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ORIGINAL ARTICLE

Sex-Based Disparities in Acute Myocardial Infarction Treatment Patterns and Outcomes in Older Adults Hospitalized Across 6 High-Income Countries: An Analysis From the International Health Systems Research Collaborative

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BACKGROUND: Sex differences in acute myocardial infarction treatment and outcomes are well documented, but it is unclear whether differences are consistent across countries. The objective of this study was to investigate the epidemiology, use of interventional procedures, and outcomes for older females and males hospitalized with ST-segment–elevation myocardial infarction (STEMI) and non–ST-segment–elevation myocardial infarction (NSTEMI) in 6 diverse countries.

METHODS: We conducted a serial cross-sectional cohort study of 1 508 205 adults aged ≥66 years hospitalized with STEMI and NSTEMI between 2011 and 2018 in the United States, Canada, England, the Netherlands, Taiwan, and Israel using administrative data. We compared females and males within each country with respect to age-standardized hospitalization rates, rates of cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass graft surgery within 90 days of hospitalization, and 30-day age- and comorbidity-adjusted mortality.

RESULTS: Hospitalization rates for STEMI and NSTEMI decreased between 2011 and 2018 in all countries, although the hospitalization rate ratio (rate in males/rate in females) increased in virtually all countries (eg, US STEMI ratio, 1.58:1 in 2011 and 1.73:1 in 2018; Israel NSTEMI ratio, 1.71:1 in 2011 and 2.11:1 in 2018). Rates of cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass graft surgery were lower for females than males for STEMI in all countries and years (eg, US cardiac catheterization in 2018, 88.6% for females versus 91.5% for males; Israel percutaneous coronary intervention in 2018, 76.7% for females versus 84.8% for males) with similar findings for NSTEMI. Adjusted mortality for STEMI in 2018 was higher for females than males in 5 countries (the United States, Canada, the Netherlands, Israel, and Taiwan) but lower for females than males in 5 countries for NSTEMI.

CONCLUSIONS: We observed a larger decline in acute myocardial infarction hospitalizations for females than males between 2011 and 2018. Females were less likely to receive cardiac interventions and had higher mortality after STEMI. Sex disparities seem to transcend borders, raising questions about the underlying causes and remedies.

Key Words: cross sectional studies ■ epidemiology ■ healthcare disparities ■ international comparison ■ mortality rates ■ myocardial infarction ■ sex differences

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WHAT IS KNOWN

- Prior analyses, primarily from individual countries, have demonstrated that females hospitalized with acute myocardial infarction are less likely to receive cardiac revascularization than males and may have higher mortality, though much of the mortality difference appears driven by older age and greater comorbidity burden in females.
- It is currently unknown whether the sex differences documented in individual countries consistent across 6 diverse countries (the United States, Canada, England, the Netherlands, Israel, and Taiwan) with different health care delivery systems, populations, and cultures.

WHAT THE STUDY ADDS

- We found that between 2011 and 2018, there were larger declines in acute myocardial infarction hospitalization rates in females than in males, resulting in acute myocardial infarction becoming increasingly male over time in all 6 countries.
- Females hospitalized with both ST-segment–elevation and non–ST-segment–elevation myocardial infarction were less likely than their male counterparts to receive cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass grafting in all 6 countries in both 2011 and 2018 with 1 exception (coronary artery bypass grafting in Taiwan in 2018).
- Sex disparities seem to transcend geopolitical borders raising questions about the mechanisms (cultural versus biological) and potential solutions.

Nonstandard Abbreviations and Acronyms

AMI	acute myocardial infarction
CABG	coronary artery bypass grafting
IHSRC	International Health System Research Collaborative
NSTEMI	non–ST-segment–elevation myocardial infarction
PCI	percutaneous coronary intervention
STEMI	ST-segment–elevation myocardial infarction

Acute myocardial infarction (AMI) is a leading cause of morbidity and mortality in high-income countries.[1] There has been longstanding concern about sex-based disparities in AMI treatment and outcomes for females relative to males.[2] In addition to potentially presenting with different symptoms than males,[3,4] females experience AMI at an older age than males and are less likely to receive coronary revascularization.[5,6] Females also have higher unadjusted mortality, but this is significantly attenuated after adjustment for age and comorbidity.[7–9]

Although sex differences in AMI treatment and outcomes have been documented in multiple individual countries,[10–13] these studies often have differed in methodological approach (eg, populations studied, inclusion/exclusion criteria, outcomes assessed) meaning that we have limited understanding of whether sex differences are consistent across countries. There are few studies that have systematically examined whether sex differences in AMI treatment and outcomes are consistent across countries when using population-representative data and a common methodological approach. The paucity of international comparisons precludes us from understanding whether observed sex differences in AMI epidemiology, treatment, and outcomes reflect isolated country-specific care gaps or generalized global phenomena. If sex differences are consistent across countries, this might suggest other possibilities including biological explanations, deeply ingrained sex differences in care-seeking behavior, or implicit biases that transcend geopolitical borders.[14,15] AMI serves as an ideal condition for cross-country comparison because criteria for diagnosis and recommended treatments (eg, early cardiac catheterization for patients with ST-segment–elevation myocardial infarction [STEMI]) are consistent across countries and males and females with AMI would typically require hospital admission in all countries, thus minimizing selection bias.[16,17]

