

Original Article

Sex Disparities in the Use and Outcomes of Temporary Mechanical Circulatory Support for Acute Myocardial Infarction-Cardiogenic Shock

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ABSTRACT

Background: There are limited sex-specific data on patients receiving temporary mechanical circulatory support (MCS) for acute myocardial infarction-cardiogenic shock (AMI-CS).

Methods: All admissions with AMI-CS with MCS use were identified using the National Inpatient Sample from 2005 to 2016. Outcomes of interest included in-hospital mortality, discharge disposition, use of palliative care and do-not-resuscitate (DNR) status, and receipt of durable left ventricular assist device (LVAD) and cardiac transplantation.

Results: In AMI-CS admissions during this 12-year period, MCS was

RÉSUMÉ

Contexte : On dispose de peu de données quant à l'influence du sexe sur les résultats pour les patients qui reçoivent une assistance circulatoire mécanique (ACM) temporaire à la suite d'un infarctus aigu du myocarde accompagné d'un choc cardiogénique (IAM-CC).

Méthodologie : Nous avons recensé dans l'échantillon national des patients hospitalisés (NIS, *National Inpatient Sample*) tous les patients admis à l'hôpital pour un IAM-CC qui ont reçu une ACM de 2005 à 2016. Les résultats d'intérêt comprenaient la mortalité hospitalière, l'état à la sortie, le recours aux soins palliatifs et à une ordonnance de

Cardiogenic shock (CS) is defined as a critical state of end-organ hypoperfusion due to primary pump failure, nearly 80% of which is due to acute myocardial infarction (AMI).¹ In addition to the primary pump failure, these patients also have systemic inflammation and hypoxemia further worsening

end-organ failure.^{2–5} Temporary mechanical circulatory support (MCS) devices, such as intra-aortic balloon pump (IABP), percutaneous left ventricular assist device (pLVAD) (Impella or TandemHeart), and extracorporeal membrane oxygenation (ECMO), can be used to support cardiovascular function in selected patients.^{6–10} However, there are conflicting data on the clinical management and outcomes of men and women who received temporary MCS for AMI-CS.^{11,12} Prior data suggest that men and women differ at baseline in terms of etiology of CS and AMI, prognosis, and the treatment strategies they receive.¹³ Alternatively, in a substudy from the **Intra-Aortic Balloon Pump in Cardiogenic Shock II** (IABP-SHOCK II) trial, despite having a worse clinical profile, women had comparable clinical outcomes with men.¹⁴

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Ethics Statement: Institutional Review Board approval was not sought due to the publicly available nature of the database.

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See page 471 for disclosure information.

used more frequently in men—50.4% vs 39.5%; $P < 0.001$. Of the 173,473 who received MCS (32% women), intra-aortic balloon pumps, percutaneous LVAD, extracorporeal membrane oxygenation, and ≥ 2 MCS devices were used in 92%, 4%, 1%, and 3%, respectively. Women were on average older (69 ± 12 vs 64 ± 13 years), of black race (10% vs 6%), and had more comorbidity (mean Charlson comorbidity index 5.0 ± 2.0 vs 4.5 ± 2.1). Women had higher in-hospital mortality than men (34% vs 29%, adjusted odds ratio [OR]: 1.19, 95% confidence interval [CI]: 1.16-1.23; $P < 0.001$) overall, in intra-aortic balloon pumps users (OR: 1.20 [95% CI: 1.16-1.23]; $P < 0.001$), and percutaneous LVAD users (OR: 1.75 [95% CI: 1.49-2.06]; $P < 0.001$), but not in extracorporeal membrane oxygenation or ≥ 2 MCS device users ($P > 0.05$). Women had higher use of palliative care, DNR status, and discharges to skilled nursing facilities.

Conclusions: There are persistent sex disparities in the outcomes of AMI-CS admissions receiving MCS support. Women have higher in-hospital mortality, palliative care consultation, and use of DNR status.

Prior work from national databases has shown persistent sex disparities in the management and outcomes of durable LVAD admissions.¹⁵ It is unclear if similar disparities exist in the clinical profile and outcomes of men and women receiving temporary MCS for AMI-CS in the United States.¹⁶⁻¹⁸

In light of these conflicting data, this study sought to assess sex differences in the use and outcomes of MCS in a 12-year nationally representative AMI-CS population. We hypothesized that women would receive MCS less frequently and have higher in-hospital mortality compared with men. We also sought to evaluate the sex differences in demographics, clinical course, and management strategies of these cohorts to better inform clinical care for these patients.

Material and Methods

Study population, variables, and outcomes

The National (Nationwide) Inpatient Sample (NIS) is the largest all-payer database of hospital inpatient stays in the United States. NIS contains discharge data from a 20% stratified sample of community hospitals and is a part of the Healthcare Quality and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality.¹⁹ Information regarding each discharge includes patient demographics, primary payer, hospital characteristics, principal diagnosis, up to 24 secondary diagnoses, and

non-réanimation (ONR), l'implantation d'un dispositif d'assistance ventriculaire gauche (DAVG) permanent et la transplantation cardiaque.

