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Factors Associated with Combined Do-Not-Resuscitate and Do-Not-Intubate Orders: A Retrospective Chart Review at an Urban Tertiary Care Center

Sara Stream, MD[1], **Anna Nolan, MD, MS**[2,3], **Sophia Kwon, DO, MPH**[2], and **Catherine Constable, MD**[3,4]

[1]New York University Internal Medicine Residency Program, NY, NY

[2]Department of Medicine, Division of Pulmonary, Critical Care and Sleep Medicine, New York University School of Medicine, NY, NY

[3]Division of Ethics, Department of Population Health, New York University School of Medicine, NY, NY

[4]Department of Medicine, New York University Langone Medical Center, NY, NY

Abstract

BACKGROUND: In clinical practice, do-not-intubate (DNI) orders are generally accompanied by do-not-resuscitate (DNR) orders. Use of do-not-resuscitate (DNR) orders is associated with older patient age, more comorbid conditions, and the withholding of treatments outside of the cardiac arrest setting. Previous studies have not unpacked the factors independently associated with DNI orders.

OBJECTIVE: To compare factors associated with combined DNR/DNI orders versus isolated DNR orders, as a means of elucidating factors associated with the addition of DNI orders.

DESIGN: Retrospective chart review.

SETTING/SUBJECTS: Patients who died on a General Medicine or MICU service (n=197) at an urban public hospital over a 2-year period.

MEASUREMENTS: Logistic regression was used to identify demographic and medical data associated with code status.

RESULTS: Compared with DNR orders alone, DNR/DNI orders were associated with a higher median Charlson Comorbidity Index (odds ratio [OR] 1.27, 95% confidence interval [CI] 1.13–1.43); older age (OR 1.02, 95% CI 1.01–1.04); malignancy (OR 2.27, 95% CI 1.18–4.37); and female sex (OR 1.98, 95% CI 1.02–3.87). In the last 3 days of life, they were associated with morphine administration (OR 2.76, 95% CI 1.43–5.33); and negatively associated with use of vasopressors/inotropes (OR 10.99, 95% CI 4.83–25.00).

Corresponding Author: Catherine Constable, MD, Assistant Professor of Internal Medicine, NYU Langone Medical Center, Room 1803, 550 First Avenue, New York, NY 10016, catherine.constable@nyumc.org, Telephone: 917-386-5451, Fax: 646-754-9986.

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CONCLUSIONS: Compared with DNR orders alone, combined DNR/DNI orders are more strongly associated with many of the same factors that have been linked to DNR orders. Awareness of the extent to which the two directives may be conflated during code status discussions is needed to promote patient-centered application of these interventions.

Keywords

Do-not-intubate (DNI); do-not-resuscitate (DNR); code status; advance directives; goals of care; medical ethics

INTRODUCTION

Advance directives limiting life-sustaining treatment have been widely utilized in the United States since the 1970s, when the American Medical Association first advocated their adoption.[1] Do-not-resuscitate (DNR) orders were introduced as a logical response to an increasing focus on patient autonomy in end-of-life decision-making, and concerns about the provision of inappropriate care, including cardiopulmonary resuscitation (CPR).[2] Given that respiratory failure may be the final common pathway for terminally ill patients with a range of diagnoses, do-not-intubate (DNI) orders entered into clinical practice at around the same time. The American Thoracic Society has issued guidelines to assist medical practitioners in honoring patients' right to refuse life-sustaining treatment, including intubation and mechanical ventilation (MV).[3] DNR orders and other advance directives limiting treatment were used in nearly two thirds of more than 31 countries recently surveyed.[4] In 2017, the World Medical Association affirmed the physician's duty to respect patient autonomy and dignity, lending broad, international support to the ethical norm of respecting preferences as stated either by the capacitated patient or their surrogate decision-maker exercising substituted judgment.[5] When properly executed, advance directives, including DNR and DNI orders, are among the most useful tools that a patient—or their surrogate—has for ensuring that preferences regarding life-sustaining treatment are honored.