In this analysis, we used population-representative administrative data from the International Health System Research Collaborative (IHSRC; https://projects.iq.harvard.edu/ihsrc) to identify older females and males hospitalized with STEMI or non–ST-segment–elevation myocardial infarction (NSTEMI) between 2011 and 2018 in 6 participating countries (the United States, Canada, England, the Netherlands, Israel, and Taiwan) with advanced health systems.[18] We compared females and males with respect to AMI hospitalization rates, receipt of cardiac interventions, and mortality in each country and over time.

METHODS

Data and Patients

Because of the sensitive nature of the data used in this study, as well as the rules and regulations of our participating countries, we are unable to share the data used in this study; questions or requests can be sent to the corresponding author. We used population-representative administrative data (Supplemental Methods 1) to identify people aged ≥66 years hospitalized for at least 1 day (or who died on the day of admission) with a primary diagnosis of STEMI or NSTEMI between January 1, 2011, and December 31, 2018, in any of our 6 IHSRC countries (between 2013-2018 in The Netherlands) (Canada represented by the provinces of Ontario and Manitoba) using the *International Classification of Diseases* (*International Classification of Diseases*, *Ninth Revision* and *International Classification of Diseases*, *Tenth Revision*) codes and methods described previously (Supplemental Methods 2).[18] Data sources were selected to ensure comparability across countries.[18,19] Patients with STEMI and NSTEMI were identified using a well-established coding schema and a common study protocol across countries; local investigators with a deep knowledge of each country's coding and care systems made minor modifications based upon local practice. We excluded patients with an AMI admission during the year prior to avoiding counting readmissions as new admissions. We also excluded patients with <1 year of preadmission or postadmission follow-up data, except in the case of death. We excluded US patients enrolled in Medicare Advantage health insurance because of concerns that Medicare part A data may not capture all Medicare Advantage hospitalizations, particularly in the earlier years of our study. We linked patients transferred between hospitals to include the complete episode of care. We applied inclusion and exclusion criteria in the same order in each country, allowing slight variations to reflect local differences in data architecture. We used data from 2010 for a 1-year look back for patients admitted in 2011 and data from 2019 for 1-year follow-up for patients admitted in 2018.

In each country, we obtained basic demographic information (age and sex) and comorbidities for each patient. Comorbid conditions present on the index admission and previous hospitalizations during the 1-year look back were captured using a Manitoba adaptation of the Elixhauser comorbidity measures, with some adjustments for country-specific differences in data (Supplemental Methods 3).[20,21] We excluded cardiovascular conditions identified in the index admission that could plausibly have arisen due to the AMI. In the Netherlands, where comorbidities identified from hospital admissions were less available, we used a medication approach to identify comorbidities.[19]

Outcomes

We evaluated outcomes separately for females and males in each country and calendar year for the STEMI and NSTEMI cohorts. Our primary outcomes were the following: (1) age-standardized AMI hospitalization rates (hospitalizations per 1000 population per year); (2) the age-standardized proportion of patients who underwent interventional cardiac procedures (catheterization [with or without percutaneous coronary intervention (PCI)]) and coronary artery bypass grafting (CABG) during the index hospitalization and within 90 days of admission; and (3) age- and comorbidity-adjusted mortality within 30 days and 1 year of admission. Secondary outcomes included hospital length of stay and hospital readmission within 30 days after discharge. Our article primarily focused on the first year (2011) and last year (2018) of data for simplicity of presentation.

Statistical Analyses

First, we compared the characteristics (age and comorbidities) of females and males hospitalized with STEMI and NSTEMI in each country. We did not perform formal statistical tests because of our large samples, multiple comparisons, and desire to focus on clinically important differences.[22] Second, we compared the STEMI and NSTEMI rates for females and males (annual hospitalizations per 1000 population) with results standardized to the age distribution of each country's population in 2018 (for additional details, see Supplemental Methods 4). We also calculated the ratio of STEMI and NSTEMI hospitalization rates in males versus females for each country and year as a measure of the overall sex balance between males and females. Third, we calculated age-standardized proportions of patients receiving cardiac interventions (catheterization, PCI, and CABG) during the index admission and within 90 days of admission; we computed the differences in the proportions of females versus males receiving each type of intervention (eg, PCI) in each country in each year; we did not adjust these comparisons for comorbid conditions because treatment approaches in AMI generally are dictated by the type of AMI rather than the presence or absence of comorbid conditions and because prior studies have demonstrated that differences persist with or without comorbidity adjustment.[7,23] Fourth, we calculated age- and comorbidity-adjusted 30-day and 1-year mortality. In each country, we fit logistic regression models with indicators for age and each comorbidity (measured using country-specific methods). Rates of measured comorbidities captured in administrative data are known to vary substantially across countries due to differences in financial incentives and completeness of coding.[24] However, these differences should not be problematic for within-country comparisons of females and males. Full details of our risk adjustment methodology are available in Supplemental Methods 3 and 5 and in our prior publications.[19] We also compared females and males with respect to age-standardized hospital length of stay and 30-day readmissions.

