Do Sex Differences Exist in the Establishment of “Do Not Attempt Resuscitation” Orders and Survival in Patients Successfully Resuscitated From In-Hospital Cardiac Arrest?

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**Background**—Women have higher utilization of “do not attempt resuscitation” (DNAR) orders during treatment for critical illness. Occurrence of sex differences in the establishment of DNAR orders after resuscitation from in-hospital cardiac arrest is unknown. Whether differences in DNAR use by sex lead to disparities in survival remains unclear.

**Methods and Results**—We identified 71,820 patients with return of spontaneous circulation (ROSC) after in-hospital cardiac arrest from the Get With The Guidelines–Resuscitation registry. Multivariable models evaluated the association between de novo DNAR (anytime after ROSC, within 12 hours of ROSC, or within 72 hours of ROSC) by sex and the association between sex and survival to discharge accounting for DNAR. All models accounted for clustering of patients within hospital and adjusted for demographic and cardiac arrest characteristics. The cohort included 30,454 (42.4%) women, who were slightly more likely than male participants to establish DNAR orders anytime after ROSC (45.0% versus 43.5%; adjusted relative risk: 1.15 [95% CI, 1.10–1.20]; P<0.0001). Of those with DNAR orders, women were more likely to be DNAR status within the first 12 hours (51.8% versus 46.5%; adjusted relative risk: 1.40 [95% CI, 1.30–1.52]; P<0.0001) and within 72 hours after ROSC (75.9% versus 70.9%; adjusted relative risk: 1.35 [95% CI, 1.26–1.45]; P<0.0001). However, no difference in survival to hospital discharge between women and men (34.5% versus 36.7%; adjusted relative risk: 1.00 [95% CI, 0.99–1.02]; P=0.74) was appreciated.

**Conclusions**—In patients successfully resuscitated from in-hospital cardiac arrest, there was no survival difference between men and women while accounting for DNAR. However, women had a higher rate of DNAR status early after resuscitation (<12 and <72 hours) in comparison to men. *(J Am Heart Assoc. 2020;9:e014200. DOI: 10.1161/JAHA.119.014200.)*

**Key Words:** cardiac arrest • disparity • DNAR • DNR • sex

In the United States, in-hospital cardiac arrest affects ≈200,000 individuals per year, with significant survival variability observed among hospitals.1,2 Sex differences have been uncovered in varying aspects of acute cardiac care,3–5 but how these demographic factors contribute to variability in cardiac arrest outcomes remains an active area of investigation. “Do not attempt resuscitation” (DNAR) orders have been associated with poor survival to hospital discharge after cardiac arrest. How sex differences affect the utilization of DNAR orders in post–cardiac arrest care is relatively unknown, and whether overall differences exist in rates of survival to hospital discharge by sex remains unclear. We hypothesized that there is significant variability by sex in the utilization and timing of DNAR orders in patients successfully

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resuscitated from an in-hospital cardiac arrest and that these differences will translate into survival differences between men and women.

Prior studies of women who experienced cardiac arrest have shown variability in survival outcome, with studies showing both similar or reduced rates of survival in comparison to men; however, few of these studies have accounted for the establishment of DNAR. This detail is relevant given that establishment of DNAR is associated with worse survival outcomes with cardiac arrest and lower utilization of potentially critical interventions and procedures that could improve the likelihood of survival. In other aspects of critical illness, investigators have found that women have more frequent and often earlier utilization of DNAR. This use has been defined in advanced heart failure and sepsis, for which women experience higher rates of DNAR and early DNAR use. The utilization and timing of DNAR by sex in in-hospital cardiac arrest has yet to be determined.

We sought to understand how patient sex affects the establishment of DNAR and, if a difference is appreciated, how DNAR affects survival to hospital discharge for women who have had cardiac arrest. Using the GWTG-R (Get With The Guidelines–Resuscitation) registry, we hypothesized that women would have more frequent early DNAR use and, as a result, worse overall survival to hospital discharge after in-hospital cardiac arrest.

Methods

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to GWTG-R (email: GWTGResuscitationResearch@heart.org).

Study Design

We performed a secondary analysis of the GWTG-R registry, which is a prospective, hospital-based, clinical registry of patients with in-hospital cardiac arrest in the United States. The design and maintenance of the registry has been described in detail previously. Briefly, the registry consists of patients with cardiac arrest, identified as loss of palpable central pulse, apnea, and impaired consciousness. Patients who have received cardiopulmonary resuscitation and meet the definition of cardiac arrest, as defined by Utstein criteria, are included. Specially trained personnel at each institution are charged with data abstraction from the medical record and inclusion in the GWTG-R database. To ensure that all cases are captured, multiple sources of case identification are explored, including hospital code logs, centralized collection of cardiac arrest flow sheets, inventory of code carts, and review of hospital-based billing for code drugs. The registry is based on standardized Utstein definitions for clinical variables and outcomes.

This study was approved by the Colorado Multiple Institutional Review Board with a waiver of the requirement for informed consent, as the study used deidentified data.