Résultats : Chez les patients admis à l'hôpital pour un IAM-CC durant la période de 12 ans étudiée, l'ACM a été utilisée plus fréquemment chez les hommes que chez les femmes (50,4 % vs 39,5 %; $p < 0,001$). Sur les 173 473 patients qui ont reçu une ACM (dont 32 % étaient des femmes), les méthodes employées se répartissaient comme suit : ballon de contre-pulsion intra-aortique, 92 %; assistance ventriculaire gauche percutanée, 4 %; oxygénation extracorporelle par membrane, 1 %; et au moins 2 types d'ACM, 3 %. Les femmes étaient plus âgées en moyenne (69 ± 12 ans vs 64 ± 13 ans), étaient plus souvent de race noire (10 % vs 6 %) et présentaient un plus grand nombre d'affections concomitantes (indice de comorbidité de Charlson moyen de $5,0 \pm 2,0$ vs $4,5 \pm 2,1$). Le taux de mortalité hospitalière était plus élevé chez les femmes que chez les hommes (34 % vs 29 %, risque relatif corrigé [RRA] corrigé : 1,19; intervalle de confiance [IC] à 95 % : de 1,16 à 1,23; $p < 0,001$) dans l'ensemble, ainsi que chez les utilisateurs d'un ballon de contre-pulsion intra-aortique (RRA : 1,20 [IC à 95 % : de 1,16 à 1,23]; $p < 0,001$), et chez les utilisateurs d'un DAVG percutané (RRA : 1,75 [IC à 95 % : 1,49 à 2,06]; $p < 0,001$), mais pas chez les utilisateurs de l'oxygénation extracorporelle par membrane ni chez les utilisateurs d'au moins 2 types d'ACM ($p > 0,05$). Le recours aux soins palliatifs, l'établissement d'une ordonnance de non-réanimation et l'orientation vers un établissement de soins infirmiers spécialisés à la sortie de l'hôpital étaient plus fréquents chez les femmes.

Conclusions : Il existe toujours des disparités entre les sexes à l'égard des résultats pour les patients admis à l'hôpital pour IAM-CC recevant une ACM. Le taux de mortalité hospitalière était plus élevé chez les femmes, et celles-ci avaient plus souvent recours à une consultation en soins palliatifs et à une ONR.

procedural diagnoses. The HCUP-NIS does not capture individual patients but captures all information for a given admission. Institutional review board approval was not sought due to the publicly available nature of this deidentified database. These data are available to other authors via the HCUP-NIS database with the Agency for Healthcare Research and Quality.

Using the HCUP-NIS data from 2005 to 2016, a retrospective cohort study of admissions with AMI in the primary diagnosis field (International Classification of Diseases 9.0 Clinical Modification [ICD-9CM] 410.x and ICD-10CM I21.x-22.x) and a secondary diagnosis of CS (ICD-9CM 785.51, ICD-10CM R57.0) receiving an IABP (ICD-9CM 37.61; ICD-10PCS 5A02110, 5A02210), pLVAD (ICD-9CM 37.68; ICD-10PCS 5A0211D, 5A0221D, 02HA3RJ, 02HA4RJ), or ECMO (ICD-9CM 39.65; ICD-10PCS 5A15223) was included.^{6,20,21} Because ICD-9CM codes were redefined in 2005 to distinguish the durable LVAD from short-term nonimplantable devices or paracorporeal devices, admissions before 2005 were excluded from this study.^{6,20,21} We also excluded AMI-CS not receiving MCS therapy, and those admissions without data on sex and in-hospital mortality. Deyo's modification of the Charlson comorbidity index was used to identify the burden of comorbid diseases (Supplemental Table S1).²² Demographic characteristics, hospital characteristics, acute organ failure, MCS, cardiac procedures, and noncardiac organ support use were identified

for all admissions using previously used methodologies from our group.²³⁻²⁵ pLVAD in this study refers to either Impella (2.5 or CP) or the TandemHeart devices.

The primary outcome was in-hospital mortality in men and women with AMI-CS supported by MCS. Temporal trends in the use of MCS in AMI-CS, type of MCS devices, and in-hospital mortality over the study period, stratified by sex, were evaluated. Secondary outcomes included length of stay, hospitalization costs, discharge disposition, use of do-not-resuscitate (DNR) status, use of palliative care consultation, receipt of durable LVAD, and cardiac transplantation.

Statistical analysis

As recommended by the HCUP-NIS, survey procedures using discharge weights provided with the HCUP-NIS database were used to generate national estimates. Using the trend weights provided by the HCUP-NIS, samples from 2005 to 2011 were reweighted to adjust for the 2012 HCUP-NIS redesign.²⁶ χ^2 and *t*-tests were used to compare categorical and continuous variables by sex, respectively. Logistic regression was used to compare the risk of outcomes over time by sex, with results presented as odds ratios (OR) with 95% confidence intervals (CI). To evaluate temporal trends, the risk of the outcome in each year of the study was compared with the year 2005. The inherent restrictions of the HCUP-NIS database related to research design, data interpretation, and data analysis were reviewed and addressed.²⁶ Pertinent considerations include not assessing individual hospital-level volumes (due to changes to sampling design detailed above), treating each entry as an “admission” as opposed to individual patients, restricting the study details to inpatient factors because the HCUP-NIS does not include outpatient data, and limiting administrative codes to those previously validated and used for similar studies. Multivariable logistic regression analysis incorporating age, race, primary payer status, socioeconomic stratum, hospital characteristics, comorbidities, acute organ failure, AMI-type, cardiac procedures, and noncardiac procedures was performed for temporal trends analyses and in-hospital mortality. For the multivariable modelling, regression analysis with purposeful selection of statistically (liberal threshold of $P < 0.20$ in univariate analysis) and clinically relevant variables was conducted. *A priori* subgroup analyses were performed stratifying admissions by race, concomitant cardiac arrest, AMI-CS type, early (hospital day zero) vs delayed (\geq hospital day 1) MCS placement, and receipt of percutaneous coronary intervention (PCI). Two-tailed $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS v25.0 (IBM Corp, Armonk, NY).

