ORIGINAL RESEARCH

Temporal Trends in Utilization of Cardiac Therapies and Outcomes for Myocardial Infarction by Degree of Chronic Kidney Disease: A Report From the NCDR Chest Pain–MI Registry

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***Background*—**We sought to determine temporal trends in use of evidence-based therapies and clinical outcomes among myocardial infarction (MI) patients with chronic kidney disease (CKD).

***Methods and Results*—**MI patients from the NCDR (National Cardiovascular Data Registry) Chest Pain–MI Registry between January 2007 and December 2015 were categorized into 3 groups by degree of CKD (end-stage renal disease on dialysis, CKD [glomerular filtration rate <60 mL/min per 1.73 m^2] not requiring dialysis, and no CKD [glomerular filtration rate ≥60 mL/min per 1.73 m^2]). Logistic regression modeling was used to determine the association between calendar years (2014–2015 versus 2007–2008) and each outcome by degree of CKD. Among 325 396 patients with ST-segment–elevation MI, 1.0% had end-stage renal disease requiring dialysis, and 26.1% had CKD not requiring dialysis. Use of primary percutaneous coronary intervention increased over time regardless of the presence or degree of CKD (P=0.40 for interaction). In-hospital mortality was temporally higher among patients with preserved renal function (odds ratio: 1.25; 95% confidence interval, 1.13–1.39; P<0.001) but not among patients with CKD (P=0.035 for interaction). Among 506 876 non–ST-segment–elevation MI patients, 3.4% had end-stage renal disease requiring dialysis, and 34.4% had CKD not requiring dialysis. $P2Y_{12}$ inhibitor use within 24 hours increased over time only among dialysis patients (P for interaction <0.001). Use of coronary angiography and percutaneous coronary intervention also increased, with the greatest increase among dialysis patients (P for interaction <0.001 and <0.001, respectively). In-hospital mortality was lower, regardless of the presence or degree of CKD (P=0.64 for interaction).

***Conclusions*—**Uptake of evidence-based medical and invasive therapies has increased over the past decade among MI patients with CKD, particularly dialysis patients, with improvement of in-hospital mortality observed among patients with non–ST-segment–elevation MI, but not ST-segment–elevation MI, and CKD. **(*J Am Heart Assoc*. 2018;7:e010394. DOI: 10.1161/JAHA.118.010394)**

Key Words: chronic kidney disease • myocardial infarction • outcomes research

Several large registries have demonstrated the high prevalence of chronic kidney disease (CKD) among patients with acute myocardial infarction (MI),[1–3] the inverse correlation between worsening renal function and use of evidence-based therapies,[1,4–6] and poor short- and long-term outcomes among these patients.[7–10] In addition to greater comorbidities and baseline risk[11] and challenges in establishing a timely diagnosis of MI because of atypical presentation characteristics,[2,12] lower use of guideline-recommended therapies has been postulated as a reason for worse outcomes among these patients.[3] Over the past decade, several medical[13–15] and interventional strategies[16] have demonstrated improvements in outcomes after MI; however, patients with renal dysfunction have typically been excluded from these studies.[17] Thus, the application of this evidence base to patients with renal disease, particularly those with end-stage renal disease (ESRD) treated with dialysis, may not be automatically extrapolated.

A study performed by the Cardiovascular Special Studies Center of the US Renal Data System showed a decrease in mortality following ST-segment–elevation MI (STEMI) in dialysis

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Clinical Perspective

What Is New?

- Uptake of evidence-based medical and invasive therapies has increased over the past decade among myocardial infarction patients with chronic kidney disease, particularly dialysis patients.
- In-hospital mortality has improved among non–ST-segment–elevation myocardial infarction patients with chronic kidney disease, but not ST-elevation–myocardial infarction patients with chronic kidney disease.

What Are the Clinical Implications?

