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Finn Husøy Andersen

Intensive care for the very old

ICU admission triage and outcomes

Doctoral thesis

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Intensivbehandling av eldre – triage og utkomme

Populasjonen av eldre kjem til å auke dei komande åra. Samtidig forventar ein ikkje at ressursar til intensivbehandling aukar like mykje. Dette kan føre til at eldre vert lågare prioriterte når det gjeld kven som skal få tilbod om intensivbehandling. Det er difor viktig å finne ut kva grupper av eldre som har nytte av intensivbehandling, og kva grupper som har lita/inga nytte. Våre tre studiar tek for seg tre fasar av intensivbehandling av eldre (≥ 80år) - før, under og etter intensivopphaldet.

Studie I handlar om prosessen som avgjer kven som skal få tilbod om intensivbehandling (triage). I denne studien ved seks ulike sjukehus i Noreg fann vi at intensivbehandling vart avvist for ca. 30% av pasientane. Avvising av pasientar vurderte til å vere «for sjuke/gamle» var knytt til høg alder og dårleg funksjonsstatus. Ved oppfølging etter meir enn eitt år viste justert overlevingsanalyse at pasientar som fekk intensivbehandling hadde høgare overleving enn avviste pasientar vurderte til å vere «for sjuke/gamle», noko som kan indikere at eldre drar nytte av intensivbehandling.

Studie II var basert på pasientopphald henta frå Norsk intensivregister frå 2006 til 2009. Pasientar ≥80 år hadde lågare korttidsoverleving enn pasientar mellom 50 og 80år, og relativt fleire døydde på sengepost. Eldre fekk mindre intensivbehandling, representert ved kortare liggetider, mindre bruk av respirasjonsstøtte og lågare bruk av pleieressursar, sjølv om dei var like sjuke.

I studie III analyserte vi utkomme i åra etter intensivopphald hos pasientar ≥80år innlagde ved Haukeland universitetssjukehus i tidsperioden frå 2000 til 2012. 42% av pasientane var i live etter eitt år, og vidare overlevingsrate per år var lik normalbefolkninga. Livskvaliteten hos pasientar som var i live > eitt år var lik den hos ei alders- og kjønnsjustert kontrollgruppe. Pasientar innlagde etter planlagt kirurgi viste betre overleving dei fyrste tre åra etter intensivopphaldet samanlikna med pasientar innlagde etter akutt kirurgi eller av medisinske årsaker.

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First, I want to express gratitude and respect to all participating patients for contributing to this project, and to research in general.

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List of papers

This thesis is based on the following original papers:

I. Andersen FH, Flaatten H, Klepstad P, Follestad T, Strand K, Kruger AJ, Hahn M, Buskop C, Rime AK, Kvale R: **Long-Term Outcomes After ICU Admission Triage in Octogenarians**. *Crit Care Med* 2017, **45**(4):e363-e371 [1]

II. Andersen FH, Kvale R: **Do elderly intensive care unit patients receive less intensive care treatment and have higher mortality**? *Acta Anaesthesiol Scand* 2012, 56(10):1298-1305 [2]

III. Andersen FH, Flaatten H, Klepstad P, Romild U, Kvale R: **Long-term survival and quality of life after intensive care for patients 80 years of age or older**. *Annals of intensive care* 2015, 5(1):53 [3]

In this thesis, the logical order of the studies is different from the chronological order of publications. We have chosen to present the studies according to the usual trajectory of ICU patients. Paper I describes the basis for selecting octogenarian patients treated in the ICU; paper I describes the short-term outcomes; and paper II describes the long-term outcomes.

Abbreviations

ANOVA - Analysis of variance

APACHE - Acute physiology and chronic health evaluation

CCI - Charlson comorbidity index

CI - Confidence interval

ED - Emergency department

EWS - Early warning score

EuroQol - 5D; European quality of life test, 5 dimensions

HUNT - The Nord-Trøndelag health study

HR - Hazard ratio

HRQOL - Health-related quality of life

ICE-CUB - Intensive care-elderly CUB-Rea database

ICU - Intensive care unit

ICU trial - ICU admission, followed by a mandatory re-evaluation

LOS - Length of stay

LST - Life-sustaining treatment

NEMS - Nine equivalents of nursing manpower

O/E-ratio - Observed to expected mortality ratio

OR- Odds ratio

NIR - Norwegian intensive care registry

ROC - Receiver operating characteristics

SAPS - Simplified acute physiology score

SD - Standard deviation

SF-36 - Short form-36

SMR- Standardized mortality ratio

VAS - Visual analog scale

ViEWS - VitalPAC early warning score

WHO - World health organization

Summary

Introduction: The older population is expected to increase markedly during the next decades. The life expectancy of older patients is increasing, but the prevalence of conditions that require ICU treatment is also growing. Currently, patients aged 80 years or older comprise about 10-15% of the patients admitted to ICUs, and this proportion is forecasted to increase in the future. However, ICU resources are not expected to expand in parallel with the potential increase in octogenarian patients that require ICU admission. Consequently, excessive demand could lead to a change in ICU admission policy, with lower priority given to older individuals. Hence, to identify very old patients that are likely to benefit from ICU treatment, it is important to elucidate the decision-making process of triage for ICU admission; to document short- and long-term outcomes of very old patients treated in the ICU; and to identify prognostic factors in very old ICU patients.

Methods: In study I, we evaluated the ICU admission triage decisions performed at six Norwegian hospitals over a one-year period. We analyzed risk factors for ICU refusal, reported the long-term survival, investigated predictors of mortality in hospital survivors, and performed a follow-up longer than one year after ICU triage, with assessments of health-related quality of life (HRQOL), functional status, and residential status. Study II was a retrospective ICU cohort study that analyzed short-term outcomes in octogenarian patients compared to patients between 50 and 80 years of age. Data were collected from the Norwegian intensive care registry (NIR) over a period of four years (2006-2009). Additionally, we performed a subgroup analysis of 5-year age groups. Study III retrospectively analyzed survival of patients ≥80 years old after ICU treatment. Patients were admitted to the Haukeland University Hospital during the time period of 2000–2012. HRQOL was prospectively analyzed in survivors at follow-up, and the assessments were compared to assessments of a portion of the general population matched for age and gender.

Results: Norwegian ICU physicians refused ICU admission to three out of 10 octogenarians; age and functional status were the risk factors for refusal in patients considered too ill/old. Compared to younger patients, patients aged 80 years or older had a lower short-term overall survival after ICU treatment; they showed a trend of dying in the ward, rather than in the ICU; they had shorter ICU

stays; and they received less mechanical ventilator support. Adjusted long-term survival of ICU admission triage patients was significantly lower in patients considered too ill/old than in ICU admitted patients. Furthermore, analyses showed that long-term survival rates among patients that survived the first year after ICU admittance were similar to long-term survival rates of octogenarian individuals in the general Norwegian population. The HRQOL of long-term survivors was comparable to (paper III) or worse than (paper I) the HRQOL of an age- and sex-matched general population group.

Conclusions: Norwegian ICU physicians refused ICU admission to 3 out of 10 octogenarians. The higher survival of octogenarians admitted to the ICU compared to patients considered too ill/old could indicate a survival benefit of ICU admission for octogenarians. In particular, patients admitted to ICUs after planned surgery showed satisfactory short- and long-term outcomes. However, once in the ICU, patients aged 80 years or older received less treatment compared to younger patients. Despite the low one-year survival rate, patients that survived the first year after ICU admittance showed long-term survival rates similar to octogenarian individuals in the general Norwegian population. Of our studies that assessed HRQOL in ICU survivors, one showed HRQOL comparable to a control population, but another showed lower HRQOL compared to the same control population.

1. Background

1.1 The term "very old"

The World health organization (WHO) used to define individuals aged 65 years or older as "elderly". However, this term has recently been considered politically incorrect. Avers et al. stated in an editorial that "…using the term *elderly* for a person who is robust and independent as well as for a person who is frail and dependent says little about the individual. Since older individuals become more heterogeneous with age, a specific descriptor such as *elderly* is inaccurate and misleading. " [4]. WHO has recently replaced the term "elderly" with "older adults", but without any thresholds of age defining that term [5]. However, the term "elderly" is still used in studies regarding intensive care, with inconsistent definitions [6]. The most common thresholds for defining older adults have been 65-75 years for the young-old, 75-80 to 85-90 for the old-old, and older than 85-90 for the oldest-old [7, 8]. Patients aged 80 years or older are often referred to as "very old" patients or "octogenarians". These terms are not static, and have changed during the last decades, in parallel with the increasing life expectancy. Although many studies continue to use the age of 65 years as a lower limit when referring to older adults, currently, in our part of the world, few would consider 65 years as particularly old. The different age limits used among studies regarding older adults represent a case-mix, which makes comparisons with previous results difficult. Currently, 80 years is the generally accepted limit for the term "very old"; therefore, this limit is used in this thesis, which deals with different aspects of intensive care in this increasingly important group of patients.

1.2 Demographic changes

The number of very old adults will increase markedly in most modern societies, due to the changes in age distribution caused by high birth rates during the first two decades post-World War II. Forecasts predict that octogenarians will represent 9.6% of the total population in Europe by the year 2050 and 8.9% of the population in Northern Europe [9, 10]. A report from the UN indicated that the largest increase will take place in Asia, where the octogenarian population is expected to increase by a factor of four. According to Statistics Norway, the octogenarian population of Norway will grow to more than double its present size; i.e., from 221,153 (4.5%) on 1 January 2011 to 450,719 (7.1%), by the year 2040 [11]. This growth was estimated from the average growth of the national population (Fig. 1). A person aged 80 years in 2010 is expected to live for another 7.6 years (males) or 9.4 years (females) [11]

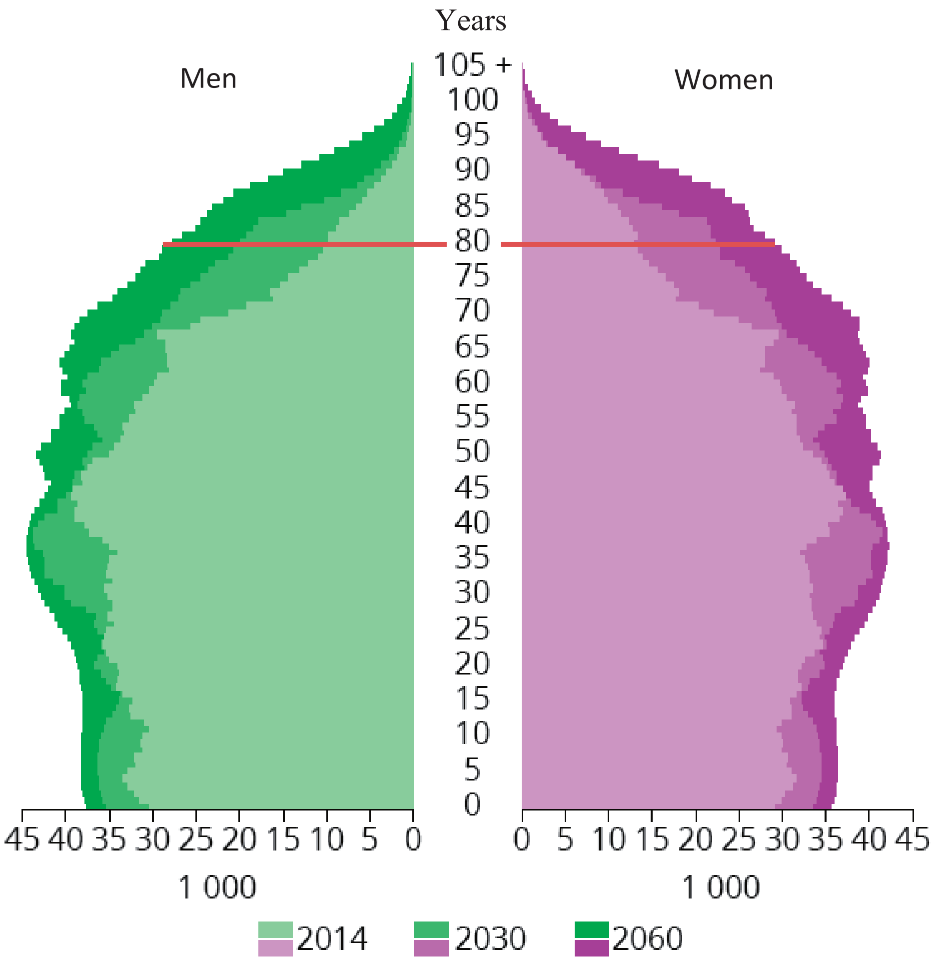

Fig. 1. Population growth predicted for Norway, distributed by age and gender. The number of individuals (X-axis) is shown for each age group (Y-axis). The population was registered in 2014 and projected for 2030 and 2060 [12].

1.3 ICU bed availability

A recent paper showed that the availability of critical care beds was highly variable among countries in Europe, ranging from 4.2 (Portugal) to 29.2 (Germany) beds per 100,000 individuals in the population [13]. The numbers of beds per 100,000 inhabitants were lower in Scandinavian countries than the European average of 11.5; i.e., 5.8 in Sweden, 6.1 in Finland, 6.7 in Denmark, and 8.0 in Norway. Moreover, the United States reported seven-fold more ICU beds per capita than in the United Kingdom [14]. However, a comparison of medical admissions to intensive care between these two countries was difficult, because the interpretation of between-country hospital outcomes was confounded by case-mix, processes of care, and discharge practices [15].

1.4 Increase in demand for intensive care

The prevalence of conditions that require ICU treatment is growing [7, 16]. Advanced treatments, like open heart surgery, are currently offered to very old adults much more frequently than only a decade ago [17, 18]. This increased frequency can be explained by the facts that (1) very old adults are healthier than a decade ago, (2) there is a greater availability or greater experience in performing advanced treatment, and (3) expectations of receiving advanced treatment have risen. Currently, very old adults receive a high proportion of healthcare services, in general, including intensive care, where the age distribution is typically highly skewed [19]. In the last decade, studies have indicated that patients aged 80 years or older comprised about 10-15% of national and large regional ICU registries, and the proportion is increasing [18, 20-22]. The average age of patients admitted to the ICU has also increased over the last 25 years [23]. In general, men appeared to be admitted to ICUs more frequently than women. However, the sex distribution in the ICU will shift with increasing age. Ihra et al. reported that, among all patients > 80 years old admitted to Austrian ICUs between 1998 and 2008, 63.2% were female [18].

Thus, we are facing a marked increase in demand for health-care services, including intensive care, for very old patients. Angus et al. pointed out that the resources for providing ICU care must also expand in the coming years [24]. Without expansion, we will have to change our current ICU admission policy. Moreover, if ICU departments are forced to increase constraints in patient triage in the years to come, very old patients will be in danger of exclusion from ICU treatment [9].

1.5 ICU admission triage

The word "triage" comes from the French word "trier", which means to sort. In this setting, the term "ICU admission triage" refers to the process of sorting referred patients in order of priority and refusing ICU treatment to patients least likely to benefit. In general, patients referred for ICU admission are evaluated by an ICU physician. Triage is influenced by several factors [7, 25], including:

1. the ICU admission request (pre-triage phase);
2. the evaluation of the ICU physician (the actual ICU triage; most often called ICU admission triage); and
3. the availability of ICU beds (post-triage phase).

A substantial number of older patients that potentially require ICU treatment are not admitted to ICUs (Fig. 2). One explanation might be that these patients are particularly at risk of being refused ICU treatment when ICU resources are limited. The lower priority compared to younger patients might be due to cultural preferences and due to shorter expected lifetime. In general, only patients that are likely to benefit from ICU treatment should be admitted. This criterion is perhaps more important when considering very old patients. However, a major challenge in modern critical care is to differentiate between very old patients that will benefit from an ICU stay and those that are either too well or too ill to benefit [26].

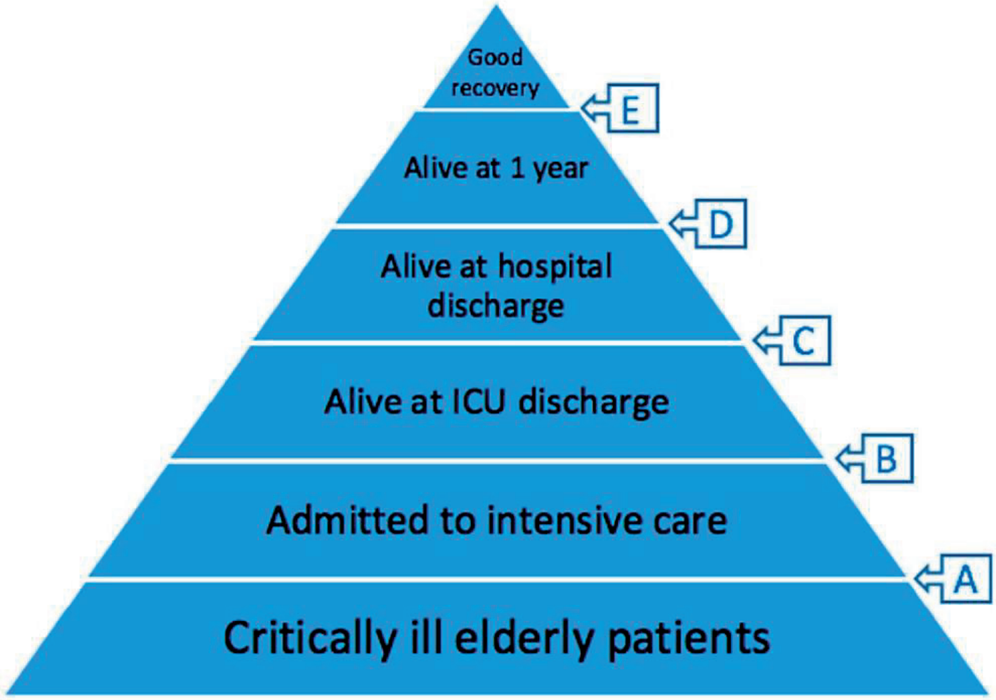

Fig. 2. Graphical representation of outcomes in critically ill elderly patients. A) A substantial number of elderly patients are not admitted to ICU as a result of a triage process. B) A high number of elderly patients die in the ICU, mostly from a withdrawal of life-sustaining therapy. C) A high number of elderly patients die in hospital after ICU discharge. D) Patients die in the first year after hospitalization mostly because of their poor baseline conditions. E) Only a small proportion of patients who survived at 1 year have recovered their functional status. *Reprinted with permission: Leblanc G, Boumendil A, Guidet B: Ten things to know about critically ill elderly patients. Intensive Care Med 2017, 43(2):217-219* [27]

To date, we lack validated criteria for accurately identifying patients that would benefit from ICU treatment. The only consensus in published guidelines is that ICU triage decisions should not be based solely on age [28]. Garrouste-Orgeas et al. showed that patients ≥ 80 years old were rarely admitted to ICUs, even when recommended triage guidelines were followed [29]. In addition, ICU severity scores are typically not purposed for triage decisions, and they are not specifically customized for very old patients; instead, they focus excessively on short-term outcomes. Due to ethical principles, it is not feasible to conduct randomized ICU triage trials for comparing groups admitted and groups not admitted to ICUs. Thus, to evaluate the overall benefit of ICU admissions for very old patients, currently, the best alternative is to analyze evaluations from observational studies. To date, only some epidemiological and observational studies are available [29-38]. These studies were based on short-term outcomes, and they showed rather conflicting results. On one hand, they showed that ICU admissions increased survival in patients ≥65 years old [34]; on the other hand, they showed decreased adjusted survival in octogenarian patients [32]. No study has provided clear evidence that very old patients benefitted from ICU treatment. However, to address the question of whether octogenarians might benefit from ICU admissions, we must look beyond the short-term outcomes, like ICU and hospital survival; instead, we must focus on long-term results, including functional status and quality of life. Although some studies define six months and beyond as long-term [32, 33], we consider that, in this setting, a more plausible definition of long-term would be one year and beyond. Previous studies have compared long-term survival between octogenarian ICU survivors and age- and gender-matched individuals in the general populations which were not treated in the ICU [3, 39, 40]. However, to our knowledge, no studies have compared long-term survival after ICU triage between octogenarian patients admitted to the ICU and those refused admittance to the ICU. Consequently, the overall long-term benefit of ICU admission for octogenarian patients remains unknown.