Results

In the period between January 1, 2005, and December 31, 2016, there were 374,920 admissions with AMI-CS, of which MCS was used in 173,473 (46.3%). Men received more frequent MCS support than women (50.4% vs 39.5%; $P < 0.001$). Of the included population, women constituted 31.7%. Compared with men, women were on average older, of black race, bearing Medicare insurance, from a lower

Table 1. Characteristics of AMI-CS admissions supported with MCS stratified by sex

Characteristics	Men (N = 118,557)	Women (N = 54,916)	<i>P</i>
Age (y)	64.4 ± 12.0	68.9 ± 12.5	< 0.001
Race			
White	75.2	74.8	< 0.001
Black	6.2	9.5	
Hispanic	9.1	8.3	
Asian	3.7	2.9	
Native American	0.8	0.6	
Others	5.1	3.8	
Primary payer			
Medicare	47.4	63.2	< 0.001
Medicaid	8.2	8.3	
Private	32.4	21.9	
Others*	12.0	6.6	
Quartile of median household income for zip code			
0-25th	25.9	28.5	< 0.001
26th-50th	26.4	27.0	
51st-75th	25.3	24.0	
75th-100th	22.4	20.4	
Hospital teaching status and location			
Rural	4.4	4.7	0.04
Urban nonteaching	35.8	35.7	
Urban teaching	59.7	59.5	
Hospital bed size			
Small	7.6	6.9	< 0.001
Medium	22.2	21.7	
Large	70.2	71.3	
Hospital region			
Northeast	16.9	18.5	< 0.001
Midwest	23.6	25.0	
South	38.0	37.4	
West	21.5	19.0	
Charlson comorbidity index			
0-3	34.7	21.8	< 0.001
4-6	48.9	57.7	
≥ 7	16.4	20.4	
AMI-CS type			
STEMI-CS	71.3	69.2	< 0.001
NSTEMI-CS	28.7	30.8	
Acute organ failure			
Respiratory	51.6	52.6	< 0.001
Renal	41.7	37.9	< 0.001
Hepatic	12.3	11.7	< 0.001
Hematologic	16.4	17.0	0.003
Neurologic	17.6	14.4	< 0.001
Out of hospital cardiac arrest	31.4	27.7	< 0.001
Coronary angiography	90.4	90.6	0.21
Percutaneous coronary intervention	65.7	66.7	< 0.001
Pulmonary artery catheterization	8.8	8.6	0.08
Invasive mechanical ventilation	45.9	46.7	< 0.001
Noninvasive ventilation	2.9	3.2	< 0.001
Hemodialysis	3.9	3.9	0.72

Represented as percentage or mean ± standard deviation.

AMI, acute myocardial infarction; CS, cardiogenic shock; MCS, mechanical circulatory support; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

* Uninsured, no charge, others.

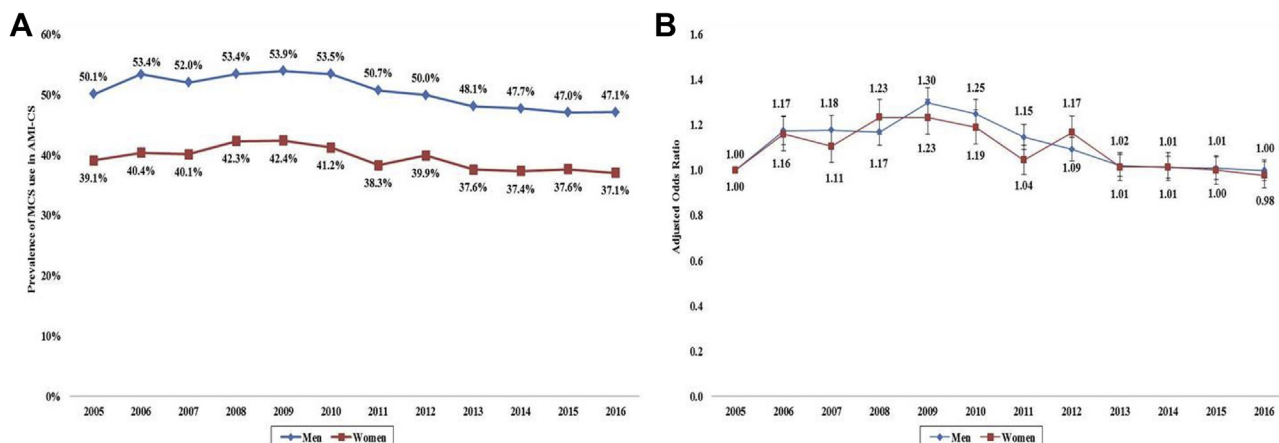


Figure 1. Temporal trends in the use of MCS in AMI-CS admissions stratified by sex. **(A)** Unadjusted temporal trends in the use of MCS for AMI-CS stratified by sex ($P < 0.001$ for trend over time). **(B)** Adjusted multivariate logistic regression for use of MCS for AMI-CS stratified by sex (referent year 2005); adjusted for age, race, comorbidity, primary payer, socioeconomic status, and hospital characteristics ($P < 0.001$ for trend over time). AMI, acute myocardial infarction; CS, cardiogenic shock; MCS, mechanical circulatory support.

socioeconomic stratum, and had a higher comorbidity burden (Table 1). Women had higher rates of non-ST-segment elevation AMI-CS, respiratory failure, and need for mechanical ventilation but lower rates of renal, hepatic, and neurologic failure (Table 1). Men and women had comparable rates of coronary angiography with a slightly higher rate of PCI in women. Median time to coronary angiography and PCI was comparable between men and women (median hospital day 0 [interquartile range (IQR): 0-0] days vs 0 [IQR: 0-0] for both procedures). The 12-year unadjusted temporal trends in the use of MCS devices in AMI-CS admissions indicated that women had consistently lower use of MCS devices compared with men

(Fig. 1A). When adjusted for age, race, comorbidity, primary payer, socioeconomic status, and hospital characteristics, women and men had comparable use of MCS during latter years compared with the referent year 2005 (these adjusted analyses did not compare men with women, but rather subsequent years to the referent year 2005) (Fig. 1B).

