Hospital Usage of Early Do-Not-Resuscitate Orders and Outcome After Intracerebral Hemorrhage

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Background and Purpose—Do-not-resuscitate (DNR) orders are commonly used after severe stroke. We hypothesized that there is significant variability in how these orders are applied after intracerebral hemorrhage and that this influences outcome.

Methods—From a database of all admissions to nonfederal hospitals in California, discharge abstracts were obtained for all patients with a primary diagnosis of intracerebral hemorrhage who were admitted through the emergency department during 1999 and 2000. Characteristics included whether DNR orders were written within the first 24 hours of hospitalization. Case-mix–adjusted hospital DNR use was calculated for each hospital by comparing the actual number of DNR cases with the number predicted from a multivariable model. Outcome (in-hospital death) was evaluated in a separate multivariable model adjusted for individual and hospital characteristics.

Results—A total of 8233 patients were treated in 234 hospitals. The percentage of patients with DNR orders varied from 0% to 70% across hospitals. Being treated in a hospital that used DNR orders 10% more often than another hospital with a similar case mix increased a patient’s odds of dying during hospitalization by 13% (P<0.001). Patients treated in the quartile of hospitals with the highest adjusted DNR use were more likely to die, and this was not just because of individual patient DNR status.

Conclusions—In-hospital mortality after intracerebral hemorrhage is significantly influenced by the rate at which treating hospitals use DNR orders, even after adjusting for case mix. This is not due solely to individual patient DNR status, but rather some other aspect of overall care. (Stroke. 2004;35:1130-1134.)

Key Words: intracerebral hemorrhage ▪ outcome ▪ physician’s practice patterns ▪ resuscitation orders

The use of measures to limit care, such as do-not-resuscitate (DNR) orders or terminal withdrawal of support, in patients with acute illness is a common aspect of care in many hospitals, especially in the setting of severe neurologic impairment.1 In a prior series, DNR orders were used in 22% of 13 337 consecutive stroke admissions and were associated with an increased risk of death, even after adjustment for other factors that predicted DNR usage.2 In this same cohort, there was significant variability in the usage of DNR orders among hospitals, with hospital rates of DNR usage ranging from 12% to 32%.3 Coma, intracerebral hemorrhage, and admission through an emergency department were independent predictors of DNR usage, while African-American race was associated with lower DNR usage.4 This racial variation in the use of DNR orders has been demonstrated in disorders other than stroke as well.4 Because usage of DNR orders is associated with outcome after stroke, variability in the way they are applied could influence outcome, even when accounting for other patient characteristics and treatments.

We sought to test the hypothesis that DNR usage at the hospital level is independently associated with outcome after spontaneous intracerebral hemorrhage (ICH) by examining a large statewide hospital discharge database, and adjusting for individual demographic characteristics that influence both outcome, and whether a patient is made DNR within the first 24 hours of hospitalization. Additionally, we wished to assess whether individual patients’ DNR status could account for any such association or whether hospital rate of early DNR usage might be a proxy for overall aggressiveness of care.

Methods

Study Cohort
A cohort of ICH patients was developed by searching the California Office of Statewide Health Planning and Development (OSHPD) database. The OSHPD database includes abstracts of all patient discharges from all nonfederal hospitals in the state of California and contains information about patient demographics, acute hospitalizations, and hospital characteristics. Beginning in 1999, the OSHPD database included whether a DNR order had been written for a patient within the first 24 hours of hospitalization. The present cohort

Received August 21, 2003; final revision received January 20, 2004; accepted January 28, 2004.

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Stroke is available at http://www.strokeaha.org DOI: 10.1161/01.STR.0000125858.71051.ca

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was developed by searching records of patients with a primary diagnosis of nontraumatic intracerebral hemorrhage (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 431) from January 1999 through December 2000. Because the purpose of this study was to identify aspects of care related to initial evaluation and treatment for ICH, patients were only included if they were admitted through an emergency department; those transferred from an outside hospital were excluded. For patients who had more than one hospitalization related to ICH (including those who were transferred from one acute care facility to another), only information from the first recorded hospitalization was used. Also, because a goal of this study was to examine hospital rates of DNR usage, patients were excluded if they were treated at hospitals with fewer than 10 ICH patients over the 2 years of the study period.