Discussions of code status commonly bundle cardiac arrest with endotracheal intubation, without recognizing pre-arrest respiratory failure as a distinct indication for intubation.[6–8] In fact, in a large multicenter survey of patients who received MV in the ICU, only 1.9% were admitted after cardiac arrest.[9] Treatment outcomes, which are known to influence patient preferences regarding life-sustaining treatment, are notably poorer for in-hospital CPR than for MV for pre-arrest respiratory failure, and vary depending on the specific indication for MV.[10–13] Studies have found that when outcomes are included in code status discussions, they are typically for CPR, but not MV for pre-arrest respiratory failure.[14] These and other observations have raised concerns that DNI orders may not accurately reflect patient preference.[15]

A related consideration is the possible effect of DNI orders on other aspects of care, as has been shown with DNR orders. DNR orders reflect a decision to forgo CPR in the setting of cardiac arrest, and are not intended to apply to any other aspect of clinical care; yet, they may be broadly interpreted. Studies have found, for example, that patients are less likely to

be triaged to the intensive care unit,[16, 17] and less likely to receive optimal medical therapy for heart failure[18] when DNR orders are in place. In addition, DNR orders are associated with certain patient characteristics such as older age, a diagnosis of cancer, and longer hospital stay.[19–21] It is of note that DNR status confers a higher risk of death even after adjusting for these characteristics.[22]

While the clinical and demographic associations with DNR status are well-documented, the potential additive effect of DNI status is not known. Patients may opt for an attempt at defibrillation and chest compressions without intubation and MV[23]. In clinical practice, isolated DNI orders are usually limited to patients with end-stage chronic respiratory failure [3]. In general, however, patients undergoing cardiopulmonary resuscitation will frequently also be intubated to maintain adequate oxygenation.[24] Thus, in order to elucidate factors associated specifically with the addition of DNI orders, we performed an observational study comparing factors associated with combined DNR/DNI status versus DNR status alone, as an indirect means of isolating the “DNI” variable. We hypothesized that many of the known associations with DNR orders would simply be strengthened by the addition of a DNI order, given that code status discussions may not adequately distinguish between the two directives. A secondary objective was to document the temporal association between DNR and DNI orders, as these directives may be more readily conflated when framed as a continuum of respiratory and cardiac arrest in a single discussion. A greater understanding of the contexts in which DNI orders are added to DNR orders—as well as the downstream effects of combining these orders—may lead providers to better distinguish between these directives, especially for patients in whom key distinctions between CPR and MV would be both clinically relevant and pertinent to the patients’ specific goals of care.

METHODS

Study Design

This was a retrospective chart review of the electronic medical record (EMR) of all patients who died on a medicine or medical intensive care unit (ICU) service between January 2012 and December 2013 at Bellevue Hospital Center (BHC), a tertiary care safety net hospital in New York City. Baseline and in-hospital characteristics were documented, including age, gender, race/ethnicity, preferred language, insurance status, length of stay, palliative care consultation, and prior hospitalization at BHC within the past six months. Dates of code status entry into the EMR were recorded. Notes were reviewed to identify the decision-maker for code status decisions, and to verify DNI status, which, in practice, is not always entered as a separate electronic order when a DNR order is entered. Code status was defined by active DNR and/or DNI orders documented in the EMR at the time of death. MOLST (Medical Orders for Life-Sustaining Treatment) forms were not analyzed, as these were not incorporated into the EMR during the study period. Comorbid conditions were identified with discharge data codes and chart review to calculate the Charlson Comorbidty Index. Records of administering inotropes, vasopressors, opioids, and benzodiazepines in the last three days of life were compiled, managed, and analyzed using SPSS (v23, IBM). The study protocol was approved by the New York University School of Medicine Institutional Review Board (#14–01268) and the Bellevue Hospital Center Research Department.