Of those receiving MCS support, the IABP, pLVAD, ECMO, and ≥ 2 MCS devices were used in 159,240 (91.8%), 7516 (4.3%), 1469 (0.8%), and 5248 (3.0%), respectively. The temporal trends in the use of IABP, pLVAD, and ECMO stratified by sex were similar in men and women (Fig. 2). Women who received any of these MCS devices were

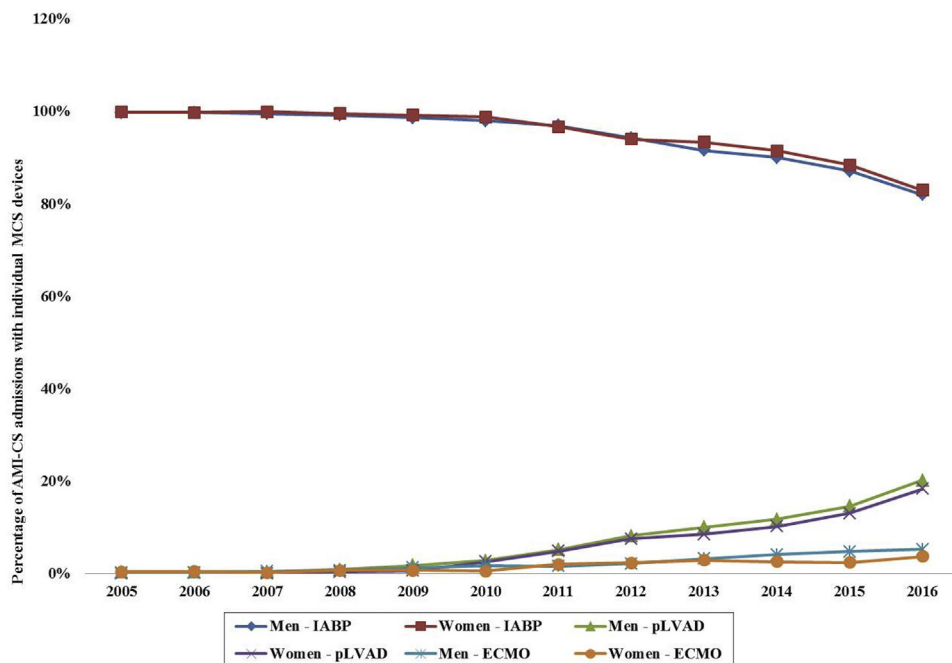


Figure 2. Trends in the use of IABP, pLVAD, and ECMO use in AMI-CS admissions stratified by sex. All $P < 0.001$ for trend over time. AMI, acute myocardial infarction; CS, cardiogenic shock; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; pLVAD, percutaneous left ventricular assist device.

Table 2. Characteristics of AMI-CS admissions supported with MCS stratified by sex and MCS type

Characteristics (N = 173,473)	IABP (N = 159,240)		pLVAD (N = 7516)		ECMO (N = 1469)		≥ 2MCS (N = 5248)		P*
	Men (N = 108,167)	Women (N = 51,073)	Men (N = 5353)	Women (N = 2163)	Men (N = 1075)	Women (N = 394)	Men (N = 3962)	Women (N = 1286)	
Age (y)	64.6 ± 12.0	69.1 ± 12.5	64.1 ± 11.8	67.5 ± 12.6	57.8 ± 10.5	58.9 ± 12.5	61.8 ± 11.2	68.9 ± 12.5	< 0.001
Race									
White	75.4	75.3	74.4	69.7	66.0	58.6	72.1	68.9	< 0.001
Black	6.0	9.1	7.1	14.4	7.8	13.3	7.6	13.6	
Hispanic	9.1	8.3	9.0	7.4	7.8	12.1	8.5	8.8	
Asian	3.8	2.9	2.2	2.5	3.8	1.5	3.5	4.0	
Native American	0.7	0.5	1.1	2.0	1.2	1.5	0.7	0.4	
Others	4.9	3.7	6.1	4.0	13.4	13.0	7.5	4.3	
Primary payer									
Medicare	47.8	63.7	47.6	65.0	31.0	32.7	40.8	48.2	< 0.001
Medicaid	8.0	8.2	8.5	8.9	12.5	11.4	10.9	9.6	
Private	32.0	21.5	32.7	19.4	46.8	44.8	36.6	36.0	
Others†	12.1	6.6	11.2	6.8	9.8	11.1	11.7	6.1	
Quartile of median household income for zip code									
0-25th	25.9	28.1	28.3	39.6	17.3	23.2	25.5	32.5	< 0.001
26th-50th	26.4	27.1	28.3	28.7	31.2	24.9	23.4	23.9	
51st-75th	25.4	24.1	23.2	19.4	25.4	24.9	24.0	27.2	
75th-100th	22.3	20.7	20.2	12.3	26.1	27.0	27.1	16.4	
Hospital teaching status and location									
Rural	4.6	4.9	3.1	3.3	0.5	0.0	3.0	1.9	0.04
Urban nonteaching	37.4	37.0	24.3	25.8	2.3	2.5	17.1	13.8	
Urban teaching	58.0	58.1	72.6	70.9	97.2	97.5	79.9	84.3	
Hospital bed size									
Small	7.7	7.1	8.3	5.9	1.9	2.5	4.6	5.1	< 0.001
Medium	22.4	21.7	23.1	26.2	11.2	10.2	16.9	18.9	
Large	69.8	71.2	68.6	67.9	87.0	87.3	78.5	76.0	
Hospital region									
Northeast	16.6	18.3	13.3	15.9	33.4	40.4	25.9	28.0	< 0.001
Midwest	23.9	25.3	18.3	18.0	21.5	23.6	22.6	21.9	
South	37.7	37.1	47.0	47.1	30.6	31.0	33.7	35.0	
West	21.7	19.3	21.4	19.0	14.5	5.1	17.7	15.1	
Charlson comorbidity index									
0-3	34.6	21.6	34.1	21.8	46.5	40.1	37.1	25.3	< 0.001
4-6	49.2	58.1	44.6	51.7	46.2	53.6	46.1	53.8	
≥ 7	16.2	20.3	21.3	26.4	7.4	6.3	16.8	20.8	
AMI-CS type									
STEMI-CS	71.6	69.7	65.0	60.5	73.1	65.0	71.0	65.5	< 0.001
NSTEMI-CS	28.4	30.3	35.0	39.5	26.9	35.0	29.0	34.5	< 0.001
Acute organ failure									
Respiratory	50.0	51.4	69.6	67.6	73.6	65.7	67.2	70.1	< 0.001
Renal	39.8	36.8	57.1	49.0	73.4	60.2	64.5	57.0	< 0.001
Hepatic	11.0	10.8	21.5	17.8	41.8	42.4	27.9	27.7	< 0.001
Hematologic	15.4	16.4	20.8	19.0	44.1	40.1	31.5	31.8	0.002
Neurologic	17.0	14.1	21.3	15.9	32.3	27.7	25.1	20.6	< 0.001
Out of hospital cardiac arrest	30.6	27.2	37.2	29.9	42.3	44.7	44.1	39.0	< 0.001
Coronary angiography	91.2	91.2	91.9	92.6	32.1	25.9	82.4	81.7	0.21

