Risk of a Diagnosis of Dementia for Elderly Medicare Beneficiaries after Intensive Care

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ABSTRACT

Background: Critical illness is likely associated with an increased risk of dementia, but the magnitude remains uncertain.

Methods: The cohort was a random 2.5% sample of Medicare beneficiaries who received intensive care in 2005 and survived to hospital discharge. Patients were matched with general population controls (age, sex, and race) with 3 yr of follow-up. The authors used an extended Cox model to assess the risk of a diagnosis of dementia, adjusting for the known risk factors for dementia, and the competing risk of death.

Results: Among 10,348 intensive care patients who survived to hospital discharge, dementia was newly diagnosed in 1,648 (15.0%) over the 3 yr of follow-up *versus* 12.2% in controls (incidence per 1,000 person-years, 73.6; 95% CI, 70.0 to 77.1 *vs.* 45.8; 95% CI, 43.2 to 48.3; hazard ratio [HR], 1.61; 95% CI, 1.50 to 1.74; P < 0.001). After accounting for the known risk factors in the year before the index hospitalization, the risk of receiving a diagnosis of dementia remained increased in patients who received intensive care (adjusted HR, 1.43; 95% CI, 1.32 to 1.54; P < 0.001). Inclusion of identifiable risk factors accrued during the quarter of critical illness accounted for almost all of the increased risks (adjusted HR, 1.09; 95% CI, 1.00 to 1.20; P = 0.06).

Conclusions: Elderly critical care survivors have a 60% increased relative risk, but only 3% increased absolute risk, of receiving a diagnosis of dementia in the subsequent 3 yr compared with the general population. This increased risk is not accounted for by risk factors preexisting the critical illness. Surveillance bias, which increases the likelihood of receiving a diagnosis of dementia, could account for some or all of these additional risks. **(ANESTHESIOLOGY 2015; 123:1105-12)**

E LDERLY patients (older than 65 yr) comprise approximately half of intensive care unit (ICU) admissions.¹ In addition, mortality rates from critical illnesses such as severe sepsis are decreasing, leading to a large population of elderly survivors.² Declining cognitive function and diagnoses of dementia increase both in severity and incidence after an acute illness among the elderly,^{3–6} and there is a mounting body of evidence suggesting potentially severe decrements follow a critical illness.^{5,6} Long-term cognitive impairment after critical illness may cause substantial disability and distress for individuals and their families. Older people fear developing dementia and experience anxiety regarding loss of self-identity and long-term care.⁷ Also, individuals may make different care choices, because they are less willing to endure burdensome treatments when faced with the possibility of severe functional or cognitive impairment.⁸

Although it has been demonstrated that cognitive impairment increases after critical illness, the magnitude of the effect at the population level has not been adequately estimated, because previous studies have had small sample sizes^{4,5} or

What We Already Know about This Topic

• Critical illness is likely associated with an increased risk of dementia, but the magnitude of that increased risk remains uncertain.

What This Article Tells Us That Is New

• By using an extended Cox model in a random sample of Medicare beneficiaries who received intensive care in 2005 in the United States and survived to hospital discharge and were matched with general population controls (age, sex, and race) with 3 yr of follow-up, it was found that the rate of incidence of diagnoses of dementia among elderly survivors of critical illness was 60% higher than in matched general population controls, but translated into only a 3% absolute increase in risk over 3 yr. This increased incidence was not accounted for by risk factors for dementia before the critical illness.

have made comparisons with population norms rather than matched controls.⁶ Furthermore, the issue of whether critically ill patients are "sicker" and thus predisposed to developing dementia has not been elucidated. Thus, the aim of

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Submitted for publication December 3, 2014. Accepted for publication June 30, 2015. From the Department of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, New York (C.G., M.H., H.W.); Department of Critical Care Medicine, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada (H.W.); Department of Anesthesiology, University of Toronto, Toronto, Ontario, Canada (H.W.); and Trauma, Emergency and Critical Care Program, Sunnybrook Research Institute, Toronto, Ontario, Canada (H.W.).

this study was to use a nationally representative Medicare population to calculate the incidence of new diagnoses of dementia for all patients who received critical care compared with matched general population controls. We also sought to determine whether patients who develop critical illness represent a high-risk population because of pre-existing conditions that might predispose this group toward an increased risk of a diagnosis of dementia.

