Mortality After Hospital Discharge in ICU Patients*

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Objectives: To assess the mortality risk of ICU patients after hospital discharge and compare it to mortality of the general Dutch population.

Design: Cohort study of ICU admissions from a national ICU registry linked to administrative records from an insurance claims database.

Setting: Eighty-one Dutch ICUs.

Patients: ICU patients (n = 91,203) who were discharged alive from the hospital between January 1, 2007, and October 1, 2010.

Interventions: None.

Measurements and Main Results: The unadjusted observed survival was inspected by Kaplan-Meier curves. Mortality risk at 1, 2, and 3 years after hospital discharge was 12.5%, 19.3%, and 27.5%, respectively. The 3-year mortality after hospital discharge in ICU patients was higher than the weighted average of the gender and age-specific death risks of the general Dutch population (27.5% versus 8.2%). The 1-year mortality after hospital discharge was adjusted for case-mix differences by a set of determinants which showed a statistically significant influence on the outcome in a 10-fold cross validation. The elective and cardiac surgical patients have statistically significantly better mortality outcomes (adjusted hazard ratio, 0.73 and 0.28, respectively), whereas medical patients and patients admitted for cancer have statistically significantly worse mortality outcomes (adjusted hazard ratio, 1.41, 1.94, respectively) compared with other ICU patients. Urgent surgery patients and patients with a subarachnoid hemorrhage, trauma, acute renal failure, or severe community-acquired pneumonia did not differ statistically from the other ICU patients after adjustment for case-mix differences.

Conclusions: In-hospital mortality underestimates the true mortality of ICU patients as the mortality in the first months after hospital discharge is substantial. Most ICU patients still have an increased mortality risk in the subsequent years after hospital discharge compared with the general Dutch population. The mortality after hospital discharge differs widely between ICU subgroups. Future studies should focus on the analysis of mortality after hospital discharge that is attributable to the former ICU admission. (*Crit Care Med* 2013; 41:1229–1236)

Key Words: critical care; intensive care unit; long-term outcome; mortality; survival

The increasing use of quality indicators to assess clinical process performance and patient outcomes is an important issue in the healthcare debate, especially in a complex and expensive environment such as the ICU (1, 2). Currently, the observed in-hospital mortality is commonly used to describe the outcome of ICU patients. The in-hospital mortality adjusted for case-mix is commonly used as quality indicator to compare the performance among hospitals. Unfortunately, for several reasons, mortality may still be higher than expected for many months after hospital discharge. First, patients may have an increased mortality risk due to critical illness-related disorders, such as weakness, immunological insufficiency, or other comorbidities. Also, patients may still be (moribundly) ill at hospital discharge, i.e., if they are discharged from one hospital to another or to a palliative care facility. Thirdly, the critical illness and ICU admission may accelerate the underlying diseases (3). A more optimal way to estimate quality of ICU care, both from the point of view of healthcare institutions and the patient, is to consider the mortality sometime after hospital discharge. It can even be argued that assessing the mortality after hospital discharge is more important than the ubiquitously used in-hospital mortality as little has been achieved when patients die soon after hospital discharge. Information on mortality after hospital discharge could help clinicians to identify groups at elevated risk after hospital discharge to identify interventions that improve their long-term mortality (4).

Clinical registries commonly register patient data and mortality up until hospital discharge and are frequently used to monitor and analyze the quality of health care based on in-hospital mortality. The in-hospital mortality can be registered quite easily and reliably while complete registration of mortality after

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hospital discharge may be more challenging and time consuming. This partly explains why ICU and hospital mortality have been described more frequently than the long-term mortality. However, linking clinical databases with administrative databases, e.g., from insurance companies, offers the opportunity to assess long-term mortality.

The aim of this study was to assess (case-mix adjusted) mortality after hospital discharge in a large Dutch ICU population and compare it to mortality of the general Dutch population. In this study we focused on the total ICU population as well as on specific ICU subgroups.