Patients are primarily refused ICU admission when they are considered either too well or too ill or old to benefit from ICU treatment. However, it is important to point out that most previous ICU triage studies have considered patients that were refused ICU admittance as a single group, which may be misleading [29-35, 41]. Actually, these patients represent two extremes, those considered too ill/old and those considered too well. When analyses combine these extremes, the results might cancel each other out; thus, average results are open to misinterpretation. A better approach might be to consider these two groups separately in comparisons with patients that were admitted to the ICU.

Several studies have tried to find factors associated with ICU refusal. All those studies, except two [38, 42], analyzed one group of patients that were refused ICU admission, with no distinction between those too ill/old and those too well. Joynt et al. studied patients considered too ill for ICU admission, and found that age, severity score, and diagnostic group were risk factors for ICU refusal [42]. Similarly, Pintado et al. studied patients ≥75 years of age considered too ill for ICU admission, and found that age, comorbidity, functional status, and the availability of beds were risk factors for ICU refusal [38].

Additionally, before making decisions about ICU admission, clinicians should assess the patient's preferences for intensive care admission and life-sustaining treatment (LST) [43]. However, many triage decisions must be made without adequate informed consent. A recent post-hoc analysis of the ICE-CUB trial showed that only about 13% of patients triaged for ICU admission were asked for their opinions prior to ICU admission. Moreover, they found that older attending physicians were less likely than younger physicians to ask for the patient's opinion [44]. The ETHICA studies showed that there was little agreement between patient and physician preferences about LST during an ICU stay, and that physicians often changed their decisions after learning the patient's preferences [45, 46].

To our knowledge, no other Scandinavian ICU admission triage study has been published on very old patients or on other specific age groups.

1.6 Outcomes

Outcomes in intensive care can be divided into two main categories:

- survival
- non-mortality outcomes

For both categories, short-term and long-term outcomes can be assessed. In paper II, we evaluated "mortality" instead of "survival", in accordance with the majority of studies that reported on outcome. However, because "survival" is a more positive word, we used the terms "survival" and "non-survival" in papers I and III and in this thesis.

The majority of epidemiological studies on very old patients admitted to the ICU were single center studies. Consequently, the results of those studies might have been affected by a selection bias, which might have limited the generalizability of the findings [9]. In recent years, other studies have been published based on large regional or national registries [18, 20-22]. Clearly, results from studies based on large national registries are likely to be more representative of a country's ICU population than single-center studies or small multi-center studies. Furthermore, all published studies on very old patients that received ICU treatment, both retrospective and prospective in design, have included patients that were selected after the ICU admission triage; therefore, those results might be influenced by an admission bias.

Several factors are important in an evaluation of short-term outcomes for very old patients that received ICU treatment. The largest problem in comparing outcomes in different studies is still case-mix, both within countries and between countries and health systems. Some important case mix factors are:

a) Age, diagnoses, and comorbidity – Given that crude survival decreases with increasing age, we might expect that patients ≥80 years old would have worse overall survival outcomes than patients ≥65 years old. Accordingly, comparisons of survival for very old patients should be made between similar age groups. Also, the spectrum of diagnoses differs between very old and younger age groups [7]. Moreover, some diagnoses may have different impacts, depending on age; for instance traumatic brain injury, was shown to have notoriously poor outcomes in very old patients [47]. Finally, very old patient groups tend to have more comorbidity than younger patient groups, but patients with severe comorbidity may be underrepresented due to ICU admission triage decisions [8].
b) ICU "profile" – Patients admitted to specialized ICUs differ from those admitted to general ICUs. Moreover, patients admitted after planned surgery were shown to achieve better outcomes than those admitted after unplanned surgery and for medical reasons. One approach to reducing the impact of this case-mix might be to adjust the results with ICU severity scores; however, different scoring systems are used in different facilities, and none are calibrated for very old patients. In general, ICU severity scores tend to be higher for patients in university hospital ICUs than for patients in non-university hospital ICUs.
c) Availability of ICU beds – the number of available ICU beds could play a central role regarding the ICU case-mix and the outcomes in very old patients admitted to ICUs [14]. Given the large variability in ICU bed availability around the world, this factor is likely to have an impact on ICU admission triage [13, 48]. When few ICU beds are available, ICU admission triage must be constrained, and ICU admission will not be justified for patients with little likelihood of benefitting from ICU treatment. Moreover, ICU admission may be

delayed until an ICU bed is available. Delays may lead to a deterioration in the illness. Moreover, very old patients may be prematurely discharged from the ICU, when younger patients with a higher probability of benefitting from ICU treatment need ICU admittance. However, many very old patients might benefit from longer ICU stays.

Functional status is generally not assessed in typical ICU severity scores. However, functional status, including physical, cognitive, and social functioning, was shown to be associated with short- and long-term outcomes in very old patients [49].

1.6.1 Short-term survival

Until recently, ICU and hospital survival rates were the most used primary outcomes in studies regarding very old patients. Currently, an increasing number of clinical studies have started using 28- or 30-day survival instead of hospital survival. This longer time frame allows assessments of the rather large proportion of deaths that occur within the first month of hospital admission. However, the majority of deaths during the first year after hospital discharge occur within the first three months [50]. Thus, the 90-day or 6-month survival would be a more appropriate outcome measurement. In this thesis, short-term is defined as the time up to one year after ICU admission.

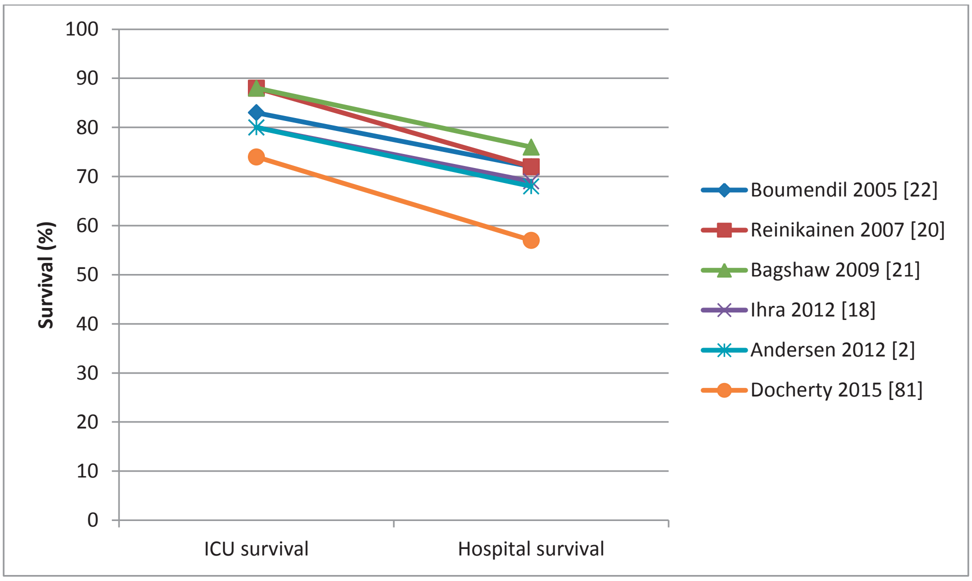

Fig. 3. Overview of short-term survival rates from large regional and national ICU registry studies.

1.6.1.1 ICU survival and length of stay

National and large regional registries from four different countries have shown ICU survival rates of 87.5-79.8% in octogenarian patients [18, 20-22] (Fig. 3), but single- or multicenter studies have reported a range between 50% [31] and 84% [49]. Few studies have reported ICU survival rates in the different admission categories. De Rooij et al. reported ICU survival rates as high as 90% in patients admitted after planned surgery; in comparison, survival rates were only 66% in patients admitted after unplanned surgery and 62% in patients admitted for medical reasons [51].

Several studies have shown that octogenarian patients received less intensive care treatment compared to younger patient groups [20-22, 50]. However, Lerolle et al. showed that ICU treatment intensity had increased for octogenarian patients over a decade, and that survival had improved during the same timeframe [52]. The therapeutic intervention scoring system (TISS) is an example of a measurement of the intensity of care [53]. However, this score is rarely used in ICUs today. Instead, ICUs mostly employ indirect measurements of the intensity of care, including the length of stay (LOS), the use of vasoactive agents, the use of mechanical ventilation, and the use of renal replacement therapy. ICUs also employ scores for measuring the nursing workload, like the nursing activities score (NAS) [54] and the nine equivalents of nursing manpower score (NEMS) [55].

It has been suggested that the ICU-LOS could serve as an indicator of the quality of ICUs. Additionally, it is often used as a resource monitor [56]. An analysis of ICU-LOS in non-survivors could be seen as a measurement of the resources spent on futile care. The ICU-LOS is also influenced by organizational and institutional factors. Therefore, it may serve to measure performance in comparisons between ICUs and hospitals. In clinical studies, the LOS is often used as a primary or secondary outcome variable, and it is particularly informative when combined with ICU survival. However, LST limitation decisions could also have an impact on ICU-LOS. A short LOS could be a consequence of treatment failure in *ICU trials* for very old patients with low prospects of survival. An *ICU trial* is referred to as an ICU admission, followed by a mandatory re-evaluation. Strand et al. reported that, in Scandinavian countries, the median ICU-LOS is generally short, and very old patients typically have shorter ICU-LOS than younger patients [57]. Compared to that study, studies from other countries on octogenarian patients have reported higher ICU-LOS [22, 40, 50, 58].

Bagshaw et al. showed in a large national registry study that age was an independent factor that influenced ICU mortality, after adjusting for severity of illness [21]. Other important predictors of ICU mortality have included the severity score, admission categories, and the use of mechanical ventilation [21, 50, 59, 60].

1.6.1.2 Hospital survival

Hospital survival is generally regarded a better outcome measurement than ICU survival, because the organizational factors in hospitals and health systems have less influence on hospital survival than on ICU survival. However, this outcome variable presupposes a well-functioning hospital information system and a satisfactory patient tracking system, in cases of transfers to other ICUs. National and large regional registries show hospital survival rates of 69-76% in octogenarian patients [18, 20-22] (Fig. 3). Hospital survival, like ICU survival, is closely linked to the distribution of admission categories and to the severity of illness.

In general, among ICU populations, approximately two thirds of non-survivors die in the ICU and one third die in the ward. For very old patients, mortality is about the same in the ICU and in the ward. Thus, for very old patients, the hospital mortality (including ICU mortality)/ICU mortality ratio is around 2, with a range of 1.53 to 2.27, in national and large regional registries. A high ratio indicates a low ICU mortality coupled with high hospital mortality; this could be a sign of premature ICU discharge or poor post-ICU care. It could also indicate that ICU treatment failed to improve the patient's condition, and thus, the patient was transferred to the ward for palliative care.

The standardized mortality ratio (SMR) is defined as the observed mortality divided by estimated mortality, where estimated mortality is based on the severity score (SAPS/APACHE); i.e., the expected number of deaths is the average of all individual mortality risks. The SMR is one of the most highly regarded quality indicators in intensive care.

In general, the predictors of hospital mortality for very old patients are age, severity scores, admission categories, admission diagnosis, comorbidity, mechanical ventilation, renal failure, and LOS [18, 21, 50, 51, 61].

1.6.2 Long-term survival

The rationale for admitting very old patients to the ICU should not be restricted to the short-term management of an acute illness. Instead, the goal should be the recovery from an acute illness with a satisfactory quality of life [9].

Few studies have published long-term survival, defined as survival beyond one year, for octogenarian patients admitted to the ICU. One explanation for this paucity could be loss to follow-up and the rather low short-term survival, which would lead to small study populations. The majority of these studies were conducted in single centers [31, 40, 49-51, 58, 62] (Fig. 4). One-year survival rates ranged from 28% [40] to 59.2% [51] in single center studies; however, the large majority of patients in the former study included patients admitted for medical reasons [40]. Recently, a national registry study in Denmark reported an overall one-year survival of 50.7% in very old patients [39].

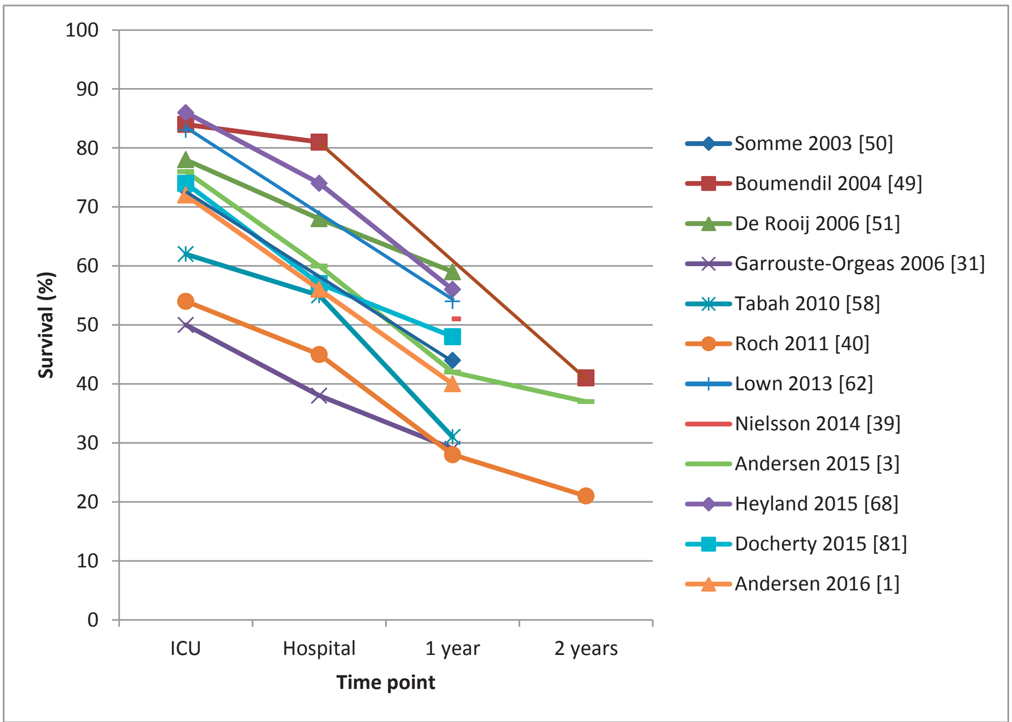

Fig. 4. Short-and long-term survival rates in some studies on octogenarian patients published after the year 2000

Long-term survival was also shown to be highly dependent on the type of reason for ICU admission. In a retrospective cohort study from the Netherlands, de Rooij et al. showed that patients admitted to the ICU after planned surgery had a one-year survival of 78.4%, significantly higher than the survival rates of patients admitted after unplanned surgery (37.9%) and for medical reasons (30.8%) [51]. The mean follow-up was 3.6 years. That study also showed that the median survival of patients admitted after planned surgery was comparable to that of the age- and sex-matched general population.

In another study, Roch et al. compared the long-term survival in octogenarian ICU patients to the survival of the general population [40]. In that study, the ICU and hospital survivors had a lower survival rate (one third to one half lower) than an age-and sex-matched, general French population, for up to two years after hospital discharge. However, after the first two years, the two groups showed comparable survival.

Only three Scandinavian studies have published long-term survival rates after intensive care in older patients. One was a national registry study from Denmark; they reported that octogenarian patients had a one-year survival of 50.7% [39]. The other two studies were conducted at single centers; they showed a one-year survival of 36% in 91 patients ≥75 years old in Denmark [63], and a three-year survival of 45% in 882 patients ≥65 years in Finland [64].

Long-term survival is limited among very old patients admitted to the ICU. Thus, it is important to establish prognostic factors for long-term survival, which can assist in identifying patients that might benefit from ICU treatment. To date, long-term mortality for very old hospital survivors was associated with age, comorbidity, severity of illness, mechanical ventilation, altered consciousness, and a diagnosis of shock [40, 49].

1.6.3 Health-related quality of life (HRQOL)

HRQOL is considered equal to survival rate in importance as an outcome parameter [65]. Moreover, HRQOL is often considered an important endpoint, when evaluating the benefit of ICU treatment.

Several studies published after 2000 included data on HRQOL in octogenarian ICU survivors. In those studies, patients were compared to a matched control group, and the follow-ups were ≥ one year after ICU discharge [31, 40, 58, 59, 63, 66], except one, which had a follow-up of six months [67]. The results of those studies were conflicting; some showed lower HRQOL [31, 59, 63, 66], and others showed similar HRQOL (or even better in some domains) for octogenarian patients, compared to a matched cohort from the general population [58, 67]. However, only two studies included more than 50 patients, and the majority of patients were either admitted after planned surgery (166/187) [66] or after orthopedic hip surgery (86/143) [59]. Only two studies reported a response rate below 80% (70% and 65%) [31, 58].

Part of the HRQOL assessment is a self-assessment of physical function. In a recent Canadian study, Heyland et al. reported that only one-quarter of octogenarian ICU survivors returned to baseline levels of physical function after one year [68].

Two Scandinavian single-center studies reported HRQOL outcomes for older patients after intensive care. Kaarlola et al. showed that the HRQOL-indexes were worse in 50 octogenarian Finnish patients compared to an age- and sex-matched general population [63]. Nevertheless, about 70% of those patients assessed their present health state as satisfactory. A Danish study reported that 36 patients ≥75 years old assessed their perceived health as good or satisfactory, despite impaired physical function, compared to their pre-admission status and compared to a general population control group [64].

Based on this background knowledge we decided the following aims for our studies:

2 Aims

2.1 Main aims of this thesis

The overall aims of this thesis were:

1. to describe the decision-making process of admitting very old patients to ICU treatment;
2. to document short-term and long-term outcomes of very old ICU patients,
3. to compare the amount of intensive care provided between older and younger ICU patients, and
4. to identify potential prognostic factors for this group of patients.

2.2 Specific study aims

2.2.1 Aims of study I: Long-term outcomes after ICU admission triage in octogenarians

- Describe and evaluate the decisions made during ICU admission triage for patients aged ≥80 years referred for ICU admission at six Norwegian hospitals;
- identify risk factors for ICU rejection;
- report long-term survival and predictors of mortality in hospital survivors;
- report HRQOL, functional status, and residential status ≥1 year after triage; and
- compare HRQOL in this patient population to HRQOLs in age- and gender-matched subjects.

2.2.2 Aims of study II: Do elderly intensive care unit patients receive less intensive care treatment and have higher mortality?

- Compare ICU and hospital survival rates between two groups of patients in the Norwegian population admitted to the ICU from January 1, 2006 to December 31, 2009. Group I: age 50–79.9 years; Group II: age ≥80 years; and
- Evaluate patients admitted to the ICU to determine whether very old patients received less ICU treatment than younger patients.