Study Population

We identified 127,172 adult patients (≥18 years of age) with an incident cardiac arrest event between April 1, 2006, and December 31, 2016, that achieved return of spontaneous circulation (ROSC), defined as a spontaneous pulse for at least 20 minutes after successful resuscitation (Figure).
Subsequent arrest events for an individual were not included in this cohort as this analysis focused on incident events. The DNAR variable was introduced into the registry on April 1, 2006; therefore, we did not consider patients in the registry before this date. Patients were excluded from the study cohort if the arrest occurred in a procedural area or the emergency department (27 566 patients) or if the patient had a DNAR that was time-stamped before the arrest event (9028 patients). Patients were also excluded if they had missing time data for the following events in order to calculate time to DNAR: time of ROSC, time of establishment of DNR, time of death, or discharge from the hospital (18 758 patients). Our final sample included 71 820 patients from 571 hospitals within the GWTG-R registry (Figure).

Study Outcomes and Variables
This study examined the relationship between patient sex and the primary outcome of de novo establishment of DNAR order at any time after ROSC, within 12 hours of ROSC, and within 72 hours of ROSC. We selected <12 hours after ROSC as a time when patients’ goals of care might be altered given the gravity of having a cardiac arrest. The 72-hour time point was selected because this is a time when patients who are comatose after cardiac arrest begin to have neurologic findings that are indicative of poor neurologic recovery.17,18 In addition, the AHA guidelines recommend that establishing a neurologic prognosis should be delayed until at least 72 hours after ROSC (or 72 hours after normothermia if temperature management was utilized), given that data have shown that neurologic prognosis cannot be predicted with sufficient accuracy before this time.19,20 The secondary outcome was survival to hospital discharge.

Statistical Analysis
Baseline characteristics including patient demographics (age, sex, race/ethnicity), premorbid medical conditions, and arrest characteristics (initial arrest rhythm, chest compressions, witnessed event, duration of resuscitation) were compared by frequencies for categorical variables. Statistical comparisons of baseline variables between men and women were made using Poisson models with a log link and accounted for clustering of patients within hospitals through the use of robust standard errors.21 The REPEATED statement in SAS PROC GENMOD was used. Multivariable models adjusting for demographics and cardiac arrest factors were constructed to examine the associations between sex and de novo establishment of DNAR orders (at any time after ROSC and within 12 or 72 hours of ROSC). All models were adjusted for clustering of patients within hospital, using SAS PROC GENMOD. Log link models with Poisson distribution using robust standard errors and an offset term for time the individual was eligible for the outcome were utilized to get adjusted relative risk (ARR) and 95% CIs for DNAR outcomes. Patient sex was included in all models, regardless of significance. To determine whether there was effect modification between sex and race, the interaction term was included in all models and removed if nonsignificant, as prior literature has shown a positive interaction among race/ethnicity, sex, and DNAR in both sepsis care and heart failure admissions. The following variables were accounted for in all models because they can be associated with prognosis: calendar year of event; age at time of event; cerebral performance category at admission; illness category; preexisting conditions; assisted or mechanical ventilation in place; any vasoactive agent in place; first pulseless rhythm; ventricular fibrillation or pulseless ventricular tachycardia anytime; event witnessed; event duration in minutes; and exposure time between ROSC and DNAR, discharge, or death. Time between ROSC and DNAR, discharge, or death was included to account for the duration of time for which the patient was susceptible to the outcome measure. The preexisting conditions that were accounted for are as follows: acute central nervous system nonstroke event, acute stroke, congestive heart failure on the index admission, congestive heart failure on prior admissions, diabetes mellitus, hepatic insufficiency, hypotension or hypoperfusion, metastatic or hematologic malignancy, metabolic electrolyte abnormality, myocardial infarction during the index admission, myocardial infarction on prior admissions, pneumonia, renal insufficiency, respiratory insufficiency, and septicemia.

To examine the association between sex and survival (as a binary outcome), we again used a log link Poisson model with robust standard errors to account for clustering of patients within hospital. There was no offset term in this model because the outcome was not dependent on length of stay. Adjustment for DNAR was also considered in the survival model, with DNAR dichotomized as early (<72 hours after ROSC) or late/no DNAR (≥72 hours after ROSC or no DNAR order).

All statistical analyses were conducted with the use of SAS software v9.4 (SAS Institute). All hypothesis tests were 2-sided with a significance level of 0.05.

Results
An initial 127 172 in-hospital cardiac arrest events were identified from the GWTG-R registry (Figure). Events were excluded if they occurred outside of the intensive care unit or ward (27 566), had significant missing data (18 758), or if the individual had a DNAR order in place before the arrest (9028). The final cohort included 71 820 in-hospital cardiac arrest events.
events across 571 hospitals, of which women accounted for 42.4% of the cohort.

In comparison to men, women were older (mean±SD: 65.5±15.8 years versus 64.6±15.1 years; \(P<0.0001\)), less frequently of non-Hispanic white race (61.7% versus 67.5%, \(P=0.0001\)), more likely to have a nonshockable cardiac arrest rhythm (pulseless electrical activity or asystole; 81.6% versus 78.0%, \(P=0.0001\)), and more likely to have a noncardiac illness at the time of admission (47.2% versus 41.1%, \(P<0.0001\)). In contrast, men had higher incidence of cardiac premorbid conditions, including myocardial infarction and congestive heart failure, compared with women (Table 1).

