MAYO CLINIC

ORIGINAL ARTICLE

Palliative Care Use in Patients With Acute Myocardial Infarction and Do-Not-Resuscitate Status From a Nationwide Inpatient Cohort

Ofer Kobo, MD, MHA; Saadiq M. Moledina, MRCP(UK); Mohamed O. Mohamed, PhD; Aynharan Sinnarajah, MD, MPH; Jessica Simon, MBChB; Louise Y. Sun, MD; Michael Slawnych, MD, PhD; David L. Fischman, MD; Ariel Roguin, MD, PhD; and Mamas A. Mamas, DPhil

Abstract

Objective: To examine the predictors, treatments, and outcomes of the use of palliative care in patients hospitalized with acute myocardial infarction (AMI) who had a do-not-resuscitate (DNR) order.

Patients and Methods: Using the National (Nationwide) Inpatient Sampling database for 2015-2018, we examined the predictors, in-hospital procedures, and outcomes of palliative care recipients among patients with AMI who had a DNR order.

Results: We identified 339,270 admissions with AMI that had a DNR order, including patients who received palliative care (n=113,215 [33.4%]). Compared with patients who did not receive palliative care, these patients were more frequently younger (median age, 81 vs 83 years; $P<.001$), were less likely to be female (50.9% [57,626 of 113,215] vs 54.7% [123,652 of 226,055]; $P<.001$), and were more likely to present with cardiac arrest (11.6% [13,133 of 113,215] vs 6.9% [15,598 of 226,055]; $P<.001$). Patients were more likely to receive palliative care at a large (odds ratio [OR], 1.47; 95% CI, 1.44 to 1.50) or teaching (OR, 2.10; 95% CI, 2.04 to 2.16) hospitals compared with small or rural ones. Patients receiving palliative care were less likely to be treated invasively, with reduced rates of invasive coronary angiography (OR, 0.46; 95% CI, 0.45 to 0.47) and percutaneous coronary intervention (OR, 0.47; 95% CI, 0.45 to 0.48), and were more likely to die in the hospital (52.4% [59,325 of 113,215] vs 22.9% [51,766 of 226,055]).

Conclusion: In patients who had a DNR status and were hospitalized and received a diagnosis of AMI, only one-third received palliative care.

 ■ Mayo Clin Proc. 2022;■■(■):1-10

Despite advances in pharmacological treatments and timely revascularization, acute myocardial infarction (AMI) remains one of the leading causes of death in the United States.[1] Documentation of a do-not-resuscitate (DNR) order is part of end-of-life care that allows patients to forgo cardiopulmonary resuscitation in the event of a cardiac arrest.[2] Hospitalized patients with AMI who have a DNR order represent a heterogeneous group of patients who are generally older, have multiple comorbidities, are less likely to receive invasive management, and have a significantly greater mortality burden.[3]

Integration of palliative care services in the care of patients with advanced illnesses has been found to have numerous benefits, including, but not limited to, helping alleviate the physical and psychological discomfort of patients and their families in addition to assisting in the transition of care after an intensive care unit (ICU) stay.[4,5] Although the use of both DNR orders[3,6] and palliative

From the Department of Cardiology, Hillel Yaffe Medical Centre, Hadera, Israel (O.K., A.R.); Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, Keele, UK (O.K., S.M.M., M.O.M., M.A.M.); Department of Medicine, Queens Uni-

Affiliations continued at the end of this article.

care[5] has been investigated independently previously in patients with AMI, little is known about the use of palliative care in patients hospitalized with AMI and a concomitant DNR order.

Thus, using data from a large nationwide database, we examined the predictors, treatments, and outcomes of the use of palliative care in patients hospitalized with AMI who had a DNR order.

PATIENTS AND METHODS

The National (Nationwide) Inpatient Sample (NIS), the largest all-payer inpatient health care database in the United States, was developed by the Healthcare Cost and Utilization Project and sponsored by the Agency for Healthcare Research and Quality.[7] Since 2012, the NIS samples discharge from all hospitals participating in the Healthcare Cost and Utilization Project, approximating a 20% stratified sample of all discharges from US community hospitals.

We analyzed all adult (≥18 years) patients hospitalized with a principal diagnosis of AMI who also had a DNR status from October 1, 2015, through December 31, 2018. Patient and procedural characteristics were extracted using the *International Classification of Diseases, Tenth Revision* codes provided in Supplemental Table 1 (available online at http://www.mayoclinicproceedings.org). Information on patient demographic characteristics were recorded for each hospital discharge, including age, sex, race, admission day (weekday or weekend), expected primary payer, and median household income according to zip code. Patients with missing data for age, sex, elective admission, weekend admission, and mortality status were excluded from the analysis. Patients with type 2 myocardial infarction (MI) or elective admissions were also excluded from the analysis (Supplemental Figure 1, available online at http://www.mayoclinicproceedings.org). Each discharge record had information on up to 30 diagnoses. A full list of *International Classification of Diseases, Tenth Revision, Clinical Modification* codes used to identify receipt of palliative care as well as other patient characteristics and complications is provided in Supplemental Table 1. We also used *International Classification of Diseases, Tenth Revision, Clinical Modification* codes to identify procedural information during hospitalization.

The main outcome measured was in-hospital all-cause mortality. Other outcomes included in-hospital major adverse cardiovascular and cerebrovascular events (MACCEs), acute ischemic cerebrovascular accident (CVA), and major bleeding. We defined MACCE as a composite of all-cause mortality and acute ischemic CVA or transient ischemic attack. Major bleeding events were defined as a composite of gastrointestinal, retroperitoneal, intracranial, and intracerebral hemorrhage; periprocedural hemorrhage; unspecified hemorrhage; or need for a blood transfusion. Destination of discharge and receipts of invasive procedures such as invasive coronary angiography (ICA), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), mechanical ventilation, and circulatory support were also measured.