Predictor Variables and Outcome
Patient characteristics that were abstracted included age, gender, race/ethnicity, insurance status, number of listed comorbidities, and whether a patient had undergone intubation or mechanical ventilation at any time during his or her hospitalization. For subsequent analyses, use of intubation or mechanical ventilation (ICD-9-CM codes 96.04 or 96.7x) was included in models as a proxy for stroke severity, as has been validated previously.3 Comorbidities were divided into 4 groups based on number of comorbidities (1, 2, 3, and 4 or more). Individual patient DNR status within the first 24 hours, whether a patient had undergone certain procedures including surgical craniotomy (identified by ICD-9-CM codes 01.2 to 01.59) during hospitalization, and the treating hospital were also abstracted and used to determine hospital level characteristics. In-hospital mortality was considered the primary individual level outcome. For patients treated at more than one hospital for their ICH, outcome for the first hospitalization was used.

Hospital characteristics abstracted directly from the OSHPD database included whether the hospital was designated as a teaching hospital, a rural hospital, or was a state designated trauma center. Several other hospital level predictors, including actual hospital DNR and craniotomy rates, were calculated from individual level patient data for those treated at each hospital. Hospital volume included all ICH patients treated at the institution during the 2-year study period.

Case-Mix–Adjusted Hospital DNR Use
From a multivariable model, the likelihood of being made DNR within the first 24 hours of hospitalization was predicted for each individual patient based on age, gender, race, insurance status, comorbidities, and mechanical ventilation. Then, for each hospital the number of predicted DNR cases was calculated by adding the probability of DNR for each patient treated at the hospital. The actual number of DNR cases at a hospital was then divided by the predicted number of DNR cases (observed/expected) to form a ratio, which we term the adjusted hospital DNR use. This adjusted hospital DNR use is therefore a unit-less measure of the actual usage of DNR orders for each hospital, relative to what would have been predicted based on the characteristics of patients presenting to that hospital (the hospital case mix). An adjusted hospital DNR use of 1 represents a hospital that used DNR orders exactly as expected, while ratios of 0.5 or 2.0 represent hospitals that used DNR half or twice as frequently as expected, respectively.

Statistical Analysis
Individual patient characteristics were expressed as mean±SD for continuous variables, median, and interquartile range for ordinal categorical variables, or overall frequencies for nominal categorical variables as appropriate. For univariate analysis, the unpaired t test was used to compare continuous variables, chi-square analysis-of-contingency tables were used to compare nominal and dichotomous variables, and the Mann-Whitney rank sum test was used for ordinal variables.

In order to assess the impact of both patient and hospital characteristics on individual patient in-hospital mortality, a 2-level multivariable model was developed.6 Individual patient in-hospital mortality was used as outcome. Individual level (patient) predictors included in this model were age, gender, race, insurance status, number of comorbidities, and use of intubation or mechanical ventilation. Hospital level predictors were included for the specific institution where each patient was treated and consisted of actual hospital DNR rate, actual rate of craniotomy at the hospital, hospital ICH volume, and whether the hospital was designated as a teaching hospital, a rural hospital, or a trauma center. Because variables may show correlation between patients treated at the same institution, logistic regression tends to overestimate the precision of results. Therefore, generalized estimating equations with robust standard errors were used to account for clustering of observations within institutions.