MATERIALS AND METHODS

Data

This study was a retrospective cohort study, comprising all ICU patients discharged from the hospital between January 1, 2007, and October 1, 2010. Data on this population were derived by linking the Dutch National Intensive Care Evaluation (NICE) registry (5) to a national administrative database of health insurance companies (insurance claims database of Vektis), covering 95% (in 2008) of the insured Dutch population (6). As a health insurance is compulsory for all citizens in the Netherlands, the claims database is representative for the total Dutch population.

The NICE registry contains demographic, physiologic, and clinical data of all consecutive ICU patients admitted to participating ICUs, including the Acute Physiology and Chronic Health Evaluation (APACHE) IV score (7), chronic comorbidity, and reason for ICU admission. During the study period, approximately 85% of all Dutch ICUs recorded data of all their admissions in the NICE registry. We used the APACHE IV score to correct the mortality 1-year after hospital discharge for the severity of illness at admission. Therefore, we could only include admissions fulfilling the inclusion criteria of the APACHE IV model (7). ICU patients discharged to other hospitals were excluded as their in-hospital outcome was unknown.

The NICE registry includes data until hospital discharge, so the mortality after hospital discharge is unavailable. However, this was obtained by linkage to the insurance claims database of Vektis, which contains information on the vital status of patients. After the insurance claims database was linked to the NICE registry, the status of the patients (either alive or death) on January 1, 2011, and if relevant, the date of death, was extracted from the insurance claims database. The data used in this study have been encrypted in a way that all patient identifying information, such as name and patient identification number, has been removed. In the Netherlands, there is no need to obtain consent to make use of registries without patient identifying information. The data are officially registered according to the Dutch Personal Data Protection Act.

The records from the NICE registry and insurance claims database are anonymously linked by a deterministic linkage algorithm (8) that used the hospital of admission, gender, date of birth, ICU admission date, and ICU discharge date. In this method, the variables in both databases must be exactly the same for a positive match. In the algorithm, the patients are first linked by using the separately declared ICU days of the insured patients, and the remaining unlinked patients are further linked by using the declared hospitalization periods for complex interventions such as cardiac surgery and transplantations. If the ICU admission registered in the NICE database occurred in the declared hospitalization period, the records were linked. In the final linked dataset, patients' vital status was assessed on January 1, 2011, and patients were assumed to be alive if there was no date of death in the insurance claims database at that time. Case-mix characteristics of the linked and nonlinked records of the NICE registry were compared using Student *t* tests for normally distributed data and Mann-Whitney *U* tests for non-normally distributed data to evaluate potential bias due to incomplete linkage.

Mortality After Hospital Discharge

To assess patient mortality after hospital discharge, we performed Kaplan-Meier and Cox proportional hazard analyses for the whole ICU population, for ICU subgroups based on admission type (elective surgery, urgent surgery, and medical [i.e., nonsurgical]), and based on reason for ICU admission (cardiac surgery, subarachnoid hemorrhage, acute renal failure, severe community-acquired pneumonia, cancer, and trauma). Choice of these subgroups was based on existing literature on long-term mortality (9–14), expert opinion, and the availability of sufficient (i.e., more than 500) ICU admissions that survived hospitalization during our study period. Definitions of the subgroups are given in **Box 1.**

Explanation of the Diagnostic Subgroups

The expected mortality for the general Dutch population was assessed by using gender- and age-specific death risks reported by the Dutch governmental institution Statistics Netherlands (15). To assess these specific death risks, the ICU patients included in the analysis were categorized in seven age groups (i.e. <40, 40–50, 50–60, 60–70, 70–80, 80–90, >90 yr) in which the percentages of women and men were calculated. According to the percentages of patients in each age group and the corresponding percentage of women and men, the weighted average of the death risks of the general Dutch population was assessed. The weighted average 1-year mortality risk of the general Dutch population was compared with that of the ICU population.