Statistical Analysis

We evaluated differences in baseline characteristics and treatment decisions between patients who were DNR/DNI and the control group—those who were DNR only—using a t-test for comparison of means for continuous variables and a Chi Square test for comparison of categorical variables. Univariate logistic regression was used to identify demographic and medical data associated with code status. Variables found to be significant at a $p < 0.05$ were included in the multivariate analysis. The performance of multivariate logistic regression models was evaluated using a Receiver Operator Characteristic (ROC) analysis, and a model was selected based on Area Under the Curve (AUC). The data are presented as adjusted odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was considered as a p-value less than or equal to 0.05.

RESULTS

A total of 796 patients died at Bellevue Hospital Center between 2012 and 2013. Of these, 197 occurred on the General Medicine or Medical Intensive Care Unit services. The majority of patients with code status (n=153) had both DNR and DNI orders (n=84; 55%), as opposed to DNR orders alone (Figure 1). DNR and DNI orders were placed on the same date in 86% of cases. No patients had DNI orders only. The median number of days until death were 2 and 2.5 following placement of DNR and DNI orders, respectively. Code status was decided by a surrogate decision-maker in 63% of cases. The demographics of the study cohort are shown in Table 1. The study cohort was diverse in terms of race and primary language, with 69% of patients who were non-white and 37% who were non-English-speaking. Common co-morbidities included malignancy (46%), diabetes mellitus (30%), chronic kidney disease (31%), and history of cerebrovascular accident or transient ischemic attack either on or before the index admission (35%).

Patient Characteristics

When compared with patients with DNR orders only, patients with DNR/DNI orders had a higher median Charlson Comorbidity Index (OR 1.27, 95% CI 1.13–1.43); were older (OR 1.02, 95% CI 1.01–1.04); were more likely to have a malignancy (OR 2.27, 95% CI 1.18–4.37); were more likely to be female (OR 1.98, 95% CI 1.02–3.87); and were more likely to have been hospitalized in the past 6 months (OR 1.95, 95% CI 1.10–3.47). There was a trend towards patients of black race being more likely to be DNR only rather than DNR/DNI when compared with patients of white race (OR 0.45, 95% CI 0.18–1.13, p=0.09). However, this trend was no longer observed when adjusting for age; patients of black race were on average younger than patients of white race (63.5 vs. 74.0, $p<0.01$). Patients who were DNR/DNI were more likely to have made their own code status decisions, as opposed to having surrogate decision-makers decide on their behalf (OR 4.52, 95% CI 2.16–9.47) (Table 2).

Treatment Characteristics

In the last 3 days of life, patients with DNR/DNI orders were more likely to receive morphine (OR 2.76, 95% CI 1.43–5.33); and less likely to receive vasopressors/inotropes (OR 10.99, 95% CI 4.83–25.00) compared to patients who were DNR only (Table 2).

Multivariate Analysis

Independent predictors of DNR/DNI status, as assessed by multivariable logistic regression, were Charlson Comorbidity Index, female sex, and the patient as the decision-maker. Malignancy was no longer significant when adjusting for Charlson Comorbidity Index. Age was not significant in the multivariate analysis, but was included to adjust for age as a possible confounder. In the final model with sex, patient as decision-maker, and Charlson Comorbidity Index, the AUC was 0.76 (0.69–0.84) (Table 3).

DISCUSSION

In this retrospective chart review of patients who died at BHC over a 2-year period with code status documented, most patients had both DNR and DNI orders. In the vast majority of these cases, the orders were placed on the same date. While likely in part reflecting patient and family preference when facing a low likelihood of recovery, the temporal association between these disparate directives may also be an indicator of code status discussions that collapse DNR with DNI orders.