Teams in each of our 6 IHSRC countries conducted the analyses locally. The study was approved by appropriate ethics committees in each country. Analyses were conducted using SAS (the United States, Ontario, Manitoba, and Taiwan), and R (Israel, England, and the Netherlands).

RESULTS

Generation of our analytic cohorts in each country can be seen in Figure S1, with final cohort sizes for STEMI ranging from 284 950 patients in the United States (889 538 with NSTEMI) to 5601 in Israel (14 909 with NSTEMI; Table S1). Females hospitalized with STEMI were 3 to 4 years older than males in all countries (Table 1). For example, in 2018, the US mean age of females and males hospitalized with STEMI were 79.7 and 75.9 years (England, 80.0 and 76.7). Females hospitalized with STEMI had higher rates of comorbid conditions than their male counterparts in the same country (Table 1). For example, in 2018 in Taiwan, 62.6% of females and 53.4% of males had recorded hypertension (9.8% and 8.1% in the Netherlands). Results for NSTEMI were similar with females being older and having higher rates of most comorbid conditions (Table 1).

Less than 50% of patients hospitalized with AMI were females in nearly all countries and years (Table 1), but the sex imbalance differed substantially across countries. For STEMI, the proportion occurring in females was lowest in Taiwan (35.7% in 2011 and 31.9% in 2018) and highest in the United States (47.5% in 2011 and

Table 1. Demographic Characteristics and Comorbid Conditions of Females and Males Hospitalized With STEMI and NSTEMI in 2011 and 2018

		The United States		Canada		England		The Netherlands		Israel		Taiwan	
		Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
STEMI													
2011*	n%	20 047 (47.5)	22 164 (52.5)	1317 (42.9)	1754 (57.1)	713 (43.1)	942 (56.9)	1718 (39.9)	2583 (60.1)	304 (40.5)	447 (59.5)	1392 (35.7)	2504 (64.3)
	Age, y; mean	80.9	77.1	79.7	75.6	80.4	76.6	78.9	75.0	79.9	76.9	79.4	76.7
	Congestive heart failure, %	10.5	7.0	3.2	2.1	2.7	1.6	NA†	NA†	7.9	10.5	NA†	NA†
	Hypertension, %	79.6	73.5	43.8	38.9	63.4	49.2	6.3	5.1	70.1	61.5	61.6	51.5
	Diabetes, %	31.4	30.7	24.2	27.5	16.0	15.7	5.7	4.5	39.8	40.5	45.8	35.5
	Hypothyroidism, %	22.8	8.7	3.5	1.1	12.3	2.3	NA†	NA†	13.5	5.4	0.7	NA†
2018	n%	12 665 (42.0)	17 520 (58.0)	1351 (40.5)	1988 (59.5)	663 (38.5)	1058 (61.5)	1933 (38.8)	3045 (61.2)	249 (35.0)	463 (65.0)	1070 (31.9)	2289 (68.1)
	Age, y; mean	79.7	75.9	79.2	75.4	80.0	76.7	79.0	75.2	79.8	74.9	79.3	75.3
	Congestive heart failure, %	7.2	4.7	1.9	2.5	3.9	2.9	NA†	NA†	10.4	2.8	NA†	NA†
	Hypertension, %	83.6	79.0	43.6	44.4	59.4	54.5	9.8	8.1	68.7	59.8	62.6	53.4
	Diabetes, %	32.6	32.6	26.0	29.6	22.8	24.4	6.5	5.9	52.2	37.1	36.3	30.3
	Hypothyroidism, %	24.3	9.9	1.0	0.7	13.0	4.4	NA†	NA†	12.0	2.6	0.7	0.2
NSTEMI													
2011*	n%	58 763 (50.7)	57 128 (49.3)	4052 (46.1)	4739 (53.9)	2978 (45.0)	3635 (55.0)	3246 (41.6)	4556 (58.4)	809 (47.1)	908 (52.9)	1736 (42.4)	2361 (57.6)
	Age, y; mean	81.6	79.0	81.2	78.2	82.2	78.7	79.6	76.8	81.6	78.8	78.9	77.9
	Congestive heart failure, %	18.6	15.7	7.8	7.4	7.7	6.9	NA†	0.5	18.8	20.2	NA†	NA†
	Hypertension, %	86.5	83.4	51.3	47.5	74.4	68.5	8.6	7.5	76.8	68.7	68.8	63.7
	Diabetes, %	39.3	41.1	36.5	39.5	27.2	30.2	7.6	7.0	54.3	54.8	58.9	45.2
	Hypothyroidism, %	26.4	11.7	3.8	1.9	14.1	4.9	NA†	NA†	13.8	7.5	0.7	0.4
2018	n%	49 390 (46.9)	55 977 (53.1)	3861 (43.2)	5069 (56.8)	1752 (42.1)	2414 (57.9)	3988 (40.0)	5977 (60.0)	760 (39.2)	1177 (60.8)	2511 (40.0)	3761 (60.0)
	Age, y; mean	80.6	78.4	80.1	77.5	82.0	78.5	79.2	76.8	80.7	77.6	79.4	77.1
	Congestive heart failure, %	17.4	15.6	6.9	6.3	9.9	9.9	NA†	0.4	16.6	15.2	NA†	NA†
	Hypertension, %	90.1	89.4	52.8	51.5	73.1	70.0	12.6	10.7	74.6	68.1	74.6	70.1
	Diabetes, %	41.5	45.3	38.5	43.8	31.4	38.5	10.0	10.3	54.7	59.3	47.8	40.5
	Hypothyroidism, %	29.4	13.6	1.5	0.9	15.8	5.7	0.4	0.2	15.4	5.1	1.0	0.4