In the literature, the long-term mortality of ICU patients is adjusted for various determinants. The most commonly used determinants are age, severity of illness, and comorbidities (16–22). Based on an extensive list of determinants that were reported at least once in the literature, we performed a 10-fold crossvalidation to identify the determinants that have a significant influence on the outcome of our ICU population and therefore should be included in the Cox proportional hazard model. During these analyses, only the ICU patients with complete data on all determinants were included. We compared the case-mix adjusted mortality 1 year after hospital discharge between the ICU subgroups by calculating the adjusted hazard ratios (HR_{adj}) and corresponding 95% confidence intervals (CIs) for the ICU subgroups with the whole ICU population (excluding the subgroup of interest) as reference.

BOX 1. Explanation of the Diagnostic Subgroups

Cardiac surgery subgroup: Patients with a postoperative cardiovascular APACHE IV reason for ICU admission. However, cardiac arrest and sepsis APACHE IV reason for ICU admission were excluded as these diagnoses can be postoperative as well as nonoperative

Subarachnoid hemorrhage subgroup: Patients with a postoperative or nonoperative subarachnoid hemorrhage/intracranial aneurysm or a nonoperative subarachnoid hemorrhage/arteriovenous malformation as APACHE IV reason for ICU admission

Acute renal failure subgroup: Patients with acute renal failure as APACHE IV reason for ICU admission and/or acute renal failure in 24 hrs after ICU admission

Severe community-acquired pneumonia subgroup: Patients with pneumonia (aspiration, bacterial, fungal, para sitic, viral, or other pneumonia) as APACHE IV reason for ICU admission and hospitalized for maximum 2 days before ICU admission

Cancer subgroup: Unplanned ICU admissions of patients with cancer (breast, colorectal, gastrointestinal, lung, urogenital, CNS, leukemia, malignant lymphoma, or other malignancy) as APACHE IV reason for ICU admission

Trauma subgroup: Patients with a postoperative or nonoperative trauma APACHE IV reason for ICU admission

APACHE = Acute Physiology and Chronic Health Evaluation.

All statistical analyses were performed using Predictive Analytics Software Statistics 18 (SPSS Inc., Chicago, IL) and SAS 9.2 (SAS Institute, Cary, NC).

RESULTS

Data

From January 1, 2007, to October 1, 2010, 149,566 patients not discharged to another hospital and fulfilling the APACHE IV inclusion criteria (9) were discharged from one of the 81 Dutch ICUs included in the study. All participating ICUs are mixed medical-surgical units located in university hospitals ($n = 7$), teaching hospitals ($n = 27$), or nonteaching hospitals ($n = 47$). Of the 149,566 records, 108,295 (72.4%) could be linked with the insurance claims database of Vektis. **Table 1** shows the demographics of the linked and nonlinked records, showing that the nonlinked records have a higher proportion of elective surgery (especially cardiac surgical) patients and

TABLE 1. Demographics of the Patients in the Linked and Nonlinked National Intensive Care Evaluation Dataset

	Linked National Intensive Care Evaluation Dataset	Nonlinked National Intensive Care Evaluation Dataset
Number of admissions	108,295	41,271
ICU mortality, %	10.4	6.8[a]
In-hospital mortality, %	15.8	10.9[a]
Men, %	58.6	61.1[a]
Admission type, %		
Medical	40.3	29.8[a]
Urgent surgery	15.5	13.2[a]
Elective surgery	44.2	57.0[a]
Age, mean (SD)	63.6 (15.9)	62.9 (15.8)[a]
Acute Physiology and Chronic Health Evaluation IV score, median (25%–75%)	51 (36–72)	48 (34–65)[a]
Diagnostic subgroups, %		
Cardiac surgery	24.2	40.3[a]
Severe community-acquired pneumonia	4.7	3.2[a]
Subarachnoid hemorrhage	1.0	1.3[a]
Renal	6.6	4.8[a]
Cancer	14.4	10.9[a]
Trauma	3.8	3.8

[a]Statistically significant difference based on $p < 0.05$.