Materials and Methods

Design Overview

This was a retrospective study using the Medicare Standard Analytic Files from the Centers for Medicare and Medicaid Services. This dataset contains all fee-for-service claims, including hospital inpatient, hospital outpatient, skilled nursing facility, and "carrier" claims (physician supplier part B files that includes all office visits), home health agency, hospice, and durable medical equipment for a random, longitudinal 5% sample of beneficiaries. We linked data from years 2004 through 2008 and derived the inception cohort from the 2005 sample with a follow-up period of 3 yr.

Setting and Participants

To generate the cohort for this study, we used the 5% sample of all beneficiaries with fee-for-service Medicare coverage for all years. We first randomly split the sample into two equal parts. From one half, we selected all Medicare beneficiaries aged 66 yr or older who received intensive care during their hospitalization in 2005 (n = 23,732). Patients were 66 yr or older to ensure at least a year of Medicare eligibility and availability of medical records before intensive care. We used International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes from data for all healthcare encounters in the previous year and during the index quarter to identify and exclude patients with any diagnosis for dementia (290.x, 294.x, 331.x, and 797.x)9 and patient with any diagnosis of mild cognitive impairment (331.83) or general symptom mental loss (780.93). We also excluded patients who either died or were sent to hospice at hospitalization discharge or in the same quarter (3 months) of their discharge date. Because cardiac surgery is generally associated with only a transient need for critical care, and also may distinctly alter a patient's risk for a diagnosis of dementia,^{10,11} we omitted anyone who had cardiac surgery (ICD-9-CM codes 35.x, 36.x, and 39.61) in the quarter of hospitalization or the previous year (fig. 1).

We used the other half of the 5% sample to select population controls and matched 1:1 with the cohort of individuals who received intensive care based on the age, gender, and race. We categorized age into 5-yr intervals, and grouped race as non-Hispanic White, non-Hispanic black, and "other" (Hispanic and other) for the matching. We used the same exclusion criteria as for the group that received critical care: no diagnosis of dementia/mild cognitive impairment/

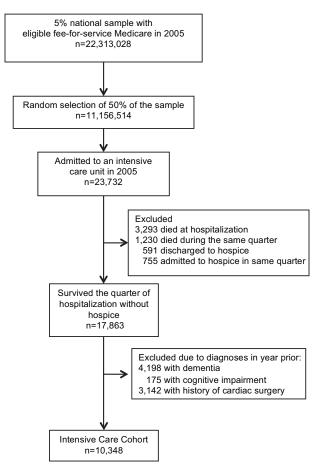


Fig. 1. Flowchart of exclusions.

general symptom mental loss, no cardiac surgery in the previous year or during the index quarter (quarter of intensive care use in the matched critical care survivor), and no death (or hospice admission) in the index quarter. In addition, eligible controls may have been hospitalized but did not receive intensive care during hospitalizations in the index quarter. We used a completely separate half of the patients to allow controls to be as representative as possible of the general population; in particular, this meant that they could have been hospitalized and received intensive care at times other than the index quarter.

Outcomes and Follow-up

The primary outcome for this study was incidence of new diagnoses of dementia, which was defined using ICD-9-CM codes (290.0 to 290.4, 294.0, 294.1, 294.8, 331.0, 331.1, 331.2, 331.7, and 797.X)^{12,13} recorded from fee-for-service claims in the subsequent 3 yr of follow-up. Because of privacy restrictions, exact dates of hospital discharge and doctor visits were not available in the Medicare Standard Analytic Files—only the quarter (3-month period) of the year. We calculated time to diagnosis of dementia and death as the number of quarters (3-month intervals) after the discharge quarter. The quarter in which the first diagnosis of dementia

occurred was used as the incident quarter to mark the diagnostic onset for that individual. For person-years at risk, each death and incident diagnosis of dementia was marked as occurring at the end of the quarter. The majority of patients who received a diagnosis of dementia during the follow-up had more than one dementia diagnosis in their records (see Supplemental Digital Content 1, table 5, http://links.lww. com/ALN/B187, for number of diagnoses).

Statistical Analysis

We used ICD-9-CM codes from all healthcare encounters in the year before the index quarter to identify specific diseases and conditions known or suspected to be related to dementia.¹² We calculated summary statistics for demographic, clinical characteristics, and preexisting conditions using percentages, means (±SDs), and medians (with interquartile ranges) as appropriate for the entire sample. Followup began with the quarter after the index hospitalization quarter and continued until the first diagnoses of dementia, death, or end of follow-up (3 yr).