Hospitals were then divided into quartiles based on adjusted hospital DNR use, with the fourth quartile representing the group of hospitals with the highest adjusted hospital DNR use and the first quartile representing the group of hospitals with the lowest. Cuzick’s nonparametric test of trend was used to assess the association of adjusted hospital DNR use quartile with mortality rate. Interaction between individual patient DNR status and adjusted hospital DNR use quartile was assessed using the Mantel-Haenszel test with individual patient in-hospital mortality as the outcome. Stratumspecific estimates were determined and the test of homogeneity was performed. Statistical analysis was performed using the Stata statistical package, version 8.0 (Stata Corp), and P<0.05 was considered statistically significant.

Results
Overall, 8,233 ICH patients were treated at 234 different hospitals. Table 1 summarizes the individual patient characteristics and the univariate association of these characteristics with in-hospital mortality. Patients who died were more likely to be older, white, have Medicare insurance, have been mechanically ventilated, and have been made DNR within the first 24 hours of hospitalization. Unadjusted hospital DNR rate varied from 0 to 0.7. Adjusted hospital DNR use also varied widely across hospitals (range 0 to 2.61), demonstrating significant variability in the usage of early DNR orders even after adjustment for hospital case mix.

In 2-level multivariable analysis, adjusting for both individual patient and treating hospital characteristics, independent predictors of in-hospital death included age, mechanical ventilation, and actual hospital DNR rate (Table 2). The odds ratio of 3.28 for actual hospital DNR rate represents the increase in odds of death for a patient treated in a hypothetical hospital that uses early DNR orders in all cases, compared with a hospital that never uses early DNR. Put in more clinically meaningful terms, each 10% increase in actual hospital DNR rate increases the odds of an individual patient dying by 13% even after adjustment for age, race, gender, insurance status, and mechanical ventilation. Being treated at a teaching hospital, a rural hospital, or a trauma center was not independently associated with in-hospital death. Also, hospital ICH volume and rate of craniotomy usage were not predictive of in-hospital mortality.

After division of hospitals into quartiles based on adjusted hospital DNR use, mortality rate was shown to increase progressively for patients treated in each quartile. The mortality rate by quartile was 1 (35%), 2 (36%), 3 (37%), and 4 (39%), (P=0.01 for trend). Patients treated in the quartile of hospitals that used DNR orders the most (adjusted for case...
mix) were more likely to be older, white, and have Medicare insurance (Table 3). Patients in the lowest quartile were more likely to be mechanically ventilated and more likely to undergo craniotomy, ventriculostomy, or cerebral angiography. Patient charges and length of stay were both less in the highest quartile of hospitals.

Hospitals in the lowest quartiles of adjusted DNR use were more likely to be teaching hospitals or trauma centers ($P<0.001$ and $P=0.04$, respectively). However, there was no significant difference in average hospital ICH volume or in the number of rural hospitals across quartiles.

We then wished to test whether the increased mortality rate in the hospitals with the highest adjusted DNR use was due to just the DNR status of the individual patients. Therefore, we evaluated the relationship between individual patient DNR status and individual patient in-hospital death; both overall and after stratifying for the adjusted hospital DNR use quartile in which the patient was treated. In the overall cohort, 68% of patients who were DNR died, whereas only 26% of patients who were not DNR died. Thus, patients who were made DNR within the first 24 hours were overall 2.6 times more likely to die than those who were not DNR ($P<0.001$).

However, this relative risk of death for DNR patients varied across all 4 adjusted hospital DNR use quartiles, actually increasing with each successive quartile. In quartile 1 DNR patients were only 2.4 times more likely to die than non-DNR patients were, whereas in quartiles 2, 3, and 4 the relative risks of death for DNR patients were 2.6, 2.8, and 3.3, respectively. Thus, an individual patient’s risk of death was not defined solely by their DNR status, but rather by the interaction between the DNR status and the hospital quartile in which the patient was treated ($P<0.001$). This means that patients with the same DNR status were treated differently in different hospitals. This strongly suggests that some additional aspect of care, which is reflected in the way hospitals use DNR orders, is at least in part responsible for the increased mortality risk in patients treated in high adjusted DNR hospitals. Since DNR orders are, by definition, measures used to limit some aspects of medical care, it is possible that adjusted hospital DNR use is actually a surrogate for an unmeasured variable perhaps indicative of overall aggressiveness of care.