TABLE 2. Demographics of Surviving ICU Patients in the Diagnostic Subgroups

	Total	Cardiac Surgery	Severe Community-Acquired Pneumonia	Subarachnoid Hemorrhage	Renal	Cancer	Trauma
Number of patients	108,295	26,234	5,102	1,057	7,167	15,625	4,135
ICU mortality, %	10.4	3.2	19.4	26.1	38.9	3.4	7.7
In-hospital mortality, %	15.8	5.0	28.2	30.9	48.5	7.8	11.6
Number of patients included in survival analyses	91,203	24,911	3,662	730	3,692	14,405	3,654
ICU length of stay, median no. of days (25%-75%)	0.98 (0.78–2.35)	0.92 (0.79–1.73)	3.71 (1.58–7.80)	3.25 (0.99–7.96)	3.83 (1.66–9.38)	0.92 (0.80–1.59)	1.07 (0.73–2.82)
Hospital length of stay median no. of days (25–75%)	10.1 (6.0–19.0)	8.0 (6.0–13.0)	14.0 (9.0–23.0)	18.0 (11.0–28.0)	20.6 (12.0–37.0)	12.0 (8.0–19.0)	11.0 (6.0–21.0)
Men, %	58.9	71.6	59.1	33.4	58.7	58.6	65.1
One or more chronic diagnoses[a], %	24.7	23.4	49.8	8.2	38.0	19.4	12.3
Admission type, %							
Medical	35.2	0.0	98.0	68.8	67.8	2.2	52.0
Urgent surgery	14.7	10.9	1.1	15.2	19.3	6.0	34.6
Elective surgery	50.1	89.1	0.9	16.0	12.9	91.8	13.4
Age, mean (SD)	62.3 (16.1)	66.7 (10.9)	63.5 (15.0)	55.7 (12.9)	65.6 (14.3)	65.6 (12.4)	53.7 (22.9)
Acute Physiology and Chronic Health Evaluation IV score median (25%–75%)	47 (34–63)	46 (36–57)	65 (50–81)	37 (27–52)	79 (64–99)	43 (33–54)	40 (26–57)

[a]Chronic diagnoses are diabetes, chronic obstructive pulmonary disease, cirrhosis, or respirator insufficiency.

TABLE 3. Demographics of the Censored and Noncensored Patients

	Noncensored Patients	Censored Patients
Number of admissions	70,075	21,128
Men, %	59.1	58.2[a]
Admission type, %		
Medical	34.3	38.2[a]
Urgent surgery	14.5	15.6[a]
Elective surgery	51.2	46.2[a]
Age, mean (SD)	62.4 (16.0)	62.2 (16.3)
Acute Physiology and Chronic Health Evaluation IV score median (25%–75%)	47 (34–62)	48 (34–64)[a]

[a]Statistically significant difference based on $p < 0.05$.