NSTEMI indicates non–ST-segment–elevation myocardial infarction; and STEMI, ST-segment–elevation myocardial infarction.
*The Netherlands data are for 2013.
†Data censored due to small cell size.

42.0% in 2018; Table 1). For NSTEMI, the proportion of females was lowest in the Netherlands (41.6% in 2011 and 40.0% in 2018), Taiwan (42.4% in 2011 and 40.0% in 2018), and Israel (47.1% and 39.2%) and highest in the United States (50.7% and 46.9%).

Between 2011 and 2018, age-standardized STEMI hospitalization rates declined in most countries for females and males (Table 2). For example, the STEMI hospitalization rate for females in the United States decreased from 1.13 per 1000 population per year in 2011 to 0.73 in 2018 and in males from 1.79 per 1000 population in 2011 to 1.26 in 2018 (2.00–1.73 for males in Canada and 1.47–1.05 for males in Taiwan). NSTEMI hospitalization rates also declined in most countries (eg, Canadian females, 3.37 in 2011 to 2.70 in 2018; English females, 2.57–1.82).

The decline in AMI hospitalization rates was proportionally smaller for males than for females in all countries, resulting in an overall shift in the sex balance over time (Table 2; Figure S2). As a result, the ratio of STEMI and NSTEMI hospitalizations in males versus females increased between 2011 and 2018 in all countries, with both conditions becoming more male. For example, STEMI hospitalization rates were 1.58× higher in males compared with females in the United States in 2011, increasing to 1.73× higher in 2018, and in England increasing from 1.43 to 1.87. NSTEMI hospitalization rates were 1.71× higher among males in Israel in 2011 (2.11 in 2018).

There were also large between-country differences in the male-female ratio of AMI hospitalizations; Taiwan

Table 2. Age-Standardized STEMI and NSTEMI Hospitalization Rates (Hospitalizations per 1000 per Year) for Males and Females Between 2011 and 2018 for the United States, Canada, England, the Netherlands, Israel, and Taiwan

Condition	Country	Sex	2011	2012	2013	2014	2015	2016	2017	2018
STEMI	US	Male	1.79	1.66	1.54	1.51	1.45	1.38	1.33	1.26
		Female	1.13	1.05	0.96	0.92	0.89	0.85	0.79	0.73
	CA	Male	2.00	1.88	1.98	1.95	1.94	1.94	1.92	1.73
		Female	1.13	1.09	1.04	1.03	1.03	1.03	0.98	0.95
	EN	Male	0.99	1.23	1.20	1.27	1.32	1.36	1.37	1.23
		Female	0.69	0.76	0.75	0.77	0.78	0.82	0.80	0.66
	NE	Male	*	*	2.79	2.80	2.63	2.32	2.01	1.87
		Female	*	*	1.55	1.56	1.40	1.28	1.13	1.04
	IS	Male	2.14	2.06	2.01	1.70	1.70	1.80	1.72	1.76
		Female	1.01	1.07	0.90	0.76	0.69	0.75	0.62	0.72
	TW	Male	1.47	1.44	1.43	1.29	1.18	1.15	1.10	1.05
		Female	0.59	0.53	0.48	0.43	0.41	0.37	0.34	0.32
NSTEMI	US	Male	4.62	4.51	4.33	4.38	4.45	4.42	4.42	4.16
		Female	3.25	3.22	3.03	3.03	3.03	3.02	3.00	2.80
	CA	Male	5.51	5.67	5.31	5.27	5.20	5.21	4.81	4.53
		Female	3.37	3.39	3.20	3.09	3.02	2.94	2.77	2.70
	EN	Male	4.20	3.92	3.68	3.68	3.37	3.42	3.60	3.07
		Female	2.57	2.45	2.28	2.15	1.96	1.98	2.02	1.82
	NE	Male	*	*	6.24	5.88	5.44	4.98	4.56	4.07
		Female	*	*	3.28	3.09	3.02	2.68	2.50	2.29
	IS	Male	4.36	4.36	4.61	4.48	4.47	4.83	4.44	4.61
		Female	2.65	2.55	2.66	2.50	2.58	2.48	2.29	2.18
	TW	Male	1.41	1.58	1.61	1.71	1.58	1.81	1.89	1.85
		Female	0.69	0.72	0.77	0.72	0.68	0.78	0.82	0.75