2.2.3 Aims of study III: Long-term survival and quality of life after intensive care for patients 80 years of age or older

- Compare survival and HRQOL between octogenarian ICU patients and age-matched control groups from the general population;
- Identify predictors for short- and long-term mortality among octogenarian ICU patients; and
- Compare survival and HRQOL scores between the different SAPS II admission categories: i.e., admissions for planned surgery, unplanned surgery, and medical reasons.

3 Materials and methods

3.1 Study settings, populations, and designs

The study settings, populations, and designs used in the three studies are summarized in Table 1.

Table 1. Study settings, populations, and designs

Studies	Topic	Outcomes	Study design	Study populations	Control groups	Study period
I.	***ICU admission triage***	Long-term survival	Multicenter, prospective, observational	355 patients ≥ 80 y old, referred to ICUs at 6 hospitals in Norway (3 university hospitals and 3 non-university hospitals)		2013 (November 1)-2014 (October 31)
		HRQOL	Prospective, observational	80 triage patients alive at follow-up	179 control subjects[#]	2015 (November)
II.	***Short-term outcomes***	ICU and hospital survival	Retrospective, national registry data	27,921 patients ≥ 50 y old, registered in NIR		2006-2009
				Group II (≥ 80 y): 6,935 subjects	Group I (50-79.9 y): 20,986 subjects	
	Amount of intensive care provided		Subgroup analysis of age dependence	Groups I and II split into 5-year age groups		
III.	***Long-term outcomes***	Long-term survival	Retrospective study; local ICU registry data	395 ICU patients ≥ 80 y old admitted to HUS	General population ≥ 80 y old (2000–2013)*	2000-2012
		HRQOL	Prospective, observational	58 ICU survivors alive at follow-up	179 Control subjects[#]	2014 (January)

HUS, Haukeland university hospital; HRQOL, Health related quality of life; ICU, Intensive care unit; NIR, Norwegian intensive care registry; y, years

[#] Control subjects in papers I and III were similar.

* Based on life tables from Statistics Norway.

3.1.1 Study parameters for study I: Long-term outcomes after ICU admission triage in octogenarians

This multicenter, prospective, observational cohort study included all patients 80 years old or older that were referred for ICU treatment in six Norwegian hospitals from November 1, 2013, to October 31, 2014. Three university hospitals and three non-university hospitals were included (Table 1). An overview of participating centers is shown in the Appendix Table. When patients were triaged more than once during this period, only the first triage was included. We excluded patients with missing personal identification numbers (IDs) or duplicate inclusions. A follow-up ≥ 1 year after inclusion was performed. HRQOL was compared with age- and sex-matched control subjects conducted in study III.

3.1.2 Study parameters for study II: Do elderly intensive care unit patients receive less intensive care treatment and have higher mortality?

This retrospective cohort study included all registered ICU admissions for patients aged 50 years or older. Data were retrieved from the Norwegian intensive care registry (NIR) for patients admitted from 1 January, 2006 to 31 December, 2009 (Table 1). Readmissions, transfers to other hospitals, and transfers between different ICUs within a single hospital were excluded.

3.1.2.1 Norwegian intensive care registry

The NIR was established in 1998 by the Norwegian Society of Anesthesiology. The registry contained data on all ICU admissions that remained in the ICU for more than 24 h, and shorter admissions that included either mechanical ventilation, a patient death, or a transfer to another ICU. NIR defined mechanical ventilator support as respiratory pressure support in a closed system (including noninvasive ventilation). During this period, the NIR received data on individual admissions from 31 surgical and mixed ICUs (5 university hospitals, 15 secondary hospitals, and 11 primary hospitals). This population constituted more than 90% of all patients admitted to Norwegian ICUs.

3.1.3 Study parameters for study III: Long-term survival and quality of life after intensive care for patients 80 years of age or older

The first part of this study was a retrospective analysis of patients ≥80 years old that had been admitted to the general ICU at Haukeland University Hospital (HUS) between January 1, 2000 and December 31, 2012 (Table 1).

The second part of the study included a prospective evaluation of HRQOL. Patients alive at follow-up (January 2014) were compared with a control group matched for age, sex, and residence. Re-admissions, non-Norwegian patients, and admissions with errors in patient ID were excluded.

3.1.3.1 Haukeland university hospital

HUS is a tertiary university hospital in Bergen, Norway, which serves approximately one million inhabitants. The general ICU had ten beds (burn, cardiac surgery, coronary, and neonatal units were separate units, and were not included in this study). The annual number of admissions to the general ICU was about 500, and 7–8% of patients were aged 80 years and older. During the study period, there were no large changes in ICU practice or organization, apart from general developments in medicine and intensive care.

3.2 Data collection and variables

3.2.1 Data and variables for study I: Long-term outcomes after ICU admission triage in octogenarians

The ICU physician assigned to on-call duty performed all triages and filled out all case report forms, which contained the following information:

1. Age, sex, and personal ID number
2. Date, time, and location of the triage
3. Triage decision (ICU admission or ICU refusal)
4. The main reason plus up to two additional reasons for ICU refusal (i.e., no available ICU beds, patient too well, patient too ill, patient too old, relative’s request, or patient’s request)
5. Main medical diagnosis at triage
6. Functional status (based on Karnofsky Performance Status [69])
7. Residential status before hospital admission.

The Simplified Acute Physiology Score 3 (SAPS 3) [70, 71] was not available to ICU physicians at triage. It was scored retrospectively, based on values and observations recorded at the time of triage or within 1 h before triage. Missing values were replaced with default values (zero points). For patients admitted to the ICU, we retrieved SAPS II results [72] from the Norwegian intensive care registry (NIR). We retrieved data on comorbidities at hospital admission, based on the Charlson comorbidity index (CCI [73]), and life-sustaining treatment (LST) limitations from the medical records. We included only statements that used the terms *withholding* or *withdrawal* of treatment during the hospital stay.

At follow-up, the date of death for non-survivors and the home addresses of survivors were collected by linking the patient's national ID number to the National Registry. An information letter and questionnaires regarding residential status, HRQOL (EuroQol-5D-3L [74]), and functional status (Karnofsky Performance Status [69]) were mailed to patients that were alive at follow-up. A single reminder was sent to non-responders after 3 weeks.

3.2.2 Data and variables for study II: Do elderly intensive care unit patients receive less intensive care treatment and have higher mortality?

The main reason for ICU admittance was recorded in the NIR, according to SAPS II definitions, as follows: planned surgical admission, unplanned surgical admission, and medical admission. Admissions with incorrect or unclear data were excluded.

For all included stays, the following variables were assessed:

1. ICU and hospital mortality
2. ICU-LOS, with a calculation of the total number of ICU days for each age group. Also, ICU days were categorized, as follows: ICU days for patients that died in the ICU (ICU-LOS of ICU non-survivors); ICU days for patients that died in the ward after ICU discharge (ICU-LOS of ward non-survivors); and ICU days for patients that survived the ICU and hospital stays (ICU-LOS of survivors)

3. Mechanical ventilator support, including mechanical ventilator support time. NIR defines mechanical ventilator support as any respiratory support provided in a closed system (including noninvasive ventilation)
4. Severity of illness, classified with the SAPS II [72]. The SAPS II was evaluated with and without age points to underline the impact of age on the score
5. The intensity of care, measured with the daily Nine Equivalents of nursing Manpower use Score (NEMS) [55]. This measurement was summarized as the NEMS during the stay, divided by the LOS.
6. SMR, defined as the observed hospital mortality divided by the SAPS II estimated mortality.

Furthermore, we performed a subgroup analysis by dividing all the patients into 5-year age groups.

3.2.3 Data and variables for study III: Long-term survival and quality of life after intensive care for patients 80 years of age or older

From the dedicated ICU database, we retrieved daily, prospectively collected data. Re-admissions, non-Norwegian patients, and admissions with errors in registered patient IDs were excluded.

For all included patients, we assessed the following:

1. Age and gender;
2. LOS;
3. Ventilator support, including invasive (mechanical) and noninvasive ventilator support;
4. Severity score (SAPS II [72]) and sequential organ failure assessment score (SOFA) [75]. We defined severe organ dysfunction as a SOFA score of 3 or 4; among daily SOFA scores, only the maximum was included in the analysis;
5. Comorbidity: we classified comorbidity into four categories (none, mild, moderate, and severe), based on the CCI [73];
6. Diagnostic groups: ICU admissions were classified into one of 13 different categories;
7. Short- and long-term survival (long-term defined as 1 year and longer); the SMR was defined as the observed hospital mortality divided by the SAPS II estimated mortality; the SMR was analyzed for all patients and for each of the SAPS II admission categories;

8. Survival at follow-up; and
9. SAPS II admission categories: planned surgery, unplanned surgery, and medical reasons.

Survival was compared with a segment of the general population that was 80 years old or over during the period of 2000–2013, based on life tables from Statistics Norway. Hospital survivors were compared to hospital non-survivors, and survival rates were compared between SAPS II admission categories.

A control group was recruited with 375 age- and sex-matched individuals was conducted based on a goal to have a control groups containing two to three times more persons than survivors at follow-up, with an estimated response rate 50%. These control subjects were randomly selected from the National Registry, with the restriction that they were similar to patients in age, sex, and catchment area.

The HRQOL was assessed with the EuroQol-5D-3L [74]. This questionnaire was mailed to ICU survivors and the control group at follow-up. A reminder was mailed to non-responders after one month, and individuals that failed to respond to the reminder were contacted by phone. Informed consent was provided by all individuals that completed the questionnaire.

We retrospectively retrieved information about end-of-life decision-making for hospital non-survivors. This retrieval required searching through each of the individual patient files from their corresponding hospital stay because that information was not entered in the ICU database. We only included statements that specifically used the terms *withholding* or *withdrawal* of ICU treatment.

3.2.3.1 EuroQol-5D

The EuroQol-5D is a validated instrument for measuring HRQOL [74]. It consists of five dimensions: mobility, self-care, usual activities, pain/disorder, and anxiety/depression. These dimensions have three response options: no problems, moderate problems, or severe problems. Respondents were asked to choose the most appropriate response option connected to each dimension; thus, there were 243 (3^5) possible health states. Each of these states was converted into a single summary index, which consisted of five numbers, ranging from one to three. Lastly, the respondents were asked to rate their present health state, on a visual analog scale (EQ VAS), which ranged from 0 (the worst imaginable health state) to 100 (the best imaginable health state).

3.3 Ethical considerations

Study II did not require approval from the regional ethics committee, because it contained only anonymous data from the NIR. The study was approved by the steering group in NIR. Studies I and III were approved by the *Regional Committee of Medical and Health Research Ethics in Central Norway* (2013/1113 and 2013/1114, respectively). In these studies, written informed consent from patients and relatives was waived. In study III, approval was received to contact the non-questionnaire responders by telephone. Informed consent to participate in the follow-up was provided when participants completed the questionnaires.

3.4 Statistical methods

The LOS, the time for mechanical ventilator support time, and the time from hospital admission to triage are expressed as the median value and quartiles, due to skewed distributions. Significance was tested with the Mann-Whitney U test/Kruskal–Wallis test. Other continuous variables are expressed as the mean value and standard deviation (SD), and comparisons were performed with the *t* test/analysis of variance (ANOVA). Categorical variables were summarized with frequencies and percentages, and significance was tested with Pearson's Chi-square test/Fisher's exact test or with the Mann-Whitney U test, as appropriate.

All statistical analyses were performed with SPSS for Windows, version 18.0-22.0 (SPSS Inc., Chicago, IL). For analyses described in the first study, we also used Microsoft Excel (Microsoft Corporation, Seattle, WA) for Mac, version 14.1.0. *P*-values <0.05 were considered statistically significant.

3.4.1 Statistics for study I: Long-term outcomes after ICU admission triage in octogenarians

Patient variables were compared between the ICU-admitted patients and the non-admitted patients. Non-admitted patients were assigned to subgroups of those considered “too well” and those considered “too ill/old”, and these subgroups were compared separately to the group of admitted patients with the t-test, Mann Whitney U test, Pearson’s chi-square test, or Fisher’s exact test, as appropriate. Predictors of ICU triage refusal were studied for both subgroups with mixed effects logistic regression. Age, Karnofsky Performance Status, CCI, and SAPS 3 were included as predictor variables. In addition, all variables that achieved a significance of $p < 0.20$ in the primary univariate analyses were included in this analysis. A random intercept for the hospital was added to account for within-center correlations. Odds ratios (ORs) were calculated with 95% confidence intervals (95% CIs). A Cox proportional hazard regression model was used to analyze predictors of mortality for hospital survivors. We evaluated the variables age, sex, hospital type, Karnofsky Performance Status, CCI, residential status, and SAPS 3. The time variable was defined as the number of days from ICU triage. Adjusted hazard ratios (HRs) were calculated with 95% CIs. Kaplan-Meier curves were constructed for patients admitted and those not admitted to the ICU, and those not admitted were separated into subgroups of those considered too well and those considered too ill/old. Adjusted Kaplan-Meier curves were generated with inverse probability weighting (IPW), according to the method described by Xie and Liu [76]. These were implemented in the IPW survival package provided by R (R Foundation for Statistical Computing, Vienna, Austria) [77]. The survival curves were compared with log-rank tests.

3.4.2 Statistics for study II: Do elderly intensive care unit patients receive less intensive care treatment and have higher mortality?

We used ANOVAs to test for differences among the 5-year age groups. The SMR was calculated for the two main age groups and for each 5-year age group. A Receiver Operating Characteristic (ROC) curve was created for each main age group.

3.4.3 Statistics for study III: Long-term survival and quality of life after intensive care for patients 80 years of age or older

We performed three separate Cox proportional hazard regression analyses to determine independent predictors of ICU mortality, hospital mortality, and 1-year mortality. The time factors were defined as the number of days from ICU admission, ICU discharge, and hospital discharge, respectively. All variables with a *P*-value <0.2 in a primary univariate analysis were included in the multivariate model, except for admission categories; all admission categories were included, even when the *P*-value was >0.2 in the univariate analysis. ICU mortality was analyzed separately. Only ICU survivors were included in the analysis of hospital mortality. Only hospital survivors were included in the 1-year mortality analysis. The remaining variables were tested separately in each model, and included when they were significant. Adjusted HRs were calculated with 95% CIs. Kaplan-Meier curves were constructed for the three SAPS II admission categories. Another Kaplan-Meier curve was constructed to compare all patients to the general octogenarian population in Norway. An adjusted mortality rate was calculated by dividing the observed mortality by the expected mortality (O/E) of an age- and gender-matched population. The adjusted mortality rate was calculated between 1 and 8 years after ICU admission. Patients who were alive at follow-up were censored. The SMR was analyzed for each of the SAPS II admission categories.

4 Summary of results

4.1 Results for study I: Long-term outcomes after ICU admission triage in octogenarians

Of the 355 included patients, 105 (29.6%) were refused ICU treatment. The percentages of rejected patients were significantly different between hospitals (range, 14.8–44.0%; $P < 0.001$) and between university hospitals and non-university hospitals (34.9 vs. 21.9%; $P = 0.008$).

Risk factors for ICU refusal in patients considered “too ill/old” were advanced age and low functional status (Table 2). Risk factors for ICU refusal for patients considered “too well” were advanced age, male sex, university hospital admission, comorbidity, and low SAPS 3 (Table 2).

Table 2. Logistic regression analysis of factors associated with ICU refusal in patients considered too well and too ill/old for ICU admission

Variables	Non-admitted patients too well (n = 45)[a]		Non-admitted patients too ill/old (n = 50)[a]	
	Multivariate OR (95% CI)	*P*-value	Multivariate OR (95% CI)	*P*-value
Age	1.23 (1.10–1.36)	*<0.001*	1.16 (1.06–1.26)	*< 0.001*
Men	2.38 (1.08–5.24)	*0.031*	1.08 (0.54–2.16	0.831
University hospital	5.79 (1.52–22.04)	*0.010*	2.25 (0.57–8.97)	0.252
Functional Status				
Karnofsky Performance Status	1.01 (0.99–1.03)	0.374	0.96 (0.94–0.98)	*<0.001*
Comorbidity				
Charlson comorbidity index	1.26 (1.04–1.52)	*0.018*	1.04 (0.87–1.26)	0.639
Severity score				
SAPS 3	0.92 (0.88–0.96)	*<0.001*	1.01 (0.98–1.05)	0.351

[a] Variables were compared for each subgroup vs. all patients admitted to the ICU (n = 244)
OR, odds ratio; CI, Confidence interval; SAPS, Simplified acute physiology score.
$P < 0.05$ were considered statistically significant. All statistically significant values are italicized.

The overall ICU survival was 71.6%. The hospital and 1-year survival rates were 56.0% and 40.0%, respectively, for ICU-admitted patients; 65.2% and 50.0%, respectively, for patients considered "too well" for ICU treatment; and 32.7% and 11.5%, respectively, for patients considered "too ill/old" for ICU treatment. The median survival times were 37 days for the ICU-admitted patients; 18 days for all non-admitted patients (merged); 330 days for patients considered too well for ICU treatment; and 2 days for patients considered too ill/old for ICU treatment. The patients admitted to the ICU had a significantly higher survival than patients not admitted (merged). Patients considered too ill/old had a significantly lower survival than ICU-admitted patients and patients considered too well for ICU treatment (Fig. 2). The median follow-up time was 610 days.

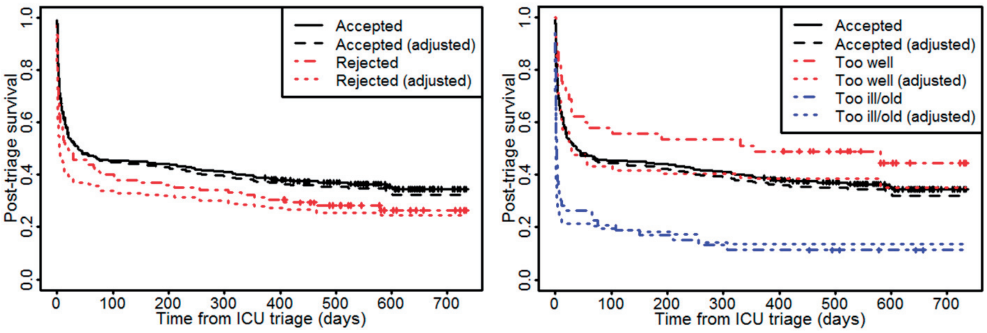

Fig. 5. Kaplan-Meier survival curves. *Left*: Survival in patients accepted for admission to the ICU (black) and patients rejected for admission to the ICU (red) (unadjusted $P = 0.13$; adjusted $P = 0.002$). *Right*: Survival in patients considered too well for ICU admission (red); patients considered too ill/old for ICU admission (blue) (unadjusted $P < 0.001$; adjusted $P = 0.004$). Patients admitted to the ICU (black) had survival rates similar to patients considered too well for ICU admission (unadjusted $P = 0.13$; adjusted $P = 0.44$), but significantly different from patients considered too ill/old for ICU admission ($P < 0.001$ for both unadjusted and adjusted). The median follow-up time was 611 days. Adjusted results reflect Kaplan-Meier curves after adjusting for age, sex, hospital, Karnofsky Performance Status, Charlson comorbidity index, residential status, and Simplified Acute Physiology Score 3.

At follow-up, patients that underwent triage had lower HRQOL values than an age- and sex-matched control group in the domains of self-care, usual care, and anxiety and depression, and a low EQ VAS.