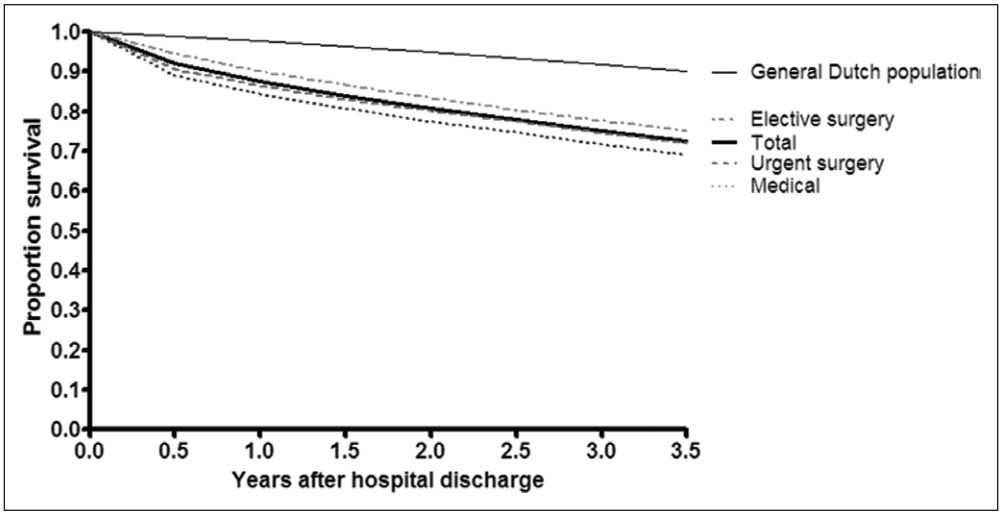

Figure 1. Kaplan-Meier curves for total ICU patients and subgroups based on admission type.

subsequently a lower in-hospital mortality. Of the 108,295 patients, 11,225 patients (10.4%) died on the ICU and another 5,867 patients (5.4%) died in the hospital after ICU discharge, resulting in a total of 17,092 in-hospital deaths (15.8%). The remaining 91,203 patients who survived hospitalization were included in the analysis of mortality after hospital discharge. Of these included patients, 17,113, 25,236, 28,736, and 20,118 patients received ICU care in 2007, 2008, 2009, and 2010, respectively. **Table 2** shows the in-hospital mortality of the total ICU population and the diagnostic subgroups and shows the characteristics of the ICU patients who survived hospitalization in which the mortality after hospital discharge is assessed.

Mortality After Hospital Discharge

At 1, 2, and 3 years after hospital discharge 21,128 (23.2%), 49,737 (54.5%), and 74,825 patients (82.0%), respectively, were censored because they were not yet discharged long enough from the hospital at the follow-up endpoint. Thus, 70,075 patients (76.8%) could be followed for 365 days after hospital discharge. **Table 3** shows the demographics of censored and noncensored patients after 1 year of follow-up, showing small differences. The observed mortality 1, 2, and 3 years after hospital discharge in the total ICU population was 12.5%, 19.3%, and 27.5%, respectively. The 1-, 2-, and 3-year mortality of the general Dutch population, according to the weighted average of the gender- and age-specific death risks, was 2.4%, 5.1%, and 8.2%, respectively (15). In **Figures 1** and **2**, the unadjusted mortality after hospital discharge of the general Dutch population, the total ICU population, and the ICU subgroups are shown in Kaplan-Meier curves. Medical admissions have a higher mortality after hospital discharge compared with surgical admissions. Among the different diagnostic subgroups, the patients admitted for acute renal failure have the highest 1-year mortality after hospital discharge. However, the patients admitted for cancer have the highest 3-year mortality after hospital discharge. The highest risk of death after hospital discharge appears to be in the first 3 months. This phenomenon is emphasized in patients with subarachnoid hemorrhage in which the mortality risk 3 months after hospital discharge is 5.4% and the additional mortality in the subsequent 9 months is only 2.6%.

Most of the ICU subgroups have an increased mortality risk during the 3 years after hospital discharge with the general Dutch population. However, 6 months after hospital discharge, the diagnostic subgroups relating to cardiac surgery and trauma have a comparable mortality risk, and subarachnoid hemorrhage seems to have a decreased mortality risk compared with the general Dutch population. Strikingly, the survival curves for patients with severe community-acquired pneumonia (sCAP), cancer, and acute renal failure continue to diverge from the general Dutch population. However, these crude survival figures are not adjusted for case-mix. The Cox proportional hazard model, which is used to calculate the case-mix adjusted mortality 1 year after hospital discharge, included the following determinants: age, gender, mechanical ventilation during