Continuous variables are presented as median and interquartile range due to skewed data, and categorical data are presented as frequencies and percentages. Categorical variables were compared using the Pearson χ^2 test, while continuous variables were compared using the Student *t* test or the Mann-Whitney *U* test, as appropriate. Sampling weights were used to calculate the estimated total discharges as specified by the Agency for Healthcare Research and Quality. Multivariable logistic regression models were used to examine the association between demographic characteristics and comorbidities and receipt of palliative care, as well as the association between receipt of palliative care and in-hospital outcomes and procedures among patients with DNR status, all expressed as odds ratios (ORs) with corresponding 95% CIs. The models were adjusted for baseline differences between the groups, controlling for the following covariates: age; sex; weekend admission; hospital size (number of beds); region and location/teaching status; ST-elevation MI (STEMI); cardiogenic shock; use of intra-aortic balloon pump, CABG, PCI, or ICA; ventricular fibrillation;

ventricular tachycardia; atrial fibrillation; heart failure; hypertension; dyslipidemia; diabetes mellitus; valvular heart disease; smoking status; chronic lung disease; chronic liver disease; chronic renal failure; anemia; obesity; thrombocytopenia; coagulopathies; and malignancies.

All statistical analyses were performed with IBM SPSS statistical software, version 26. Statistical significance was set at the 2-tailed $P=.05$ level, without multiplicity adjustment.

RESULTS

Between October 2015 and December 2018, 2,959,244 patients were admitted to US hospitals and during the hospitalization received a principal diagnosis of AMI. Application of relevant inclusion and exclusion criteria (Supplemental Figure 1) produced a study cohort of 339,270 patients, 113,215 (33.4%) of whom received palliative care. Differences in clinical characteristics between the 2 groups (those with and without palliative care) at admission are presented in Table 1. Recipients of palliative care were younger (median age, 81 vs 83 years; $P<.001$), less likely to be female (57,626 of 113,215 [50.9%] vs 123,652 of 226,055 [54.7%]; $P<.001$), less often White (89,664 of 113,215 [79.2%] vs 185,366 of 226,055 [82.0%]; $P<.001$), and less likely to have Medicare insurance (92,096 of 113,215 [81.4%] vs 197,701 of 226,055 [87.7%]; $P<.001$), while the highest proportion of patients receiving palliative care were admitted to large (61,703 of 113,215 [54.5%] vs 110,541 of 226,055 [48.9%]; $P<.001$) and teaching (81,062 of 113,215 [71.6%] vs 142,640 of 226,055 [63.1%]; $P<.001$) hospitals. Patients who received palliative care were more likely to be admitted with STEMI (23,090 of 113,215 [20.4%] vs 33,004 of 226,055 [14.6%]; $P<.001$) and to experience cardiac arrest (13,133 of 113,215 [11.6%] vs 15,598 of 226,055 [6.9%]; $P<.001$), cardiogenic shock (19,248 of 113,215 [17.0%] vs 19,441 of 226,055 [8.6%]; $P<.001$), or ventricular arrhythmias (ventricular fibrillation, 5,887 of 113,215 [5.2%] vs 6,556 of 226,055 [2.9%]; ventricular tachycardia, 9,855 of

TABLE 1. Characteristics of 339,270 Study Patients With DNR Orders, Stratified by Receipt of Palliative Care[a,b]

Variable	No palliative care	Palliative care	*P* value
No. of weighted records	226,055 (66.6)	113,215 (33.4)	NA
Age (y), median (IQR)	83 (74-90)	81 (71-89)	<.001
Female	123,652 (54.7)	57,626 (50.9)	<.001
Race			<.001
White	185,366 (82.0)	89,664 (79.2)	
Black	16,728 (7.4)	10,982 (9.7)	
Hispanic	13,111 (5.8)	6,340 (5.6)	
Asian/Pacific Islander	5,651 (2.5)	3,283 (2.9)	
Native American	904 (0.4)	453 (0.4)	
Other	4,295 (1.9)	2,493 (2.2)	
Hospital location			<.001
Northeast	51,315 (22.7)	22,545 (19.9)	
Midwest	60,131 (26.6)	30,723 (27.1)	
South	75,728 (33.5)	41,368 (36.5)	
West	38,881 (17.2)	18,579 (16.4)	
Hospital size			<.001
Small	47,019 (20.8)	18,114 (16.0)	
Medium	68,495 (30.3)	33,398 (29.5)	
Large	110,541 (48.9)	61,703 (54.5)	
Hospital location/teaching status			<.001
Rural	27,353 (12.1)	7,585 (6.7)	
Urban nonteaching	56,062 (24.8)	24,568 (21.7)	
Teaching	142,640 (63.1)	81,062 (71.6)	
Weekend admission	61,939 (27.4)	30,790 (27.2)	.16
Median zip code income			<.001
1st quartile	61,919 (27.4)	31,134 (27.5)	
2nd quartile	63,190 (28.0)	30,565 (27.0)	
3rd quartile	55,835 (24.7)	27,851 (24.6)	
4th quartile	45,111 (20.0)	23,665 (20.9)	
Expected primary payer			<.001
Medicare	197,701 (87.5)	92,096 (81.4)	
Medicaid	7,380 (3.3)	5,492 (4.9)	
Private	14,920 (6.6)	10,805 (9.5)	
Uninsured	2,713 (1.2)	1,801 (1.6)	
No charge	226 (0.1)	105 (0.1)	
Other	3,115 (1.4)	2,916 (2.6)	
Record characteristics			
STEMI	33,004 (14.6)	23,090 (20.4)	<.001
Cardiac arrest	15,598 (6.9)	13,133 (11.6)	<.001
Ventricular fibrillation	6,556 (2.9)	5,887 (5.2)	<.001
Ventricular tachycardia	14,015 (6.2)	9,855 (8.7)	<.001
Cardiogenic shock	19,441 (8.6)	19,248 (17.0)	<.001
Comorbidities			
Previous MI	33,682 (14.9)	13,925 (12.3)	<.001
Cerebrovascular disease	19,989 (8.4)	9,398 (8.3)	.71
Heart failure	127,721 (56.5)	64,080 (56.6)	.5
Valvular disease	48,602 (21.5)	20,718 (18.3)	<.001
Atrial fibrillation/flutter	83,414 (36.9)	42,342 (37.4)	<.001
Hypertension	186,948 (82.7)	87,170 (77.0)	<.001
Dyslipidemia	118,452 (52.4)	48,342 (42.7)	<.001