- These trends likely reflect a combination of accumulation of evidence supporting the benefit of these therapies in patients with chronic kidney disease and increased awareness and less therapeutic nihilism on the part of the practitioner.
- Although encouraging, persistent high residual early mortality rates demonstrate opportunities for further improvement in care of this high-risk population.

patients between 1993 and 2008 but not among non-STEMI (NSTEMI) patients.[18] This report, however, was limited by the precision needed to reliably distinguish STEMI from NSTEMI and by data on the use of concomitant evidence-based therapies. Trends in the use of these evidence-based therapies and in outcomes among patients with CKD in the contemporary era are unknown. Therefore, in this study, we utilized the NCDR (National Cardiovascular Data Registry) ACTION Registry (Acute Coronary Treatment and Intervention Outcomes Network Registry)–Get With the Guidelines (ACTION Registry–GWTG) database to examine temporal trends in the use of evidence-based therapies and in-hospital clinical outcomes of MI patients with CKD over the past decade. We specifically sought to determine whether the use of guideline-recommended in-hospital and discharge therapies and in-hospital clinical outcomes differed over time by MI type (STEMI versus NSTEMI) and by presence and degree of renal dysfunction.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Data Source and Analysis Population

All patients enrolled with MI in the NCDR ACTION Registry–GWTG from January 1, 2007, to December 31, 2015, were included in the initial study population (n=1 077 521 from 1177 hospitals). The NCDR ACTION Registry–GWTG serves as a hospital data collection and evaluation mechanism for MI patients in the United States and has been described previously.[19] All participating hospitals were required to comply with local regulatory and privacy guidelines and, if required, to secure institutional review board approval. Because data were used primarily at the local site for quality improvement, sites were granted a waiver of informed consent under the common rule. The Duke Clinical Research Institute served as the data analysis center and has an agreement to analyze the aggregate deidentified data for research purposes. For this analysis, patients who were missing information for the dialysis variable (n=1523), missing initial creatinine (n=7146), missing initial estimated glomerular filtration rate (GFR; n=6296), treated in a hospital without percutaneous coronary intervention (PCI) capability (n=30 874), given an abbreviated version of the data collection form (n=170 257), or transferred to another hospital (n=29 153) were excluded. The final study population consisted of 832 272 patients treated at 872 hospitals.

Statistical Analysis

Descriptive statistics were summarized as medians with interquartile ranges for continuous variables and as percentages for categorical variables. GFR was estimated for each patient with the Modification of Diet in Renal Disease equation using the initial creatinine value on presentation. Patients were stratified into 3 groups based on the presence and degree of CKD (ESRD on dialysis, moderate to severe CKD [GFR <60 mL/min per 1.73 m^2] not on dialysis, and preserved renal function [GFR$\geq$60 mL/min per 1.73 m^2]). Baseline demographics, presentation characteristics, in-hospital investigations, treatments, and outcomes were compared among the 3 groups, separately for STEMI and NSTEMI cohorts. In particular, frequency of primary PCI among eligible candidates, timeliness of reperfusion therapy (door-to-balloon [D2B] time), and frequency of medical therapy within 24 hours of presentation and at hospital discharge were determined among STEMI patients. Among NSTEMI patients, the frequency of medical therapy within 24 hours of presentation and at hospital discharge and the frequency of cardiac catheterization and revascularization in the hospital were determined. In-hospital clinical outcomes examined included mortality, major bleeding,[20] and moderate to severe acute kidney injury (AKI), defined as a $\geq$0.5-mg/dL change between peak and initial absolute creatinine values.

Finally, we determined the association between time period and in-hospital treatments, as well as outcomes stratified by presence and degree of CKD. Logistic regression modeling was used to evaluate the association between calendar year (binary variable: 1=patients discharged in

2014–2015, 0=patients discharged in 2007–2008) and each outcome according to the presence and degree of CKD separately for STEMI and NSTEMI patients. The interaction *P* value tested differences in outcomes between the last 2 years (2014–2015) and the first 2 years (2007–2008) by degree of CKD. Generalized estimating equations were used to account for clustering within hospitals. The unadjusted analysis included calendar year (binary variable), CKD groups, and their interactions in the model. $P<0.05$ was considered significant for all tests. All statistical analyses were performed by the Duke Clinical Research Institute with SAS software (v9.4; SAS Institute).

Results

STEMI Cohort

Among 325 396 patients with STEMI, 3121 (1.0%) had ESRD requiring dialysis, 85 068 (26.1%) had moderate to severe CKD but did not require dialysis, and 237 207 (72.9%) had preserved renal function. Compared with patients with preserved renal function, STEMI patients with CKD were older and had more comorbidities and higher risk features on presentation (Table 1). The proportion of STEMI patients with CKD remained constant between 2007–2008 and 2014–2015; patient demographics and features on presentation were also similar between 2007–2008 and 2014–2015 in the overall cohort and in each group stratified by presence and degree of CKD.