Percutaneous coronary intervention	65.4	66.5	76.7	78.9	25.3	25.1	68.9	68.1	< 0.001
Pulmonary artery catheter	8.7	8.5	8.7	7.7	9.6	10.4	12.8	12.0	0.08
Invasive mechanical ventilation	45.0	46.3	54.0	50.6	65.4	55.8	53.0	53.3	0.001
Noninvasive ventilation	3.0	3.3	3.0	3.7	1.1	0.0	1.7	1.2	< 0.001
Hemodialysis	3.6	3.8	6.6	4.6	15.7	6.1	6.5	5.8	0.70

Represented as percentage or mean ± standard deviation.

AMI, acute myocardial infarction; CS, cardiogenic shock; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; NSTEMI, non-ST-segment elevation myocardial infarction; pLVAD, percutaneous left ventricular assist device; STEMI, ST-segment elevation myocardial infarction.

* *P* value for intergroup comparison.

[†] Uninsured, no charge, others.

on average older, of non-white race, belonged to a lower socioeconomic stratum, and presented with non-ST-segment elevation AMI-CS, compared with men (Table 2). The cohort receiving ECMO support had lower comorbidity and higher acute organ failure compared with the cohorts receiving IABP and pLVAD. Women receiving the IABP (50.0 vs 51.4%), but not the pLVAD (67.6% vs 69.6%) or ECMO (65.7% vs 73.6%) had higher respiratory failure and lower rates of all other acute noncardiac organ failure compared with men (Table 2). Women less frequently received ≥ 2 MCS devices—IABP + pLVAD (men 30.7% vs women 28.3%); IABP + ECMO (men 49.5% vs women 49.0%), and pLVAD + ECMO (men 15.7% vs women 14.8%) (all *P* < 0.001). There were no differences in the timing of MCS placement between men and women—IABP (median hospital day 0 [IQR: 0-0] days vs 0 [IQR: 0-0]), pLVAD (hospital day 0 [IQR: 0-1] vs hospital day 0 [IQR: 0-1]), and ECMO (hospital day 1 [IQR: 0-2] vs hospital day 1 [IQR: 0-2]).

All-cause in-hospital mortality was higher in women compared with men (34.3% vs 29.3%; unadjusted OR: 1.26 [95% CI: 1.24-1.29]; *P* < 0.001). In a multivariable logistic regression model adjusting for demographic characteristics, hospital-level characteristics, comorbidity, severity of illness, cardiac, and noncardiac procedures and DNR status, women had higher in-hospital mortality compared with men (OR: 1.19 [95% CI: 1.16-1.23]; *P* < 0.001) (Supplemental Table S2). Women had higher unadjusted in-hospital mortality over the entire 12-year period (Fig. 3A). The adjusted mortality shows a steady decrease in the in-hospital mortality in 2016 as compared with 2000 in both groups (Fig. 3B). The increased risk of in-hospital mortality in women vs men extended to all racial and ethnic groups, those with and without concomitant cardiac arrest, both types of AMI-CS, patients with early and delayed MCS placement, and those who did and did not receive PCI (Fig. 4). Women had comparable length of hospital stay, lower hospitalization costs, and were less often discharged to home and more often discharged to skilled nursing facilities compared with men (Table 3). Although women and men had comparable rates of durable LVAD placement and cardiac transplantation during the AMI-CS hospitalization, women had higher use of DNR status and palliative care consultation (Table 3). Women had higher all-cause unadjusted in-hospital mortality across all MCS devices except in those using ECMO (Table 4). In a multivariable logistic regression model including all variables from Supplemental Table S2, women had higher in-hospital mortality in admissions receiving IABP (OR: 1.20 [95% CI: 1.16-1.23]; *P* < 0.001), pLVAD (OR: 1.75 [95% CI: 1.49-2.06]; *P* < 0.001), but not in those receiving ECMO (OR: 0.94 [95% CI: 0.63-1.40]; *P* = 0.76) or ≥ 2 MCS devices (OR: 0.98 [95% CI: 0.83-1.17]; *P* = 0.83). Women had lower hospitalization costs, greater use of DNR status and palliative care consultation, fewer discharges to home, and more frequent discharges to skilled nursing facilities across all MCS device types (Table 4).