Continued on next page

TABLE 1. Continued

Variable	No palliative care	Palliative care	*P* value
Comorbidities, continued			
Diabetes	85,448 (37.8)	28,070 (24.8)	<.001
Smoking	80,928 (35.8)	38,708 (34.2)	<.001
Peripheral vascular disease	26,222 (11.6)	12,230 (10.8)	<.001
Chronic lung disease	66,913 (29.6)	32,275 (28.5)	<.001
Chronic renal failure	90,189 (39.9)	43,020 (38.0)	<.001
Obesity	20,334 (9.0)	8,945 (7.9)	<.001
Anemia	84,994 (37.6)	44,275 (39.1)	<.001
Thrombocytopenia	19,2107 (8.5)	12,785 (11.3)	<.001
Coagulopathy	7,911 (3.5)	7,360 (6.5)	<.001
Dementia	55,603 (24.6)	28,525 (25.2)	<.001
Chronic liver disease	2,476 (1.1)	1,590 (1.4)	<.001
Homelessness	385 (0.2)	232 (0.2)	.03
Solid malignancy	13,770 (6.1)	11,770 (10.4)	<.001
Hematologic malignancies	5,185 (2.3)	3,857 (3.4)	<.001
Metastatic cancer	7,469 (3.3)	8,040 (7.1)	<.001
In-hospital procedures			
Coronary angiography	47,026 (20.8)	16,650 (14.7)	<.001
PCI	25,989 (11.5)	9,175 (8.1)	<.001
CABG	2,476 (1.1)	915 (0.8)	<.001
Thrombolysis	206 (0.1)	42 (0.04)	<.001

[a]CABG, coronary artery bypass grafting; DNR, do-not-resuscitate; IQR, interquartile range; MI, myocardial infarction; NA, not applicable; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation MI.

[b]Data are presented as No. (percentage) of patients unless indicated otherwise.

113,215 [8.7%] vs 14,015 of 226,055 [6.2%]; both *P*<.001).

Patients who received palliative care had a lower prevalence of previous MI (13,925 of 113,215 [12.3%] vs 33,682 of 226,055 [14.9%]; *P*<.001), valvular heart disease (20,718 of 113,215 [18.3%] vs 48,602of 226,055 [21.5%]; *P*<.001), and cardiovascular risk factors including hypertension (87,170 of 113,215 [77.0%] vs 186,948 of 226,055 [82.7%]; *P*<.001), dyslipidemia (48,342 of 113,215 [42.7%] vs 118,452 of 226,055 [52.4%]; *P*<.001), and diabetes mellitus (28,070 of 113,215 [24.8%] vs 85,448 of 226,055 [37.8%]; *P*<.001). Conversely, they had a higher prevalence of thrombocytopenia (12,785 of 113,215 [11.3%] vs 19,2107 of 226,055 [8.5%]; *P*<.001), coagulopathy (7,360 of 113,215 [6.5%] vs 7,911 of 226,055 [3.5%]; *P*<.001), and malignancies (solid, 11,770 of 113,215 [10.4%] vs 13,770 of 226,055 [6.1%]; hematologic, 3,857 of 113,215 [3.4%] vs 5,185 of 226,055 [2.3%]; metastatic, 8,040 of 113,215 [7.1%] vs 7,469 of 226,055 [3.3%]; all *P*<.001) compared with those who did not receive palliative care.

The destination of discharge for patients is shown in Supplemental Figure 2 (available online at http://www.mayoclinicproceedings.org). Recipients of palliative care were less likely to be discharged home (3,290 of 113,215 [2.9%] vs 42,510 of 226,055 [18.8%]) and to receive home health care (16,417of 113,215 [14.5%] vs 38,437 of 226,055 [17.0%]) and were more likely to die in the hospital (59,325 of 113,215 [52.4%] vs 51, 766 of 226,055 [22.9%]).

Factors independently associated with receipt of palliative care are summarized in Supplemental Table 2 (available online at http://www.mayoclinicproceedings.org). Positive predictors included Black (OR,1.12; 95% CI, 1.09 to 1.15) or Asian/Pacific Islander (OR, 1.17; 95% CI, 1.11 to 1.22) race and medium (OR,1.26; 95% CI, 1.23 to 1.29), large (OR, 1.47; 95% CI, 1.44 to 1.50), urban (OR, 1.59; 95% CI, 1.54 to 1.64), and teaching (OR, 2.10; 95% CI, 2.04 to 2.16) hospitals. Comorbidities including thrombocytopenia (OR, 1.19; 95% CI, 1.16 to 1.22), dementia (OR, 1.22; 95% CI, 1.20 to 1.24), malignancies (solid—OR,1.32; 95% CI, 1.28 to 1.36; hematologic—OR, 1.32; 95% CI, 1.26 to 1.38), and metastases (OR, 1.62; 95% CI, 1.55 to 1.69) were positive predictors of palliative care receipt. Female sex was a negative predictor for receipt of palliative care (OR, 0.93; 95% CI, 0.91 to 0.95), as were traditional cardiovascular risk factors (hypertension—OR, 0.83; 95% CI, 0.81 to 0.95; dyslipidemia—OR, 0.75; 95% CI, 0.74 to 0.76; diabetes—OR, 0.92; 95% CI, 0.91 to 0.94; smoking—OR, 0.88; 95% CI, 0.87 to 0.90; and obesity—OR, 0.86; 95% CI, 0.84 to 0.88).