4.2 Results for study II: Do elderly intensive care unit patients receive less intensive care treatment and have higher mortality?

We analyzed data for 27,921 patients. The ICU and hospital survival rates were 85.7% and 78.6%, respectively in Group I (50-79.9 years) and 80.2% and 67.6%, respectively in Group II (≥80 years). A subgroup analysis of patients in 5-year age groups showed that overall survival decreased with increasing age, and the decrease was more pronounced in the hospital survival rate than in the ICU survival rate. The ratio of hospital mortality/ICU mortality increased from 1.29 in patients aged 50–54.9 to 1.85 in patients aged over 90. Thus, for older patients, death was more likely to occur on the ward than in the ICU (Fig. 6).

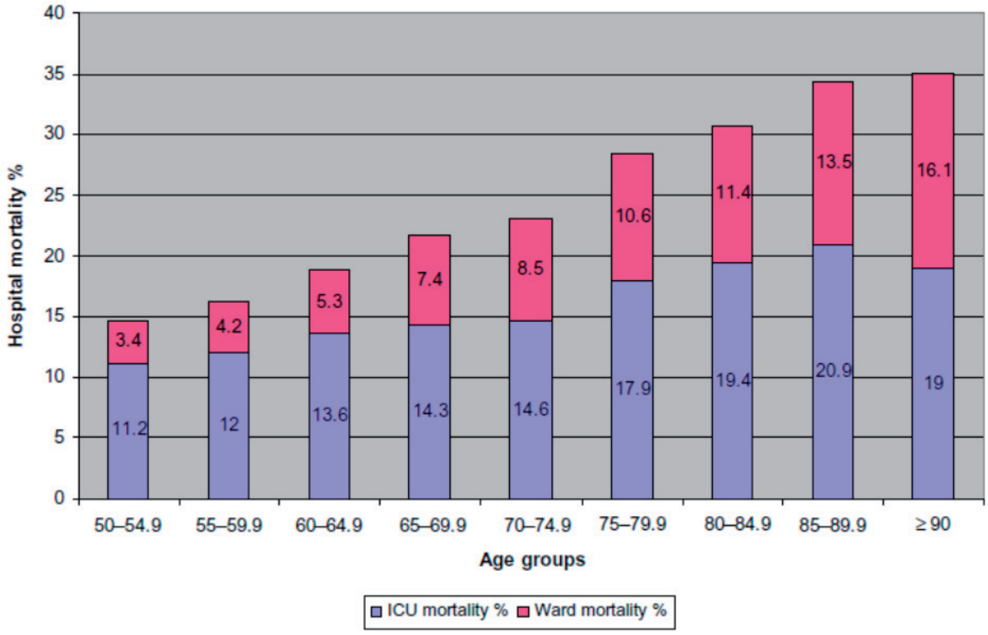

Fig. 6 Mortality for different 5-year age groups. Numbers indicate the percentages of deaths that occurred in the intensive care unit (ICU, blue), in the hospital ward (red), and in the hospital (merged)

The observed difference in admission categories could not explain the significant difference in the median length of stay (LOS) between Group I (2.3 days) and Group II (2.0 days). The subgroup analysis of 5-year age groups showed quite consistent LOS values (2.2 to 2.4 days) for patients up to 79.9 years old, but then, LOS dropped significantly for patients 80 years old and older. The proportion of ICU days spent by hospital non-survivors was smallest for the 50–54.9 year-old age group (15.8%), and the proportions increased with age in each group up to the 75–79.9 year-old age group (35.2%). The proportions of ICU days spent by hospital non-survivors in the very old age groups were 33.3% (80–84.9 years), 34.6% (85–89.9 years), and 28.3% (≥90 years) (Fig. 7).

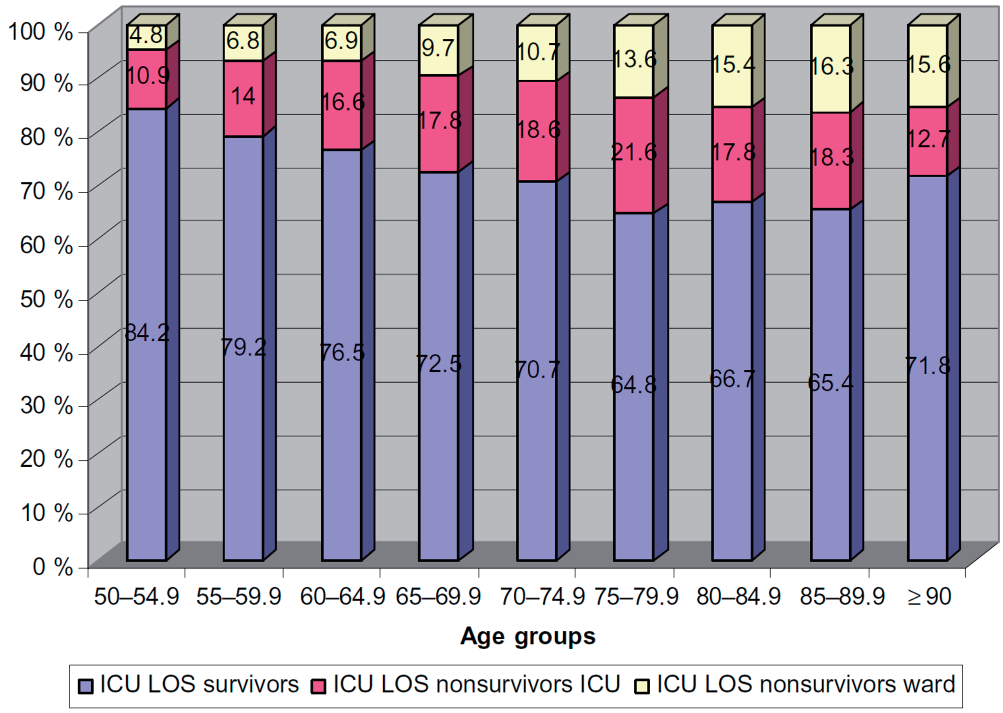

Fig. 7. Accumulated days in intensive care unit (ICU) [length of stay (LOS)]

Compared to younger patients, the very old patients received less mechanical ventilator support (40.6% vs. 56.1%) and had shorter median ventilator support times (0.8 days vs. 1.9 days). The median LOS decreased with age after around 80 years old, and ventilator support time decreased with age after around 65–70 years old.

The main results between Group I and Group II showed that the mean SAPS II score increased from 38.3 in the younger group to 44.2 in the octogenarian group. After filtering out the age points from the SAPS II score, there was no difference; the adjusted means were 26.1 (50–79.9 years) and 26.2 (≥80 years). The subgroup analysis also showed no significant differences in SAPS II scores.

4.3 Results for study III: Long-term survival and quality of life after intensive care for patients 80 years of age or older

The 395 patients included in this study (mean age 83.8 years, 61.0% males) had overall survival rates of 75.9% (ICU) and 59.5% (hospital). A high ICU mortality risk was predicted by older age, mechanical ventilator support, high SAPS II, high maximum SOFA, and the presence of multi-trauma with head injury. High hospital mortality risk was predicted by an unplanned surgical admission.

The overall 1- and 2-year survival rates were 42.0 and 36.6%, respectively. After 5 years, 22.2% of all admitted patients remained alive. A comparison between these patients (n = 395) and the individuals in the general population aged 80 or older in Norway (n = 426,773) showed excess mortality among patients in the first year, with an adjusted mortality rate of 6.35 (95% CI: 5.58–7.23). After the first year, survival rates were similar between these groups; the adjusted mortality rate during the second year was 1.34 (95% CI 0.86–2.07; Fig. 8).

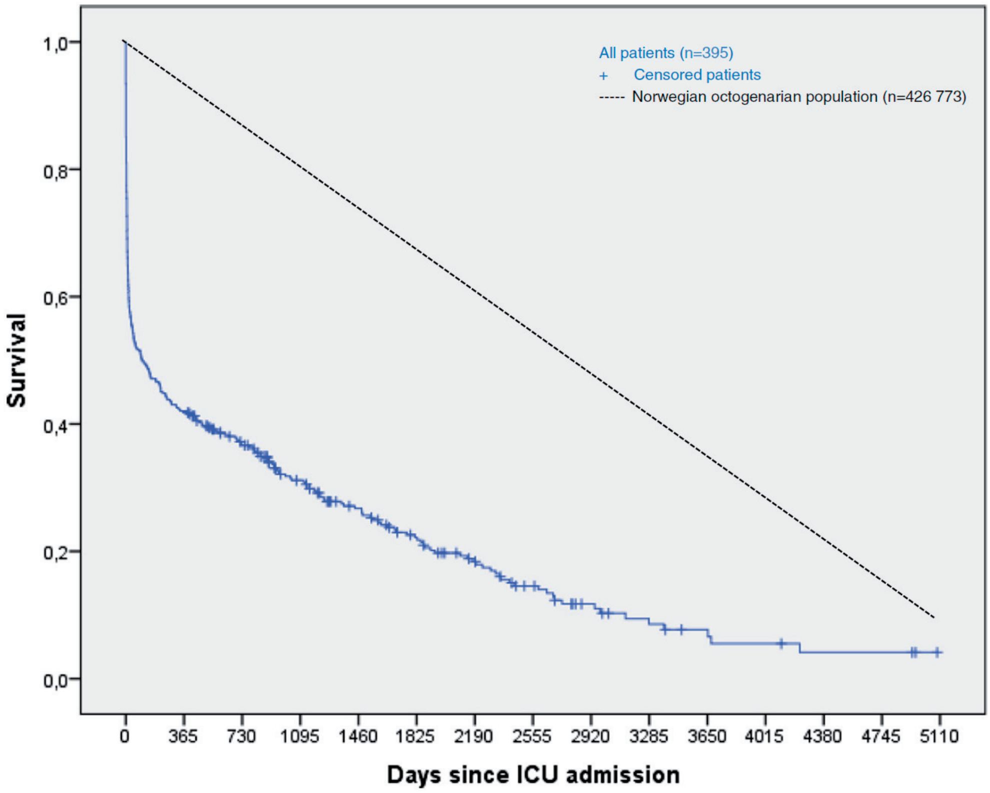

Fig. 8. Kaplan-Meier survival curve for all patients (solid blue line) compared to the Norwegian octogenarian population (dashed black line) in 2000–2013

Among patients alive after 1 year, the mean survival time, starting from the 1- year point, was 5.1 years. Respiratory failure and isolated head injury were independent predictors of 1-year mortality.

Patients admitted for planned surgery had significantly higher survival rates than those admitted for medical reasons or unplanned surgery, for up to 3 years after ICU admittance (Fig. 9).

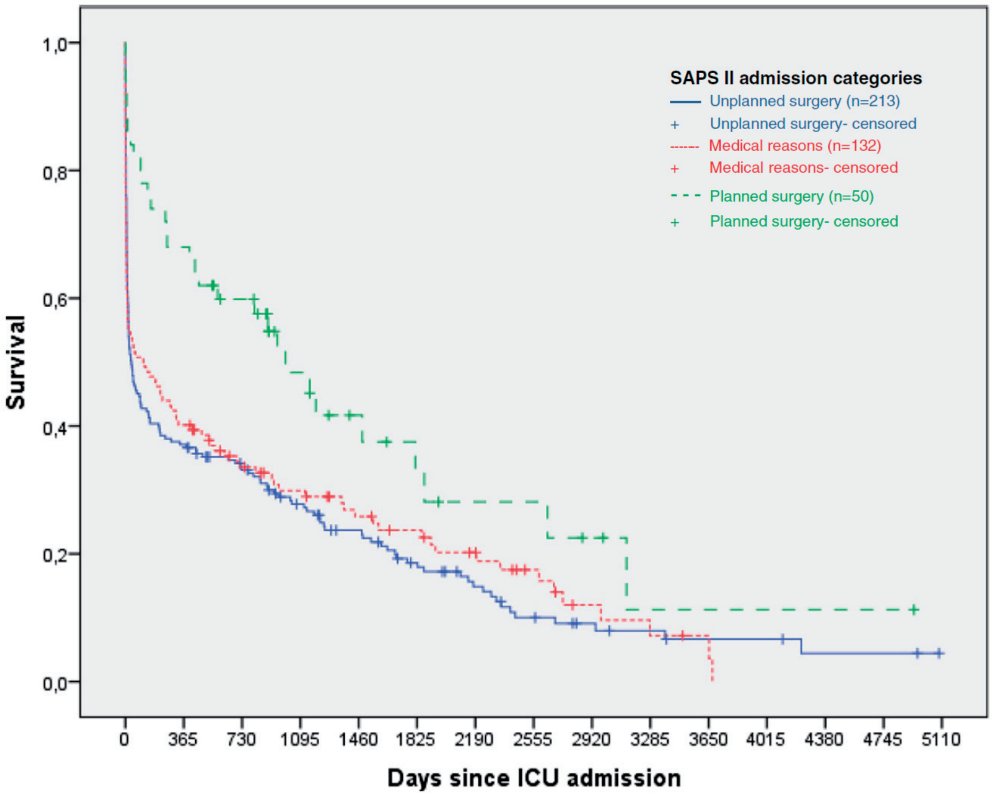

Fig. 9. Kaplan-Meier survival curves of SAPS II admission categories

The EuroQol-5D questionnaire was sent to the 73 patients that were alive at follow-up. The response rate was 83.6% (n = 61). The response rate in the control group was 47.7% (179/375), which constituted 2.5 controls per survivor at follow-up. The HRQOLs were similar between the patients and the general population and among the different admission categories.

Of the ICU non-survivors, 70.5% (n = 67) had been given treatment limitations. Of these ICU non-survivors, 63.2% died within 2 days after ICU admission (n = 60), and 68.3 % of these patients had received LST limitations (n = 41), including withheld (60.0%) and withdrawal (51.7%).

5 Discussion

The main findings in study I were that Norwegian ICU physicians refused ICU admission to three out of 10 octogenarians. For patients considered too ill/old, the risk factors for ICU refusal were advanced age and low functional status. For patients considered too well, the risk factors for ICU refusal were advanced age, male sex, university hospital admission, comorbidities, and low SAPS 3. The adjusted long-term survival was significantly lower in patients considered too ill/old for ICU admission than in patients admitted to the ICU. Overall, the follow-up of patients that underwent triage showed lower HRQOL in very old patients than in an age- and sex-matched control group.

In study II, we observed that the very old patients (aged 80 years or more) had lower ICU and hospital survival rates, showed a trend of dying in the ward rather than in the ICU, had shorter ICU stays, and received less mechanical ventilator support, compared to younger patients. We found no significant difference in the mean SAPS II scores between these groups (after adjusting for age). There was a significantly lower daily NEMS score in the group over 80 years old.

Study III had three major results. First, patients $\geq$ 80 years old that survived the first year after ICU admittance had long-term survival rates similar to those of octogenarians in the general Norwegian population. The HRQOL of these long-term survivors was comparable to that of an age- and sex-matched general population group. Second, the planned surgery group exhibited higher survival rates than the medical and unplanned surgery groups, for up to 3 years after ICU admittance. However, at follow-up, HRQOL did not differ between these three groups of patients. Third, increased ICU mortality was predicted by age, mechanical ventilator support, SAPS II score, maximum SOFA score, and the presence of multi-trauma with head injury. High hospital mortality was predicted only by an unplanned surgical admission. Respiratory failure and isolated head injury were independent predictors of 1-year mortality. The majority of the ICU non-survivors died within 2 days, and most of these had been given LST limitations. Similarly, nearly three quarters of hospital non-survivors had been given treatment-limitation decisions.

5.1 ICU admission triage decisions (Paper I)

To our knowledge, this was the first prospective observational multicenter study to describe the actual ICU admission triage in patients aged ≥80 years. Other studies on ICU triage in older adults were either single center studies, or they were conducted in other age groups [31, 34, 35]. The ICE-CUB study evaluated triage for octogenarian patients with implementation of a two-step triage process, where an initial triage performed by ED physicians was followed by the actual ICU triage [29, 32, 33]. Studies that employ this two-step triage approach tend to focus on the first step; thus, they do not include patients that are considered ineligible for ICU treatment at the time of hospital admission. These patients may deteriorate in the wards, in recovery, or in intermediate ICUs, and then, they become candidates for ICU admission. Our study showed that only 38.6% of ICU triage decisions were made in the ED. Furthermore, Norwegian EDs generally do not have permanent emergency medicine specialists, and junior doctors typically perform the first patient assessments. Therefore, a two-step triage study conducted in Norway would not be representative of the standard ICU admission triage decisions made by ICU physicians on a daily basis. Most patients treated in our ICU, including very old patients, came to the ICU from locations other than the ED. Therefore, our study was designed to represent the typical ICU admission triage for octogenarian patients that potentially require ICU treatment. These triages were performed by ICU physicians, after a request from a referring physician.

We lack ICU triage guidelines tailored for very old adults and validated criteria to facilitate identifying very old patients that might benefit from ICU treatment. Consequently, ICU triage decisions are highly variable for older patients [27]. This was illustrated by the large differences in ICU refusal rates reported in previous studies. Our study showed a refusal rate of 29.6%, consistent with those reported in several other general ICU triage studies (24.1%–37.8%) [30, 41, 42, 78] and with the Eldicus study, which showed a 25.5% ICU refusal rate for patients ≥75 years old [34]. However, the Eldicus study showed high variability in the ICU refusal rates across countries (2%–48%). These differences might be explained by differences in organization, culture, ICU bed availability, and case-mix [34].

The only previous actual ICU admission triage study conducted with octogenarian patients reported a refusal rate of 73.3% [31]. In the large ICE-CUB study, which used a two-step triage process, the refusal rates were high and variable across centers within the Paris area (67%–94%), although there were no clear differences in hospital characteristics [33]. In comparison, our study revealed lower refusal rates; moreover, we found significant differences in ICU refusal rates between centers and between university and non-university hospitals.

There are several approaches to ICU admission triage. Presumably, ideal ICU admission triage decisions would be based on detailed information about functional status, comorbidities, the preferences of patients and relatives, frailty, and current disease status. Often, the most realistic approach is to admit patients to the ICU and start basic LST, despite uncertainties about the potential benefit, and then gather more information *(ICU trial)*. In many cases, the patient's condition does not improve, despite ICU treatment, or the physician acquires additional information that indicates that further treatment would be futile, and therefore, it should be limited. This scenario was reflected in our study results, which showed a rather high proportion of LST limitations among the ICU non-survivors (83.1%), and of those patients, 64.4% died within 2 days after triage.

A lack of available beds could also contribute to triage decisions. Norwegian ICUs are typically staffed with a nurse-to-patient ratio of 1:1 or more. However, in many units, the physical bed capacity exceeds the number of staffed beds, which represents a buffer area capacity that can be utilized by either hire more nurses or temporarily reduce the nurse-to-patient ratio. Thus, most Norwegian ICUs admit patients, even when there is lack of staffed beds.