Qualitative studies have indeed observed that code status discussions commonly bundle these interventions together, failing to distinguish between MV for respiratory failure in the pre-arrest setting and MV used to ensure tissue perfusion during CPR.[6–8] Nuanced preferences are notoriously difficult to capture with intervention-based directives. In the recent TRIAD VI and VII studies, health care workers inconsistently followed Physician Orders for Life Sustaining Treatment for any combination of directives other than full medical treatment and CPR.[25, 26] DNR status may be interpreted as intent to avoid other life-sustaining therapies, such as intubation, despite the fact that many patients who are documented as DNR/DNI express a desire to be intubated for more readily reversible processes such as pneumonia and angioedema.[27] Given the importance to patients of outcomes when weighing medical interventions, it is vitally important that providers capture the disparate indications and outcomes for MV and CPR when discussing code status. In a recent editorial, Breu and Herzig suggested that defaulting to consolidation of DNR and DNI orders carries the risk of impeding autonomous decision-making.[15] Our data showing the tight linkage of DNR and DNI orders support this concern.

As expected, our study found that when combined, DNR and DNI orders are more strongly associated with many of the patient characteristics previously linked to DNR status,[19, 20, 28] including older age, malignancy, and higher Charlson Comorbidity Index. In the multivariate analysis, however, malignancy and age were no longer significant when adjusted for Charlson Comorbidity Index. While these differences may be explained as the appropriate preferences of patients at higher risk of death, they may also be driven by providers placing a greater emphasis on avoidance of interventions—including intubation—for older patients with more comorbidities.

We found that females were more likely than males to be DNR/DNI versus DNR. Previous studies have found an association with female sex and DNR status.[19, 29, 30] It has been suggested that this may be due to the preferences of women,[31] or gender disparities in patient-physician communication facilitating more end-of life discussions with female

patients, who may in turn be more likely to voice their preferences to surrogate decision-makers.[32, 33] In a study by Bedell and colleagues, DNR status was associated with discontinuation of medical support outside of the arrest setting (e.g. blood draws, dialysis) in women as compared with men.[21] The more frequent coupling of DNI with DNR orders in women seen in our study could reflect an inappropriately perceived preference of women for less aggressive care when DNR orders are in place. Alternatively, it may accurately reflect a gender disparity in end-of-life decision-making. Further investigation is needed to elucidate the underlying factors.

Race was a variable of interest given the literature showing that black patients are less likely to have advance directives limiting treatment. We found a trend towards black patients being less likely to have DNR/DNI orders compared with white patients, but which did not bear out when adjusted for age.

While we found that patients making their own code status decisions were more likely to be DNR/DNI, this finding should be interpreted with caution, given that patients who were DNR only received more aggressive treatment, including intubation. In this population of patients who died in the hospital, 91% of patients without combined DNR/DNI orders were intubated during their hospitalization, rendering them unable to participate in further code status discussions due to medically-induced coma, or due to critical illness itself. Overall, most patients in our study had code status decisions made for them by surrogates due to incapacity, consistent with the multi-national study by van der Heide and colleagues, which showed that among non-sudden deaths that were preceded by end-of-life decision-making, patients lacked capacity to participate in most cases.[34] In light of the finding in our study, as in the SUPPORT trial, that most code status decisions were made within the last 3 days of life, the preponderance of code status decisions made by surrogates may be viewed as less surprising.[35]

We found that patients who were DNR/DNI were more likely to receive morphine, and less likely to receive pressors/inotropes versus those who were DNR alone, consistent with a more pronounced shift away from aggressive treatment for patients who were DNR/DNI versus DNR. Chu and colleagues reported that patients with DNI orders had worse survival than patients without, but postulated that that this could be attributed entirely to their older age and greater number of comorbid conditions, rather than any differences in treatment.[36] However, our findings showing more liberal use of morphine and more restrictive use of pressors/inotropes in DNR/DNI vs DNR patients call this assertion into question, and raise the specter of a self-fulfilling prophecy; i.e., patients expected to fare more poorly may be treated in a manner which contributes to the realization of that expectation. As already alluded to, this is in line with previous studies on the effect of DNR orders alone, which have demonstrated a tendency to provide less aggressive care to patients who are DNR, as opposed to “full code”, outside of the arrest setting.[16, 18, 37] The finding that adding a DNI order to a DNR order merely strengthened the association with the same treatment decisions known to be associated with DNR status alone could again signify a failure to distinguish appropriately between the two, creating a net effect equivalent to “double DNR”.