**DNAR by Sex**

Of the total cohort, 44.1% (31695/71820) had an initial DNAR order placed after ROSC. Within the entire cohort, 45.0% (13692/30454) of women and 43.5% (18003/41366) of men had a DNAR order after ROSC (unadjusted RR: 1.16; 95% CI, 1.12–1.21). Subject demographics, pre-morbid conditions, and arrest characteristics by sex and DNAR are reported in Table S1. Adjusting for these factors through a multivariable model, women were 15% more likely to become DNAR at any time after ROSC (RR: 1.15; 95% CI, 1.10–1.20; Table 2).

When analyzing the incidence of DNAR by time from ROSC, a higher proportion of female patients had early DNAR. Of those who had any DNAR during the hospital admission (n=31695), 51.8% (7096) of women and 46.5% (8367) of men had a DNAR order placed <12 hours after ROSC and 75.9% (10388) of women and 70.9% (12759) of men had a DNAR order placed <72 hours after ROSC. When accounting for the same patient and arrest characteristics as described previously, female sex was associated with a higher likelihood of early DNAR <12 hours after ROSC among those who made DNAR orders at any time (ARR: 1.40; 95% CI, 1.30–1.52) and DNAR <72 hours after ROSC (ARR: 1.35; 95% CI, 1.26–1.45; Table 2).

**Survival by Sex**

Unadjusted rates of survival to hospital discharge were 34.5% for women and 36.7% for men. After accounting for patient and arrest characteristics, except DNAR, female sex was associated with modestly lower rates of survival to hospital discharge (ARR: 0.98 [95% CI, 0.96–1.00]; \(P=0.04\)), which were essentially unchanged after additional adjustment for DNAR within 72 hours (ARR: 1.00 [95% CI, 0.99–1.02]; \(P=0.74\)). Within this same model, when patients had a DNAR established within 72 hours of ROSC, their chance of surviving was much lower than those without a DNAR placed (RR: 0.15 [95% CI, 0.14–0.17]; \(P<0.0001\); Table 3). The interaction effect between sex and DNAR within 72 hours was nonsignificant (\(P=0.16\)).

**Discussion**

In this national registry of in-hospital cardiac arrest, we found that women were more likely to become DNAR after successful resuscitation from an in-hospital cardiac arrest. Notably, among those made DNAR at any time after ROSC, the likelihood of early DNAR, defined as <12 and <72 hours after ROSC, was also higher among women compared with men. However, this variability in DNAR application did not translate to a meaningful survival difference between men and women. When exploring the association between DNAR and survival to hospital discharge, early DNAR was associated with worse survival than subjects who had late DNAR, defined as >72 hours after ROSC, or no DNAR. What is notable about these findings is that despite the higher prevalence of early DNAR, women were as likely to survive to discharge as men.

Studies exploring the incidence of DNAR in episodes of acute, unplanned, critical illness have found similar sex-based trends. Specifically, the incidence of DNAR is higher among women who have had cerebrovascular accidents and unplanned acute surgeries22–24 in comparison to men. In these studies, authors attributed the differences in rates of DNAR to women better expressing their wishes before an unplanned illness or to physician bias that resulted in women having increased rates of DNAR use.23,24 We expanded on these observations to explore incidence and timing of DNAR use in post–cardiac arrest care. Timing of DNAR is not without consequence. Richardson et al found that early DNAR placement is associated with fewer critical interventions and procedures and with reduced survival to hospital discharge.12 Conversely, it is possible that the early DNAR is indicative of a worse prognosis based on factors that cannot be measured within this study but that were apparent to the care team and family. Although a portion of this variability will be due to patient wishes, establishing an accurate neuroprognosis is critical to ensuring that families are able to align patient wishes with the potential for neurologic recovery.

A prior study based on the GWTG-R registry similarly demonstrated that DNAR placement after ROSC is strongly associated with death before hospital discharge25; our study builds on this work by exploring sex differences in the timing of DNAR. Because early DNAR is associated with worse outcomes and we found that women have higher rates of early DNAR, we hypothesized that reducing the difference in early DNAR in women could potentially improve current survival rates for women who have cardiac arrest. Elmer et al found that in patients in the Resuscitation Outcomes Consortium
Table 1. Baseline Characteristics by Patient Sex (n=71,820)