Medical and invasive therapy use

Early in-hospital use of aspirin, $P2Y_{12}$ receptor inhibitors, β-blockers, statins, glycoprotein IIb/IIIa inhibitors, and coronary angiography was lower among STEMI patients with CKD, with the lowest use among ESRD patients requiring dialysis (Table 2). Rates of primary PCI and coronary artery bypass grafting among STEMI patients undergoing coronary angiography were similar regardless of the presence or degree of CKD; however, the use of stents, including drug-eluting stents, and achievement of D2B time within recommended targets were lower among CKD patients, particularly among ESRD patients requiring dialysis. At hospital discharge, the use of $P2Y_{12}$ receptor inhibitors, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, and statins was lower among patients with CKD, particularly among patients with ESRD requiring dialysis.

There was a differential increase in aspirin use within 24 hours from 2007–2008 to 2014–2015 stratified by presence of CKD ($P=0.049$ for interaction); aspirin use increased among patients with preserved renal function but not among patients with CKD. Use of $P2Y_{12}$ receptor inhibitors within 24 hours, coronary angiography, primary PCI, percentage of patients with D2B time within guideline-recommended goal, and aspirin at discharge also increased over time regardless of the presence or degree of CKD (*P* values for interaction: $P2Y_{12}$ receptor inhibitor, $P=0.44$; coronary angiography, $P=0.24$; primary PCI, $P=0.40$; D2B time within guideline-recommended goal, $P=0.17$; aspirin at discharge, $P=0.34$). $P2Y_{12}$ receptor inhibitor use at discharge also increased over time, with a greater increase among patients with CKD ($P<0.001$ for interaction).

Clinical outcomes

In-hospital outcomes in STEMI patients are shown in Table 3. Compared with STEMI patients with preserved renal function, in-hospital mortality was ≈5-fold higher among patients with moderate to severe CKD not requiring dialysis and 7-fold higher among ESRD patients requiring dialysis. Major bleeding was also significantly higher among patients with CKD, particularly among ESRD patients requiring dialysis. Moderate to severe AKI occurred in 16% of patients with moderate to severe CKD and 4.6% of patients with preserved renal function.

In-hospital mortality rates were similar in 2007–2008 and 2014–2015 among patients with moderate to severe CKD (odds ratio: 1.07; 95% confidence interval, 0.98–1.16; $P=0.11$) and patients with ESRD requiring dialysis (odds ratio: 1.20, 95% confidence interval, 0.87–1.66; $P=0.26$), with a relative increase in in-hospital mortality among patients with preserved renal function (odds ratio: 1.25, 95% confidence interval, 1.13–1.39; $P<0.001$; $P=0.035$ for interaction; Figure 1A). In-hospital major bleeding rates were lower in 2014–2015 compared with 2007–2008, with the greatest reduction in bleeding observed among patients with ESRD on dialysis ($P=0.023$ for interaction; Figure 1B).

NSTEMI Cohort

Among 506 876 patients with NSTEMI, 17 104 (3.4%) had ESRD requiring dialysis, 174 543 (34.4%) had moderate to severe CKD but did not require dialysis, and 315, 229 (62.2%) had preserved renal function. NSTEMI patients with CKD had lower body weight, more comorbidities, and higher risk features on presentation (Table 4). The proportion of NSTEMI patients who had ESRD on dialysis but not moderate to severe CKD not requiring dialysis increased from 2007–2008 to 2014–2015 (2.8% versus 3.5% and 38.3% versus 32.7%, respectively). Compared with 2007–2008, NSTEMI patients in 2014–2015 had greater body weight and higher burden of diabetes mellitus, dyslipidemia, hypertension, and prior PCI but were less likely to have ECG changes on presentation.