We calculated the incidence rates for a diagnosis of dementia during the follow-up for the cohort that received intensive care and the control group stratified by 5-yr age categories and also stratified by gender. Crude time to a diagnosis of dementia was examined with a cumulative incidence competing risks method using Kaplan-Meier curves accounting for the competing risk of death. By using an extended Cox model, we estimated hazard ratios (HRs) for diagnoses of dementia. We created four models to examine the relative incidence of diagnoses of dementia. First, we generated unadjusted HRs to determine the overall increase in risk for the intensive care cohort. Second was a model adjusting for preexisting conditions that are known to be associated with an increased risk of dementia to determine whether intensive care patients were at an increased risk of diagnoses of dementia because of previously known disease. As a third model, we included diagnoses accrued by the intensive care cohort during the index hospitalization. A final, fourth model included all potential diagnoses viewed as risk factors for dementia accrued during the quarter of critical illness for both the intensive care cohort and controls. Because of date restrictions within the data, we could not determine whether the diagnoses that occurred during the index quarter outside of the index hospitalization occurred before or after the hospitalization. Thus, we refer to diagnoses as "accrued during the index quarter." We used a stepwise selection to create parsimonious multivariable models for dementia. These models also accounted for matched characteristics. Covariates that were statistically significant (P < 0.05) were kept in the model. We assessed the Cox proportionality assumption graphically and added time-dependent covariates where the effect of a covariate varied during follow-up. This meant that for some diagnoses, the effect was not constant over time. However, because the emphasis of this study was on the risk of dementia, we do not provide a detailed breakdown of these effects of other variables, but note them in the tables.

For our supplementary analysis, we replicated the models splitting the patients as medical or surgical and then stratified by whether they had a documented infection with or without severe sepsis, because this is a group of patients well established to be at increased risk of subsequent cognitive impairment and dementia.^{4,12} We identified the subsample of the intensive care cohort with any infection (with and without severe sepsis) using an established definition¹⁴ and compared these patients with their matched controls.

On the basis of our previous work,¹² we estimated a sample size (n = 12,000 for the 2.5% sample, with approximately 17% with dementia in 3 yr). We calculated that we had greater than 90% power to show a difference of 2% in the rates of diagnosis of dementia over 3 yr. Findings were considered statistically significant with a *P* less than 0.05. Database management and statistical analyses were performed using Excel (Microsoft, USA), and SAS version 9.2 (SAS Institute Inc., USA) software. For the cumulative incidence competing risks models, we used a SAS macro (comprisk). This research was reviewed and approved by the Columbia University Medical Center Institutional Review Board, New York, New York (IRB AAAE9908).

Results

Cohort Characteristics

After appropriate exclusions, 10,348 Medicare beneficiaries were hospitalized with admission to intensive care and survived to the end of the index hospitalization quarter. The average age of the intensive care cohort was 76.7 ± 6.8 yr, with 53.1% female and the majority (88.7%) were white, non-Hispanic (table 1). The known risk factors for dementia were common, with the majority of both the intensive care cohort and matched controls having at least one risk factor identified. Average follow-up time was 2.3 ± 1.0 yr for the intensive care cohort and 2.8 ± 0.6 yr for the matched controls. Three-year mortality for the intensive care cohort was 38.3%, more than double that of matched controls (14.7%).

Risk of a Diagnosis of Dementia in 3 yr of Follow-up

In the intensive care cohort, 1,648 (15.9%) received a new diagnosis of dementia during the 3 yr of follow-up *versus* 1,266 (12.2%) of the matched controls (table 2). The overall rate of new diagnoses of dementia was 73.6 per 1,000 person-years (95% CI, 70.0 to 77.1) for the intensive care cohort *versus* 45.8 per 1,000 person-years (95% CI, 43.2 to 48.3) for matched controls, with a HR of 1.61; 95% CI, 1.50 to 1.74, P < 0.001 (table 2). Among intensive care survivors, approximately 40% of all new diagnoses of dementia occurred in the first year, but the cumulative incidence of diagnoses of dementia remained larger for the intensive care cohort throughout the entire period of follow-up (fig. 2). This higher rate was consistent across every age group (fig. 3) and was also higher in women than in men (data not shown).