Differences in the management strategy and outcomes between the 2 groups are presented in Table 2. Patients who received palliative care were less likely to undergo ICA (16,670 of 113,215 [14.7%] vs 47,026 of 226,055 [20.8%]; *P*<.001), PCI (9,230 of 113,215 [8.1%] vs 25,989 of 226,055 [11.5%]; *P*<.001), or CABG (915of 113,215

[0.8%] vs 2,476 of 226,055 [1.1%]; $P<.001$). They were more likely to receive circulatory support (5,890 of 113,215 [5.2%] vs 7,230 of 226,055 [3.2%]; $P<.001$) or undergo mechanical ventilation during admission (37,140 of 113,215 [32.8%] vs 37,980 of 226,055 [16.8%]; $P<.001$).

In-hospital mortality (59,325 of 113,215 [52.4%] vs 51,766 of 226,055 [22.9%]; $P<.001$), acute ischemic CVA (10,313 of 113,215 [9.1%] vs 10,178 of 226,055 [4.5%]; $P<.001$), major bleeding (12,230 of 113,215 [10.8%] vs 16,720 of 226,055 [7.4%]; $P<.001$), and MACCE (64,772 of 113,215 [57.2%] vs 61,045 of 226,055 [27.0%]; $P<.001$) were all significantly more frequent in the palliative care group.

When adjusted for important baseline characteristics and comorbidities (Table 3), patients receiving palliative care had lower odds of ICA (OR, 0.46; 95% CI, 0.45 to 0.47) and PCI (OR, 0.47; 95% CI, 0.45 to 0.48) and higher odds of adverse in-hospital clinical outcomes such as mortality (OR, 3.18; 95% CI, 3.13 to 3.23), acute ischemic CVA (OR, 2.01; 95% CI, 1.95 to 2.06), MACCE (OR, 3.08; 95% CI, 3.03 to 3.13), and major bleeding (OR, 1.30; 95% CI, 1.26 to 1.33).

Our key study findings are summarized in the Figure.

TABLE 2. In-Hospital Procedures and Outcomes Among 339,270 Study Patients With DNR Status, Stratified by Receipt of Palliative Care[a,b]

Variable	No palliative care, No. (%)	Palliative care, No. (%)	*P* value
No. of weighted records	226,055 (66.6)	113,215 (33.4)	NA
In-hospital procedures			
Coronary angiography	47,026 (20.8%)	16,670 (14.7%)	<.001
PCI	25,989 (11.5%)	9,230 (8.1%)	<.001
CABG	2,476 (1.1%)	915 (0.8%)	<.001
Thrombolysis	206 (0.1%)	42 (0.04)	<.001
Circulatory support (including IABP, LV assist device, and ECMO)	7,230 (3.2%)	5,890 (5.2%)	<.001
Mechanical ventilation	37,980 (16.8%)	37,140 (32.8%)	<.001
In-hospital outcomes			
MACCE[b]	61, 045 (27.0%)	64, 775 (57.2%)	<.001
Mortality	51,766 (22.9%)	59,325 (52.4%)	<.001
Acute ischemic CVA	10,178 (4.5%)	10,313 (9.1%)	<.001
Major bleeding	16,720 (7.4%)	12 ,230 (10.8%)	<.001
GI bleed	13,150 (5.8%)	8,270 (7.3%)	<.001
Procedure-related bleeding	930 (0.4%)	455 (0.4%)	.07
Retroperitoneal bleed	460 (0.2%)	448 (0.4%)	<.001
Intracranial hemorrhage	2,490 (1.1%)	3405 (3.0%)	<.001

[a]CABG, coronary artery bypass grafting; CVA, cerebrovascular accident; DNR, do-not-resuscitate; ECMO, extracorporeal membrane oxygenation; GI, gastrointestinal; IABP, intra-aortic balloon pump; LV, left ventricle; MACCE, major adverse cardiovascular and cerebrovascular event; NA, not applicable; PCI, percutaneous coronary intervention.

[b]MACCE is defined as a composite of all-cause mortality, acute ischemic CVA or transient ischemic attack, and cardiac complications.

DISCUSSION

The results of this analysis of more than 300,000 patients with a DNR status who were admitted to US hospitals between 2015 and 2018 and during the hospitalization received a diagnosis of AMI revealed several important findings. First, only 1 of 3 patients in this heterogeneous group received palliative care. Second, patients less frequently received palliative care if they were female or presented with cardiovascular risk factors including previous MI, hypertension, dyslipidemia, diabetes, or smoking, whereas they were more likely to receive palliative care if they had comorbidities including heart failure, malignancy (solid or hematologic), or metastatic cancer. Third, they were less likely to obtain palliative care if they presented at a small hospital compared with a medium or large hospital or presented to a rural hospital compared with a suburban or teaching hospital. Fourth, patients who were in receipt of palliative care were less likely to receive in-hospital procedures including ICA and PCI. Finally, patients with a DNR status who obtained palliative care had increased adjusted odds of in-hospital mortality, acute ischemic CVA, major bleeding, and MACCE.