Consensus statements on ICU triage, including the "*Guidelines for intensive care unit admission, discharge, and triage"*, and the "*Triage of intensive care patients: identifying agreement and controversy",* have stated that age should never be the sole determining factor in triage decisions [28, 48]. This statement was supported by a recently updated consensus, from 2016, entitled "*ICU Admission, Discharge, and Triage Guidelines: A Framework to Enhance Clinical Operations, Development of Institutional Policies, and Further Research"* [43]. Our study found that advanced age nevertheless was an independent risk factor for ICU refusal in patients considered too ill/old for ICU admission, consistent with a general ICU triage study [42]. Similar results were also reported by other studies, but these studies analyzed risk factors of ICU refusal in general, meaning that they did not differentiate between patients considered too ill and patients considered too well [29, 31, 36, 41]. Two of these studies were performed in octogenarians [29, 31]. However, we also found that advanced age was a risk factor for ICU refusal in patients considered too well for ICU admission. This finding may seem surprising because, despite the relatively low severity scores in these patients, they had relatively high comorbidity burdens. A potential explanation for this finding might be that patients considered too well for ICU admission were more frequently refused ICU admittance at university hospitals, where 41.7% of patients considered too well for ICU admission were referred to intermediate units. However, we considered that the rather small, but significant, difference in age between ICU admitted and non-admitted patients considered too well for ICU admission was unlikely to be clinically important. Our study also showed that functional status was associated with ICU refusal in patients considered too ill/old for ICU admission, consistent with the study by Pintado et al. [38], and with most studies that analyzed factors that influenced ICU refusal in general for older patients [29, 30, 36]. A study by Rodriguez-Molinero et al. also found that a physician's evaluation of functional status was associated with ICU refusal. However, that association disappeared when the multivariate model was changed to include functional status evaluated by reliable informants, instead of basing it solely on physician evaluations [79].

A study from Boumendil et al. was, to our knowledge, the only study to evaluate adjusted survival between patients admitted and those not admitted to the ICU, beyond the first month after hospital discharge [32]. Adjustments were made for age, sex, main diagnosis category, functional and nutritional status, cancer, severity of illness and a random center effect. That study showed that the adjusted survival after a median follow-up of 185 days decreased for patients admitted compared to those not admitted to ICUs. Our study was the first to analyze survival between these groups in octogenarian patients at ≥1 year after ICU triage. We found that non-admitted patients seen as one group, exhibited lower survival than patients admitted to ICUs, after adjusting for age, sex, functional status, comorbidities, residential status, severity score, and a fixed center effect. After the group of non-admitted patients was divided into those considered too well and those considered too ill/old for ICU admission, we found that overall survival for patients admitted to ICUs was lower than the survival of patients considered too well for ICU admission and significantly higher than the survival of patients considered too ill/old for ICU admission. Accordingly, our survival analysis indicated a survival benefit for octogenarians admitted to the ICU compared to those not admitted that were considered too ill/old. Although the latter finding was expected, our study was the first to conduct separate analyses for the two main groups of patients not admitted to the ICU; those considered too well and those considered too ill/old for ICU admission. We believe this separation is important, because these groups were clearly different, and the difference was missed in studies that combined all patients that were not admitted into a single group. This failure to separate the patients that were refused ICU admission into two groups might partly explain why no previous studies had shown that ICU admission provided a survival benefit compared to ICU refusal, among older adults.

Some precautions must be taken in interpreting our findings. First, an ICU refusal may have changed the physicians' perspective on the patient's condition, which could have led to a subsequent LST limitation. There is a substantial risk attached to LST limitations, because these decisions may be self-fulfilling. We assumed that no LST limitations were imposed in advance of the request of referral. Second, the low survival in patients considered too ill/old for ICU admission could reflect well-made triage decisions by Norwegian ICU physicians regarding these patients, rather than a lack of ICU treatment. Third, the results might have been influenced by confounding factors that we did not adjust for in the analyses. Fourth, most of the difference between Kaplan-Meier curves for patients admitted to the ICU and patients considered too ill/old for ICU admission arose within the first 100–200 days post triage; thus, the benefit of ICU admittance might only apply over a short term. Hence, further studies are needed on ICU triage in octogenarian patients with long-term outcomes.

Mortality among hospital survivors was influenced by advanced age, lower functional status and pre-ICU residential status. The ICE-CUB and the Eldicus studies also reported that functional status was a major predictor of short-and mid-term outcome [33, 34]. To the best of our knowledge, functional status was identified as a predictor of mortality in all previous ICU admission triage studies that performed such analyses in older adults [29-31, 36]. Therefore, functional status should be one of the main factors emphasized in future ICU admission triage decisions. Ideally, we should have performed similar analyses for patients refused ICU admission, but this was not feasible, due to the small patient cohorts. Future research should focus on predictors of long-term mortality in groups refused ICU admission, because information about predictive factors would most likely improve ICU admission triage decisions for octogenarian patients. However, large trials would be required to recruit sufficient hospital survivors among patients considered too ill/old for ICU admission, and moreover, to show significant differences among predictors. Future research should also include comparisons of survival between triaged patients and a matched general population.

Intuitively, one might expect that patients considered too ill/old for ICU admission were refused, because the likelihood of survival was considered very low, and ICU treatment was not expected to improve survival significantly. However, in study I, we found that about one third of these patients were discharged from the hospital alive. Conversely, the expectation for patients considered too well for ICU admission would be that these patients would survive, even without intensive care. However, one third of these patients died during the hospital stay. One interpretation of these findings might be that the ICU admission triage decisions were "inaccurate" in one third of the cases. However, we believe that ICU physicians go beyond life expectancy when they make triage decisions. For example, apart from the aforementioned factors associated with ICU refusal, ICU physicians may consider other important factors, like the patient's and relatives' preferences and the predicted post-hospital quality of life. Thus, ICU physicians might limit ICU admissions for patients with dementia or patients confined to living in a nursing home [29]. Consequently, the decision to refuse patients for ICU admission is not necessarily linked to certain death for patients too ill for ICU admission or certain survival for patients too well for ICU admission. In fact, perhaps ICU admittance could have further increased survival in patients considered too well for ICU admission.

Future ICU triage studies may have other designs. A recent interesting study by Boumendil et al. highlighted the methodology, the feasibility, and the ethical and logistical constraints in designing and conducting a cluster-randomized trial of ICU admission for octogenarian patients [80]. The participating centers in that study included patients in the ED, which were randomly assigned to either a systematic ICU admission, or to follow the standard practices regarding ICU admission. However, the follow-up was only 6 months, and the patients included were ≥75 years of age. Interestingly, that study only included patients with clinical conditions that potentially required organ support. These clinical conditions were retrieved from an earlier ICE-CUB 1 study [29], established by a Delphi consensus method among emergency physicians, and adapted from the *Guidelines for intensive care unit admission, discharge, and triage* [28]. Patients with factors of poor prognosis, identified from the ICE-CUB 1 study [33], like the presence of cachexia, active cancer, or a declining functional status were excluded. By using similar exclusion criteria in our study, we may have had fewer patients considered too ill/old for ICU admission, and thereby different results.

5.2 Short-term outcomes after intensive care (Papers I, II, and III)

Traditionally, studies regarding outcomes in very old ICU patients were mostly based on short-term survival. Although, recently, more papers have acknowledged the importance of survival, HRQOL, and functional status from a longer-term perspective, short-term outcomes remain important as a foundation for long-term outcomes.

5.2.1 Short-term survival

ICU survival in our three studies ranged from 71.6% to 80.2%. These findings were consistent with most previous studies on very old patients admitted to the ICU. However, case-mix differences between our papers and others, regarding ICU-LOS, severity of illness, and the percentage of patients that received mechanical ventilation, most likely had an impact on the results. Table 3 shows a comparison of short-term outcomes in ICU patients for studies I-III.

Table 3. Comparisons of outcomes in studies I-III

Studies	**n**	**ICU-LOS***	**Mechanical ventilation (%)**	**SAPS II (mean)**	**ICU survival (%)**	**Hospital survival (%)**	**1-y survival (%)**
I	250≠	2.5	65.6	52.3	71.6	56.0	40.0
II	7,556	2.0#	40.6	44.2	80.2	67.6	NA
III	395	1.9	61.3	44.3	75.9	59.5	42.0

ICU, Intensive care unit; LOS, length of stay; NA, Not available; SAPS, Simplified acute physiology score. *in survivors; ≠patients admitted to the ICU; #only patients with LOS >1 day

Because study II was based on a national registry, we compared these results with similar studies. In our study, the ICU and hospital survival rates were 80.2% and 67.6%, respectively. These results were similar to populations in Austria and in the Paris area [18, 22]. The Austrian study also showed a similar percentage of ICU admittance for patients ≥ 80 years old and a similar distribution among SAPS II admission categories. However, the patients in our study had a higher mean SAPS II score and a lower rate of mechanical ventilation than those studies [18]. Studies from Finland, Australia, and New Zealand showed higher survival rates than we found in study II. A plausible explanation might be that those patients had lower severity scores than our patients [20, 21].

In study II, we evaluated whether the lower short-term survival in very old patients was related to a lower supply of ICU treatment intensity, compared to younger patients. The ICU-LOS can be seen as a measurement of resource use during the ICU stay. However, because the ICU-LOS is highly dependent on survival, we excluded the ICU non-survivors. We found that very old patients had significantly shorter ICU-LOS compared to a younger population, which is consistent with previous studies [18, 22, 50]. This difference was observed within each of the three SAPS II admission categories (planned surgery admissions, unplanned surgery admissions, and medical admissions), but the difference between age groups was not statistically significant for patients admitted for planned surgery. A large Scandinavian registry study also showed that Scandinavian countries generally had short ICU-LOS [57], consistent with our findings in studies I and III. The short ICU-LOS could be related to the low ICU-bed availability in Scandinavia compared to other countries [13], but it may have also been due to a cultural preference of withdrawing or withholding treatment rather rapidly, when patients did not respond to treatment. This practice was also reflected in the short LOS for ICU non-survivors. The ICU days used by patients that did not survive the hospital stay could be considered futile care, but a certain amount of “futility” is mandatory, when offering intensive care to patients with an uncertain outcome. There is no general recommendation on what percentage of ICU days “should be” used for non-survivors, but our data indicated that we were closer to the lower threshold than the higher threshold. An analysis of the total number of days spent in the ICU by non-survivors in the 5-year subgroups (study II) showed that the number of days used by non-survivors increased with age, up to age 75 to 79.9 years; then, the number decreased with age in patients aged 80 years or more. After 80 years, the decrease was mainly due to short stays for patients dying in the ICU.

Compared to a younger population, we found that octogenarian patients (study II) received less mechanical ventilation, consistent with other studies [18, 21, 22]. We also found shorter mechanical ventilator support times and a lower nurse workload (NEMS/day) for older compared to younger groups. A plausible explanation for less extensive ICU treatment in very old groups compared to younger groups could be the higher severity of illness among very old patients in the ICU. That is, many very old patients might have been considered too ill/old to benefit from aggressive ICU treatments. However, after filtering out the age points in the SAPS II score, the difference between older and younger patients disappeared. This finding indicated that the two groups had similar severity of illness, also consistent with findings in other studies [22, 50]. After determining that very old patients received less intense ICU treatment than younger patients, we investigated at what age this change appeared. To that end, we performed subgroup analyses with 5-year age groups. To our knowledge, no other studies have performed this type of analysis. We observed consistent values for the median ICU-LOS, the proportion of patients that received mechanical ventilation (%), and the nursing workload (NEMS/day), up to the age of about 80. Above age 80, these values decreased. Accordingly, the age of about 80 years appeared to represent some kind of threshold, whereupon ICU treatment decreased. We might speculate that Norwegian ICU physicians considered patients above 80 years of age too old to benefit from ICU treatment.

In study II, we observed that both ICU survival and hospital survival were lower for octogenarian patients than for younger patients, and that survival rates decreased with age. However, hospital survival decreased with age more steeply than ICU survival, which indicated that increasing age was associated with a shift from dying in the ICU to dying in the ward. To our knowledge, no other studies have shown this gradual increase in the hospital mortality/ICU mortality ratio with increasing age. We found a hospital/ICU mortality ratio of 1.63 in octogenarian patients. This ratio is comparable to that reported in a study from the Paris area [22] and to that recently reported for a Scottish population [81]. However, our ratio was lower than those in similar studies from Finland (ratio=2.27) [20] and from Australia and New Zealand (ratio=2.0) [21]. The higher numbers of very old patients dying in the ward compared to the ICU might be related to premature discharges from the ICU, poor post-ICU care, or transfers to post-ICU care after a failed ICU trial with prospects of a poor outcome. Because SAPS II scores that excluded age points were not significantly different between the two main age groups or among the 5-year age groups, the severity of illness alone could not explain the age-related increase in the hospital mortality/ICU mortality ratio.

Survival decreases with increasing age. The immediate conclusion from this statement should be that age is associated with mortality. Although we found age to be associated with ICU mortality in a multivariate analysis in study III, these findings contrast with findings from some previous studies [49-51]. When we further analyzed the ICU survivors in study III, we did not find that age was associated with increased hospital mortality. Conflicting results on the impact of age on short-term mortality among older patients may be explained by variations between different studies in adjustments for severity of illness and comorbidities. At minimum, adjustments for illness severity should be performed when evaluating the influence of age on mortality.

In general, short-term mortality is most frequently predicted by severity scores and by abnormal physiological and biochemical data [5]. However, it is questionable whether these models, which were developed for short-term ICU mortality, can be used to predict long-term outcome. Long-term mortality is probably influenced more by age and other diseases than short-term mortality. Thus, other models should be developed for predicting the long-term consequences of ICU treatment.

5.2.1.1 Life-sustaining treatment limitation decisions

Decisions to limit LST during the ICU stay were assessed in all patients admitted to the ICU in study I and hospital non-survivors in study III. The majority of patients that did not survive the ICU were given LST limitations; 83.1% in study I, and 70.5% in study III. These decisions were mostly made within the first two days after ICU admission. Based on our finding that the median ICU-LOS was also about two days, our data suggested that ICU physicians limited the intensity of LST within the first two days after ICU admission, if the patient showed no improvement. Very old patients were probably then transferred early to post-ICU care, which in turn, could account for the higher hospital/ICU mortality ratio, due to a low likelihood of post-ICU survival. A recent Canadian study on octogenarian patients found a lower proportion of LST limitation decisions than we found in our study. Compared to our study, the most striking differences of that study were the long LOS in ICU non-survivors (median 10 days), coupled with the LST modalities employed before death and on the day of death [82]. That study also showed that, although one quarter of family members preferred comfort measures, almost all patients received LSTs during ICU stays, with a time from ICU admission to death of 12 days. We lacked information in our studies about patient preferences regarding LST limitations; therefore, we do not know whether the patient preferences were congruent with the LST limitation decisions.

5.3 Long-term outcomes after intensive care (Papers I and III)

5.3.1 Long-term survival

Among patients admitted to the ICU, one-year survival was 40.0% in study I and 42.0% in study III (Table 3). These survival rates were higher than those reported in similar French studies, despite similar severity scores and the higher percentage of our patients that received mechanical ventilation [31, 40, 58]. However, those previous studies included mostly patients admitted for medical reasons. Other Scandinavian studies have shown similar one-year survival (45%) among patients ≥65 years old [63], and lower survival rates among patients ≥75 years old [64].

Few studies have reported long-term outcomes for aged patients in different SAPS II admission categories. De Rooij et al. reported that long-term survival in patients admitted after planned surgery was higher (similar to the expected survival of the age- and sex-matched general population) than in patients admitted for medical reasons and unplanned surgery (mean follow-up, 3.6 years) [51]. Our results from study III support that finding, but only up to 3 years after ICU admittance. Thereafter, our patients showed similar long-term survival between groups. However, only 50 patients were admitted after planned surgery. We speculate that, if our study had included a larger number of patients in this group, we might have demonstrated a significant difference in survival between groups beyond three years. Recent, larger national studies also reported significantly higher 1-year survival rates in very old patients admitted to the ICU after planned surgery, compared to the other two SAPS II groups [39, 81]. Those studies did not include survival rates beyond one year. Therefore, we can postulate that patients admitted to the ICU after planned surgery generally will have better outcomes than patients in the other two SAPS II admission categories, and that this group is likely to benefit from ICU admission.

The ICU and post-ICU hospital non-survivors constituted the majority of patients that died within the first year. Thus, inclusion of these hospital non-survivors in long-term analyses would, to a large extent, reflect short-term predictors, instead of the intended long-term predictors. Thus, analyses of long-term predictors should exclusively be performed with hospital survivors, or with patients that survived the first 30 days, like the cohort analyzed in a large Danish study [39]. Some previous studies have reported prognostic factors for long-term mortality among older individuals [39, 40, 49-51, 62]. However, due to the inclusion of hospital non-survivors, some of those studies failed to identify factors specifically associated with long-term mortality [50, 62].

In study III, we found that octogenarian patients had greater than six-fold higher mortality rates during the first year after ICU admittance compared to a matched octogenarian general population. We did not make comparisons to ICU survivors or hospital survivors, but we assumed that far less excess mortality occurred during the first year, given the high ICU and ward mortality rates. After one year, survival rates became comparable to those of the general octogenarian population. Interestingly, Roch et al. found a similar trend after 2 years [40]. The low 1-year survival rate in our study may indicate that many aged patients did not benefit from ICU treatment. Accordingly, to improve our ability to predict which patients would be most likely to gain long-term benefit from ICU treatment, we analyzed factors that might influence mortality during the first year after ICU discharge.

It has been increasingly recognized that chronological age is poorly correlated to physiologic reserve and functional status (physiologic age), and that outcomes in older patients cannot be determined by age alone [83]. Nevertheless, we continue to use chronological age as a variable of interest in ICU outcome studies, due to the difficulties in measuring physiological age. Furthermore, increasing age has been associated with worse outcomes in patients admitted to the ICU, and thus, age is a strong predictor of mortality in most models and risk scores [72, 83, 84]. In study I, we found that increasing age was an independent predictor of long-term mortality in hospital survivors. This contrast with some other studies that reported long-term outcomes in patients aged 80 years or more [40, 49, 51], including results from our study III. These conflicting results may be explained by variations in adjustments for severity of illness and comorbidities. However, studies that employed younger control groups have tended to show age as an independent predictor of long-term mortality, compared to studies that use age as a continuous variable in patients ≥ 80 years [39, 50, 85].

In some ICU studies on octogenarian patients, comorbidity was also found to be a predictor of long-term mortality [40, 49]. Those studies used the McCabe classification, where comorbidity was based on the presence of underlying fatal diseases. In studies II and III, we found no association between long-term mortality and comorbidity, where comorbidity was based on the CCI. This finding was supported by similar findings from other studies [39, 59] that also used the CCI. Moreover, long-term consequences from organ dysfunctions acquired during ICU stays might have greater effects on outcomes than pre-existing comorbidities. This issue has not been elucidated to date in any long-term outcome studies regarding octogenarian patients.

In study I, pre-ICU functional status was identified as a predictor of long-term mortality. This is also supported by findings from other studies [40, 49]. A recent study by Heyland et al. showed that octogenarian patients with higher baseline physical function were more likely to survive the ICU than those with low baseline function. However, at one year after ICU discharge, only 26% of the survivors had recovered their baseline physical function [68]. Another alternative measure of good physical recovery after intensive care might be the proportion of patients that were able to return to their homes. In study I, 78% of the responders were living in their own homes at follow-up.

Several studies have reported that brain injury was associated with poor long-term outcomes in older patients [47]. Most of those results were retrieved from registries prone to selection bias, and they lacked statistical methods to control for important confounders [86]. In our study II, an isolated head injury was one of the factors associated with 1-year mortality among hospital survivors. Although this result was based on a multivariate Cox proportional hazard model, which was adjusted for severity of illness, comorbidity, and admission categories, only four hospital survivors (2.5%) had isolated head injuries, and three died within one year. Thus, we must be cautious in drawing conclusions from the data. We also found that an admission diagnosis of respiratory failure was independently associated with 1-year mortality (study II). To our knowledge, only one previous study that investigated very old patients admitted to the ICU included admission diagnoses as a potential predictor of long-term mortality in a multivariate analysis. That study, by Roch et al, found no association between long-term mortality and respiratory failure [40].