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Characteristics	Intensive Care Cohort (N = 10,348), n (%)	Matched General Population Controls (N = 10,348), n (%)	
Age (yr)			
Mean ± SD	76.7 ± 6.8	76.7 ± 6.8	
66–69	1,920 (18.6)	1,920 (18.6)	
70–74	2,505 (24.2)	2,505 (24.2)	
75–79	2,467 (23.8)	2,467 (23.8)	
80–84	2,044 (19.8)	2,044 (19.8)	
≥85	1,412 (13.7)	1,412 (13.7)	
Gender	,	,	
Female	5,496 (53.1)	5,496 (53.1)	
Male	4,852 (46.9)	4,852 (46.9)	
Race		, , , ,	
White, non-Hispanic	9,182 (88.7)	9,182 (88.7)	
Black, non-Hispanic	752 (7.3)	752 (7.3)	
Other	414 (4.0)	414 (4.0)	
Preexisting risk factor for dement	ia*	()	
None	1,155 (11.2)	2,449 (23.7)	
Cerebrovascular accident	473 (4.6)	205 (2.0)	
Cerebrovascular disease	1,423 (13.8)	830 (8.0)	
Myocardial infarction	1,113 (10.8)	441 (4.3)	
Congestive heart failure	2,684 (25.9)	999 (9.7)	
Valvular disease	1,901 (18.4)	995 (9.6)	
Pulmonary circulation disease	518 (5.0)	178 (1.7)	
Peripheral vascular disease	2,316 (22.4)	1,109 (10.7)	
Hypertension	7,367 (71.2)	5,956 (57.6)	
Depression	857 (8.3)	467 (4.5)	
Diabetes	3,349 (32.4)	2,233 (21.6)	
Hypoglycemia	462 (4.5)	172 (1.7)	
Chronic renal failure	796 (7.7)	195 (1.9)	
Head trauma	102 (1.0)	52 (0.5)	
Chronic pulmonary disease	3,269 (31.6)	1,615 (15.6)	
Hypothyroidism	1,851 (17.9)	1,606 (15.5)	
Obesity	529 (5.1)	266 (2.6)	
Weight loss	624 (6.0)	340 (3.3)	
Fluid and electrolyte disorders	2,018 (19.5)	777 (7.5)	
Deficiency anemia	2,835 (27.4)	1,573 (15.2)	
Alcohol abuse	123 (1.2)	62 (0.6)	
Drug abuse	44 (0.4)		
Epilepsy	82 (0.8)	51 (0.5)	
Parkinson disease	154 (1.5)	137 (1.3)	
Rheumatoid arthritis/collagen vascular diseases	558 (5.4)	346 (3.3)	
Follow-up time, mean \pm SD (yr)	2.3 ± 1.0	2.8 ± 0.6	
3-yr mortality	3,963 (38.3)	1,525 (14.7)	

Table 1. Characteristics of Intensive Care Cohort and Matched

General Population Controls

Follow-up time in quarters (3-mo intervals) was converted to years and includes all observed time in the study up to death.

* Based on the International Classification of Diseases, Ninth Revision, Clinical Modification codes from all healthcare encounters during the year before the index quarter.

Adjusted Risk of a Diagnosis of Dementia

Only a third of the increased risk of a diagnosis of dementia was explained by adjusting for preexisting conditions that are known to be associated with dementia (adjusted hazard ratio [aHR] for intensive care cohort *versus* matched controls, 1.43; 95% CI, 1.32 to 1.54, P < 0.001; table 2). Inclusion of diagnoses accrued during the index hospitalization partially attenuated this difference (aHR, 1.16; 95% CI, 1.05 to 1.27, P < 0.001). Overall, the intensive care cohort received many additional diagnoses during the index quarter that were risk factors for development of dementia (see Supplemental Digital Content 1, table 1, http://links.lww.com/ALN/B187). Inclusion of all additional diagnoses that were risk factors for dementia accrued during the index quarter accounted for most of the difference between groups (aHR, 1.09; 95% CI, 1.00 to 1.20, P = 0.06). See Supplemental Digital Content 1, tables 2 to 4, http://links.lww.com/ALN/B187, for the full models.

Among the subgroup of intensive care patients who were medical, the risk of a diagnosis of dementia was higher (HR, 1.84; 95% CI, 1.69 to 2.00, P < 0.001) and remained increased even after accounting for all preexisting diagnoses (aHR, 1.56; 95% CI, 1.43 to 1.70, P < 0.001), and all new risk factors accrued during the index hospitalization quarter (aHR, 1.17; 95% CI, 1.06 to 1.29, P = 0.002; table 3). There was also an increased risk of a diagnosis of dementia for patients with infection only or severe sepsis during critical illness, with the higher risk for those with severe sepsis (HR, 2.04; 95% CI, 1.77 to 2.34, P < 0.01; table 3). Adjusting for preexisting conditions did not explain all of the increased risk. All diagnoses accrued during the index quarter accounted for most, but not all of the additional risks (aHR, 1.24; 95% CI, 1.06 to 1.45, P = 0.006).