Our study identified several patient-related characteristics that were associated with palliative care use, including ventricular arrhythmias, cardiogenic shock or arrest, STEMI, and malignancy. It is likely that physicians recognize these high-risk factors and subsequently provide palliative care to these patients. Importantly, the frequency of patients receiving circulatory support or mechanical ventilation was significantly higher in the cohort that received palliative care. This is an unexpected finding because one

of the key principles of palliative care is de-escalation of treatments. Thus, it is possible that this finding is a reflection of treatment failures. This finding raises questions about the appropriateness of such interventions when it may have been more appropriate to get early involvement with palliative care.

Our analysis, like that of others,[5] revealed that both the size and type of hospital played an important role in which patients received palliative care. Patients in teaching and urban hospitals were more likely to receive palliative care than those in rural ones. Access to palliative care has been found to be an important proxy outcome measure to determine the quality of care patients receive prior to death, such that in 2014 the World Health Organization made a global resolution to improve palliative care access as a core component of health care.[8,9] Although access to health care is both a complex and multidimensional concept,[10] it is likely that institutional factors and geography are implicated in less frequent palliative care in patients who were treated in rural and small hospitals. Chukwusa et al[9] found considerable variations in geographic access to inpatient hospice, with evidence that patients who lived further away from hospice locations were less likely to die in a hospice facility. There may be both a lack of availability of palliative care and awareness of the need for this care in the AMI population. Observations that this disparity of care exists for this heterogeneous group of patients with AMI are an important step forward because better access to palliative care is likely to reduce this disparity gap.

Our analysis demonstrates that sex disparities exist, with women who have a DNR status being less likely than their male counterparts to receive a palliative care consultation. This finding is surprising because another recent study in an unselected cohort of patients with AMI reported that females were more likely to receive palliative care.[5] Similarly, Saeed et al[11] reported that in patients diagnosed with cancer, women were significantly more likely to prefer palliative care than men, whereas a multisite prospective cohort study by Sharma et al[12] found that men with cancer were more likely to receive aggressive non-beneficial intensive care near the end of their life. We previously reported that females who were diagnosed with AMI were more likely than men to have a DNR order.[3] In this high-risk cohort of patients, it is likely that there is a complex interplay between a person's own wishes and priorities toward the end of their life. Given that the presentation and perception of the symptoms of AMI differ between the sexes, it is possible that

TABLE 3. Adjusted OR of Patients With DNR Orders and Receipt of Palliative Care for In-Hospital Procedures and Outcomes During Hospitalization for AMI[a,b]

Variable	OR (95% CI)	*P* value
In-hospital procedures		
Invasive coronary angiography[c]	0.46 (0.45-0.47)	<.001
PCI[c]	0.47 (0.45-0.48)	<.001
Circulatory support (including IABP, LV assist device, and ECMO)[c]	0.90 (0.86-0.94)	<.001
Mechanical ventilation[c]	1.95 (1.91-1.99)	<.001
In-hospital outcomes		
MACCE[d]	3.08 (3.03-3.13)	<.001
Mortality[d]	3.18 (3.13-3.23)	<.001
Acute ischemic CVA[d]	2.01 (1.95-2.06)	<.001
Major bleeding[d]	1.30 (1.26-1.33)	<.001

[a]AF, atrial fibrillation; AMI, acute myocardial infarction; CVA, cerebrovascular accident; DNR, do-not-resuscitate; ECMO, extracorporeal membrane oxygenation; HF, heart failure; IABP, intra-aortic balloon pump; LV, left ventricle; MACCE, major adverse cardiovascular and cerebrovascular event; MI, myocardial infarction; OR, odds ratio; PVD, peripheral vascular disease; STEMI, ST-elevation MI; VF, ventricular fibrillation; VT, ventricular tachycardia.

[b]Reference: DNR with no palliative care.

[c]Adjusted for age, sex, weekend admission, hospital size (number of beds), region and location/teaching status, STEMI, cardiogenic shock, VF, VT, AF, previous MI, HF, hypertension, dyslipidemias, diabetes mellitus, valvular heart disease, smoking status, chronic lung disease, chronic liver disease, chronic renal failure, PVD, obesity, anemia, thrombocytopenia, coagulopathies, and malignancies.

[d]Adjusted for age, sex, weekend admission, hospital size (number of beds), region and location/teaching status, STEMI, cardiogenic shock, VF, VT, AF, previous MI, HF, hypertension, dyslipidemias, diabetes mellitus, valvular heart disease, smoking status, chronic lung disease, chronic liver disease, chronic renal failure, PVD, obesity, anemia, thrombocytopenia, coagulopathies, malignancies, and in-hospital procedures.