Medical and invasive therapy use

Use of aspirin, $P2Y_{12}$ receptor inhibitors, β-blockers, angiotensin-converting enzyme inhibitors, and statins within 24 hours and anticoagulation in the hospital were lower

Table 1. Demographics and Features on Presentation by Degree of CKD Among Patients with STEMI

	Overall 2007–2015			2007–2008			2014–2015		
	ESRD on Dialysis (n=3121)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=85 068)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=237 207)	ESRD on Dialysis (n=335)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=10 102)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=25 620)	ESRD on Dialysis (n=1013)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=27 908)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=80 235)
Demographics									
Age, y	65 (56–73)	69 (60–79)	58 (51–67)	65 (55–74)	70 (61–80)	57 (50–66)	65 (56–73)	68 (60–78)	59 (51–67)
Sex, male	56.8	59.1	74.6	53.4	55.4	75.6	56.6	60.7	74.4
Race, white	57.3	85.1	81.7	66.0	88.4	84.5	52.3	83.3	80.1
Weight, kg	79.3 (67.0–93.0)	82.0 (70.0–96.4)	86.0 (74.0–99.8)	78.0 (68.0–91.0)	81.4 (68.2–95.0)	85.4 (74.0–99.0)	79.2 (67.0–93.1)	83.0 (70.8–97.5)	86.0 (74.0–99.8)
Medical history									
Diabetes mellitus	61.4	32.4	22.1	61.4	28.7	19.6	60.6	34.4	23.5
Dyslipidemia	67.9	57.9	50.3	61.5	52.9	47.6	67.0	58.1	49.8
Hypertension	90.6	76.6	60.3	86.8	73.7	55.5	91.1	76.9	61.2
Current/recent smoker	23.6	28.4	47.0	23.8	28.1	49.9	22.9	27.7	44.6
Prior MI	34.6	21.6	17.4	31.5	22.0	18.1	32.3	20.7	17.1
Prior PCI	33.6	22.4	18.8	31.6	20.9	18.8	30.8	22.7	18.7
Prior CABG	15.2	9.5	5.2	17.3	10.0	5.7	13.4	8.7	4.9
Prior HF	29.5	9.9	3.2	27.0	9.9	2.7	28.6	9.4	3.3
Prior stroke	16.5	8.4	3.8	13.8	8.6	3.5	14.2	8.2	3.8
Prior PAD	23.7	8.9	4.1	29.0	9.0	4.1	20.2	8.0	4.0
Atrial fibrillation/flutter	11.3	8.2	3.4	9.8	7.3	2.5	12.6	8.7	3.8
Features on presentation									
Heart rate, bpm	86 (71–101)	79 (64–96)	78 (66–92)	84 (70–100)	79 (64–96)	77 (65–91)	86 (70–100)	79 (63–96)	79 (66–92)
Systolic BP, mmHg	131 (104–156)	134 (109–158)	143 (123–163)	130 (104–155)	133 (110–155)	140 (120–158)	128 (102–157)	135 (109–160)	144 (124–166)
Cardiogenic shock	16.2	14.2	4.7	13.6	10.5	3.4	16.6	14.4	4.7
Cardiac arrest	13.0	12.1	5.8	NA	NA	NA	13.4	12.1	5.8
ACTION Registry–GWTG risk score for mortality	50 (43–58)	38 (32–46)	31 (26–36)	50 (44–58)	38 (32–45)	31 (26–36)	50 (43–58)	38 (31–46)	31 (26–36)
ACTION Registry–GWTG risk score for bleeding	47 (42–53)	33 (28–39)	27 (24–32)	46 (42–52)	33 (28–39)	27 (24–31)	47 (42–53)	33 (27–39)	27 (23–32)

ACTION Registry–GWTG indicates Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines; BP, blood pressure; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HF, heart failure; MI, myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; NA, not available; STEMI, ST-segment–elevation myocardial infarction.

among NSTEMI patients with CKD, particularly among ESRD patients requiring dialysis (Table 5). Similar to the STEMI cohort, coronary angiography was performed less frequently among NSTEMI patients with CKD; however, unlike the STEMI population, among patients undergoing coronary angiography, PCI and coronary artery bypass grafting was performed less frequently among patients with CKD. At hospital discharge, use of $P2Y_{12}$ receptor inhibitors, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, and statins was also lower among NSTEMI patients with CKD.