Discussion

By using population-level data, we estimated that elderly survivors of intensive care are diagnosed with dementia at a 60% higher rate than matched general population controls, but with only a 3% absolute increase in risk over 3 yr. We demonstrated that the increase in risk of a diagnosis of dementia for patients who required intensive care was not explained by existing conditions that predispose people to dementia. Given the low absolute increased risk, this suggests that the population does not represent an identifiably high-risk group before the development of critical illness.

Our findings provide accurate numbers for the absolute increased risk of a diagnosis of dementia in the elderly ICU population relative to the general population; it expands on a study that showed an increase in subsequent dementia after hospitalization but lacked sufficient power to quantify the risk in the critically ill population.³ Our results are also consistent with the findings from a two-center cohort study of patients with respiratory failure or shock that found an increased risk of cognitive impairment for these patients relative to population means,⁶ as well as a study that focused on survivors of severe sepsis from the Health and Retirement Study that found increased rates of cognitive impairment after sepsis.⁴ However, it is important to note that our study focuses specifically on dementia and does not identify subtle changes in cognition or severity of impairment, so we
 Table 2.
 Incident Risk and Hazard Ratios for Receiving a Diagnosis of Dementia during 3 yr of Follow-up for Intensive Care Cohort

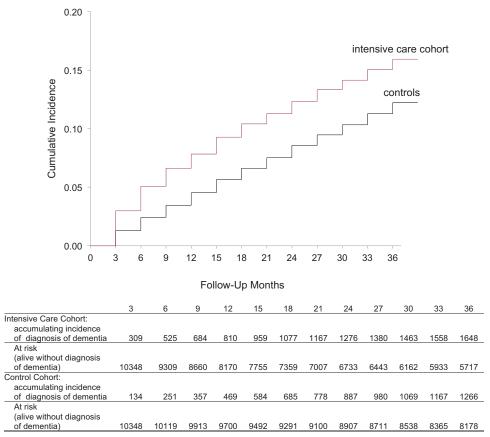
 versus General Population Controls

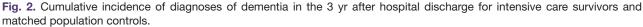
	Matched Control Cohort (n = 10,348)	Intensive Care Cohort (n = 10,3	48)	
Cases of incident dementia, n (%) Person-years (n) Crude incidence rate per 1,000 person-years (95% CI)	1,266 (12.2) 27,666 45.8 (43.2–48.3)	1,648 (15.9) 22,399 73.6 (70.0–77.1)		
		HR (95% CI)	P Value	
Cox proportional hazards models				
1. Unadjusted	Reference	1.61 (1.50–1.74)	< 0.001	
2. Adjusted for preexisting risk factors for dementia*	Reference	1.43 (1.32–1.54)	< 0.001	
3. Adjusted for preexisting risk factors for dementia* and diagnoses from the index hospitalization	Reference	1.16 (1.05–1.27)	<0.001	
 Adjusted for preexisting risk factors for dementia* and potential mediators and other risk factors accrued during the quarter of the index hospitalization 	Reference	1.09 (1.00–1.20)	0.06	

Models account for matching variables and a previous year history of conditions/diseases associated with dementia. Covariates: Quarters (3-mo intervals) of follow-up time was converted to person-years to calculate incidence rate. See Supplemental Digital Content 1, tables 2 to 4, http://links.lww.com/ALN/B187, for the full models with all covariates.

* Identified from all Medicare claims in the year previous to the quarter of index hospitalization.

HR = hazard ratio.





cannot compare rates with the previously mentioned studies. We found an increased rate of diagnoses of dementia among all survivors of critical illness, but also confirmed that infection, and severe sepsis in particular, seems to be associated with an even higher risk relative to the general intensive care cohort and not all of this risk could be explained by accrued diagnoses. The risk of dementia among medical patients also seemed to be higher relative to the general population

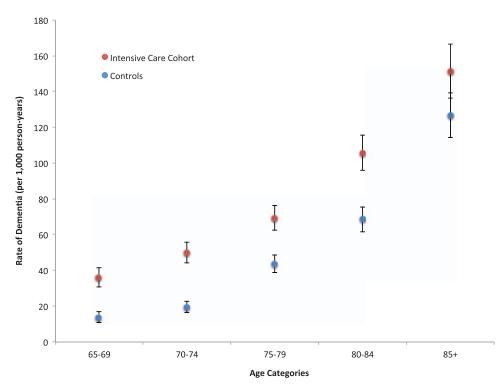


Fig. 3. Rate of dementia over 3 yr after hospital discharge for intensive care survivors and matched population controls stratified by age.