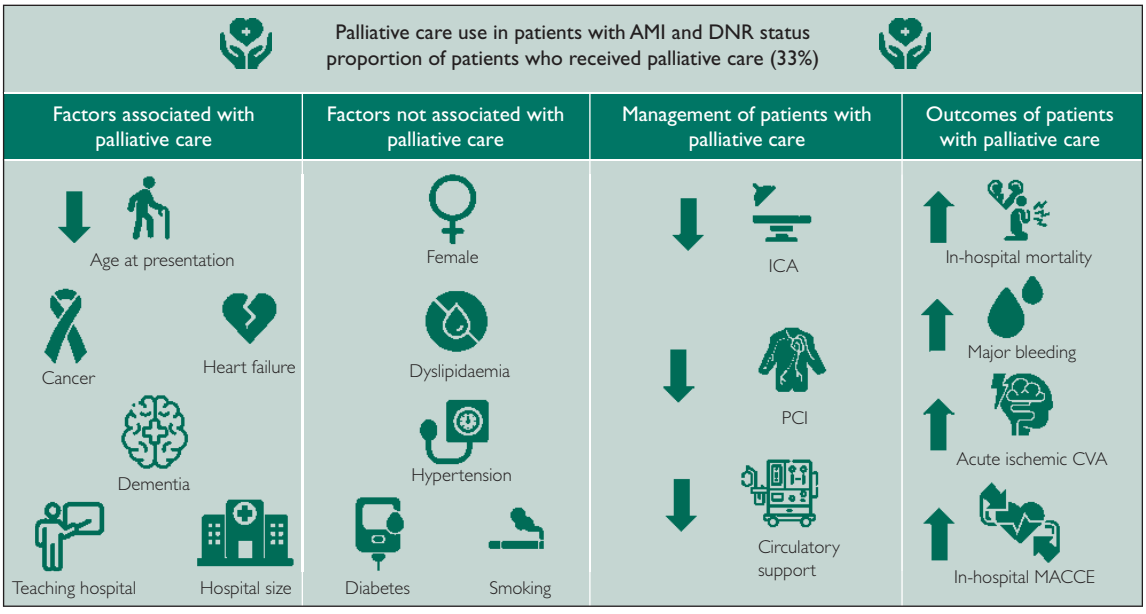

FIGURE. Key study findings. AMI, acute myocardial infarction; CVA, cerebrovascular accident; DNR, do-not-resuscitate; ICA, invasive coronary angiogram; MACCE, major adverse cardiovascular and cerebrovascular event; PCI, percutaneous coronary intervention.

this may also be a factor in the differences of management.[13,14] It is important to recognize that there are differences in the use of palliative care in this cohort based on race. In our study, patients who were Black and Asian/Pacific Islander were more likely to receive palliative care consultation than White patients, whereas Hispanic patients were less likely to receive such care than White patients. In a previous population-based study of 1212 patients, Ornstein et al[15] found that Black individuals were significantly less likely to use hospice and more likely to undergo intensive treatment in the last 6 months of their lives than White individuals regardless of cause of death. Although patient preference and cultural differences are a key factor in differences in the use of palliative care, it is reassuring to see that in this high-risk cohort of patients, Black individuals are not disadvantaged in the receipt of palliative care.

Although the AMI cohort of patients who have a DNR order represents a group that generally has poor outcomes and is less likely to receive invasive management compared with those without a DNR order,[3] our analysis revealed that patients who receive palliative care are even less likely to undergo invasive management. One of the key facets of palliative care is "active listening," in which equal importance is placed on patients' attitude regarding their condition and understanding their fears, concerns, and priorities.[16-18] In conditions such as heart failure and cancer, patients with advanced disease often have a preference to not be treated aggressively, with the focus on prioritizing their quality of life.[19] Our results suggest a similar pattern in this high-risk cohort of patients with AMI in which the focus of management is likely to be patient-centered and less focused on interventions that prolong life. The clinical outcomes for patients with AMI including mortality, acute ischemic CVA, major bleeding, and MACCE were significantly worse in patients who received palliative care. This finding is likely multifactorial and in part may be that the patients receiving palliative care are likely to represent a more unwell group of patients who would generally have worse clinical outcomes and may thus be less likely to be offered life-prolonging—focused interventions.

Importantly, our study does not have temporal data on the timing of the DNR order, receipt of palliative care, or its relationship with the timing of the AMI. Thus, it is important to recognize that the group of patients who received palliative care in this cohort reflects a highly heterogeneous group of patients. For instance, patients may range from those who had a multimorbidity burden and a preexisting DNR order who were subsequently hospitalized with a noncardiac cause and had an AMI in the hospital to those who were previously well, were admitted to the hospital with an AMI, and initiated a DNR order and palliative care in the hospital following a catastrophic complication. Thus, there exists a highly complex interplay of the receipt of palliative care and its timing in relationship to both a DNR order and the timing of the AMI. For many conditions such as cancer, the initiation of a DNR order has become synonymous with the involvement of palliative care and recognition that the priority of care for the patient and their families should be switched to prioritizing comfort.[20] Importantly, this relationship has not been well defined for AMI, and differences are likely given the varied patient populations and treatments in comparison to patients who have cancer.[21] Thus, our study raises questions about the timing of palliative care within the realms of AMI in view of the immediate lifesaving treatments available, particularly PCI for patients with STEMI. In the past decade, both DNR orders and palliative care have been used increasingly in an ICU setting, both for patients who are expected to die in the ICU and for those discharged either to home or to another department within the hospital, where early involvement has been found to be beneficial.[22,23] Given the parallels between ICU care and cardiac diseases, it is likely there are lessons to be learned on the timing of involvement of palliative care for patients with AMI by looking at successful use in the ICU.

Our analysis has important clinical implications for practice. Cardiology as a specialty has often been criticized for its reluctance to utilize palliative care, largely attributed to advances in cardiovascular sciences over the past 20 years that allow patients with advanced heart disease to survive events that previously would have been fatal.[24-26] It is important to recognize that a DNR order only reflects the desires of a patient once they experience a full cardiopulmonary arrest and does not reflect their preferences about other forms of life-sustaining treatment. Thus, in this high-risk cohort of patients with poor outcomes, it is likely that increased use of palliative care will have significant benefits for patients and their families in deciding which treatments they would be willing to accept and focusing on their key priorities.[27] Of concern, the lower rates of discharge to home with home health care or to a nursing home suggests that in this cohort, palliative care was mostly being reserved as end-of-life care for those identified as at high risk of dying during that hospitalization. "Late" use of palliative care has been reported similarly by others,[28] and cardiologists are increasingly being asked to reframe palliative care as a useful added layer of support for those with advanced illness, not just in the final weeks of life but potentially over months and years.[29,30] There are several barriers to earlier referral,[31] but greater education for physicians and integrated-care pathways with palliative care teams are likely to facilitate a more timely patient-centered approach.

This study has several strengths. Our analysis represents the largest study to date that examined the use of palliative care in a heterogeneous high-risk group of patients with a diagnosis of AMI who had a DNR status. The NIS database gives insight into the real-world in-hospital outcomes in a large and unselected cohort of patients with AMI, including those who are at high risk and have multiple comorbid illnesses, such that they are underrepresented in clinical trials. The size of the database provides sufficient power to detect differences in adverse outcomes between the 2 cohorts of interest.