Discussion

In the largest study evaluating the use of temporary MCS in AMI-CS, there were significant sex disparities in the use of MCS, patient characteristics, and outcomes. Women with AMI-CS received MCS devices less frequently, had higher

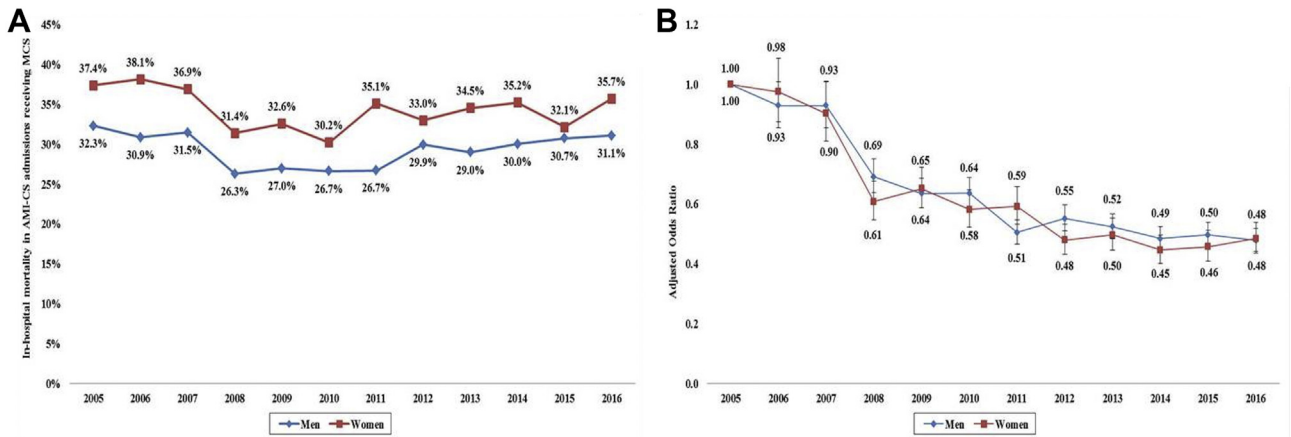


Figure 3. Temporal trends in in-hospital mortality in AMI-CS admissions receiving MCS stratified by sex. **(A)** Unadjusted in-hospital mortality in AMI-CS admissions receiving MCS stratified by sex ($P < 0.001$ for trend over time). **(B)** Adjusted multivariate logistic regression for in-hospital mortality temporal trends in AMI-CS admissions receiving MCS stratified by sex (referent year 2005); adjusted for age, race, comorbidity, primary payer, socioeconomic stratum, hospital characteristics, comorbidities, AMI type, acute organ failure, cardiac arrest, cardiac and noncardiac procedures ($P < 0.001$ for trend over time). AMI, acute myocardial infarction; CS, cardiogenic shock; MCS, mechanical circulatory support.

comorbidity, and higher rates of respiratory failure and mechanical ventilation use. Over the 12-year study period, there was a decrease in the use of IABP with increases in the use of pLVAD and ECMO in both men and women. Women had higher in-hospital mortality, more frequent use of DNR status and palliative care consultation, and higher postacute care resource utilization. Women receiving IABP or pLVAD

support, but not ECMO support, had higher in-hospital mortality in AMI-CS.

Although the overall mortality from AMI-CS has decreased over the last few decades, there remain significant challenges and opportunities for improvement in the care of these patients.⁴ As noted previously, patient- and hospital-specific demographic factors continue to be associated with

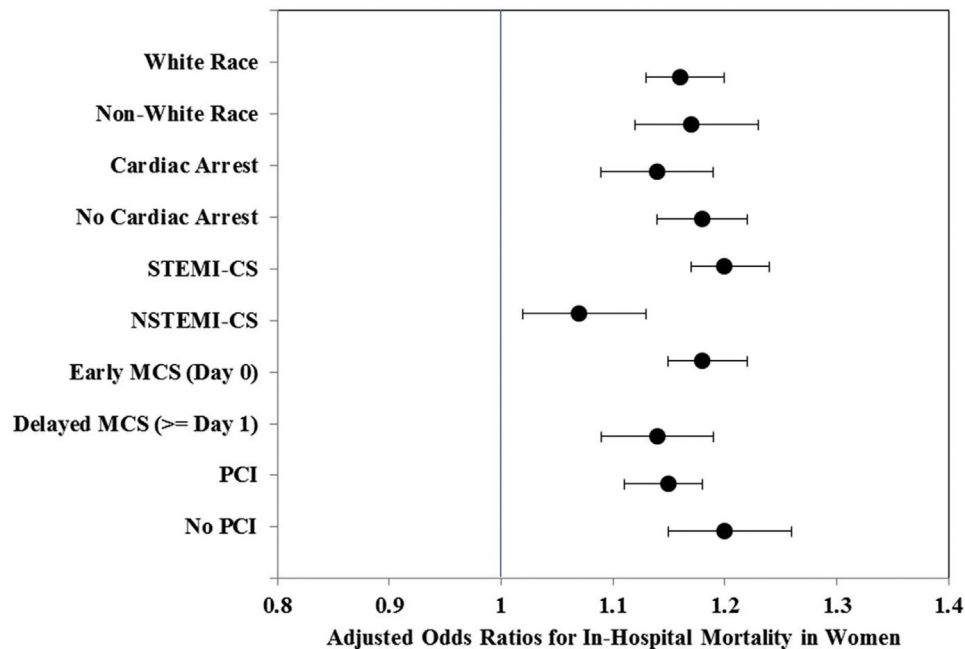


Figure 4. Multivariate logistic regression analysis for in-hospital mortality in women with AMI-CS receiving MCS compared with men. Multivariable adjusted odds ratios (95% confidence intervals)* for in-hospital mortality in women compared with men stratified by race, presence of cardiac arrest, type of AMI, timing of MCS placement, and receipt of PCI; all $P < 0.001$. *Adjusted for age, race, year of admission, primary payer, socioeconomic status, hospital location/teaching status, hospital bed size, hospital region, year of admission, comorbidity, type of AMI-CS, acute organ failure, cardiac arrest, coronary angiography, PCI, pulmonary artery catheterization, mechanical ventilation, and hemodialysis. AMI, acute myocardial infarction; CS, cardiogenic shock; MCS, mechanical circulatory support; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