Table 3.	Hazard Ratios for Receiving a Diagnosis of Dementia during 3 yr of Follow-up for Intensive Care Cohort versus General
Populatic	on Controls, for Specific Subgroups of Patients

		Unadjusted		Adjusted for Preexisting Risk Factors for Dementia*		Adjusted for Preexisting Risk Factors for Dementia and Other Risk Factors Accrued during the Quarter of the Index Hospitalization		
	N (Total)	N (Dementia)	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value
Controls	10,348	1,266	Reference		Reference		Reference	
ICU-surgical	4,596	625	1.30 (1.18–1.43)	<0.001	1.26 (1.15–1.39)	<0.001	0.99 (0.89–1.09)	0.77
ICU-medical	5,752	1,023	1.84 (1.69–2.00)	<0.001	1.56 (1.43–1.70)	<0.001	1.17 (1.06–1.29)	0.002
Controls	10,348	1,266	Reference		Reference		Reference	< 0.001
ICU-no infection	6,658	1,010	1.43 (1.32–1.56)	<0.001	1.33 (1.22–1.44)	< 0.001	1.04 (0.95–1.14)	0.45
ICU—infection only	2,300	400	1.85 (1.66–2.08)	< 0.001	1.57 (1.40–1.76)	< 0.001	1.19 (1.05–1.35)	0.005
ICU-severe sepsis	1,390	238	2.04 (1.77–2.34)	<0.001	1.80 (1.56–2.07)	<0.001	1.24 (1.06–1.45)	0.006

Models account for matching variables.

* Identified from all Medicare claims in the year previous to the quarter of index hospitalization.

HR = hazard ratio; ICU = intensive care unit.

compared with surgical patients. This may represent a selection bias associated with the likelihood of receiving surgery at all and is an intriguing finding given that none of these patients had a diagnosis of dementia before the hospitalization. However, we have previously focused on specific risk factors within an ICU cohort associated with a diagnosis of dementia; thus, we chose not to further assess this question here.¹²

The mechanism for this increased risk is unknown and likely to be complex. As expected for the Medicare population aged 65 yr and older, the majority of our sample had at least one known risk factor for dementia in their previous history. However, our models help to establish that the increased risk for patients who are critically ill seems attributable to the pericritical illness period, because preexisting risk factors did not fully account for the increased risk. Several studies hypothesize an event during critical illness that causes or begins long-term neurocognitive damage such as inflammatory response to infection,^{15,16} and the duration of delirium has been associated with an increased risk of

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cognitive impairment after respiratory failure or shock.⁶ A bidirectional relationship has also been suggested; a process in which subclinical changes in cognition can increase the risk of an acute illness that then accelerates long-term cognitive decline leading to dementia.¹⁷ We found that patients who received critical care acquired additional identifiable risk factors for dementia during the index hospitalization quarter. Some of these diagnoses may define the critical illness (such as a cerebrovascular accident) and may be seen as "mediators" that could directly impact on cognitive function; others may be unrelated or only partially related to the acute events (such as depression) and have a less clear mechanism of action. Because of restrictions in dates, it was impossible to determine the timing of these additional diagnoses in relation to the hospitalization with critical care.

A key strength to our study was our use of Medicare claims, which remain a vital data source for studies of dementia because beneficiaries are a nationally representative sample of the main at-risk population. The incident rate of dementia across age in our matched controls is typical of other studies of dementia,¹⁸⁻²⁰ with an exponential pattern and an approximate doubling of the rate for 5-yr increases in age from 70 to 74 to 75 to 79.^{20,21} We also found that women were more likely than men to receive a diagnosis of dementia and that non-Hispanic blacks had a higher rate of diagnoses. This use of population-level data sets our work apart from other studies of critically ill cohorts of patients; we were not limited to a subpopulation of critical care survivors and we were able to generate matched controls using the general population and conduct subgroup analyses. Recent studies evaluated the potential risk factors and protective factors using similar methods for incident dementia with Medicare data.^{22,23}