CA indicates Canada; EN, England; IS, Israel; NE, the Netherlands; NSTEMI, non–ST-segment–elevation myocardial infarction; STEMI, ST-segment–elevation myocardial infarction; TW, Taiwan; and US, the United States.

* 2011-2012 data was unavailable for The Netherlands.

and Israel had notably higher male-female ratios and the United Sates had lower male-female ratios than the other countries.

Revascularization Patterns

For STEMI, females in all countries had lower age-standardized rates of both cardiac catheterization and PCI within 90 days of admission in both 2011 and 2018 (Figure 1). For example, in 2018, the percentage of females who received PCI within 90 days of admission ranged from 3.0% lower than males in the United States to 8.5% lower in Taiwan (3.5% lower in Canada). Looking longitudinally, between 2011 and 2018, the female gap in receipt of PCI (compared with men) decreased in the United States, was unchanged in Canada, and increased in England, the Netherlands, Israel, and Taiwan. Females hospitalized with STEMI also were less likely to receive CABG within 90 days of admission than males in all countries in both 2011 and 2018 with the exception of Taiwan in 2018 (Figure 1). The disparity in receipt of interventional procedures among females hospitalized with STEMI was maintained when analyses were limited to procedures performed during the index hospitalization (Figure S3). Results for NSTEMI were generally similar, with females less likely to receive cardiac catheterization, PCI, and CABG than males in all countries and all years both within 90 days of hospitalization (Figure 2) and when limited to the index hospital admission (Figure S4). For example, in England, compared with males, within 90 days of hospitalization, females received 4.3% less cardiac catheterization, 5.3% less PCI, and 1.2% less CABG with similar findings in other countries.

Mortality

For STEMI, age- and comorbidity-adjusted 30-day mortality was modestly higher for females compared with males in most countries and years (Figure 3). For example, in 2011, STEMI mortality was higher for females than males in 5 countries (the United States [+1.7%], Canada [+0.8%], and England [+0.1%]), Israel [+3.1%], and England [+5.7%]) but lower in 1 country (the Netherlands [–0.6%]). In 2018, STEMI mortality

Country	Year	Cardiac catheterization, % Female rate	Cardiac catheterization, % Male rate	Cardiac catheterization, % Female minus male	PCI, % Female rate	PCI, % Male rate	PCI, % Female minus male	CABG, % Female rate	CABG, % Male rate	CABG, % Female minus male
US	2011	77.5	82.5	-4.9	61.4	66.6	-5.2	7.1	11.0	-3.9
	2018	88.6	91.5	-2.9	76.1	79.1	-3.0	5.5	8.9	-3.4
CA	2011	78.9	83.3	-4.4	66.2	69.8	-3.6	3.8	5.9	-2.1
	2018	86.0	88.4	-2.4	77.1	80.6	-3.5	1.9	4.4	-2.5
EN	2011	76.6	73.6	-2.9	63.6	57.6	-6.0	2.6	3.9	-1.4
	2018	81.1	74.2	-7.0	72.2	65.0	-7.2	1.9	3.4	-1.5
NE	2013	41.8	44.0	-2.2	34.3	36.7	-2.4	2.1	3.0	-0.9
	2018	50.7	54.6	-3.9	47.6	52.0	-4.5	1.1	1.7	-0.6
IS	2011	75.9	81.6	-5.8	65.7	70.9	-5.2	5.6	8.0	-2.4
	2018	84.7	91.5	-6.9	78.7	84.8	-6.1	2.4	5.2	-2.8
TW	2011	65.6	68.9	-3.3	46.7	55.3	-8.7	4.5	6.6	-2.1
	2018	77.3	82.2	-4.9	68.4	76.9	-8.5	3.6	3.0	0.6

Figure 1. Cardiac catheterization, percutaneous coronary intervention (PCI), and coronary artery bypass graft surgery (CABG) within 90 days of admission for ST-segment–elevation myocardial infarction in 2011 and 2018 by country (age standardized).
CA indicates Canada; EN, England; IS, Israel; NE, the Netherlands; TW, Taiwan; and US, the United States.

was marginally lower for females than for males in 1 country (−0.9% in England) but higher for females in 5 countries (the United States, Canada, the Netherlands, Israel, and Taiwan; range, +1.3% in the United States to +4.1% in Taiwan; Figure 3). Results were generally similar for STEMI when looking at 1-year mortality (Figure S5) with higher mortality for women in most countries and years.