**Discussion**

Respect for patient and family decisions to forgo futile medical and surgical treatments in a setting of devastating
illness with little hope of meaningful recovery is now emphasized as an important aspect of compassionate care in many settings. However, decisions to limit care are often predicated on the assumption that treating physicians are able to accurately predict outcome in the specific case at hand. A prior single institution study suggested that physicians tended to be overly pessimistic in early prognostication after ICH and that this may lead to a "self-fulfilling prophecy" of poor outcome. In that study, a decision to withdraw medical support for patients with ICH was the most important predictor of outcome. Strictly taken, DNR orders are fundamentally different than orders to withdraw medical support. Because DNR orders indicate that no resuscitation should be attempted in the event of cardiopulmonary arrest, if no cardiopulmonary arrest occurs, then DNR orders should not have any actual impact on a patient’s hospital course. In fact, it may be that DNR orders written later in a patient’s hospital course have a different impact than those written earlier.

Given the heterogeneity of other aspects of care for ICH, it is not surprising that there is heterogeneity across hospitals in the usage of early DNR orders. However, the fact that this heterogeneity, even after adjusting for hospital case mix, is associated with heterogeneity in outcome is an important observation. That the increased risk of death in patients treated in high adjusted DNR hospitals is not due solely to the patients’ DNR status is even more important. This implies that DNR is not reserved for patients with particularly poor prognosis at hospitals that use early DNR orders frequently. In this study, adjusted hospital DNR use is serving as a proxy for some other aspect of care at the hospital level, and this aspect of care is independently associated with in-hospital mortality. We believe this strongly suggests that an overall "nonaggressive" approach, reflected as high use of DNR orders within the first 24 hours of hospital admission, influences outcome, even in the absence of a treatment of proven efficacy for ICH. Less frequent use of aggressive procedures, such as craniotomy and ventriculostomy, at hospitals that use DNR more frequently supports this concept.

| TABLE 3. Patient Characteristics between Lowest and Highest Adjusted Hospital DNR Quartiles |
|-----------------------------------------------|-----------------------------------------------|---|
| Died in-hospital                              | 780 (35)                                      | 737 (39)                                      | 0.01 |
| Age (mean± SD)                                | 68±16                                         | 71±15                                         | <0.001 |
| Female                                        | 1078 (49)                                     | 985 (52)                                      | 0.02 |
| Race                                          |                                               |                                               | <0.001 |
| White                                         | 1139 (51)                                     | 1222 (65)                                     | <0.001 |
| Asian                                         | 412 (19)                                      | 252 (13)                                      | <0.001 |
| Hispanic                                      | 278 (13)                                      | 154 (8)                                       | <0.001 |
| Black                                         | 222 (10)                                      | 122 (6)                                       | <0.001 |
| Other                                         | 168 (8)                                       | 135 (7)                                       | <0.001 |
| Insurance status                              |                                               |                                               | <0.001 |
| Medicare                                      | 1237 (56)                                     | 1218 (65)                                     | <0.001 |
| MediCal                                       | 504 (23)                                      | 257 (14)                                      | <0.001 |
| HMO                                           | 267 (12)                                      | 244 (13)                                      | <0.001 |
| Non-HMO                                       | 194 (9)                                       | 153 (8)                                       | <0.001 |
| Other                                         | 17 (1)                                        | 13 (1)                                        | <0.001 |
| Intubation or mechanical ventilation          | 772 (35)                                      | 489 (26)                                      | <0.001 |
| Comorbidities (median, IQR)                   | 3 (1,3)                                       | 3 (1,3)                                       | 0.49 |
| DNR within 24 hours                           | 230 (10)                                      | 803 (43)                                      | <0.001 |
| Procedures performed                          |                                               |                                               |<0.001 |
| Craniotomy                                    | 205 (9)                                       | 80 (4)                                        | <0.001 |
| Ventriculostomy                               | 139 (6)                                       | 40 (2)                                        | <0.001 |
| Cerebral Angiogram                            | 164 (7)                                       | 87 (5)                                        | <0.001 |
| MRI                                           | 136 (6)                                       | 133 (7)                                       | 0.23 |
| Length of stay (median, IQR)                  | 7 (4,15)                                      | 6 (3,11)                                      | <0.001 |
| Hospital charges ($1000) (median, IQR)        | 29 (14,70)                                     | 22 (12,48)                                    | <0.001 |