A known limitation to the use of administrative data is the accurate assessment of dementia and risk factors. Early dementia was found to be underreported in claims data, and the severity of dementia is unknown.^{13,24} Very mild dementia that may be present before critical illness, but not identified, could alter conclusions to incorrectly implicate major illness as a risk factor for continued cognitive decline.²⁵ Given this challenge, we used a definition found to capture 82% of dementia cases identified with a neuropsychology battery and also used 3 yr of claims data;¹³ in another study, claims data were found to have a sensitivity of 85% and specificity of 89% when compared with in-home dementia assessment by clinical staff.⁹ Despite our exclusion of diagnosed dementia and cognitive impairment, prevalent cases of undiagnosed mild dementia may have existed in our sample. We were also unable to assess cognitive function before critical illness. A previous study found a high prevalence of preexisting cognitive impairment in patients admitted to the medical ICU (42%),^{26,27} and this would suggest that critical care survivors may already have a downward trajectory that we may not have fully captured. We also assessed whether patients had at least two diagnoses of dementia, which would provide additional information to suggest that this was not an erroneous diagnosis. Two thirds of the cohort had two or more diagnoses, with the additional caveat of a relatively high death rate during the 3 yr of follow-up (38.3%), which may reduce the likelihood of additional diagnoses.

Finally, a critical illness hospitalization clearly leads to more healthcare encounters after discharge and therefore increases opportunities to diagnose dementia among our intensive care group. Moreover, encounters with specific types of healthcare professionals (such as neurologists) may increase the likelihood of evaluation and diagnosis of dementia. However, we demonstrate that the increase in rate for incident dementia continued throughout the second and third years of follow-up. We were also careful to describe our finding in terms of receiving a diagnosis of dementia. This represents an outcome that is patient (and family) centered, because a new diagnosis represents a large event for many people. A diagnosis of dementia, in particular, comes with huge implications for life trajectory and care planning.^{28,29}

Conclusion

In conclusion, we have determined that the rate of incidence of diagnoses of dementia among elderly survivors of critical illness is 60% higher than in the matched general population controls, but translates into only a 3% absolute increase in risk over 3 yr. This increased incidence is not accounted for by risk factors for dementia before the critical illness, suggesting that elderly patients who become critically ill do not represent a particularly high-risk group for dementia before the illness. Our findings are limited by the differential rates of overall diagnoses associated with the repeated healthcare encounters, which were more frequent in the intensive care cohort.

Acknowledgments

This work was supported by K08AG038477 from the National Institute on Aging, Bethesda, Maryland (to Dr. Wunsch). The funder had no role in the study's design, conduct, or reporting.

Competing Interests

The authors declare no competing interests.

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References

1. Angus DC, Kelley MA, Schmitz RJ, White A, Popovich J Jr; Committee on Manpower for Pulmonary and Critical Care Societies (COMPACCS): Caring for the critically ill patient. Current and projected workforce requirements for care of the critically ill and patients with pulmonary disease: Can we

meet the requirements of an aging population? JAMA 2000; $284{:}2762{-}70$

- 2. Iwashyna TJ: Survivorship will be the defining challenge of critical care in the 21st century. Ann Intern Med 2010; 153:204–5
- Ehlenbach WJ, Hough CL, Crane PK, Haneuse SJ, Carson SS, Curtis JR, Larson EB: Association between acute care and critical illness hospitalization and cognitive function in older adults. JAMA 2010; 303:763–70
- 4. Iwashyna TJ, Ely EW, Smith DM, Langa KM: Long-term cognitive impairment and functional disability among survivors of severe sepsis. JAMA 2010; 304:1787–94
- Davydow DS, Hough CL, Levine DA, Langa KM, Iwashyna TJ: Functional disability, cognitive impairment, and depression after hospitalization for pneumonia. Am J Med 2013; 126:615–24.e5
- 6. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, Brummel NE, Hughes CG, Vasilevskis EE, Shintani AK, Moons KG, Geevarghese SK, Canonico A, Hopkins RO, Bernard GR, Dittus RS, Ely EW; BRAIN-ICU Study Investigators: Long-term cognitive impairment after critical illness. N Engl J Med 2013; 369:1306–16
- 7. Corner L, Bond J: Being at risk of dementia: Fears and anxieties of older adults. J Aging Stud 2004; 18:143–55
- Fried TR, Bradley EH, Towle VR, Allore H: Understanding the treatment preferences of seriously ill patients. N Engl J Med 2002; 346:1061–6
- 9. Taylor DH Jr, Østbye T, Langa KM, Weir D, Plassman BL: The accuracy of Medicare claims as an epidemiological tool: The case of dementia revisited. J Alzheimers Dis 2009; 17:807–15
- Newman MF, Kirchner JL, Phillips-Bute B, Gaver V, Grocott H, Jones RH, Mark DB, Reves JG, Blumenthal JA; Neurological Outcome Research Group and the Cardiothoracic Anesthesiology Research Endeavors Investigators: Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med 2001; 344:395–402
- Selnes OA, Royall RM, Grega MA, Borowicz LM Jr, Quaskey S, McKhann GM: Cognitive changes 5 years after coronary artery bypass grafting: Is there evidence of late decline? Arch Neurol 2001; 58:598–604
- Guerra C, Linde-Zwirble WT, Wunsch H: Risk factors for dementia after critical illness in elderly Medicare beneficiaries. Crit Care 2012; 16:R233
- Taylor DH Jr, Fillenbaum GG, Ezell ME: The accuracy of medicare claims data in identifying Alzheimer's disease. J Clin Epidemiol 2002; 55:929–37
- 14. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR: Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001; 29:1303–10
- Hopkins RO, Weaver LK, Collingridge D, Parkinson RB, Chan KJ, Orme JF Jr: Two-year cognitive, emotional, and qualityof-life outcomes in acute respiratory distress syndrome. Am J Respir Crit Care Med 2005; 171:340–7