Recently, frailty has gained attention in ICU outcome studies, and also in studies regarding octogenarian patients. Frailty can broadly be defined as a gradually accumulating, multidimensional loss of physiologic reserve [83]. It may therefore serve as a substitute for biological age, anticipating better biological markers. Although none of our studies included frailty as a variable, recent studies have shown that frailty had an important impact on 6-month mortality in older patients admitted to the ICU [87]. Furthermore, frailty was a more significant predictor of physical recovery at 1 year after ICU admission than age, illness severity, and comorbidity [68].

5.3.2 Health-related quality of life

To date, no studies have compared long-term HRQOL in patients that were admitted versus those not admitted because they were too ill or too well. Overall, our follow-up of patients that underwent triage showed a lower HRQOL than age- and sex-matched control subjects in terms of self-care, usual activities, anxiety and depression, and EQ VAS. These findings correspond to those from a study by De Rooij et al. where patients at follow-up had more problems with usual activities and had lower mean EQ VAS scores than a general British population [66]. Other recent studies on HRQOL in older ICU survivors have reported impaired physical function [40, 64]. Those findings contrast with the findings in study III and in two other studies, where ICU survivors had HRQOLs comparable to those of age- and sex-matched populations [58, 67]. Tabah et al. reported that, in some domains, ICU survivors displayed even better HRQOL compared to the general population matched for age and sex [58]. We found differences in HRQOL assessments between two of our studies. This difference might be due to the higher severity scores and lower proportion of planned surgery in the cohort of study I compared to the ICU cohort of study III; alternatively, differences might have been due to the inclusion of patients not admitted to the ICU in study I. Moreover, the median time to follow-up was shorter in study I than in study III (1.6 vs. 3.3 years); the shorter follow-up could have led to a lower evaluation of the current HRQOL, due to better patient recall of their pre-illness HRQOL. Although many very old patients do not fully recover their physical ability, they probably settle into accepting their physical impairment as time goes by. Thus, they might have lower expectations from life after a critical illness, and this shift would be reflected in their assessments of HRQOL outcomes. Overall, patients with short follow-up times tend to report more physical problems than those with longer follow-ups, and patients with follow-ups exceeding 1-2 years tend to report more emotional problems than those with shorter follow-ups [65].

The most important problem in a study with long follow-up times is that more patients will be lost to follow-up. In study III, patients were included over a period of more than thirteen years; thus, a large proportion of eligible patients died before follow-up, which could represent an important bias. The hospital survivors that died before follow-up had a median survival of 3.1 years after hospital discharge. In comparison, patients that survived to follow-up had a median follow-up of 3.4 years after ICU discharge. These groups were otherwise comparable, and we speculated that hospital survivors that had died before follow-up had about the same HRQOL as those that survived to follow-up, at least for much of the time.

Responders to follow-up questionnaires may represent healthier patients. Therefore, responders should be compared to non-responders to identify a potential selection bias. In study I, responders and non-responders were comparable in terms of age, comorbidity, functional status before ICU admission, and severity score. Study III revealed that non-responder and responder groups had similar severity scores and similar proportions of severe organ failure, but the non-responder group had slightly longer times to follow-up after the hospital discharge (medians, 4.6 vs. 3.3 years; $P = 0.350$).

There is no consensus about which tool should be used for HRQOL measurements among critical care patients [60]. The two most frequently used instruments are the SF-36 [64] and the EuroQol-5D [65], and both are considered valid and reliable [60, 66]. We chose the EuroQol-5D, because this tool was less extensive and simpler to answer compared to the SF-36. In our opinion, this feature is important in achieving the highest possible response rate, particularly among very old hospital survivors. A response rate of 80% among eligible patients at follow-up is considered good for QOL studies [65]. We achieved that response rate in study III, but not in study I, or in the control group, which was used in both studies. A plausible explanation for this difference might be that, in study III, but not in study I, the regional ethics committee allowed us to make telephone contact with individuals that had not responded to the questionnaire.

The ideal outcome of ICU treatment would be for patients to regain their pre-ICU quality of life, or attain a quality of life similar (or better) to that of individuals that are the same age and sex [88]. To determine whether the long-term HRQOL assessment is the result of critical illness, or rather, a reflection of a poor baseline pre-ICU status, HRQOL measurements should be performed before the ICU admission [60]. There are two approaches to assessing pre-ICU HRQOL; (1) information can be estimated from proxies, and (2) patients can retrospectively assess their previous status, based on recall, at the time of ICU discharge or later. To our knowledge, only one study has compared HRQOL pre- and post-ICU in octogenarian patients [67]. That study reported that patients steadily recovered towards baseline values during the first six months after ICU discharge. Although it would be desirable to evaluate patient HRQOL before ICU admission, we chose not to implement that measurement in two of our studies. In study I, the main reason for this decision was that HRQOL was not the main issue in the study. That study aimed to investigate ICU admission triage, and we reasoned that increasing the workload on physicians during patient inclusion into the study would have reduced the inclusion rate. Study III was based on retrospective material collected over thirteen years. There, we reasoned that asking patients to recall pre-ICU HRQOL status from many years ago would have led to major recall biases. In that scenario, the primary risk was that patients might overestimate their previous health status.

There are reasons to believe that there is a natural decline in HRQOL over time, due to aging, both for patients formerly admitted to the ICU and for individuals in the general population. This was shown by Hopman et al. in a normative population, where HRQOL changes were more pronounced in older than in younger age groups and in physical domains [89]. We cannot generalize these findings to very old ICU populations, but this aspect should be kept in mind when interpreting HRQOL outcomes in very old ICU patients. In general, ongoing morbidity in ICU patients suggests that they will experience a worse QOL, both before and after intensive care, compared to the general population [90].

A systematic review by Oeyen et al. stated that it is nearly impossible to draw generalized overall conclusions about HRQOL in older ICU survivors due to differences between studies in the study populations, study designs, QOL instruments, follow-up times, and response rates [65]. To assess the study quality of HRQOL studies, Oeyen et al. listed four important criteria [65]: (1) QOL assessment before ICU admission, (2) descriptions of key inclusion and exclusion criteria, (3) description of non-responders and a comparison with responders, and (4) adjustments for confounders, like age and sex. All these criteria were fulfilled in our studies I and III, apart from the assessment of HRQOL before ICU admission.

5.4 Strengths

Study I described a prospective multicenter study that included both university and non-university hospitals, and employed a median follow-up time > 600 days. The main strength of this study was that patients that were not admitted to the ICU were divided into two main groups: those considered too ill/old and those considered too well. Another strength of the study was that the data on HRQOL was compared to data from sex- and age-matched individuals from the general population, and it included documentation on LST limitation decisions.

Study II described the analysis of a large national registry data set. The main strength of this study was that it included the vast majority of patients > 50 years old that had been admitted to Norwegian ICUs over a four-year period. Other strengths were that the data set included information on the severity of illness (SAPS II, with and without age points) and variables that could be used as surrogates for evaluating the intensity of intensive care given (LOS, mechanical ventilator support, NEMS).

The main strength of the study described in paper III was its long follow-up time (> 13 years) for an octogenarian cohort treated in the ICU. This follow-up time was longer than those applied in previous studies. Another important strength was the comparison of survival between very old patients and octogenarian individuals in the general population. Moreover, the analyses of Kaplan-Meier curves from the different SAPS II admission categories provided valuable information about the probable benefit of admitting patients after planned surgery for ICU treatment. That study also included a prospective analysis of HRQOL in survivors at follow-up compared to a matched control group.

5.5 Limitations

All three studies had some limitations. The main limitation in study I was that we only studied ICU triage performed by ICU physicians. Thus, we lacked information about pre-ICU triage decisions performed by other physicians, who may not have referred patients to the ICU if they had anticipated ICU refusal. However, there were no indications of systematic errors regarding patient inclusion, and the groups of rejected patients were relatively small. Studies II and III did not include information about ICU admission triage decisions. The main limitation in study II was the rather high proportion of excluded patients (9.5%). However, most patients had evaluable data. Despite significantly shorter median LOS and shorter median ventilator times in the excluded group, the short-term mortality rates were quite similar between excluded and included groups, which increased the internal validation of this study. Other limitations in study II were the lack of information about LST limitation decisions and the lack of long-term outcomes. In study III, the main limitation was the study design; it was a partly retrospective study conducted in only one center; therefore, it included relatively small groups. In particular, the number of patients for HRQOL assessment was limited. This problem is relatively common in single-center studies of aged populations admitted to ICUs. The small group size was also a limitation in study I, even though we included patients from several centers. The main cause for the low number of eligible patients at long-term follow-up was the rather low short-term survival. Another limitation in study III was that HRQOL was evaluated at different follow-up times; however, every patient was followed-up after at least 1 year, which was the recommended minimum time [65]. Another limitation in study I was the low response rate of eligible patients at follow-up (65%); in contrast, the response rate was above 80% in study III. In study I and III we evaluated HRQOL only once in each patient; thus, we could not evaluate possible changes in HRQOL over time. Ideally, a baseline measurement should be made before the ICU stay. Another limitation in study III was the omission of the effects of changes in admission policy and medical practice, which might have occurred over the long inclusion period. However, we determined that the catchment area and basic functions of the hospital remained the same during the study period, with a slowly growing population; the hospital included all medical services, except organ transplant surgery. Moreover, there were no major changes in practice or organizational changes in the ICU during the study period. Therefore, we considered this limitation a minor weakness. An overall limitation was that the findings from our studies might not be generalizable to other countries. Moreover, because study I included only six hospitals in the southern part of Norway and study III was a single center study, the results may not be generalizable to the entire country. Also, in studies I and III, the findings were not compared to younger age groups; this limitation might have increased the apparent impact of age on the outcomes of these studies. Finally, as mentioned above (see the Discussion), all of our studies were limited by the lack of information about frailty.

6 Conclusions

This work showed that Norwegian ICU physicians refused ICU admission to three out of 10 octogenarian patients. We found higher survival rates among octogenarian patients admitted to the ICU compared to patients considered too ill/old for ICU admission. That result could indicate that ICU admission provided a survival benefit for octogenarian patients. In particular, patients admitted to ICUs after a planned surgery showed satisfactory short- and long-term outcomes. However, once in the ICU, very old patients received less treatment compared to younger patients. We also found that, despite low 1-year survival rates, very old patients that survived the first year after ICU admittance showed long-term survival rates at later times that were similar to octogenarians in the general Norwegian population. In one of our studies, assessments of HRQOL showed comparable results between very old ICU survivors and a control population. However, another of our studies showed that very old survivors after ICU triage had lower HRQOL assessments compared to the same control population.

7 Areas of future research

In Scandinavian countries, the unique civil registration number given to every citizen offers great potential for thoroughly tracking long-term survival. Consequently, loss to follow-up is minimal. Crosslinking between several different national registries further extends this potential. Admission diagnoses and categories are important factors in evaluating long-term survival, but information on the cause of death (provided by a different registry) might be equally important. A collaboration among Scandinavian ICU registries with a longer follow-up time might reveal better predictors of long-term mortality. These predictors can facilitate the development of much-awaited triage scores for very old patients that might potentially require ICU admission.

No studies to date have evaluated the performance of pre-existing risk scores in triage studies. Well-established ICU risk scores are time-consuming to use, and they are not specifically meant for ICU triage purposes. An alternative to those scores is the early warning score (EWS), an aggregated, weighted track and trigger system. The EWS is a simple, rapid bedside tool; it only comprises physiological variables for early assessments of adult patients at risk of death [91]. A recent study from South Korea reported a modified version of an EWS, called the ViEWS-L (VitalPAC Early Warning Score [92] with Serum Lactate). The ViEWS-L performed equivalent to or better than the most common scoring systems (SAPS II, SAPS 3, and APACHE II) for predicting mortality among adult critically ill medical patients admitted to intensive care treatments via EDs [93]. A future trial might analyze the value of ViEWS for predicting hospital mortality compared to other established risk scoring systems in ICU admission triage decisions for octogenarian patients.

Another potential future study could be to identify patients formerly admitted to the ICU that are registered in both the NIR and the Nord-Trøndelag health study (HUNT) database, and to link information from these two sources. The HUNT database is Norway's largest collection of health data about a population. It includes population health data obtained through three population studies, dating from 1984. It might also be particularly interesting to use information from the HUNT biobank, which is a collection of biological material, and which includes, for example, DNA and proteins.

To our knowledge, no studies have been conducted based on collaborations between intensivists and geriatricians. It would be interesting to determine whether that type of collaboration could improve pre-ICU admission triage, care in the ICU, and post-ICU care.

Another interesting study would be to determine the potential benefits of using intermediate units as an alternative to ICUs in specific groups of patients.

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Appendix

Appendix Table. Characteristics of participating hospitals and ICUs (2014)

	Characteristics of hospitals				Characteristics of ICUs									
Hospital	**Number of beds in Hospital** (approx.)	**Total ICU beds in Hospital**	**Other ICUs in Hospital**	**Intermediate ICUs in Hospital**	**ICU type**	**Number of beds in ICU**	**Number of ICU admissions in 2014***	**Median age***, years	**LOS***, median	**Respiratory support***, %	**Respiratory support time***, median days	**NEMS/24h***	**SAPS II***, mean	**SMR*** mean
Ålesund Hospital	250	8	1	no	Surgical	5	245	71.0	1.9	33.1	0.4	30.1	31.5	0.97
St. Olavs Hospital	700	16	2	yes	Mixed	10	598	64.1	2.2	90.0	1.8	31.1	39.5	0.84
Haukeland University Hospital	1000	24	4	yes	Mixed	10	471	61.0	2.7	86.8	0.9	31.2	46.8	0.63
Haugesund Hospital	230	5	-	no	Mixed	5	306	67.0	1.8	56.9	0.8	32.1	36.3	0.64
Stavanger University Hospital	570	7	-	yes	Mixed	7	467	61.0	2.1	87.2	1.4	36.6	46.5	0.73
Østfold Hospital	500	8	-	yes	Mixed	8	482	66.2	2.8	75.1	2.0	31.0	44.2	0.65

* Numbers collected from the Norwegian Intensive Care Registry (NIR), 2014; LOS: length of stay; NEMS: nine equivalents of nursing power; SAPS II: Simplified acute physiology score-II; SMR: standardized mortality ratio

Paper I

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Paper II

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Paper III

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Long-term survival and quality of life after intensive care for patients 80 years of age or older

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Abstract

Background: Comparison of survival and quality of life in a mixed ICU population of patients 80 years of age or older with a matched segment of the general population.

Methods: We retrospectively analyzed survival of ICU patients ≥80 years admitted to the Haukeland University Hospital in 2000–2012. We prospectively used the EuroQol-5D to compare the health-related quality of life (HRQOL) between survivors at follow-up and an age- and gender-matched general population. Follow-up was 1–13.8 years.

Results: The included 395 patients (mean age 83.8 years, 61.0 % males) showed an overall survival of 75.9 (ICU), 59.5 (hospital), and 42.0 % 1 year after the ICU. High ICU mortality was predicted by age, mechanical ventilator support, SAPS II, maximum SOFA, and multitrauma with head injury. High hospital mortality was predicted by an unplanned surgical admission. One-year mortality was predicted by respiratory failure and isolated head injury. We found no differences in HRQOL at follow-up between survivors (n = 58) and control subjects (n = 179) or between admission categories. Of the ICU non-survivors, 63.2 % died within 2 days after ICU admission (n = 60), and 68.3 % of these had life-sustaining treatment (LST) limitations. LST limitations were applied for 71.3 % (n = 114) of the hospital non-survivors (ICU 70.5 % (n = 67); post-ICU 72.3 % (n = 47)).

Conclusions: Overall 1-year survival was 42.0 %. Survival rates beyond that were comparable to those of the general octogenarian population. Among survivors at follow-up, HRQOL was comparable to that of the age- and sex-matched general population. Patients admitted for planned surgery had better short- and long-term survival rates than those admitted for medical reasons or unplanned surgery for 3 years after ICU admittance. The majority of the ICU non-survivors died within 2 days, and most of these had LST limitation decisions.

Keywords: Intensive care unit; Elderly; Octogenarians; Survival; Mortality; HRQOL; Long-term outcome

Background

In many countries, aged populations may increase by 40–50 % in the coming decades [1–3]. A similar increase is expected in the proportion of older patients admitted to intensive care units (ICU). Patients 80 years of age or older currently constitute between 8.9 and 13.8 % of large national ICU registries [4–7]. Australia and New Zealand showed 5.6 % annual increases in the numbers of octogenarians that entered the ICU [4]; in Denmark, an 18 % increase was observed from 2005 to 2011 [5].

Few recent studies have focused on long-term health-related quality of life (HRQOL) in aged ICU survivors, and even fewer have compared octogenarian ICU patients to an older segment of the general population. These studies were mainly performed in medical ICUs and included small sample sizes, due to high short-term mortality [8, 9]. One- and 2-year mortalities in octogenarians are reported to be as high as 72.0 and 79 % [9], respectively. Thus, it is important to identify factors among the older population that predict benefit from ICU treatment, establish prognostic factors for long-term survival, and elucidate the HRQOL.

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This study aimed to:

1. Compare survival and HRQOL between older patients and age-matched control groups from the general population;
2. Identify predictors for short- and long-term mortality among older ICU patients; and
3. Compare survival and HRQOL scores between the different SAPS II admission categories: admissions for planned surgery, unplanned surgery, and medical reasons.

Methods

Haukeland University Hospital is a tertiary university hospital in Bergen, Norway, which serves approximately one million inhabitants. The general ICU has ten beds (burn, cardiac surgery, coronary, and neonatal units are separate units, and are not included in this study). The annual number of admissions is about 500, and 7–8 % of patients are 80 years of age or older. There were no large changes in practice or organization of the ICU during the study period besides general development in medicine and intensive care.

Study design

The first part of this study was a retrospective analysis of patients ≥80 years old, which were admitted to this general ICU between the 1st of January 2000 and the 31st of December 2012. These data were extracted from the dedicated ICU database with daily, prospectively collected data. Re-admissions, non-Norwegian patients, and admissions with errors in patient ID were excluded. For all included patients, we assessed the following:

1. Age and gender;
2. Length of stay (LOS);
3. Ventilator support, invasive (mechanical) and non-invasive ventilator support;
4. Severity score (simplified acute physiology score II (SAPS II) [10]) and organ dysfunction (sequential organ failure assessment score (SOFA) [11]): we defined severe organ dysfunctions as a SOFA score of 3 or 4; among daily SOFA scores, only the maximum was included in the analysis;
5. Comorbidity: we separated comorbidity in four categories (none, mild, moderate, and severe) based on the Charlson comorbidity index (CCI) [12];
6. Diagnostic groups: ICU admissions were allocated into one of thirteen different categories;
7. Short- and long-term survival (long-term defined as 1 year and longer): the standardized mortality ratio (SMR) was defined as the observed hospital mortality divided by the SAPS II estimated mortality; the SMR was analyzed for all patients and for each of the SAPS II admission categories;
8. Survival at follow-up; and
9. SAPS II admission categories, planned surgery, unplanned surgery, and medical reasons.