Table 3. Clinical outcomes of AMI-CS admissions supported with MCS stratified by sex

Outcomes	Men (N = 118,557)	Women (N = 54,916)	P
In-hospital mortality	29.3	34.3	< 0.001
Length of stay (d)	11.3 ± 11.9	11.4 ± 12.2	0.11
Hospitalization costs (×1000 USD)	208 ± 222	195 ± 199	< 0.001
Do-not-resuscitate status	5.6	7.0	< 0.001
Palliative care consultation	5.3	6.1	< 0.001
Durable left ventricular assist device	0.7	0.6	0.003
Cardiac transplantation	0.1	0.0	0.003
Disposition			
Home	45.6	33.0	< 0.001
Transfer	12.0	11.1	
Skilled nursing facility	25.1	36.6	
Home with home health care	16.9	19.0	
Against medical advice	0.5	0.3	

Represented as percentage or mean ± standard deviation.

AMI, acute myocardial infarction; CS, cardiogenic shock; MCS, mechanical circulatory support; USD, United States Dollars.

differences in clinical outcomes in this population.²⁷⁻²⁹ In this study, there were significant sex differences in the outcomes for patients receiving MCS for AMI-CS. The results are consistent with prior research that has shown pervasive sex disparities in acute cardiovascular care.^{29,30} Compared with men, women experiencing an AMI are often older, present with delayed and atypical symptoms, often have longer total ischemic time, and are revascularized less often.³⁰ Furthermore, women have higher comorbidity, higher rates of heart failure, were less likely to undergo primary reperfusion, and had higher rates of in-hospital complications.³¹ Similar results were also noted in prior studies from the HCUP-NIS database.³² In our study, despite noting that women were older and had greater comorbidity, there were no differences in the use of angiography and PCI between the sexes. This observation could be related to a selection bias because all admissions in this study had received MCS devices. It is conceivable that given the concerns with large bore access-related complications, women were considered for MCS further along their “hemo-metabolic” cascade compared with men.^{4,31} Prior data have shown that clinicians worry about higher complications with large-bore MCS in women due to smaller calibre of femoral vessels, lower body surface area, and higher rates of bleeding.^{18,30,33} Prior studies have shown that sex disparities in ST-segment elevation AMI-CS have less pronounced sex differences.³⁴ Therefore, it is conceivable that the worse outcomes in women in this study may be related to the higher prevalence of non-ST-segment elevation AMI-CS. Further dedicated studies of non-ST-segment AMI-CS are needed to better understand this phenomenon. Lastly, women had higher rates of respiratory failure and mechanical ventilation use, which might reflect higher severity of heart failure. The lower rates of angiography and PCI in this population are consistent with prior real-world literature that reflects reluctance to perform angiography in higher risk cohorts despite robust guideline recommendations.³⁵

As compared with AMI, there are limited data on the sex disparities in AMI-CS. In the **Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock** (SHOCK) registry, women had higher comorbidity and higher rates of mechanical complications.¹¹ In a population study from Ontario including 9750 patients, female sex was

associated with lower rates of revascularization and less frequent transfers to PCI-capable centres.³⁶ However, these studies did not show any differences in mortality despite the significant differences in the clinical profiles between men and women. In AMI-CS, reports of higher mortality in women are often confounded by small sample sizes, inadequate adjustment for delays since symptom onset and incomplete accounting for race, age, and socioeconomic status.^{11,30} In this large study using administrative data, these limitations were circumvented. Importantly, the study added to the sex-specific outcomes in AMI-CS literature in the contemporary MCS era.^{16-18,29} In 600 patients with AMI-CS from the IABP-SHOCK II study, although women had higher comorbidity and greater hemodynamic instability, they did not experience higher short- or long-term mortality compared with men.¹⁴ Using the catheter-based ventricular assist device registry (Impella 2.5 or CP), Alraies et al.¹⁶ did not note any sex-specific differences in clinical outcomes in Impella-supported PCI, including in 303 patients with AMI. In a retrospective registry of 81 patients with AMI-CS receiving Impella 2.5 or CP support, Doshi et al.¹⁷ did not note any differences in in-hospital and 30-day mortality between women and men.