Early in-hospital and discharge use of aspirin increased from 2007–2008 to 2014–2015, regardless of the presence

or degree of CKD (*P* values for interaction: *P*=0.51 and *P*=0.16, respectively). $P2Y_{12}$ receptor inhibitor use within 24 hours increased only among ESRD patients requiring dialysis (*P*<0.001 for interaction), whereas discharge $P2Y_{12}$ receptor inhibitor use increased among all patients, with the greatest increase among patients with ESRD requiring dialysis (*P*<0.001 for interaction). In-hospital anticoagulation use increased among ESRD patients requiring dialysis and patients with preserved renal function but not patients with moderate to severe CKD not requiring dialysis (*P*=0.004 for

Table 2. Medical and Invasive Therapy Among Patients With STEMI Stratified by Degree of CKD

	Overall 2007–2015			2007–2008			2014–2015		
	ESRD on Dialysis (n=3121)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=85 068)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=237 207)	ESRD on Dialysis (n=335)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=10 102)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=25 620)	ESRD on Dialysis (n=1013)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=27 908)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=80 235)
Medications within 24 h									
Aspirin	96.1	97.5	98.9	97.2	97.5	98.8	96.1	97.6	99.0
$P2Y_{12}$ receptor inhibitor	76.0	81.8	89.8	71.4	76.7	87.8	80.0	85.6	92.5
β-Blocker	79.8	84.0	90.2	93.3	94.5	96.9	74.0	79.7	87.6
ACEi/ARB	37.8	42.9	54.7	47.4	51.8	60.6	33.1	38.8	51.8
Statin	62.8	67.9	77.8	55.6	63.2	73.2	65.1	71.4	81.2
Glycoprotein IIb/IIIa inhibitor	31.5	46.2	51.1	53.1	69.6	77.0	23.0	36.0	39.4
Any anticoagulant	91.7	95.3	96.6	90.0	94.2	94.8	92.0	95.9	97.3
Bivalirudin	31.4	36.0	40.0	16.0	12.7	14.1	35.2	42.8	46.5
Invasive procedures									
Coronary angiography	90.7	93.3	98.5	86.3	88.0	96.3	93.1	95.0	98.8
Primary PCI*	90.8	91.6	92.2	83.3	82.1	82.0	91.8	93.8	94.4
D2B within guideline recommendation	77.0	82.3	85.7	52.1	64.2	69.1	84.6	87.0	89.7
DES (among stented primary PCI patients)	61.7	63.9	69.4	40.3	44.9	48.7	73.8	75.6	80.6
CABG*	5.8	5.9	5.4	6.9	8.7	7.1	6.1	5.0	4.5
Medications at hospital discharge									
Aspirin	97.7	98.6	99.0	96.1	98.6	98.9	98.3	98.7	99.0
Any $P2Y_{12}$ receptor inhibitor	85.1	88.5	91.8	79.9	83.5	89.7	87.2	92.9	94.9
Clopidogrel	71.4	69.4	64.2	85.7	88.4	92.8	59.7	55.9	49.3
Prasugrel	12.4	16.6	24.5	…	…	…	10.0	15.2	21.5
Ticagrelor	18.1	21.9	24.1	…	…	…	19.8	23.4	25.6
β-Blocker	96.7	97.8	98.0	95.1	97.5	97.7	97.2	98.2	98.2
ACEi/ARB	72.5	75.5	78.5	75.9	77.3	79.4	65.1	73.9	77.1
Aldosterone blocker	2.1	5.4	4.3	3.0	5.7	4.0	1.7	5.3	4.5
Statin	91.6	95.4	96.9	81.7	90.2	93.7	94.8	97.6	98.3

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor inhibitor; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; D2B, door to balloon; DES, drug-eluting stent; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction.

*Among patients undergoing angiography.

Table 3. In-Hospital Outcomes Among Patients With STEMI Stratified by Degree of CKD

	Overall 2007–2015			2007–2008			2014–2015		
	ESRD on Dialysis (n=3121)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=85 068)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=237 207)	ESRD on Dialysis (n=335)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=10 102)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=25 620)	ESRD on Dialysis (n=1013)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=27 908)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=80 235)
Death	21.3	14.0	2.9	19.4	13.4	2.4	22.6	14.2	3.0
Major bleeding	20.2	16.1	7.2	28.5	18.4	8.9	15.8	14.1	6.3
AKI									
No	…	78.3	91.0	…	76.2	90.2	…	79.3	91.4
Mild	…	5.7	4.5	…	6.7	4.9	…	5.4	4.1
Moderate	…	7.4	2.7	…	8.2	3.1	…	7.1	2.6
Severe	…	8.6	1.9	…	8.8	1.8	…	8.2	1.9

AKI indicates acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; STEMI, ST-segment–elevation myocardial infarction.

interaction). Use of coronary angiography and PCI also increased, with the greatest increase among ESRD patients requiring dialysis (both $P<0.001$ for interaction). Use of coronary artery bypass grafting decreased in 2014–2015 compared with 2007–2008, with the greatest decrease among patients with preserved renal function ($P=0.047$ for interaction).