In contrast, for NSTEMI, females tended to have lower mortality than males across countries and years (Figure 3). For example, in 2018 for NSTEMI, females had higher mortality in Israel (+1.4%) but slightly lower mortality in the United States, Canada, England, the Netherlands, and Taiwan (range, −0.1% to −0.7%; Figure 3). Age- and comorbidity-adjusted 1-year mortality results for NSTEMI were generally similar (Figure S5).

There were no clear differences for females versus males in either age-standardized hospital length of stay or 30-day readmissions for STEMI or NSTEMI in 2018 (Figure S6).

Country	Year	Cardiac catheterization, % Female rate	Cardiac catheterization, % Male rate	Cardiac catheterization, % Female minus male	PCI, % Female rate	PCI, % Male rate	PCI, % Female minus male	CABG, % Female rate	CABG, % Male rate	CABG, % Female minus male
US	2011	58.3	63.2	-4.9	28.9	33.5	-4.6	8.5	13.2	-4.7
	2018	62.1	68.9	-6.8	31.7	37.3	-5.6	8.4	15.1	-6.7
CA	2011	55.6	59.5	-3.9	28.6	31.3	-2.7	6.7	11.5	-4.8
	2018	67.7	72.2	-4.5	37.5	43.2	-5.7	6.9	12.4	-5.5
EN	2011	57.6	51.2	-6.5	29.5	23.7	-5.8	3.9	8.7	-4.8
	2018	62.4	58.5	-4.0	35.0	29.9	-5.0	4.5	8.4	-3.9
NE	2013	32.1	34.7	-2.6	17.2	19.3	-2.1	2.3	3.0	-0.7
	2018	29.9	34.8	-4.8	25.3	29.3	-4.0	1.8	2.9	-1.0
IS	2011	49.9	56.0	-6.1	29.8	34.5	-4.8	7.9	10.9	-3.0
	2018	57.9	66.8	-8.9	39.8	47.9	-8.1	4.5	7.7	-3.2
TW	2011	59.5	63.3	-3.8	37.0	43.3	-6.3	5.2	6.8	-1.6
	2018	70.4	73.9	-3.5	50.5	57.0	-6.5	3.9	5.3	-1.4

Figure 2. Cardiac catheterization, percutaneous coronary intervention (PCI), and coronary artery bypass graft surgery (CABG) within 90 days of admission for non–ST-segment–elevation myocardial infarction in 2011 and 2018 by country (age standardized).
CA indicates Canada; EN, England; IS, Israel; NE, the Netherlands; TW, Taiwan; and US, the United States.