Survival was compared with a segment of the general population that was 80 years of age or older during 2000–2013, based on life tables from Statistics Norway.

The second part of the study included a prospective analysis of HRQOL. Patients alive at follow-up (16th of January 2014) were compared with a control group of 375 individuals matched for age, sex, and residence, which were randomly drawn from the National Registry. The HRQOL was assessed with EuroQol-5D (EQ-5D-3L) [13], a questionnaire sent by mail to ICU survivors and the control group at follow-up. EQ-5D has five dimensions, each with three response options. It also included a visual analog scale (EQ-VAS; Table 4). A reminder was sent to the non-responders after 1 month. ICU survivors were also contacted by phone. Informed consent was given by persons who answered the questionnaire.

We compared hospital survivors with hospital non-survivors and also compared the SAPS II admission categories. Information about end-of-life decision-making was retrospectively found for hospital non-survivors by searching through the individual patient files of their current hospital stay since such information was not entered in the ICU database. We only included statements which clearly used the terms withholding or withdrawal of ICU treatment.

The study was approved by the Regional Committee of Medical and Health Research Ethics in Central Norway (REC Central, 2013/1113).

Statistics

The length of stay (LOS) and ventilator time are expressed in terms of medians and quartiles. Significance was tested with the Mann-Whitney U test/Kruskal-Wallis test. Other continuous variables are expressed as the mean with standard deviation (SD) and compared with the t test/analysis of variance (ANOVA). Qualitative and dichotomous data are reported as the percent of n, and they were compared with Pearson's chi-square test/Fisher's exact test or with the Mann-Whitney U test. Three separate Cox proportional hazard regression analyses were used to determine independent predictors of ICU mortality, hospital mortality, and 1-year mortality. The time factor was defined as the number of days from ICU admission, ICU discharge, and hospital discharge, respectively. All variables with a p value of <0.2 in a primary univariate analysis were included in the multivariate model, except for admission categories; admission categories were included even when the p value was >0.2 in the univariate analysis. ICU mortality was analyzed separately. Only ICU survivors were included in the analysis of hospital mortality. Only hospital survivors were included in the 1-year mortality analysis. The remaining variables were then tested separately in the models, and included if they were significant. Adjusted hazard ratios (HR) were calculated with 95 % confidence intervals (95 % CI). Kaplan-Meier curves were constructed from the three SAPS II admission categories. Another Kaplan-Meier curve was constructed to compare all patients to the general octogenarian population in Norway. An adjusted mortality rate was calculated by dividing the observed mortality rate by the expected mortality rate from an age- and gender-matched population. The adjusted mortality rate was calculated between 1 and 8 years after ICU admission. Patients who were alive at follow-up were censored. All statistical analyses were performed with SPSS 21.0 (SPSS Inc., Chicago, IL, USA). *P* values <0.05 were considered statistically significant.

Results

From 2000 to 2012, 402 patients ≥80 years were admitted to our ICU, with a total of 419 ICU stays. Re-admissions (during the same hospital stay (n = 10) and during another later hospital stay (n = 7)), non-Norwegian patients (n = 4), and admissions with errors in patient ID (n = 3) were omitted from the analysis. Thus, 395 patients were included in the current study (Fig. 1).

Patient characteristics

Age and gender

At ICU admittance, the mean age was 83.8 years (range 80–101; median 83.1) and 61.0 % were males (Table 1). Males had longer median ICU-LOS (2.1 vs. 1.5 days, p = 0.006), a higher mean maximum SOFA score (8.3 vs. 7.0,

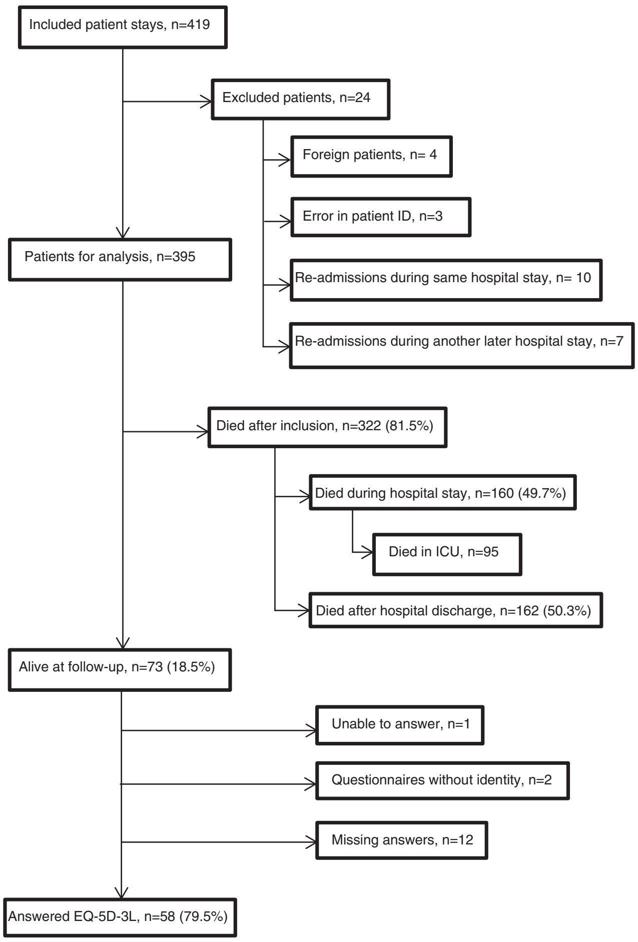

Fig. 1 Data collection process

Table 1 Differences in characteristics between hospital survivors and hospital non-survivors

	Total (*n* = 395)	Hospital survivors (*n* = 235)	Hospital non-survivors (*n* = 160)	*p* value
Age, mean ± SD	83.8 ± 2.9	83.5 ± 2.9	84.1 ± 2.8	0.049[a]
Male, %	61.0	60.9	61.3	0.511[b]
Length of stay (LOS), median (IQR)				
ICU-LOS	1.8 (0.9–3.9)	1.9 (1.0–4.3)	1.7 (0.8–3.2)	0.097[c]
Hospital LOS	11.3 (4.0–19.3)	14.2 (7.6–25.1)	5.5 (1.9–12.8)	<0.001[c]
Ventilator support				
Mechanical ventilator support, % (*n*)	61.3 (242)	51.9 (122)	75.0 (120)	<0.001b
Mechanical ventilator support time, median (IQR)	1.2 (0.5–3.3)	1.3 (0.5–3.8)	1.0 (0.4–3.0)	0.235[c]
Non-invasive ventilator support, % (*n*)	33.2 (131)	35.8 (84)	29.6 (47)	0.344[b]
Non-invasive ventilator support time, median (IQR)	1.5 (0.5–2.8)	1.6 (0.5–3.2)	1.3 (0.4–2.5)	0.164[c]
Severity score, mean ± SD				
SAPS II	44.3 ± 15.0 (*n* = 390)	40.6 ± 12.9 (*n* = 230)	49.5 ± 16.3 (*n* = 160)	<0.001[a]
Max. SOFA	7.8 ± 3.8 (*n* = 389)	6.7 ± 3.3 (*n* = 229)	9.5 ± 3.8 (*n* = 160)	<0.001[a]
Comorbidity				
Charlson comorbidity index, mean ± SD	2.6 ± 1.9 (*n* = 390)	2.7 ± 1.8 (*n* = 234)	2.5 ± 1.9 (*n* = 156)	0.389[a]
Charlson comorbidity index (CCI) categories, % (*n*)				0.602[b]
None (CCI 0)	12.3 (48)	11.1 (26)	14.1 (22)	
Mild (CCI 1–2)	40.8 (159)	39.3 (92)	42.9 (67)	
Moderate (CCI 3–4)	32.3 (126)	34.2 (80)	29.5 (46)	
Severe (CCI ≥5)	14.6 (57)	15.4 (36)	13.5 (21)	
Severe organ dysfunction, % (*n*)				
Respiration	66.3 (262)	62.6 (147)	71.9 (115)	0.034[b]
Circulation	47.1 (186)	38.7 (91)	59.4 (95)	<0.001[b]
Renal	28.1 (111)	20.9 (49)	38.8 (62)	<0.001[b]
CNS	26.1 (103)	18.7 (44)	36.9 (59)	<0.001[b]
Coagulation	9.9 (39)	9.8 (23)	10.0 (16)	0.537[b]
Liver	1.3 (5)	0.9 (2)	1.9 (3)	0.399[d]
Admission categories, % (*n*)				<0.001[b]
Planned surgery	12.7 (50)	17.9 (42)	5.0 (8)	
Unplanned surgery	53.9 (213)	49.8 (117)	60.0 (96)	
Medical reasons	33.4 (132)	32.3 (76)	35.0 (56)	
Diagnostic groups, % (*n*)				
Respiratory failure	28.1 (111)	31.1 (73)	23.8 (38)	0.112[b]
Circulatory failure	8.1 (32)	7.7 (18)	8.8 (14)	0.697[b]
Combined respiratory and circulatory failure	10.4 (41)	8.9 (21)	12.5 (20)	0.254[b]
Neurologic failure	10.1 (40)	9.4 (22)	11.3 (18)	0.541[b]
Isolated head injury	2.5 (10)	1.7 (4)	3.8 (6)	0.328[d]
Sepsis	8.9 (35)	7.2 (17)	11.3 (18)	0.168[b]
Gastroenterological failure	4.8 (19)	4.7 (11)	5.0 (8)	0.884[b]
Multiple organ failure	5.6 (22)	3.0 (7)	9.4 (15)	0.007[b]
Multitrauma without head injury	3.8 (15)	5.1 (12)	1.9 (3)	0.099[b]
Multitrauma with head injury	2.3 (9)	1.7 (4)	3.1 (5)	0.495[d]

Table 1 Differences in characteristics between hospital survivors and hospital non-survivors *(Continued)*

Planned surgery	3.3 (13)	5.5 (13)	0.0 (0)	0.002[b]
Acute operation	6.6 (26)	7.2 (17)	5.6 (9)	0.527[b]
Unspecified	5.6 (22)	6.8 (16)	3.8 (6)	0.193[b]

IQR interquartile range, *SD* standard deviation, *CI* confidence interval, *ICU* intensive care unit, *SAPS II* simplified acute physiology score II, *SOFA* sequential organ failure assessment, *CCI* Charlson comorbidity index
[a]Independent *t* test
[b]Pearson's chi-square
[c]Mann-Whitney U test
[d]Fisher's exact test

$p = 0.031$), and severe circulatory failure more frequently (52.3 vs. 39.0 %, $p = 0.010$) than females.

Length of stay

The overall median ICU-LOS and hospital-LOS were 1.8 and 11.3 days, respectively. The median LOS for ICU non-survivors was 1.3 days (see Table 1). Among all patients, 26.8 % stayed less than 1 day in the ICU.

Ventilator support

Of 395 patients, 61.3 % received mechanical ventilator support for a median time of 1.2 days. Of the hospital non-survivors, 75.0 % ($n = 120$) received mechanical ventilator support (Table 1). A fraction of 69.2 % ($n = 83$) of these 120 patients had life-sustaining treatment limitation decisions.

Severity scores and severe organ dysfunction

Overall, the mean SAPS II and mean maximal SOFA scores were 44.3 and 7.8, respectively. Hospital non-survivors had a mean SAPS II of 49.5 and a mean maximal SOFA score of 9.5 (Table 1). All patients with maximal SOFA scores ≥17 died in the ICU; all those with scores ≥16 died during the hospital stay.

Comorbidity

Overall mean Charlson comorbidity index was 2.6. Patients admitted for planned surgery showed the highest index score among the admission categories (3.2). Only 12.3 % of the patients had no preexisting comorbidity (see Table 1 and 2).

Diagnostic groups

The most frequent cause for ICU admission was respiratory failure (28 %). Respiratory failure was most common in the planned surgery group (44 %; Table 2).

Survival and predictors of mortality

Short-term survival

The overall ICU and hospital survival were 75.9 and 59.5 %, respectively. Of the ICU non-survivors, 63.2 % died within 2 days after ICU admission ($n = 60$), and 68.3 % of these patients had life-sustaining treatment (LST) limitations (($n = 41$); withholding 60.0 % and withdrawal 51.7 %). The SMR was 1.06, with large differences between the planned surgery (0.55) and unplanned surgery (1.15) groups. For survival at 30, 90, and 180 days, see Table 2.

Predictors of high ICU mortality were age, mechanical ventilator support, SAPS II, maximum SOFA, and multi-trauma with head injury. Increased hospital mortality was predicted by an unplanned surgical admission (Table 3).

Long-term survival (1 year and longer)

The overall 1- and 2-year survival rates were 42.0 and 36.6 %, respectively. After 5 years, 22.2 % of all patients remained alive. A comparison between patients ($n = 395$) and the general population greater than 80 years old in Norway ($n = 426\,773$) showed excess mortality among patients in the first year, with an adjusted mortality rate of 6.35 (95 % CI 5.58–7.23). After the first year, the survival rates were similar between groups; patients had an adjusted mortality rate during the second year of 1.34 (95 % CI 0.86–2.07; Fig. 2). Among patients alive after 1 year, the mean survival time, starting from the 1-year point, was 5.1 years.

Respiratory failure and isolated head injury were independent predictors of 1-year mortality (Table 3).

Survival at follow-up

At follow-up (January 2014), 322 (81.5 %) patients had died, including 160 during the hospital stay and 162 after hospital discharge. Seventy-three patients (18.5 %) survived, with a mean age of 86.9 years at follow-up. The median time from hospital discharge to follow-up was 3.3 years (range 1–13.8 years; Fig. 1). The survivors at follow-up ($n = 73$) had, compared to hospital survivors not alive at follow-up ($n = 162$), similar ICU-LOS (1.9 vs. 1.8 days; $p = 0.465$), fraction of ventilator support (52.1 vs. 51.9 %; $p = 0.977$), severity of illness (SAPS II 43.2 vs. 39.4, $p = 0.658$; max. SOFA 6.5 vs. 6.7, $p = 0.313$), and comorbidity (Charlson comorbidity index 2.4 vs. 2.8, $p = 0.156$; Additional file 1: Table S1). However, hospital survivors not alive at follow-up had a lower median survival after hospital discharge (3.1 years), compared to the follow-up of 3.4 years in survivors.

Table 2 Characteristics of SAPS II admission categories

	Planned surgery (*n* = 50)	Unplanned surgery (*n* = 213)	Medical reasons (*n* = 132)	Total (*n* = 395)	*p* value
Age, mean ± SD	83.5 ± 2.7	84.0 ± 2.7	83.5 ± 3.2	83.8 ± 2.9	0.217[a]
Male, %	64.0	60.6	60.6	61.0	0.889[b]
Length of stay (LOS), median (IQR)					
ICU-LOS	2.0 (1.0–4.4)	2.2 (1.0–5.0)	1.2 (0.6–2.6)	1.8 (0.9–3.9)	<0.001[b]
Hospital LOS	15.1 (10.2–26.2)	12.9 (4.3–20.6)	6.5 (2.0–14.3)	11.3 (4.0–19.3)	<0.001[b]
Ventilator support					
Mechanical ventilator support, % (*n*)	48.0 (24)	69.5 (148)	53.0 (70)	61.3 (242)	0.001[b]
Mechanical ventilator support time, median (IQR)	1.1 (0.4–3.7)	1.3 (0.5–3.8)	0.9 (0.3–2.0)	1.2 (0.5–3.3)	0.050[b]
Non-invasive ventilator support, % (*n*)	44.0 (22)	33.8 (72)	28.0 (37)	29.6 (47)	0.119[b]
Non-invasive ventilator support time, median (IQR)	1.2 (0.5–2.6)	2.0 (0.6–3.0)	1.0 (0.3–2.0)	1.3 (0.4–2.5)	0.056[b]
Severity score, mean ± SD					
SAPS II	39.0 ± 13.2 (*n* = 47)	44.6 ± 14.8 (*n* = 212)	45.6 ± 15.6 (*n* = 131)	44.3 ± 15.0 (*n* = 390)	0.030[a]
Max. SOFA	6.3 ± 4.1 (*n* = 47)	8.3 ± 3.6 (*n* = 212)	7.5 ± 3.8 (*n* = 130)	7.8 ± 3.8 (*n* = 389)	0.002[a]
Comorbidity					
Charlson comorbidity index, mean ± SD	3.2 ± 1.8 (*n* = 50)	2.5 ± 2.0 (*n* = 209)	2.5 ± 1.7 (*n* = 131)	2.6 ± 1.9 (*n* = 390)	0.050[a]
Charlson comorbidity index (CCI) categories, % (*n*)					
None (CCI 0)	4.0 (2)	13.4 (28)	13.7 (18)	12.3 (48)	0.159[b]
Mild (CCI 1–2)	34.0 (17)	43.1 (90)	39.7 (52)	40.8 (159)	0.436[b]
Moderate (CCI 3–4)	46.0 (23)	26.3 (55)	36.6 (48)	32.3 (126)	0.009[b]
Severe (CCI ≥5)	16.0 (8)	17.2 (36)	9.9 (13)	14.6 (57)	0.163[b]
Severe organ dysfunction, % (*n*)					
Respiration	68.0 (34)	71.8 (153)	56.8 (75)	66.3 (262)	0.016[b]
Circulation	38.0 (19)	53.1 (113)	40.9 (54)	47.1 (186)	0.035[b]
Renal	30.0 (15)	28.6 (61)	26.5 (35)	28.1 (111)	0.868[b]
CNS	20.0 (10)	23.5 (50)	32.6 (43)	26.1 (103)	0.100[b]
Coagulation	16.0 (8)	8.5 (18)	9.8 (13)	9.9 (39)	0.273[b]
Liver	2.0 (1)	0.0 (0)	3.0 (4)	1.3 (5)	0.034[d]
Survival, % (*n*)					
ICU	90.0 (45)	74.2 (158)	73.5 (97)	75.9 (300)	0.045[b]
Hospital	84.0 (42)	54.9 (117)	57.6 (76)	59.5 (235)	0.001[b]
30 days	86.0 (43)	51.2 (109)	54.5 (72)	56.7 (224)	<0.001[b]
90 days	82.0 (41)	44.6 (95)	50.8 (67)	51.4 (203)	<0.001[b]
180 days	74.0 (37)	40.4 (86)	47.7 (63)	47.1 (186)	<0.001[b]
1 year	68.0 (34)	37.1 (79)	40.2 (53)	42.0 (166)	<0.001[b]
2 years	59.9 (28)	33.1 (64)	33.6 (39)	36.6 (130)	0.001[b]
3 years	48.4 (15)	27.8 (50)	29.9 (32)	31.2 (96)	0.088[b]
5 years	32.8 (7)	18.6 (28)	23.7 (22)	22.2 (55)	0.290[b]
Diagnostic groups, % (*n*)					
Respiratory failure	44.0 (22)	24.4 (52)	28.0 (37)	28.1 (111)	0.021[b]
Circulatory failure	8.0 (4)	8.5 (18)	7.6 (10)	8.1 (32)	0.959[b]
Combined respiratory and circulatory failure	8.0 (4)	12.7 (27)	7.6 (10)	10.4 (41)	0.270[b]

Table 2 Characteristics of SAPS II admission categories *(Continued)*

Neurologic failure	2.0 (1)	7.0 (15)	18.2 (24)	10.1 (40)	<0.001[b]
Isolated head injury	0.0 (0)	1.9 (4)	4.5 (6)	2.5 (10)	0.165[d]
Sepsis	4.0 (2)	8.9 (19)	10.6 (14)	8.9 (35)	0.308[d]
Gastroenterological failure	0 (0)	5.6 (12)	5.3 (7)	4.8 (19)	0.276[d]
Multiple organ failure	4.0 (2)	7.5 (16)	3.0 (4)	5.6 (22)	0.205[d]
Multitrauma without head injury	0.0 (0)	5.6 (12)	2.3 (3)	3.8 (15)	0.107[d]
Multitrauma with head injury	0.0 (0)	2.3 (5)	3.0 (4)	2.3 (9)	0.638[d]
Planned surgery	18.0 (9)	1.4 (3)	0.8 (1)	3.3 (13)	<0.001[d]
Acute operation	2.0 (1)	10.3 (22)	2.3 (3)	6.6 (26)	0.004[d]
Unspecified	10.0 (5)	3.8 (8)	6.8 (9)	5.6 (22)	0.150[d]
SMR (95 % CI)	0.55 (0.28–1.11) (*n* = 47)	1.15 (0.94–1.40) (*n* = 212)	1.05 (0.81–1.37) (*n* = 131)	1.06 (0.90–1.23) (*n* = 390)	

Survival times were derived from the life table method
IQR interquartile range, *SD* standard deviation, *CI* confidence interval, *ICU* intensive care unit, *SAPS II* simplified acute physiology score II, *SOFA* sequential organ failure assessment, *CCI* Charlson comorbidity index, *SMR* standardized mortality ratio
[a]With ANOVA (analysis of variance)
[b]Pearson's chi-square test
[c]With Kruskal-Wallis test
[d]Fisher's exact test

SAPS II admission categories

Patients admitted for planned surgery had significantly higher survival rates than those admitted for medical reasons and unplanned surgery up to 3 years after ICU admittance (Table 2). The median survival times were 33.4 months (95 % CI 21.2–45.6) for planned surgery, 1.2 months (95 % CI 0.0–2.7) for unplanned surgery, and 2.7 months (95 % CI 0.0–9.1) for medical admissions (Fig. 3).