| Characteristic                  | Category                        | All Patients, n | All Patients, % | Female (n=30,454, 42.4%), n (%) | Male (n=41,366, 57.6%), n (%) | P Value* |
|--------------------------------|---------------------------------|-----------------|-----------------|---------------------------------|-------------------------------|----------|
| Year of event                  |                                 |                 |                 |                                 |                               |          |
| 2006                           |                                 | 3395            | 4.7             | 1457 (4.8)                      | 1938 (4.7)                    | 0.07     |
| 2007                           |                                 | 4943            | 6.9             | 2219 (7.3)                      | 2724 (6.6)                    |          |
| 2008                           |                                 | 5651            | 7.9             | 2398 (7.9)                      | 3253 (7.9)                    |          |
| 2009                           |                                 | 5851            | 8.2             | 2527 (8.3)                      | 3324 (8.0)                    |          |
| 2010                           |                                 | 4936            | 6.9             | 2142 (7.0)                      | 2794 (6.8)                    |          |
| 2011                           |                                 | 5375            | 7.5             | 2296 (7.5)                      | 3079 (7.4)                    |          |
| 2012                           |                                 | 6218            | 8.7             | 2676 (8.8)                      | 3542 (8.6)                    |          |
| 2013                           |                                 | 8161            | 11.4            | 3421 (11.2)                     | 4740 (11.5)                   |          |
| 2014                           |                                 | 8777            | 12.2            | 3654 (12.0)                     | 5123 (12.4)                   |          |
| 2015                           |                                 | 9354            | 13.0            | 3863 (12.7)                     | 5491 (13.3)                   |          |
| 2016                           |                                 | 9159            | 12.8            | 3801 (12.5)                     | 5358 (13.0)                   |          |
| Age at time of event, y        | 18–49                           | 11,014          | 15.3            | 4759 (15.6)                     | 6255 (15.1)                   | <0.0001  |
|                                | 50–59                           | 12,862          | 17.9            | 5115 (16.8)                     | 7747 (18.7)                   |          |
|                                | 60–69                           | 17,638          | 24.6            | 7104 (23.3)                     | 10,534 (25.5)                 |          |
|                                | 70–79                           | 17,188          | 23.9            | 7272 (23.9)                     | 9916 (24.0)                   |          |
|                                | 80+                             | 13,118          | 18.3            | 6204 (20.4)                     | 6914 (16.7)                   |          |
| Race/ethnicity                 | Non-Hispanic white              | 46,708          | 65.0            | 18,774 (61.7)                   | 27,934 (67.5)                 | <0.0001  |
|                                | Non-Hispanic black              | 15,938          | 22.2            | 7916 (26.0)                     | 8022 (19.4)                   |          |
|                                | Hispanic/other/unknown           | 9,174           | 12.8            | 3764 (12.4)                     | 5410 (13.1)                   |          |
| Cerebral performance category  | 1: Good cerebral performance    | 32,750          | 45.6            | 13,341 (43.8)                   | 19,413 (46.9)                 | <0.0001  |
| at admission                   | 2: Moderate cerebral disability | 10,773          | 15.0            | 4817 (15.8)                     | 5956 (14.4)                   |          |
|                                | 3: Severe cerebral disability   | 5,817           | 8.1             | 2653 (8.7)                      | 3169 (7.7)                    |          |
|                                | 4,5: Coma/brain death           | 3,878           | 5.4             | 1,594 (5.2)                     | 2,296 (5.6)                   |          |
|                                | 6: Missing                      | 18,601          | 25.9            | 8,049 (26.4)                    | 10,532 (25.5)                 |          |
| Illness category               | Medical-cardiac                 | 24,726          | 34.4            | 10,055 (33.0)                   | 14,671 (35.5)                 | <0.0001  |
|                                | Medical-noncardiac              | 31,369          | 43.7            | 14,388 (47.2)                   | 16,981 (41.1)                 |          |
|                                | Surgical-cardiac                | 5,952           | 8.3             | 2,186 (7.2)                     | 3,766 (9.1)                   |          |
|                                | Surgical-noncardiac             | 7,660           | 10.7            | 3,252 (10.7)                    | 4,408 (10.7)                  |          |
|                                | Trauma/other                    | 2,113           | 2.9             | 573 (1.9)                       | 1,540 (3.7)                   |          |
| Acute CNS nonstroke event      |                                 | 47,15           | 6.6             | 20,95 (6.9)                     | 26,20 (6.3)                   | 0.006    |
| Acute stroke                   |                                 | 28,75           | 4.0             | 12,62 (4.1)                     | 16,13 (3.9)                   | 0.10     |
| CHF this admission             |                                 | 12,420          | 17.3            | 5,115 (16.8)                    | 7,305 (17.7)                  | 0.003    |
| CHF prior admission            |                                 | 15,759          | 21.9            | 6,548 (21.5)                    | 9,211 (22.3)                  | 0.01     |
| Diabetes mellitus              |                                 | 24,785          | 34.5            | 10,586 (34.8)                   | 14,199 (34.3)                 | 0.26     |
| Hepatic insufficiency          |                                 | 5,942           | 8.3             | 2,222 (7.3)                     | 3,720 (8.0)                   | <0.0001  |
| Hypotension/hypoperfusion      |                                 | 17,614          | 24.5            | 7,504 (24.6)                    | 10,110 (24.4)                 | 0.57     |
| Metastatic/hematologic malignancy |                             | 8,096           | 11.3            | 3,492 (11.5)                    | 4,604 (11.1)                  | 0.22     |
| Metabolic electrolyte abnormality |                             | 13,668          | 19.0            | 5,926 (19.5)                    | 7,742 (18.7)                  | 0.03     |

Continued
who had withdrawal of life-sustaining therapy <72 hours after being resuscitated from out-of-hospital cardiac arrest, ≈3.5% of patients may have survived to hospital discharge neurologically intact had guidelines recommending delaying neuroprognostication until 72 hours after achieving normothermia been followed.26 In this study, investigators also found an association between women and early withdrawal of life-sustaining therapy for neurologic reasons,26 further supporting our hypothesis that sex differences exists in how patients are managed after cardiac arrest.