Numbers are expressed as totals with percentages of total in parentheses, except where indicated. IQR indicates interquartile range for specific parameter. *P values for race and insurance status are for difference between groups by quartile.
Several limitations are inherent in an observational study using administrative data. The OSHPD database does not contain patient-specific information on many factors that have been shown to be associated with outcome after ICH, such as Glasgow Coma Scale (GCS) score, location or size of hematoma, or presence of intraventricular hemorrhage. Mechanical ventilation has been demonstrated as a reasonable proxy for coma in a large sample of Medicare patients with acute stroke and, when used, is usually initiated very early on in the course of acute stroke. However, the possibility of residual confounding due to stroke severity cannot be entirely excluded. In this cohort, we did not adjust for any potential differences among different physicians, as this information is not available in the OSHPD database. Finally, and most importantly, assessment of outcome is limited to in-hospital death. No functional outcome using validated measures, such as the modified Rankin Scale or the Glasgow Outcome Scale, is available at the time of hospital discharge or at later time points, such as 3 to 6 months post-ICH. It is possible that patients in low DNR usage hospitals are surviving to hospital discharge but remain very functionally impaired. However, given that patients must survive in order to improve, we believe that in-hospital mortality is still a meaningful outcome measure when examining a large cohort such as this.

Despite these limitations, several strengths are apparent from this analysis. First, the very large size of this cohort and the large number of hospitals represented make possible an evaluation of hospital-level and individual-level characteristics not previously described for ICH. By including these patient and hospital characteristics in the 2-level analysis (Table 2), and leaving out individual treatments that patients received such as being made a DNR or undergoing craniotomy, we were able to identify factors predictive of in-hospital mortality which were not dependent on the treatments later received by the patient. Of note, in this analysis we chose to use actual hospital DNR rate, rather than adjusted hospital DNR use, and adjust for other individual characteristics in order to provide a more easily interpretable hospital predictor of individual patient in-hospital mortality; an analysis using adjusted hospital DNR use was essentially the same. Also, the comprehensive nature of the included hospitals (all nonfederal hospitals in California) reduces the likelihood of bias and suggests that the basic findings of this study are generalizable. We found it interesting that of all the hospital level variables, only DNR rate (or adjusted hospital DNR use) was independently associated with in-hospital mortality and that hospital ICH volume, or status as a teaching, rural, or trauma center hospital did not matter.

This is a complex issue. We believe it would be wrong to suggest that DNR orders or other measures to limit care are inappropriate after ICH. The challenge lies in determining for which patients this is the most appropriate plan of care. Even so, use of DNR orders within the first 24 hours after acute ICH is common and heterogeneous across different hospitals. Higher than predicted use of early DNR orders is associated with increased risk of in-hospital mortality after acute ICH, even after adjusting for individual and hospital characteristics. This higher mortality is not due solely to individual patient DNR status, suggesting that adjusted hospital DNR use is a proxy, likely reflective of overall aggressiveness of care.

**Acknowledgments**

Dr Hemphill is funded by grant K23 NS41240 from the NIH/NINDS. Dr Johnston is funded by grant K02 NS02254 from the NIH/NINDS.

**References**

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Stroke. 2004;35:1130-1134; originally published online March 25, 2004;
doi: 10.1161/01.STR.0000125858.71051.ca

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/35/5/1130

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