- Jackson JC, Hart RP, Gordon SM, Shintani A, Truman B, May L, Ely EW: Six-month neuropsychological outcome of medical intensive care unit patients. Crit Care Med 2003; 31:1226–34
- 17. Shah FA, Pike F, Alvarez K, Angus D, Newman AB, Lopez O, Tate J, Kapur V, Wilsdon A, Krishnan JA, Hansel N, Au D, Avdalovic M, Fan VS, Barr RG, Yende S: Bidirectional relationship between cognitive function and pneumonia. Am J Respir Crit Care Med 2013; 188:586–92
- Andersen K, Nielsen H, Lolk A, Andersen J, Becker I, Kragh-Sørensen P: Incidence of very mild to severe dementia and Alzheimer's disease in Denmark: The Odense Study. Neurology 1999; 52:85–90
- Fitzpatrick AL, Kuller LH, Ives DG, Lopez OL, Jagust W, Breitner JC, Jones B, Lyketsos C, Dulberg C: Incidence and prevalence of dementia in the Cardiovascular Health Study. J Am Geriatr Soc 2004; 52:195–204
- Jorm AF, Jolley D: The incidence of dementia: A meta-analysis. Neurology 1998; 51:728–33
- 21. Gao S, Hendrie HC, Hall KS, Hui S: The relationships between age, sex, and the incidence of dementia and Alzheimer disease: A meta-analysis. Arch Gen Psychiatry 1998; 55:809–15
- 22. Baxter NN, Durham SB, Phillips KA, Habermann EB, Virning BA: Risk of dementia in older breast cancer survivors: A population-based cohort study of the association with adjuvant chemotherapy. J Am Geriatr Soc 2009; 57:403–11
- 23. Hebert PL, McBean AM, O'Connor H, Frank B, Good C, Maciejewski ML: Time until incident dementia among Medicare beneficiaries using centrally acting or non-centrally acting ACE inhibitors. Pharmacoepidemiol Drug Saf 2013; 22:641–8
- 24. Bynum JP, Rabins PV, Weller W, Niefeld M, Anderson GF, Wu AW: The relationship between a dementia diagnosis, chronic illness, medicare expenditures, and hospital use. J Am Geriatr Soc 2004; 52:187–94
- 25. Avidan MS, Searleman AC, Storandt M, Barnett K, Vannucci A, Saager L, Xiong C, Grant EA, Kaiser D, Morris JC, Evers AS: Long-term cognitive decline in older subjects was not attributable to noncardiac surgery or major illness. ANESTHESIOLOGY 2009; 111:964–70
- 26. Pisani MA, Redlich CA, McNicoll L, Ely EW, Friedkin RJ, Inouye SK: Short-term outcomes in older intensive care unit patients with dementia. Crit Care Med 2005; 33:1371–6
- Pisani MA, Inouye SK, McNicoll L, Redlich CA: Screening for preexisting cognitive impairment in older intensive care unit patients: Use of proxy assessment. J Am Geriatr Soc 2003; 51:689–93
- Schulz R, Martire LM: Family caregiving of persons with dementia: Prevalence, health effects, and support strategies. Am J Geriatr Psychiatry 2004; 12:240–9
- 29. Yaffe K, Fox P, Newcomer R, Sands L, Lindquist K, Dane K, Covinsky KE: Patient and caregiver characteristics and nursing home placement in patients with dementia. JAMA 2002; 287:2090–7

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