Although we were unable to clearly identify the reasons why DNAR was established in this large cohort, we assume that a proportion are due to concerns about poor neurologic recovery. In the study of out-of-hospital cardiac arrest by Elmer et al,26 overall 38% of the study cohort had withdrawal of life sustaining therapy for neurologic reasons, of which 57% underwent early withdrawal of life-sustaining therapy (<72 hours after ROSC) due to poor perceptions of neurologic recovery. Current guidelines for determining neuroprognostication after cardiac arrest recommend delaying testing and

| Characteristic                        | Category            | All Patients, n | All Patients, % | Female (n=30 454, 42.4%), n (%) | Male (n=41 366, 57.6%), n (%) | P Value*  |
|--------------------------------------|---------------------|-----------------|----------------|---------------------------------|-------------------------------|-----------|
| MI this admission                    |                     | 10 132          | 14.1           | 3786 (12.4)                     | 6346 (15.3)                   | <0.0001   |
| MI prior admission                   |                     | 10 334          | 14.4           | 3661 (12.0)                     | 6673 (16.1)                   | <0.0001   |
| Pneumonia                            |                     | 11 141          | 15.5           | 4611 (15.1)                     | 6530 (15.8)                   | 0.03      |
| Renal insufficiency                  |                     | 27 163          | 37.8           | 11 107 (36.5)                   | 16 056 (38.8)                 | <0.0001   |
| Respiratory insufficiency            |                     | 32 611          | 45.4           | 14 023 (46.1)                   | 18 588 (44.9)                 | 0.007     |
| Septicemia                           |                     | 14 027          | 19.5           | 6237 (20.5)                     | 7790 (18.8)                   | <0.0001   |
| Assisted or mechanical vent in place |                     | 23 793          | 33.1           | 10 133 (33.3)                   | 13 660 (33.0)                 | 0.51      |
| Any vasoactive agent in place        |                     | 17 838          | 24.8           | 7428 (24.4)                     | 10 410 (25.2)                 | 0.03      |
| Induced hypothermia initiated        | Yes                 | 3503            | 4.9            | 1333 (4.4)                      | 2170 (5.2)                    | <0.0001   |
|                                      | No/ND               | 59 499          | 82.8           | 25 297 (83.1)                   | 34 202 (82.7)                 |           |
|                                      | NA                  | 7437            | 10.4           | 3230 (10.6)                     | 4207 (10.2)                   |           |
|                                      | Missing             | 1381            | 1.9            | 594 (2.0)                       | 787 (1.9)                     |           |
| First pulseless rhythm               | Asystole            | 19 642          | 27.3           | 8741 (28.7)                     | 10 901 (28.4)                 | <0.0001   |
|                                      | PEA                 | 37 441          | 52.1           | 16 101 (52.9)                   | 21 340 (51.6)                 |           |
|                                      | pVT                 | 6841            | 9.5            | 2555 (8.4)                      | 4286 (10.4)                   |           |
|                                      | VF                  | 7896            | 11.0           | 3057 (10.0)                     | 4839 (11.7)                   |           |
| VF or pVT at any time                |                     | 23 136          | 32.2           | 9031 (29.7)                     | 14 105 (34.1)                 | <0.0001   |
| Event witnessed                      |                     | 61 887          | 86.2           | 26 324 (86.4)                   | 35 563 (86.0)                 | 0.15      |
| Compressions                         |                     | 70 770          | 98.5           | 30 030 (99.6)                   | 40 740 (98.5)                 | 0.18      |
| Event duration, min                  | 0–5                 | 23 146          | 32.2           | 9902 (32.5)                     | 13 244 (32.0)                 | 0.15      |
|                                      | 6–10                | 17 006          | 23.7           | 7243 (23.8)                     | 9763 (23.6)                   |           |
|                                      | 11–20               | 17 118          | 23.8           | 7124 (23.4)                     | 9994 (24.2)                   |           |
|                                      | ≥21                 | 14 550          | 20.3           | 6185 (20.3)                     | 8365 (20.2)                   |           |
| Survived to hospital discharge       |                     | 25 663          | 35.7           | 10 491 (34.5)                   | 15 172 (36.7)                 | <0.0001   |
| Declared DNAR order during this admission |             | 31 695          | 44.1           | 13 692 (45.0)                   | 18 003 (43.5)                 | 0.0004    |
| If declared DNAR,1 DNAR was established <12 h after ROSC | | 15 463 | 48.8 | 7096 (51.8) | 8367 (46.5) | <0.0001 |
| If declared DNAR,1 DNAR was established <72 h after ROSC | | 23 147 | 73.0 | 10 388 (75.9) | 12 759 (70.9) | <0.0001 |

CHF indicates congestive heart failure; CNS, central nervous system; NA, not applicable; ND, not documented; DNAR, do not attempt resuscitation; MI, myocardial infarction; PEA, pulseless electrical activity; pVT, pulseless ventricular tachycardia; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

*All P values are adjusted for clustering within site.

†n=31 695.
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**Table 2. ARR of Establishment of DNAR for Female Versus Male Patients**

| Characteristic | Denominator | ARR | Lower 95% CI | Upper 95% CI | P Value |
|---------------|-------------|-----|--------------|--------------|---------|
| DNAR at any time | 71 820 | 1.15 | 1.10 | 1.20 | <0.0001 |
| Of those with DNAR at any time, DNAR <12 h | 31 695 | 1.40 | 1.30 | 1.52 | <0.0001 |
| Of those with DNAR at any time, DNAR <72 h | 31 695 | 1.35 | 1.26 | 1.45 | <0.0001 |

All models adjusted for significant demographic variables, clinical characteristics, arrest characteristics, and length of time at risk for the outcome. ARR indicates adjusted relative risk; DNAR, do not attempt resuscitation.

examination until patients are without the effects of sedating medications, have become normothermic, and have had sufficient time for neurologic recovery.\(^2^0\) As of 2015, the International Liaison Committee on Resuscitation and the American Heart Association stated that the earliest time when one could establish a neurologic prognosis is 72 hours after arrival at normothermia.\(^2^0\) Investigators have begun to encourage even longer delays in establishing neuroprognosis because of a cohort of patients, called delayed awakensers, who return to prearrest conditions well after 72 hours following normothermia.\(^2^7^2^8\) To this end, we a priori selected 72 hours as a cutoff for early DNAR. In our analysis, just >1 in 4 patients had early DNAR, and early DNAR was slightly more common for women. Understanding the contributors to goals of care decisions early after arrest will assist with future guidelines informing quality of care.