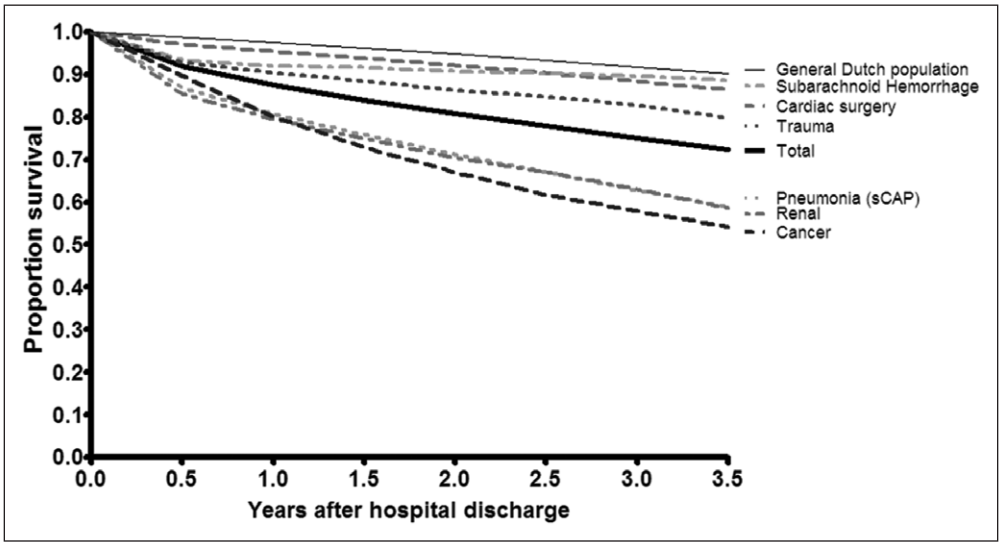

Figure 2. Kaplan-Meier curves of total ICU population and subgroups based on admission diagnosis. sCAP = severe community-associated pneumonia.