Our study also has several important limitations. Despite the NIS using *International Classification of Diseases, Tenth Revision* codes and being a validated data set for the

purposes of cardiovascular research,[32,33] it is an administrative data set, and coding error may be a source of bias. The identification of AMI, DNR status, palliative care, comorbidities, and procedural data was based on the use of administrative codes. Second, the NIS data set only records in-hospital outcomes, and therefore, longer-term follow-up of mortality or other adverse outcomes is missing from our analysis. Third, because the database does not include pharmacotherapy, we were unable to determine if there was a significant disparity in care between the 2 groups regarding pharmacotherapy or to see if the use of pharmacotherapy altered clinical outcomes for those patients with palliative care. Furthermore, the NIS does not capture when the DNR order was instituted, whether it was in place prior to admission,[34] at the point of admission, or during the inpatient episode following a complication/adverse outcome. Thus, the intention of the palliative care is unknown. Similarly, we do not know the timing of the palliative care in relationship to the diagnosis of AMI (even though there is a suggestion that it might be late) or to the DNR status. Importantly, we also don't know whether receipt of palliative care means that patients received high-quality palliative care, nor that they received specialist palliative care consultation. It is also possible that unmeasured confounders such as frailty or malnutrition may contribute to the adverse association that we report in patients referred for palliative treatment. Finally, the process by which the palliative care was established and how patients' preferences were elicited in decision making is unknown.

CONCLUSION

Our study found that in hospitalized patients who had a DNR status and received a diagnosis of AMI, only one-third received palliative care. Females, patients presenting at small or rural hospitals, and those with cardiovascular comorbidities were less likely to receive palliative care, whereas patients who had multiple comorbidities with heart failure or malignancy were more likely to receive palliative care. Patients who received palliative care had increased adjusted odds of in-hospital mortality, acute ischemic CVA, major bleeding, and MACCE. Further evaluation of the use of palliative care, particularly in patients who had a DNR order in place prior to admission with an AMI, is required to determine its appropriateness and to facilitate greater use in this high-risk cohort of patients.

POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

ACKNOWLEDGMENTS

Drs Kobo and Moledina are joint first authors of this article.

Authors contributions: Dr Kobo—Data curation, formal analysis, writing/original draft; Dr Moledina—Writing/original draft; Dr Mohamed—Writing, review editing; Dr Sinnarajah—Writing, review editing; Dr Simon—Writing, review editing; Dr Sun—Writing, review editing; Dr Slawnych—Writing, review editing; Dr Fischman—Writing, review editing; Dr Roguin—Writing, review editing; Dr Mamas—Conceptualization, project administration, supervision, writing, review editing.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **AMI,** acute myocardial infarction; **CABG,** coronary artery bypass grafting; **CVA,** cerebrovascular accident; **DNR,** do-not-resuscitate; **ICA,** invasive coronary angiography; **ICU,** intensive care unit; **MACCE,** major adverse cardiovascular and cerebrovascular event; **MI,** myocardial infarction; **NIS,** National (Nationwide) Inpatient Sample; **OR,** odds ratio; **PCI,** percutaneous coronary intervention; **STEMI,** ST-elevation myocardial infarction

Affiliations (Continued from the first page of this article.): versity, Kingston, Ontario, Canada (A.S.); Libin Cardiovascular Institute and Division of Palliative Care (M.S.), Department of Oncology (J.S., M.S.), University of Calgary, Calgary, Alberta, Canada; Division of Cardiac Anesthesiology, University of Ottawa Heart Institute, and School of Epidemiology and Public Health, University of Ottawa,

Ottawa, Ontario, Canada (L.Y.S.); and Department of Cardiology, Thomas Jefferson University, Philadelphia, PA (D.L.F., M.A.M.).

Correspondence: Address to Mamas A. Mamas, DPhil, Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, Stoke-on-Trent, UK (mamasmamas1@yahoo.co.uk; Twitter: @mmamas1973).

ORCID

Jessica Simon: https://orcid.org/0000-0002-0865-4231; Michael Slawnych: https://orcid.org/0000-0002-9822-2650