Although the variable nature of DNAR utilization found in this study might indicate better end-of-life planning by women or worse prognosis in women, the results of this study have implications for postarrest critical care practice moving forward. Guideline adherence has been found to reduce practice variability, and the provision of post–cardiac arrest care and neuroprognostic practice would benefit from further adherence to expert guideline. In addition, implicit bias has been culprit in previous findings of different practice between men and women; therefore, increasing awareness may reduce unequal practice.\(^5^9\) We intend for these data to serve as a topic for further investigation to understand the barriers and facilitators to equal healthcare delivery and end-of-life decisions in post–cardiac arrest care.

This retrospective study has limitations that must be highlighted. First and foremost, we cannot account for patient preference, which is integral to making end-of-life decisions or decisions about aggressiveness of hospital intervention. More robust qualitative data are necessary to clearly understand the drivers of variability in DNAR use that were uncovered in this study. Understanding patient preference, provider implicit bias, and surrogate decision making in post–cardiac arrest care may be revealing in understanding the phenomenon uncovered in this quantitative study. Second, these data explore DNAR use and not withdrawal of life-sustaining therapy, and families might opt for a DNAR order in case their loved one rearssets but wish to have no restrictions on care. However, prior literature has shown the presence of a DNAR is associated with less aggressive interventions and is not restricted to cardiopulmonary resuscitation in the setting of rearser.\(^1^2\) How the establishment of a DNAR order correlates with the decision to withdraw life-sustaining therapy cannot be elucidated from the data maintained in this registry. In addition, we were unable to compare the severity of illness after ROSC between men and women. Understanding the processes, data interpretation, and humanistic properties of complex end-of-life decision making requires granular exploration with qualitative methodology.

**Table 3. ARR of Survival to Hospital Discharge Utilizing a Multivariable Log Poisson Model With Robust SEs Adjusted For Clustering Within Hospital**

| Characteristic | ARR | Lower 95% CI | Upper 95% CI | P Value |
|---------------|-----|--------------|--------------|---------|
| Female | 1.00 | 0.99 | 1.02 | 0.74 |
| DNAR status | | | | |
| No DNAR or DNAR ≥72 h | Referent | ... | ... | ... |
| DNAR <72 h | 0.15 | 0.14 | 0.17 | <0.0001 |

All models adjusted for demographic variables, clinical characteristics, arrest characteristics. ARR indicates adjusted relative risk; DNAR, do not attempt resuscitation.

Conclusions

In comparison to men, women who experience in-hospital cardiac arrest have a greater likelihood of having a DNAR established anytime after ROSC and early (<12 and <72 hours) after ROSC. This association persisted after accounting for observed differences in demographics and in patient and cardiac arrest characteristics. Despite higher rates of DNAR use, women were as likely to survive to hospital discharge as men. Future studies are needed to determine whether higher rates of early establishment of DNAR orders after ROSC have an effect on women’s overall survival from cardiac arrest or reflect more appropriate end-of-life decision making.

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Appendix

Get With The Guidelines–Resuscitation Investigators

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Disclosures

None.