Health-related quality of life

The EQ-5D questionnaire was sent to the 73 patients who were alive at follow-up. The response rate was 83.6 % (*n* = 61), but one questionnaire was incomplete, and two questionnaires had no patient identity. Fourteen patients responded to the questionnaire by telephone. The response rate in the control group was 47.7 % (179/375), constituting 2.5 controls per survivor at follow-up. HRQOL was similar between patients and the general population and among the admission categories (Table 4).

Life-sustaining treatment limitation in hospital non-survivors

Of the ICU non-survivors, 70.5 % (*n* = 67) had treatment-limitation decisions; withholding 68.4 % (*n* = 65) and withdrawal 51.6 % (*n* = 49). The majority of these LST limitation decisions were taken within the first 2 days after ICU admission (61.2 % (*n* = 41)). Post ICU 72.3 % (*n* = 47) of the hospital non-survivors had treatment-limitation decisions; withholding 72.3 % (*n* = 47) and withdrawal 32.3 % (*n* = 21). We lack information on LST decisions in six ICU non-survivors and two ICU survivors.

Discussion

This study establishes three major results. First, patients who survived the first year after ICU admittance showed long-term survival rates similar to those of the normal Norwegian octogenarian population. The HRQOL of long-time survivors was comparable to that of an age- and sex-matched general population group. Second, the planned surgery group exhibited higher survival rates than the medical and unplanned surgery groups up to 3 years after ICU admittance. However, at follow-up, HRQOL did not differ among these three groups. Third, high ICU mortality was predicted by age, mechanical ventilator support, SAPS II, maximum SOFA score, and multitrauma with head injury. High hospital mortality was predicted by an unplanned surgical admission. Respiratory failure and isolated head injury were independent predictors of 1-year mortality. The majority of the ICU non-survivors died within 2 days, where most of these had life-sustaining treatment (LST) limitations. Almost three quarters of the hospital non-survivors had treatment-limitation decisions.

Our finding of age as an independent predictor of ICU mortality contrasts with several previous studies [14, 15]. Conflicting results about the impact of age on outcome for older patients in the ICU may be explained by variations in adjustments for severity and comorbidities among different studies. Moreover, in some institutions, older individuals may have been denied ICU admission, based on advanced age [16]. In addition, treatment is often withheld for older ICU patients with severe comorbidity [17]. In our study, advanced age may also have influenced preferences in decision-making among patients, relatives, or caregivers. The influence of age on mortality must be adjusted for severity of illness.

Table 3 Predictors of mortality in the ICU, in hospital, and at 1 year after admission

	ICU mortality (n = 389)	Hospital mortality for ICU survivors (n = 294)	1-year mortality for hospital survivors (n = 230)
	Adjusted HR (95 % CI)	Adjusted HR (95 % CI)	Adjusted HR (95 % CI)
Age, years	1.10 (1.03–1.18)[a]		
Male			
Ventilator support			
Mechanical ventilator support	1.99 (1.10–3.60)[a]	1.40 (0.81–2.43)	
Non-invasive ventilator support	0.87 (0.51–1.49)		
Severity score, mean			
SAPS II	1.03 (1.01–1.04)[a]	1.01 (0.99–1.03)	1.01 (0.99–1.03)
Max. SOFA	1.20 (1.10–1.31)[a]	1.03 (0.95–1.12)	
Comorbidity			
None (CCI 0)	1.00		1.00
Mild (CCI 1–2)	0.68 (0.35–1.30)		1.02 (0.43–2.46)
Moderate (CCI 3–4)	0.53 (0.25–1.11)		1.06 (0.42–2.65)
Severe (CCI ≥ 5)	0.53 (0.23–1.25)		2.09 (0.99–5.39)
Severe organ dysfunction			
Respiration	1.05 (0.55–1.97)		
Circulation	0.76 (0.39–1.48)		
Renal	1.50 (0.88–2.54)		
CNS	1.19 (0.71–1.99)		
Coagulation			
Liver			
Admission categories			
Planned surgery	1.00	1.00	1.00
Unplanned surgery	1.40 (0.54–3.65)	3.46 (1.06–11.24)[a]	2.02 (0.88–4.64)
Medical reasons	2.11 (0.80–5.58)	3.17 (0.94–10.76)	1.97 (0.83–4.70)
Diagnostic groups			
Respiratory failure	1.03 (0.55–1.90)		1.86 (1.13–3.07)[a]
Circulatory failure			
Combined respiratory and circulatory failure			
Neurologic failure		1.67 (0.86–3.25)	
Isolated head injury	1.56 (0.58–4.18)		9.12 (2.44–34.14)[a]
Sepsis	1.20 (0.63–2.69)		
Gastroenterological failure			
Multiple organ failure	1.27 (0.60–2.69)	1.67 (0.64–4.31)	
Multitrauma without head injury			
Multitrauma with head injury	2.99 (1.04–8.60)[a]		
Planned surgery			
Acute operation			
Unspecified			

ICU intensive care unit, *SAPS II* simplified acute physiology score II, *SOFA* sequential organ failure assessment, *HR* hazard ratio, *CI* confidence interval, *CCI* Charlson comorbidity index

[a]Significant differences

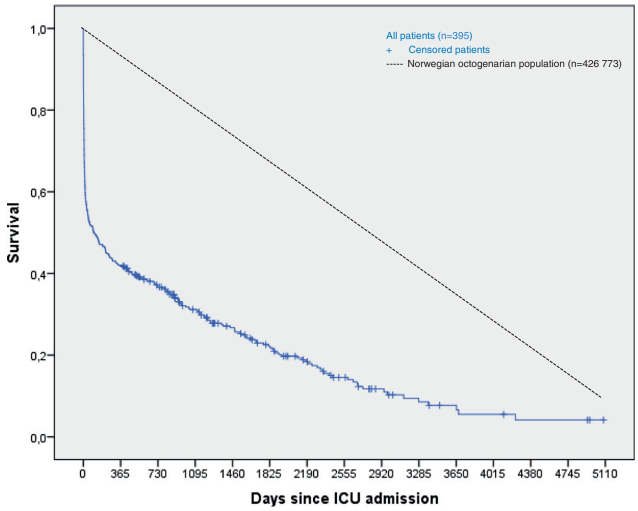

Fig. 2 Kaplan-Meier survival curve for all patients (*solid blue line*) compared to the Norwegian octogenarian population (*dashed black line*) in 2000–2013

In general, ICU length of stay is short in Scandinavian countries [6, 7, 18]. One explanation can be the low availability of ICU beds compared to many other European countries [3, 19]. Also, octogenarians are in general found to have shorter ICU stays than younger patients [6, 20, 21]. This is probably reflected in our study. The overall median ICU-LOS was 1.8 days, which was 3.2–4.2 days shorter than that reported in recent French studies [8, 9]. Also, our ICU and hospital mortality rates were lower than reported in those studies. These findings might be explained by differences in "case-mix" within the SAPS II admission categories, where the French studies included mostly medical cases. However, our medical group had significantly shorter ICU stays (median 1.2 days) than the unplanned surgery group. This finding could not be explained by differences in mortalities or SAPS II scores. Even though ICU-LOS is short in our study, the mean SAPS II scores and mechanical ventilator support rates are comparable to other octogenarian cohort studies [8, 9, 14, 21–23]. In general, our survivors had longer ICU stays than non-survivors, due to

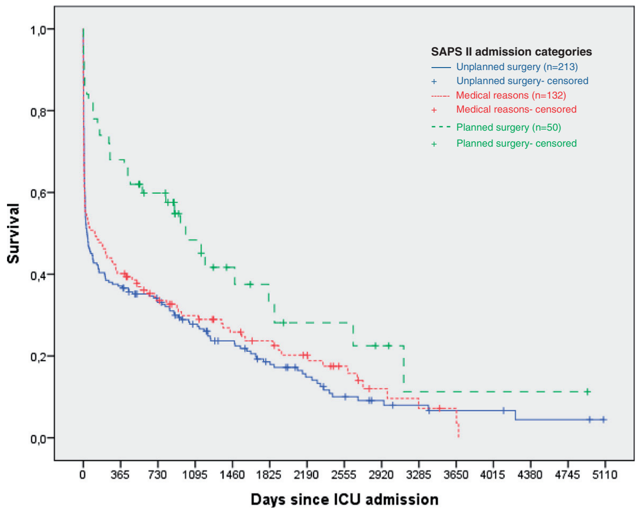

Fig. 3 Kaplan-Meier survival curves of SAPS II admission categories

Table 4 Comparison of frequency distributions (profiles) of the EQ-5D-3L for patient and control groups

Variable	Total patients (*n* = 58)	Control group (*n* = 179)	*p* value
Age, years, mean ± SD	87.4 ± 4.0	86.7 ± 4.4	0.265[a]
Male, % (*n*)	69.0 (40)	66.5 (119)	0.726[b]
Mobility, % (*n*)			0.504[c]
No problem	41.4 (24)	43.6 (78)	
Some problems	51.7 (30)	54.7 (98)	
Confined to bed	6.9 (4)	1.7 (3)	
Self-care, % (*n*)			0.957[c]
No problem	75.9 (44)	74.9 (134)	
Some problems	15.5 (9)	21.8 (39)	
Unable to	8.6 (5)	3.4 (6)	
Usual activities, % (*n*)			0.237[c]
No problem	43.1 (25)	49.7 (89)	
Some problems	41.4 (24)	41.3 (74)	
Unable to	15.5 (9)	8.9 (16)	
Pain and discomfort, % (*n*)			0.229[c]
None	43.1 (25)	34.6 (62)	
Moderate	51.7 (30)	58.1 (104)	
Extreme	5.2 (3)	7.3 (13)	
Anxiety and depression, % (*n*)			0.258[c]
None	77.6 (45)	69.8 (125)	
Moderate	20.7 (12)	27.9 (50)	
Extreme	1.7 (1)	2.2 (4)	
EQ index, mean ± SD	0.71 ± 0.28	0.73 ± 0.23	0.924[c]
EQ VAS, mean ± SD	63.9 ± 20.3 (*n* = 53)	67.7 ± 22.0 (*n* = 170)	0.219[c]

SD standard deviation, *EQ* EuroQol, *VAS* visual analog scale (range 0–100)
[a]Independent *t* test
[b]Pearson's chi-square
[c]Mann-Whitney U test

death shortly after ICU admittance (63.2 % within 2 days). The large proportion of LST limitations among ICU non-survivors during the first 2 days after ICU admission may contribute to the short length of stay. Our data could indicate that ICU physicians limit the intensity of life-sustaining treatment if there is no improvement in the condition of the octogenarian patient within the first 2 days after ICU admission. Although we lack data on triage decisions prior to ICU admission, we might speculate that a more thorough pre-ICU triage process could have decreased the rather high fraction of LST limitation decisions by rejecting patients who probably would not benefit from ICU treatment.

After the first year, we found our ICU patients to have survival rates similar to those of the general octogenarian population. Interestingly, Roch et al. found a similar trend after 2 years [9]. The low 1-year survival rate may indicate that many aged patients did not benefit from ICU treatment. Therefore, we need better predictors to determine which patients are likely to gain long-term benefit from ICU treatment. Several studies have reported prognostic factors for short- and long-term mortality among older individuals [14, 17, 24]. In general, short-term mortality is most frequently predicted by severity scores and the number of organ failures [17]. Commonly used prognostic models for aged patients in the ICU lack calibration. Nevertheless, our study showed that severity scores were good predictors for ICU mortality, in addition to age, mechanical ventilator support, and multitrauma with head injury. One study developed a prognostic model for predicting in-hospital mortality in older patients in the ICU, and found low Glacow coma scale (GCS) scores to be strongly related to short-term mortality [24]. Several other studies have reported that brain injury is associated with poor outcomes in older patients [25, 26]. Comorbidity is also found to be a predictor of long-term survival in some octogenarian ICU studies [9, 14]. However, these studies used the McCabe classification, where comorbidity is based on the presence of underlying fatal diseases. In our study, we found no association between long-term mortality and comorbidity, using the Charlson comorbidity index. This is supported in other studies [5, 27], also using Charlson comorbidity index. The regression analysis of ICU mortality showed decreasing hazard of death with increasing comorbidity. This was probably mainly due to admission of patients with no comorbidity who suffered severe trauma and bleeding events, with high mortality. We might speculate that the admission policy of these patients was more liberal due to lack of comorbidity, even if the prospects of survival was low, compared to patients with higher comorbidity. In our opinion, comorbidity is not a very useful predictor for ICU mortality in general nor for the elderly population.

To our knowledge, this study is the first to report HRQOL in older patients over a 13-year post-ICU follow-up. We found similar HRQOLs in ICU survivors and the general Norwegian octogenarian population at follow-up. Other recent studies on HRQOL in older ICU survivors have reported impaired physical function [9, 28]. De Rooij et al. found that patients had more problems with usual activities and lower mean EQ VAS scores than the general British population [29]. In contrast, Tabah et al. reported a similar HRQOL, or better in some domains, compared to a matched general population [8]. Good HRQOL perceptions, despite physical impairment, could be due to lower expectations of life after critical illness. However, HRQOL evaluations may be prone to selection bias, because responders may represent healthier patients. Our study revealed that non-responders and responders had similar severity scores and similar fractions of severe organ failures. But non-responders were evaluated at slightly longer times after hospital discharge (median 4.6 vs. 3.3 years; $p = 0.350$). Patients alive after 1 year had a mean further survival time of 5.1 years. Furthermore, survivors at follow-up had longer time to follow-up compared to the median survival in hospital survivors not alive at follow-up. Nevertheless, these groups were otherwise comparable, and we can speculate that hospital survivors no longer alive had about the same HRQOL as survivors at follow-up, at least for much of the time left (Additional file 1: Table S1).

Very few studies have reported outcomes for aged patients in different SAPS II admission categories. De Rooij et al. reported higher short- and long-term survival in patients admitted for planned surgery compared to those admitted for medical reasons and unplanned surgery, with a mean follow-up of 3.6 years [22]. Our results supported that finding, but only up to 3 years after ICU admittance. Thereafter, long-term survival was similar among the groups. We also found that an unplanned surgery admission could predict high hospital mortality in ICU survivors.

Limitations

This study has several limitations. First, it was partly a retrospective study and clinical data were confined to those registered in the ICU database. Thus, we had no information about triage decisions made before ICU admission. Variability in these decisions may influence the results [30–32]. Second, the long inclusion period could contain changes in admission policy and medical practice. However, the catchment area and basic functions of the hospital remained the same during the study period, with a slowly growing population and all medical services except organ transplant surgery offered. There were no large changes in practice or organizational changes in the ICU during the study period. Third, due to our single-center study design, the group sizes were relatively small. In particular, the number of patients for HRQOL assessment was limited (n = 73); this is common in single-center studies of aged ICU populations. Furthermore, the HRQOLs of different groups were evaluated at different follow-up times. Nevertheless, every patient was followed-up after at least 1 year, the recommended minimum [33]. Furthermore, the high response rate for the EQ-5D questionnaire (n = 58, 79.5 %) provided valuable HRQOL information among older, long-term ICU survivors in Norway, particularly compared to the age- and gender-matched control group. We evaluated HRQOL once in each patient; thus, we did not study changes in HRQOL over time. Ideally, a baseline measurement should be made before the ICU stay. Finally, we had no information on living status or cognitive functions.

Conclusions

One-year survival was 42.0 %, with further survival comparable to the general octogenarian population. HRQOL in survivors was comparable with an age- and sex-matched general population, with a follow-up of 1–13.8 years. Up to 3 years after ICU admittance, patients admitted for planned surgery had better short- and long-term outcomes than those admitted for medical reasons and unplanned surgery. The majority of the ICU non-survivors died within 2 days, and most of these had life-sustaining treatment (LST) limitations. Almost three quarters of the hospital non-survivors had treatment-limitation decisions. Our results indicate that older ICU patients have poor short-term outcomes due to high mortalities, but good long-term outcomes in those who survive beyond 1 year. Predictors identified in this study may facilitate triage decisions in older patients regarding ICU treatment. Future research should focus on improving prognostic models for aged patients.

Key messages

- One-year survival was 42.0 %; thereafter, survival was comparable to that of the general octogenarian population.
- HRQOL in our survivors at follow-up (n = 58) was comparable with an age- and gender-matched

general population (n = 179), for a follow-up of 1–13.8 years.

- Patients admitted for planned surgery had better short- and long-term survival rates than those admitted for medical reasons or unplanned surgeries for three years after ICU admittance.
- The majority of the ICU non-survivors died within 2 days (63.2 %), and most of these had life-sustaining treatment (LST) limitations (68.3 %).

Additional file

Additional file 1: Table S1. Differences in characteristics between hospital survivors not alive at follow-up (n = 162) and survivors at follow-up (n = 73).

Abbreviations

HRQOL: health-related quality of life; ICU: intensive care unit; LOS: length of stay; SAPS II: simplified acute physiology score II; SOFA: sequential organ failure assessment score; CCI: Charlson comorbidity index; SMR: standardized mortality ratio; SD: standard deviation; CI: confidence interval; IQR: interquartile range; ANOVA: analysis of variance; HR: hazard ratio; LST: life-sustaining.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FHA conceived the study, participated in its coordination, performed the statistical analyses, and drafted the manuscript. RK, HF, and PK made substantial contribution to the conception and design of the study and helped to draft the manuscript. UR participated in the design of the study and supervised during the statistical analyses. All authors read and approved the final manuscript.

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