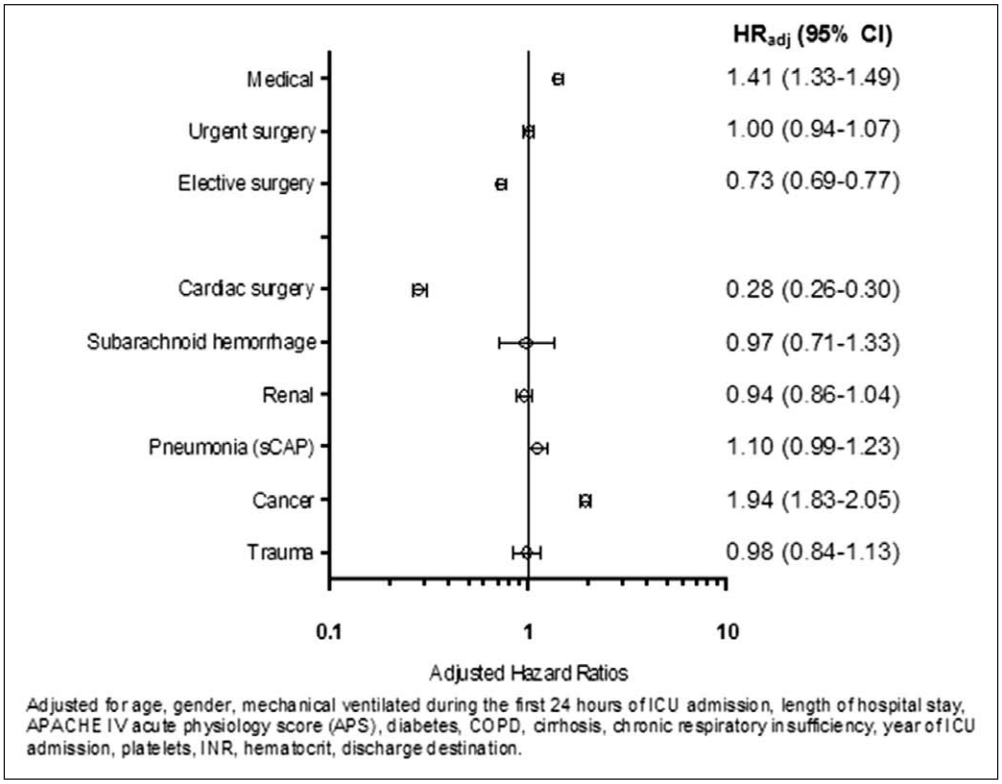

Figure 3. Adjusted hazard ratio (HR$_{adj}$) for the 1-yr mortality risk, after hospital discharge for different subgroups compared to the total ICU population excluding the subgroup of interest as reference group. APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; sCAP = severe community-associated pneumonia; COPD = chronic obstructive pulmonary disorder; INR = international normalized ratio.

the first 24 hours of ICU admission, length of hospital stay, physiological condition expressed as the acute physiology score according to the APACHE IV model, the comorbidities diabetes, chronic obstructive pulmonary disease, cirrhosis, and chronic respiratory insufficiency (oxygen at home, positive pressure ventilation at home, the so-called New York Health Association IV of respiratory disease), year of ICU admission, platelets, international normalized ratio, hematocrit, and discharge destination. During the analysis, 59,157 ICU patients with complete data on all determinants could be included. The Cox model showed that particularly the presence of cirrhosis and chronic respiratory insufficiency led to a statistically significant higher 1-year mortality after hospital discharge. In **Figure 3** the adjusted hazard ratios for the 1-year mortality after hospital discharge of the subgroups are compared with that of the whole ICU population, excluding the patients in the subgroup of interest as the reference group. This figure shows that the elective surgical and cardiac surgical patients have statistically significantly better mortality outcomes (HR$_{adj}$ 0.73 and 0.28, respectively) than the rest of the ICU patients. In contrast, medical patients and patients admitted for cancer have statistically significantly worse mortality outcomes (HR$_{adj}$ 1.41, 1.94, respectively) compared with the rest.

DISCUSSION

This study shows that the 3-year mortality risk after hospital discharge in ICU patients is higher than that of the weighted average of gender- and age-specific death risks of the general Dutch population (27.5% versus 9.8%), indicating that ICU patients who survived the hospital still have an increased risk of dying in the subsequent years. However, the mortality risk after hospital discharge differs among ICU subgroups. The cardiac surgery, subarachnoid hemorrhage, and trauma patients have a relatively lower unadjusted observed mortality after hospital discharge compared with the patients with sCAP, acute renal failure, and cancer. Generally, the highest post-hospital mortality of ICU patients is in the first 3 months after hospital discharge. Since we excluded the patients who were discharged to other hospitals, the higher mortality risk in the first 3 months cannot be explained by the in-hospital mortality of patients who were transferred to another hospital. The mortality of ICU patients after hospital discharge can be at least partially explained by the additional mortality associated with the ICU admission or by the pre-existing comorbidities. Not unexpectedly, the Cox proportional hazard model showed that comorbidities have statistically significant influence on mortality after hospital discharge. This is consistent with findings of Azoulay et al (3). The cardiac surgery, subarachnoid hemorrhage, and trauma patients probably have less comorbidities compared with sCAP, acute renal failure, and cancer patients partly explaining the differences found in the unadjusted observed mortality after hospital discharge of these diagnostic subgroups.