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SUPPLEMENTAL MATERIAL
| Variable                  | Category            | Females (n=30454) | Males (n=41366) | P-value* |
|---------------------------|---------------------|-------------------|-----------------|----------|
|                          | DNAR During Admission | Yes (N=13692)    | Yes (N=18003)  |          |
|                          |                     | No (N=16762)      | No (N=23363)    |          |
| Calendar year of event   | 2006                | 633 (4.6%)        | 780 (4.3%)      | 0.01     |
|                          |                     | 824 (4.9%)        | 1158 (5.0%)     |          |
|                          | 2007                | 925 (6.8%)        | 1084 (6.0%)     | 0.001    |
|                          |                     | 1294 (7.7%)       | 1640 (7.0%)     |          |
|                          | 2008                | 963 (7.0%)        | 1309 (7.3%)     | 0.001    |
|                          |                     | 1435 (8.6%)       | 1944 (8.3%)     |          |
|                          | 2009                | 1086 (7.9%)       | 1336 (7.4%)     | 0.001    |
|                          |                     | 1441 (8.6%)       | 1988 (8.5%)     |          |
|                          | 2010                | 896 (6.5%)        | 1130 (6.3%)     | 0.001    |
|                          |                     | 1246 (7.4%)       | 1664 (7.1%)     |          |
|                          | 2011                | 1002 (7.3%)       | 1262 (7.0%)     | 0.001    |
|                          |                     | 1294 (7.7%)       | 1817 (7.8%)     |          |
|                          | 2012                | 1155 (8.4%)       | 1457 (8.1%)     | 0.001    |
|                          |                     | 1521 (9.1%)       | 2085 (8.9%)     |          |
|                          | 2013                | 1591 (11.6%)      | 2110 (11.7%)    | 0.001    |
|                          |                     | 1830 (10.9%)      | 2630 (11.3%)    |          |
|                          | 2014                | 1749 (12.8%)      | 2372 (13.2%)    | 0.001    |
|                          |                     | 1905 (11.4%)      | 2751 (11.8%)    |          |
|                          | 2015                | 1866 (13.6%)      | 2583 (14.3%)    | 0.001    |
|                          |                     | 1997 (11.9%)      | 2908 (12.4%)    |          |
|                          | 2016                | 1826 (13.3%)      | 2580 (14.3%)    | 0.001    |
|                          |                     | 1975 (11.8%)      | 2778 (11.9%)    |          |
| Age at event in years    | 18-49               | 1678 (12.3%)      | 2014 (11.2%)    | 0.001    |
|                          |                     | 3081 (18.4%)      | 4241 (18.2%)    |          |
|                          | 50-59               | 1986 (14.5%)      | 3015 (16.7%)    | 0.001    |
|                          |                     | 3129 (18.7%)      | 4732 (20.3%)    |          |
|                          | 60-69               | 3155 (23.0%)      | 4435 (24.6%)    | 0.001    |
|                          |                     | 3949 (23.6%)      | 6099 (26.1%)    |          |
|                          | 70-79               | 3508 (25.6%)      | 4698 (26.1%)    | 0.001    |
|                          |                     | 3764 (22.5%)      | 5218 (22.3%)    |          |
|                          | 80+                 | 3365 (24.6%)      | 3841 (21.3%)    | 0.001    |
|                          |                     | 2839 (16.9%)      | 3073 (13.2%)    |          |
| Race/Ethnicity           | Non-Hispanic White  | 8703 (63.6%)      | 12423 (69.0%)   | 0.001    |
|                          |                     | 10071 (60.1%)     | 15511 (66.4%)   |          |
|                          | Non-Hispanic Black  | 3503 (25.6%)      | 3476 (19.3%)    | 0.001    |
|                          |                     | 4413 (26.3%)      | 4546 (19.5%)    |          |
| Variable                                      | Category                        | Females (n=30454) | Males (n=41366) | P-value* |
|----------------------------------------------|---------------------------------|-------------------|-----------------|----------|
|                                              |                                 | Yes (N=13692)     | No (N=16762)    |          |
| Females                                      |                                 | 1486 (10.9%)      | 2278 (13.6%)    |          |
| Males                                        |                                 | 2104 (11.7%)      | 3306 (14.2%)    |          |
| Cerebral Performance Category at Admission   | Hispanic / Other / Unknown      | 5626 (41.1%)      | 7715 (46.0%)    | <0.001   |
|                                              | 2424 (17.7%)                    | 2393 (14.3%)      | 2949 (16.4%)    |          |
|                                              | 1417 (10.3%)                    | 1236 (7.4%)       | 1694 (9.4%)     |          |
|                                              | 864 (6.3%)                      | 730 (4.4%)        | 1177 (6.5%)     |          |
| Illness Category                             | Medical-Cardiac                 | 4200 (30.7%)      | 5855 (34.9%)    | <0.001   |
|                                              | Medical-Noncardiac              | 7256 (53.0%)      | 7132 (42.5%)    |          |
|                                              | Surgical-Cardiac                | 582 (4.3%)        | 1604 (9.6%)     |          |
|                                              | Surgical-Noncardiac             | 1428 (10.4%)      | 1824 (10.9%)    |          |
|                                              | Trauma/Other                    | 226 (1.7%)        | 347 (2.1%)      |          |
|                                              | Acute CNS Non-Stroke Event      | 1016 (7.4%)       | 1079 (6.4%)     | 0.02     |