Our study had several limitations. First, our analysis reveals associations, but not causality, given the observational nature of the study. Secondly, our study may not be generalizable to other institutions, given that it was performed at a single, academic, urban hospital, albeit with a highly diverse patient population. Hakim and colleagues found institutional variability in factors associated with DNR status; this suggestion of institutional and physician-level factors at work in what is intended to be a patient-centered decision regarding code status is of clinical and ethical concern, and warrants further study in patients with combined DNR/DNI status.[35] The generalizability of our results may be further limited by the fact that all subjects in this sample of patients died on the index admission, implying a severely ill study population. While this introduces a selection bias, we chose this population with the knowledge that code status is more frequently addressed near the end of life, when it is most likely to be relevant. A related consideration is the fact that code status orders were written close to the time of death in this study, which is consistent with results from the multi-center SUPPORT trial, where nearly half of DNR orders were written in the last 2 days of life.[38] Previous research has suggested that DNR orders written late in the hospitalization may be more likely to reflect futility of treatment in the setting of imminent death, as opposed to patient preferences and prognosis at admission.[22]

In conclusion, our data support the concern that DNI orders, in association with DNR orders, may be interpreted by providers to signify a more palliative approach, in much the same way that has been observed with DNR orders alone. While avoidance of aggressive care, including intubation, may well be the goal of patients who are DNR, this cannot be presumed. Providers should educate patients and surrogate decision-makers that MV and CPR are not simply two sequential steps on a continuum of care, but discrete interventions that may be utilized in different settings, with different expected outcomes. Further research is needed to determine prospectively the effect of linked DNR/DNI orders on treatment in a larger patient population, and to qualitatively elucidate the attitudes and beliefs surrounding the use of these directives.

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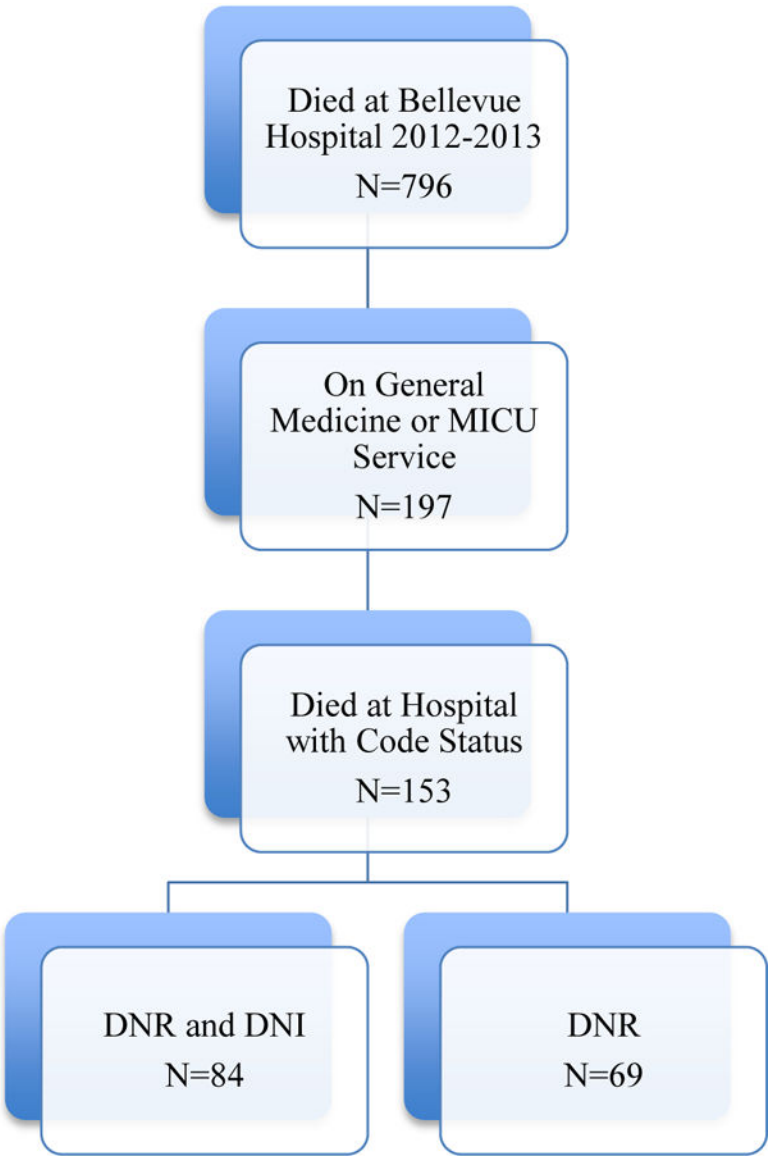