In contrast, an older study of 180 patients with AMI-CS receiving Impella 2.5 support for AMI-CS showed that women had lower in-hospital mortality compared with men.¹⁸ In contrast to these smaller studies, the present study of 173,473 AMI-CS admissions shows persistent sex-specific disparities in clinical outcomes across the total cohort of MCS users and in the cohorts receiving the IABP and pLVAD. Although both sexes showed a temporal decrease in in-hospital mortality, female sex was an independent predictor of in-hospital mortality. These disparities persisted in the stratified analyses. Importantly, women have lower use of guideline-directed therapy after AMI complicated by heart failure/CS and have higher in-hospital mortality after durable LVAD placement, suggestive of a systematic bias along the spectrum of care of these patients.¹⁵ As evidenced in our study, women had higher rates of palliative care referrals, higher use of DNR status, and higher discharges to skilled nursing facilities. Prior data have demonstrated that women with AMI discharged to skilled nursing facilities have higher in-hospital mortality.³⁷ Taken in aggregate, these findings

Table 4. Clinical outcomes of AMI-CS admissions supported with MCS stratified by sex and MCS type

Outcomes	IABP (N = 159,240)		pLVAD (N = 7516)		ECMO (N = 1469)		≥ 2 MCS (N = 5248)		P
	Men (N = 108,167)	Women (N = 51,073)	Men (N = 5353)	Women (N = 2163)	Men (N = 1075)	Women (N = 394)	Men (N = 3962)	Women (N = 1286)	
In-hospital mortality	27.5	33.1	42.8	47.5	61.0	59.6	51.4	52.8	< 0.001
Length of stay (d)	11.1 ± 11.3	11.2 ± 11.6	11.4 ± 13.2	10.8 ± 11.6	18.8 ± 25.2	17.4 ± 19.1	15.4 ± 17.6	16.2 ± 26.5	< 0.001
Hospitalization costs (×1000 USD)	189 ± 183	181 ± 174	313 ± 265	316 ± 243	571 ± 610	552 ± 529	589 ± 488	451 ± 410	< 0.001
Do-noe-resuscitate status	5.0	6.5	13.4	15.3	10.7	7.6	10.1	12.8	< 0.001
Palliative care consultation	4.7	5.6	10.9	13.3	18.7	16.2	12.6	9.8	< 0.001
Durable LVAD	0.4	0.3	1.3	2.0	11.9	15.5	4.9	3.9	< 0.001
Cardiac transplantation	0.1	0.0	0.1	0.0	0.5	0.0	0.1	0.8	< 0.001
Race									
Home	46.3	33.5	40.8	30.4	26.6	20.2	20.7	8.1	< 0.001
Transfer	11.5	10.8	15.9	13.2	18.8	16.1	27.3	26.9	
SNF	24.6	36.5	32.4	34.0	32.9	59.7	36.5	44.2	
Home with HHC	17.1	18.9	10.9	22.4	21.6	4.0	15.2	20.8	
AMA	0.5	0.3	0.0	0.0	0.0	0.0	0.3	0.0	

Represented as percentage or mean ± standard deviation.

AMA, against medical advice; AMI, acute myocardial infarction; CS, cardiogenic shock; ECMO, extracorporeal membrane oxygenation; HHC, home health care; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; MCS, mechanical circulatory support; pLVAD, percutaneous left ventricular assist device; SNF, skilled nursing facility; USD, United States Dollars.

may suggest that women have a poorer social support system and potentially face earlier withdrawal of care. In this administrative database, it was not possible to quantify these qualitative measures including marital status, presence of advanced directives, and the outcomes from palliative care consultation. It is conceivable that we may note a similar picture as a consequence of higher severity of illness; however, the lower rates of end-organ perfusion and overall lower use of MCS support argue otherwise. Greater recognition of subconscious biases, sex-specific therapeutic strategies, and involvement of multidisciplinary teams for shared decision making are potential avenues to address these health care disparities.^{7,28} Lastly, in an exploratory subgroup analysis, we identified multiple subgroups wherein female sex was associated with worse in-hospital mortality. Consistent with similar literature from other AMI studies, non-white women had higher in-hospital mortality.³⁸ The worse outcomes of female and racial minorities, in addition to insurance status, are closely related to social, economic, and environmental factors that need to be considered in future qualitative studies.

Limitations

This study has several limitations, some of which are inherent to the analysis of a large administrative database. Coding errors, misrepresentation of procedural volumes, and underreporting of comorbidities are potential limitations of using administrative codes. The HCUP-NIS attempts to mitigate potential errors by using internal and external quality control measures. The administrative codes for AMI, CS, and MCS have been previously validated that reduces the inherent errors in the study. Although adjustments were made for differences in characteristics using multivariable analysis, it is possible that the observed outcomes could have been influenced, to some extent, by other unidentified confounders because of the inherent limitations of a retrospective study. Concomitant use of MCS with other devices/procedures was defined as those performed on the same procedure day. However, because further granularity in timing is unavailable and AMI-CS often evolves dynamically, the exact sequence of events cannot be discerned. The HCUP-NIS does not record duration of support or explantation of organ support; this study did not evaluate duration of MCS support alone or in combination with other MCS devices. The lack of universal health care, individual institutional practices, and patient preferences might impact the use and outcomes associated with the MCS devices and need a careful study in the future. The angiographic data, such as PCI location, lesion classification, presence of multivessel disease, and revascularization failure, that may significantly influence outcomes were not available in this database. From a CS standpoint, the database does not record echocardiographic, hemodynamic, and physiological data, which may limit the ability to risk-stratify the CS in these patients.³⁹ It is conceivable that similar to the long-term outcomes of an all-comer AMI population, these sex disparities may be less pervasive in the long term.⁴⁰ However, further data are needed to study this high-risk population, that is, those with CS and receiving MCS therapy. The strengths of this analysis include the large sample size, the ability to provide longitudinal data across the 12-year study period, and the identification of sex-specific disparities in this complex population.

Conclusions

In this retrospective, observational, and administrative database study, persistent sex disparities in care and outcomes of AMI-CS admissions supported with temporary MCS were noted. Women who received MCS had higher in-hospital mortality and posthospitalization resource utilization. Further dedicated research into the pathobiology of AMI-CS and MCS use with a sex-specific focus is needed to improve care and ensure equitable outcomes between men and women.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjcoopen.ca/> and at <https://doi.org/10.1016/j.cjco.2020.06.001>.