|                                              | Acute Stroke                    | 652 (4.8%)        | 610 (3.6%)      | <0.001   |
|                                              | CHF Prior Admission             | 3115 (22.8%)      | 3433 (20.5%)    | 0.001    |
|                                              | CHF This Admission              | 2309 (16.9%)      | 2806 (16.7%)    | 0.83     |
|                                              | Diabetes Mellitus               | 4882 (35.7%)      | 5704 (34.0%)    | 0.009    |
|                                              | Hepatic Insufficiency           | 1181 (8.6%)       | 1041 (6.2%)     | <0.001   |
|                                              | Hypotension or Hypoperfusion    | 3853 (28.1%)      | 3651 (21.8%)    | <0.001   |
| Variable                                | Females (n=30454) | Males (n=41366) |                           | Females (n=30454) | Males (n=41366) |                           |
|-----------------------------------------|-------------------|-----------------|---------------------------|-------------------|-----------------|---------------------------|
|                          | DNAR During Admission | DNAR During Admission |                           | DNAR During Admission | DNAR During Admission |                           |
|                          | Category          | Yes (N=13692)   | No (N=16762)   | P-value* | Yes (N=18003)   | No (N=23363)   | P-value* |                           |
| Metastatic / Hematologic Malignancy    |                   | 1955 (14.3%)    | 1537 (9.2%)    | <0.001   | 2599 (14.4%)    | 2005 (8.6%)    | <0.001   |                           |
| Metabolic Electrolyte Abnormality      |                   | 2994 (21.9%)    | 2932 (17.5%)   | <0.001   | 3964 (22.0%)    | 3778 (16.2%)   | <0.001   |                           |
| MI this Admission                     |                   | 1611 (11.8%)    | 2175 (13.0%)   | 0.007    | 2404 (13.4%)    | 3942 (16.9%)   | <0.001   |                           |
| MI Prior Admission                     |                   | 1711 (12.5%)    | 1950 (11.6%)   | 0.04     | 2863 (15.9%)    | 3810 (16.3%)   | 0.35     |                           |
| Pneumonia                              |                   | 2284 (16.7%)    | 2327 (13.9%)   | <0.001   | 3252 (18.1%)    | 3278 (14.0%)   | <0.001   |                           |
| Renal Insufficiency                    |                   | 5509 (40.2%)    | 5598 (33.4%)   | <0.001   | 7869 (43.7%)    | 8187 (35.0%)   | <0.001   |                           |
| Respiratory Insufficiency              |                   | 6885 (50.3%)    | 7138 (42.6%)   | <0.001   | 8830 (49.0%)    | 9758 (41.8%)   | <0.001   |                           |
| Septicemia                             |                   | 3306 (24.1%)    | 2931 (17.5%)   | <0.001   | 4032 (22.4%)    | 3758 (16.1%)   | <0.001   |                           |
| Assisted or Mechanical Vent            |                   | 4900 (35.8%)    | 5233 (31.2%)   | <0.001   | 6284 (34.9%)    | 7376 (31.6%)   | <0.001   |                           |
| Any Vasoactive Agent                   |                   | 3632 (26.5%)    | 3796 (22.6%)   | <0.001   | 4928 (27.4%)    | 5482 (23.5%)   | <0.001   |                           |
| Induced hypothermia initiated           |                   | 718 (5.2%)      | 615 (3.7%)     | <0.001   | 1177 (6.5%)     | 993 (4.3%)     | <0.001   |                           |
| No / Not Documented                    |                   | 11218 (81.9%)   | 14079 (84.0%)  | 14637 (81.3%) | 19565 (83.7%)  |                           |
| N/A                                    |                   | 1534 (11.2%)    | 1696 (10.1%)   | 1945 (10.8%) | 2262 (9.7%)     |                           |
| Missing                                |                   | 222 (1.6%)      | 372 (2.2%)     | 244 (1.4%) | 543 (2.3%)      |                           |
| First Pulseless Rhythm                 | Asystole          | 4120 (30.1%)    | 4621 (27.6%)   | <0.001   | 4932 (27.4%)    | 5969 (25.5%)   | <0.001   |                           |
|                                         | Pulseless Electrical Activity (PEA) | 7740 (56.5%) | 8361 (49.9%) | <0.001 | 10112 (56.2%) | 11228 (48.1%) |           |                           |
|                                         | Pulseless Ventricular Tachycardia | 861 (6.3%) | 1694 (10.1%) | 1474 (8.2%) | 2812 (12.0%) |                           |
| Variable | Category | Females (n=30454) | Males (n=41366) | P-value* |
|----------|----------|-------------------|-----------------|----------|
|          |          | DNAR During Admission | DNAR During Admission |          |
| Ventricular Fibrillation (VF) | Yes (N=13692) | 971 (7.1%) | 1485 (8.2%) | <0.001 |
|          | No (N=16762) | 2086 (12.4%) | 3354 (14.4%) | <0.001 |
| VFib or Pulseless VTach at any time | Yes (N=18003) | 5391 (29.9%) | 8714 (37.3%) <0.001 |
|          | No (N=23363) | 3641 (12.4%) | 20373 (87.2%) <0.001 |
| Event Witnessed | Yes (N=13692) | 11686 (85.3%) | 15190 (84.4%) | <0.001 |
|          | No (N=16762) | 14638 (87.3%) | 20373 (87.2%) <0.001 |
| Compressions | Yes (N=13692) | 13572 (99.1%) | 17845 (99.1%) | <0.001 |
|          | No (N=16762) | 16458 (98.2%) | 22895 (98.0%) <0.001 |
| Event duration in minutes | 0-5 min | Yes (N=13692) | 3842 (28.1%) | 4860 (27.0%) | <0.001 |
|          | No (N=16762) | 6060 (36.2%) | 8384 (45.9%) <0.001 |
|          | 6-10 min | Yes (N=13692) | 3455 (25.2%) | 4471 (24.8%) | <0.001 |
|          | No (N=16762) | 3788 (22.6%) | 5292 (27.7%) | <0.001 |
|          | 11-20 min | Yes (N=13692) | 3470 (25.3%) | 4760 (26.4%) | <0.001 |
|          | No (N=16762) | 3654 (21.8%) | 5234 (22.4%) | <0.001 |
|          | 21 min or more | Yes (N=13692) | 2925 (21.4%) | 3912 (21.7%) | <0.001 |
|          | No (N=16762) | 3260 (19.4%) | 4453 (21.1%) | <0.001 |
| Died | Yes (N=13692) | 12419 (90.7%) | 16357 (90.9%) | <0.001 |
|          | No (N=16762) | 7544 (45.0%) | 9837 (42.1%) | <0.001 |

* All p-values are adjusted for clustering within site