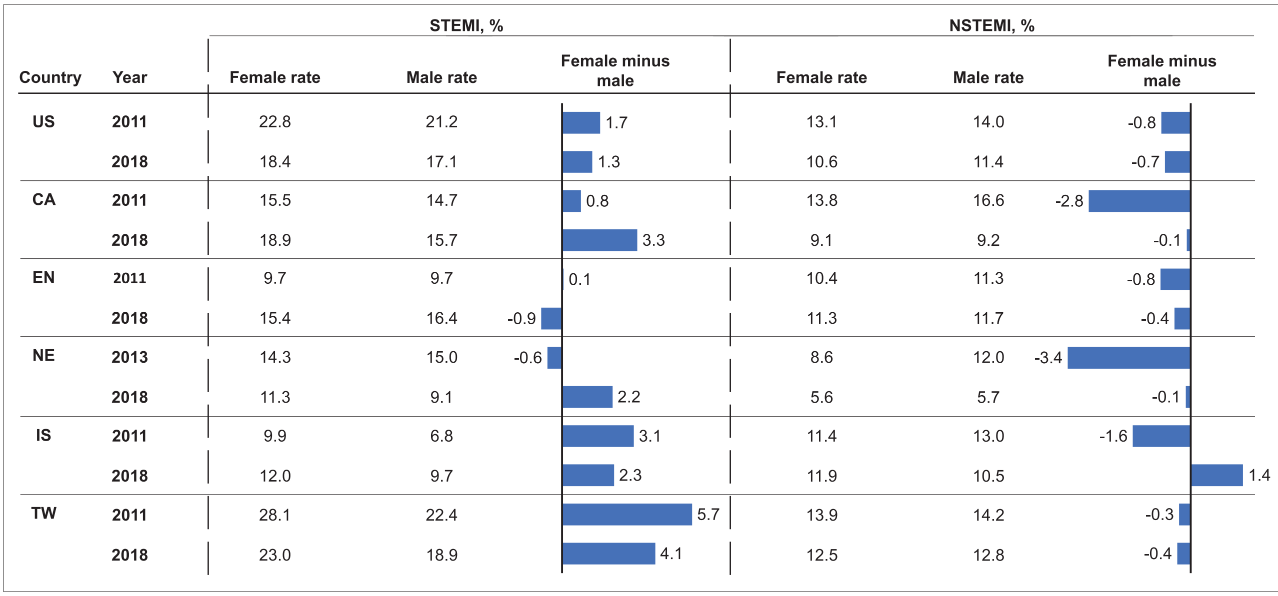

Figure 3. Thirty-day mortality for ST-segment–elevation myocardial infarction (STEMI) and non–segment-ST–elevation myocardial infarction (NSTEMI) for men and women in 2011 and 2018 by country (age and comorbidity adjusted).
CA indicates Canada; EN, England; IS, Israel; NE, the Netherlands; TW, Taiwan; and US, the United States.

DISCUSSION

In this analysis of population-representative administrative data from 6 high-income countries, we found 3 noteworthy differences in older females and males hospitalized with AMI. First, between 2011 and 2018, males comprised an increasing share of both STEMI and NSTEMI hospitalizations across all 6 countries. Second, females were less likely than males to receive cardiac catheterization or revascularization in all countries, with a particularly large gap for STEMI; moreover, the deficit did not appreciably decline over time. Third, females hospitalized with STEMI had modestly higher adjusted mortality than males in most countries but slightly lower mortality rates for NSTEMI.

Each of our key findings warrants elaboration. First, over the time period of our study, we found that STEMI and NSTEMI hospitalizations became increasingly male (and less female) across all 6 IHSRC countries—a finding that has not been well described previously. Overall, AMI hospitalizations had been declining for decades in most countries,[25–28] though this decline may have been smaller in certain populations such as younger females.[23,29] Interestingly, recent data suggest that we may have reached a nadir and that rates of AMI may now be increasing, potentially driven by increasing rates of obesity and diabetes.[30]

The shift in the sex balance that we observed between 2011 and 2018 was driven by a larger relative reduction in AMI hospitalizations for females than males and raises important questions about the causes of this differential reduction in AMI: why are AMI rates falling more in females than males? One potential explanation would be changing patterns of cardiovascular disease risk factors (eg, diabetes, hypertension, obesity, or smoking) among females and males occurring contemporaneously in all 6 countries. Given that we found relatively similar trends in the prevalence of diabetes and hypertension in females and males among the STEMI and NSTEMI populations within individual countries, we would suggest that shifting risk factors are unlikely causes. Another potential cause would be differential shifts in smoking rates. According to 1 large international comparison, rates of decline in smoking prevalence from 1990 to 2019 were larger among females than males in all our countries,[31] making it at least plausible that differential declines in smoking could be a potential explanation. Other potential causes could include secular changes in the prescribing of or adherence to guideline-recommended medications (eg, antihypertensives, statins) for females and males that are occurring simultaneously in all 6 countries; while such a hypothesis is appealing,[32] we are unaware of empirical data to this effect.[33] Given the potential importance of our finding of a widespread shift in the sex balance of AMI, our findings require further confirmation and, if verified, investigation of definitive contributors to this shift.

We also found large between-country differences in the male-female imbalance: specifically, much larger male-female hospitalization ratios in Taiwan and Israel compared with other countries. One possible explanation would be a larger male-female difference in cardiovascular risk factors (higher risk in males relative to females) in Israel and Taiwan than in other countries; differential smoking rates for males and females in Israel and Taiwan (as compared with other countries) offers 1 potential explanation.[31,34] Data from the Global Burden of Disease study group suggest that males in Taiwan are ≈8-fold more likely to smoke than females, the largest male-to-female ratio of smoking prevalence among all our countries.[31] Israel, with the second largest male-female AMI ratio, also had the second highest male-to-female smoking difference.

Although it is plausible that differential cardiovascular risk factors such as smoking in males and females explain the between-country sex differences in AMI epidemiology, other explanations must be considered. Studies have demonstrated that females experiencing AMI are less likely to seek care and that females with cardiac symptoms are less likely to receive a cardiac evaluation than men.[3,35] If, for example, females in Taiwan and Israel were less likely to seek care for cardiac symptoms than their male counterparts, this would also produce the pattern of male-female AMI imbalance that we observed. A different mechanism that would yield similar findings would occur if females in Taiwan and Israel were less likely to receive electrocardiograms or receive high-sensitivity troponin testing; this could result in systematic underdiagnosis of AMI in females and an appearance of a larger male-female ratio. The underlying mechanisms of the between-country differences in male-female AMI balance is important as different mechanisms require different solutions. For example, lower rates of care seeking among women with AMI symptoms might be addressed through public awareness campaigns whereas underdiagnosis of AMI in women by health professionals would necessitate a different approach. Our study should generate further inquiry in Taiwan and Israel.