Figure 1.
Patients Included in the Data Analysis and Distribution of Code Status

Table 1.

Characteristics of Patients Who Died on a Medicine or MICU Service with Advance Directives in Place (N=153) [Mean (SD) or N(%)]

		Total N=153	DNR/DNI N=84	DNR N=69	P
Age		66.6(18.1)	69.9(17.3)	62.5(18.2)	0.01
Female		60(39%)	39(46%)	21(30%)	0.04
Race	White	47(31%)	29(35%)	18(26%)	0.26
	Black	31(20%)	13(15%)	18(26%)	0.08
	Hispanic	18(12%)	12(14%)	6(9%)	0.29
	Other	57(37%)	30(36%)	27(39%)	0.66
Primary Language	English	97(63%)	48(57%)	49(71%)	0.11
	Spanish	14(9%)	7(8%)	7(10%)	0.70
	Chinese	14(9%)	11(13%)	3(4%)	0.06
	Other	28(18%)	18(21%)	10(14%)	0.27
Charlson Comorbidity Index		7.0(3.4)	8.1(3.2)	5.7(3.1)	<0.01
Malignancy		70(46%)	46(55%)	24(35%)	0.01
Patient as Decision-Maker		56(37%)	43(51%)	13(19%)	<0.01
Length of Stay, Days		16.4(30.1)	16.0(25.0)	17.0(35.5)	0.83
Palliative Care Consulted		87(57%)	53(63%)	34(49%)	0.09
Intubated		81(53%)	18(21%)	63(91%)	<0.01
Treatment Course in the Last 3 Days of Life					
Morphine		74(48%)	50(60%)	24(35%)	<0.01
Pressors/Inotropes		50(33%)	10(12%)	40(60%)	<0.01

Table 2.

Univariate Logistic Regression Predicting DNR/DNI

Characteristics/Treatment	OR	95%CI
Age	1.02	1.01–1.04
Female Sex	1.98	1.02–3.87
Charlson Comorbidity Index	1.27	1.13–1.43
Malignancy	2.27	1.18–4.37
Hospitalized < 6 Months Ago	1.95	1.10–3.47
Patient as Decision-Maker	4.52	2.16–9.47
Morphine	2.76	1.43–5.33
No Pressors/Inotropes	10.99	4.83–25.00

Table 3.

Multivariate Regression Predicting DNR/DNI

Characteristics	OR	95%CI
Age	1.01	0.98–1.03
Patient as Decision-Maker	3.44	**1.57–7.51**
Charlson Comorbidity Index	1.20	**1.05–1.38**
Sensitivity 64%, Specificity 70%		
Female Sex	2.09	**1.01–1.44**
Patient as Decision-Maker	3.48	**1.59–7.63**
Charlson Comorbidity Index	1.22	**1.08–1.38**
Sensitivity 61%, Specificity 73%		