These results were not unexpected as previous publications showed that the unadjusted mortality after hospital discharge is substantial. Our results are similar to the study by Keenan et al, in which the unadjusted 1-year mortality after hospital discharge in a Canadian ICU population (n = 27,103) was 10.9% (23). In a study by Iribarren-Diarasarri et al, the unadjusted 1-year mortality after hospital discharge in a Spanish ICU population was higher than in our study, namely 21.2% (24). However, the sample size of that study was small (n = 283) and might be not generalizable to the general Spanish ICU population. In a study by Williams et al, the unadjusted 1-year mortality after hospital discharge in an Australian population (n = 19,921) was lower, namely 5.4% (21). This apparent difference can, at least partially, be explained by the smaller proportion of patients admitted after cardiac surgery in our study (27%), compared with the Australian study

(44%). However, the overall 1-year mortality of the total ICU population is an oversimplification. There are huge apparent differences between ICU subgroups. We defined specific ICU subgroups of which various 1-year risks have been reported with either higher (9, 10, 12) or lower (11, 14) mortality risks than those we have found for those subgroups. However, the direct comparison of different studies investigating long-term mortality of ICU patients is difficult. First,the case-mix of ICU populations may markedly differ, and that explains some of the differences between the studies. This is illustrated by the subgroups of patients with sCAP and acute renal failure. Their unadjusted 1-year mortality is impressively increased in comparison to the general ICU population (Fig. 2). However, after adjustment for several determinants the hazard ratio of these subgroups is no longer statistically significantly different from the total ICU population (Fig. 3). Therefore, direct comparison of Kaplan-Meier curves without adjustment may lead to wrong conclusions. Second, the starting point of the follow-up (ICU admission, ICU discharge, or hospital discharge) and its endpoint differs among the previously reported studies. We have chosen to focus on the outcome after hospital discharge and used the hospital discharge as the starting point of follow-up as the short-term outcome of ICU patients (e.g., ICU and hospital mortality) is already extensively described.

Although we used a large dataset, this study is subject to some limitations. In our data, the reasons for death are not known and might be unrelated to the reason of ICU admission. However, if the cause for death is unrelated to the former ICU admission it is likely that these cases are evenly distributed between the ICU and non-ICU patients and thus have no effect on our conclusions concerning the difference between ICU subgroups and between the ICU and the general Dutch population. In this study the patients who were readmitted to the ICU during the same hospitalization period were excluded. However, patients who were admitted more than once to the ICU during different hospitalization periods were not excluded. Furthermore, in this study 28.6% of the NICE registry records could not be linked with the insurance claims database. This could lead to some bias in the selection of included patients (Table 1). The nonlinked records mainly concerned cardiac surgery patients, suggesting that the overall mortality of the total ICU population might have been lower if these patients could have been included. We used deterministic linkage which overall produces a low number of false-positive links (25), meaning that the linked dataset is reliable. Vice versa, it also explains the rather high percentage of nonlinked records as deterministic linkage can miss matches due to errors in the linking variables (false-negative links). Furthermore, the insurance claims database of Vektis covers 95% of the Dutch insured population, meaning that 5% of the insured admitted ICU patients may not be present in the insurance claims database. The nonlinked patients are predominantly cardiac surgery patients, and the amount of patients with sCAP, acute renal failure, and cancer are somewhat lower in the nonlinked group. It is, therefore, safe to assume that inclusion of these patients would decrease the overall 1-year mortality and strengthen the already found differences between the subgroups with higher mortality risks. Of course, the linkage could be greatly improved if a paitent's social security code would have been registered in both databases. Unfortunately, such identifier was not available in The Netherlands during the study period due to existing Dutch privacy protection rules. In some Scandinavian countries; however, the social security code is already being used to assess long-term mortality (26). Yet, the strength of this observational study is its size and our ability to correct for various known determinants. We were able to show that the excess of mortality in certain subgroups was related to comorbidities more than to the direct influence of the diseases themselves.

CONCLUSION

In the general ICU population, the mortality after hospital discharge is substantial and much higher than the weighted average of gender- and age-specific death risks of the general Dutch population. The mortality after hospital discharge differs widely between ICU subgroups, though the highest risk of death after hospital discharge occurs in the first three months. Reporting the ubiquitously used in-hospital mortality may hence lead to an important underestimation of the true mortality of ICU patients. Future studies should focus on the analysis of mortality after hospital discharge that is attributable to the former ICU admission and on ways to improve long-term mortality.

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