Second, our finding of clinically relevant differences in rates of cardiac interventions, with lower utilization of catheterization, PCI, and CABG for females as compared with males is consistent with prior single-country studies.[7,36,37] Our results are also consistent with a recently published 28-country analysis using data from 2 prospective international registries (EPICOR [long-term follow-up of anti-thrombotic management patterns In acute coronary] and EPICOR Asia), Those studies focused on the interaction between sex-differences, country-level differences, and income inequality rather than country-specific sex differences.[38] Lower rates of cardiac catheterization and PCI among females hospitalized with STEMI warrant special attention because of the strong evidence that early PCI reduces mortality for STEMI. Cardiac catheterization with PCI within 120 minutes of symptom onset is recommended in virtually all clinical practice guidelines.[39,40] The magnitude of the PCI deficit in females (in 2018 ranging from 3.0% [the United States] to 8.5% [Taiwan] lower for females) is large enough to warrant concern and corrective action.

In considering potential causes or mechanisms for the disparities we have observed it may be useful to think about patient factors (eg, demographic characteristics, comorbid conditions, anatomy, patient preference) but also broader social constructs. Our and others analyses have demonstrated that demographic characteristics and comorbidity do not fully explain the lower rates of cardiovascular procedures in females relative to males.[41,42] While it is possible that anatomic differences (eg, myocardial infarction with nonobstructive coronary arteries) would lead to lower rates of PCI in females presenting with STEMI,[41] this would not explain the lower rates of cardiac catheterization, as catheterization is a prerequisite to visualizing coronary anatomy. While some single-country studies have shown declines in the female-male gap in recent years, our study suggests that these disparities are both persistent and widespread.[41,42] If patient factors are not the predominant driver of differential rates of revascularization, it is important to think about other potential contributing causes including misdiagnosis and bias.[43]

Third, the higher age- and comorbidity-adjusted mortality for females after STEMI warrants attention. Multiple studies, usually using data from individual countries have demonstrated higher mortality for females hospitalized with AMI in general, and STEMI specifically, when compared with their male counterparts.[7,29,42,44,45] Potential causes of and explanations for the higher mortality observed in females after STEMI are complex. Available data suggest that patient factors (older age and a greater burden of comorbid conditions at presentation) play a role in higher mortality among females but also health-system factors including lower rates of revascularization and lower rates of guideline concordant therapies.[44–48] Females are also more likely to have delays in presentation to the emergency department and delayed or misdiagnosis, which are also likely to be contributing factors for the increased mortality in females that we observed.[4,37] Campaigns to increase awareness of myocardial infarction as a condition that afflicts females should continue.[49] In considering the higher mortality we observed for women with STEMI, it is also interesting to contemplate the potential role of social determinants of health including income; a recent study by Rossello et al[38] found a strong association between lower country-level wealth and higher income inequality with larger sex disparities (increased mortality for females). The observation of Rossello et al is particularly interesting in the context of our own recent finding that females hospitalized with AMI in our IHSRC countries tend to reside in lower income neighborhoods than males, further suggesting that lower income and associated social determinants of health may play an important mechanism.[19]

This analysis has several limitations. First, we used administrative data that lack important clinical details such as time to presentation, coronary artery anatomy, and ejection fraction that could influence treatment decisions. Second, our study was limited to adults aged ≥66 years who were hospitalized for AMI, and, therefore, does not generalize to other conditions or younger patients. Third, the large between-country differences in comorbid conditions warrant comment. These findings are concordant with previous international research using administrative data and likely reflect a combination of differential coding practices and financial incentives across countries to capture comorbid conditions rather than true health differences[18,50] Fourth, we excluded the Medicare Advantage population because there were concerns that hospitalizations in these patients were not consistently captured in the Medicare part A data, particularly during the earlier years of our study period.[22] Fifth, our 90-day catheterization and PCI rates did not capture outpatient procedures in any of the countries and thus 90-day procedure rates could be somewhat higher, particularly in countries where a large proportion of percutaneous interventions are performed in the outpatient setting. Sixth, we cannot exclude the possibility that some aspects of our results could be influenced by between-country differences in coding practices. Finally, our findings of higher rates of AMI in males and a larger reduction in AMI hospitalizations in females than males over time, suggests a worsening of male-female disparities in the incidence of both STEMI and NSTEMI with higher rates in males[51]; further work is needed to verify our finding and understand the underlying mechanisms at play.

In conclusion, we found that between 2011 and 2018 in 6 diverse high-income countries the declines in AMI hospitalization were smaller for males than females. We also extend prior research by demonstrating that females were less likely to receive cardiac interventions than males in all countries and had higher mortality after STEMI. In aggregate, our analysis exemplifies how international health system comparisons can be used to better discern patterns of care within and across countries.[52]

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

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