REFERENCES

1. Menees DS, Peterson ED, Wang Y, et al. Door-to-balloon time and mortality among patients undergoing primary PCI. *N Engl J Med*. 2013;369(10):901-909.
2. Loertscher L, Reed DA, Bannon MP, Mueller PS. Cardiopulmonary resuscitation and do-not-resuscitate orders: a guide for clinicians. *Am J Med*. 2010;123(1):4-9.
3. Kobo O, Moledina SM, Slawnych M, et al. Predictors, treatments, and outcomes of do-not-resuscitate status in acute myocardial infarction patients (from a nationwide inpatient cohort study). *Am J Cardiol*. 2021;159:8-18.
4. Jneid H, Addison D, Bhatt DL, et al. 2017 AHA/ACC clinical performance and quality measures for adults with ST-elevation and non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol*. 2017;70(16):2048-2090.
5. Elgendy IY, Elbadawi A, Sardar P, el al. Palliative care use in patients with acute myocardial infarction. *J Am Coll Cardiol*. 2020;75(1):113-117.
6. Pollock BD, Herrin J, Neville MR, et al. Association of do-not-resuscitate patient case mix with publicly reported risk-standardized hospital mortality and readmission rates. *JAMA Netw Open*. 2020;3(7):e2010383.
7. HCUP Nationwide Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2011. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/nisoverview.jsp
8. Carrasco JM, Inbadas H, Whitelaw A, Clark D. Early impact of the 2014 World Health Assembly resolution on palliative care: a qualitative study using semistructured interviews with key experts. *J Palliat Med*. 2021;24(1):103-106.
9. Chukwusa E, Verne J, Polato G, Taylor R, Higginson IJ, Gao W. Urban and rural differences in geographical accessibility to inpatient palliative and end-of-life (PEoLC) facilities and place of death: a national population-based study in England, UK. *Int J Health Geogr*. 2019;18(1):8.
10. Gulliford M, Figueroa-Munoz J, Morgan M, et al. What does 'access to health care' mean? *J Health Serv Res Policy*. 2002;7(3):186-188.
11. Saeed F, Hoerger M, Norton SA, Guancial E, Epstein RM, Duberstein PR. Preference for palliative care in cancer patients: are men and women alike? *J Pain Symptom Manage*. 2018;56(1):1-6.e1.
12. Sharma RK, Prigerson HG, Penedo FJ, Maciejewski PK. Male-female patient differences in the association between end-of-life discussions and receipt of intensive care near death. *Cancer*. 2015;121(16):2814-2820.
13. Lichtman JH, Leifheit EC, Safdar B, et al. Sex differences in the presentation and perception of symptoms among young patients with myocardial infarction: evidence from the VIRGO study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). *Circulation*. 2018;137(8):781-790.
14. Zucker DR, Griffith JL, Beshansky JR, Selker HP. Presentations of acute myocardial infarction in men and women. *J Gen Intern Med*. 1997;12(2):79-87.
15. Ornstein KA, Roth DL, Huang J, et al. Evaluation of racial disparities in hospice use and end-of-life treatment intensity in the REGARDS cohort. *JAMA Netw Open*. 2020;3(8):e2014639.
16. Wittenberg-Lyles E, Goldsmith J, Platt CS. Palliative care communication. *Semin Oncol Nurs*. 2014;30(4):280-286.
17. Wentlandt K, Seccareccia D, Kevork N, et al. Quality of care and satisfaction with care on palliative care units. *J Pain Symptom Manage*. 2016;51(2):184-192.
18. Shaw M, Shaw J, Simon J. Listening to patients' own goals: a key to goals of care decisions in cardiac care. *Can J Cardiol*. 2020;36(7):1135-1138.
19. Duberstein PR, Kravitz RL, Fenton JJ, et al. Physician and patient characteristics associated with more intensive end-of-life care. *J Pain Symptom Manage*. 2019;58(2):208-215.e1.
20. Espeli VG, Fusi-Schimdhauser T, Mangan D, Gamondi C. The role of palliative care in relapsed and metastatic head and neck cancer patients in a single ESMO integrated oncology and palliative care centre [published online ahead of print July 12, 2022; correction published online August 5, 2022 (https://doi.org/10.1007/s00405-022-07583-5)]. *Eur Arch Otorhinolaryngol*. https://doi.org/10.1007/s00405-022-07535-z
21. Kobo O, Moledina SM, Raisi-Estabragh Z, et al. Emergency department cardiovascular disease encounters and associated mortality in patients with cancer: a study of 20.6 million records from the USA. *Int J Cardiol*. 2022;363:210-217.
22. Aslakson RA, Curtis JR, Nelson JE. The changing role of palliative care in the ICU. *Crit Care Med*. 2014;42(11):2418-2428.
23. Cook D, Rocker G. Dying with dignity in the intensive care unit. *N Engl J Med*. 2014;370(26):2506-2514.
24. Warraich HJ, Hernandez AF, Allen LA. How medicine has changed the end of life for patients with cardiovascular disease. *J Am Coll Cardiol*. 2017;70(10):1276-1289.
25. Hanratty B, Hibbert D, Mair F, et al. Doctors' understanding of palliative care. *Palliat Med*. 2006;20(5):493-497.
26. Ecarnot F, Meunier-Beillard N, Seronde M-F, et al. End-of-life situations in cardiology: a qualitative study of physicians' and nurses' experience in a large university hospital. *BMC Palliat Care*. 2018;17(1):112.
27. Hoare S, Morris ZS, Kelly MP, Kuhn I, Barclay S. Do patients want to die at home? a systematic review of the UK literature, focused on missing preferences for place of death. *PLoS One*. 2015;10(11):e0142723.
28. Warraich HJ, Wolf SP, Mentz RJ, Rogers JG, Samsa G, Kamal AH. Characteristics and trends among patients with cardiovascular disease referred to palliative care. *JAMA Netw Open*. 2019;2(5):e192375.
29. Klinedinst R, Kornfield ZN, Hadler RA. Palliative care for patients with advanced heart disease. *J Cardiothorac Vasc Anesth*. 2019;33(3):833-843.
30. Braun LT, Grady KL, Kutner JS, et al. American Heart Association Advocacy Coordinating Committee. Palliative care and cardiovascular disease and stroke: a policy statement from the American Heart Association/American Stroke Association. *Circulation*. 2016;134(11):e198-e225.
31. Bonares MJ, Mah K, MacIver J, et al. Referral practices of cardiologists to specialist palliative care in Canada. *CJC Open*. 2020;3(4):460-469.
32. Birman-Deych E, Waterman AD, Yan Y, Nilasena DS, Radford MJ, Gage BF. Accuracy of ICD-9-CM codes for identifying cardiovascular and stroke risk factors. *Med Care*. 2005;43(5):480-485.
33. DeShazo JP, Hoffman MA. A comparison of a multistate inpatient EHR database to the HCUP Nationwide Inpatient Sample. *BMC Health Serv Res*. 2015;15:384.
34. Saczynski JS, Gabbay E, McManus DD, et al. Increase in the proportion of patients hospitalized with acute myocardial infarction with do-not-resuscitate orders already in place between 2001 and 2007: a nonconcurrent prospective study. *Clin Epidemiol*. 2012;4:267-274.