Clinical outcomes

Compared with NSTEMI patients with preserved renal function, in-hospital mortality was ≈4-fold higher among patients with moderate to severe CKD and 5-fold higher among ESRD patients requiring dialysis (Table 6). Major bleeding was also significantly higher among patients with CKD, particularly among ESRD patients requiring dialysis. Moderate to severe AKI occurred in 17.6% of patients with moderate to severe CKD and 5.3% of patients with preserved renal function. In-hospital mortality and bleeding rates were lower in 2014–2015 compared with 2007–2008, regardless of the presence or degree of CKD (*P* values for interaction: $P=0.64$ and $P=0.63$, respectively; Figures 2A and 2B).

Discussion

In this largest, contemporary evaluation of in-hospital treatment and outcomes of MI patients with CKD in the United States, several important observations emerge. First, CKD

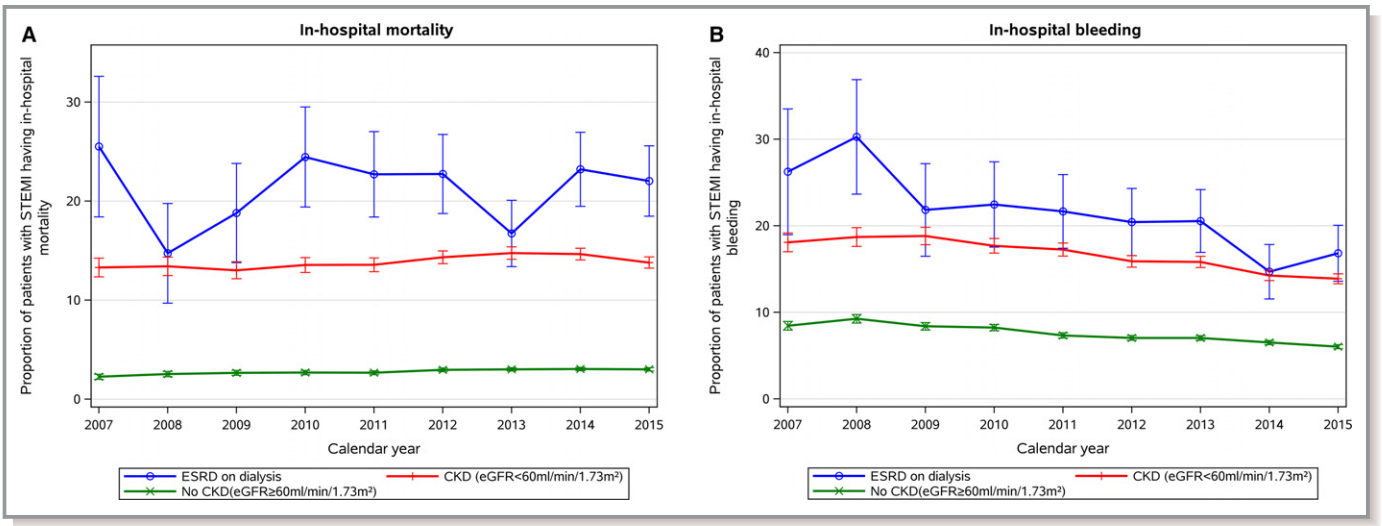

Figure 1. Temporal trends in (**A**) in-hospital mortality and (**B**) in-hospital bleeding by degree of CKD among patients with STEMI. CKD indicates chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; STEMI, ST-segment–elevation myocardial infarction.

Table 4. Demographics and Features on Presentation by Degree of CKD Among Patients With NSTEMI

	Overall 2007–2015			2007–2008			2014–2015		
	ESRD on Dialysis (n=17 104)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=174 543)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=315 229)	ESRD on Dialysis (n=1512)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=20 790)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=31 950)	ESRD on Dialysis (n=6120)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=56 508)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=110 429)
Demographics									
Age, y	66 (58–75)	74 (65–83)	62 (53–72)	67 (58–76)	76 (66–84)	61 (52–72)	66 (58–74)	74 (65–82)	62 (54–72)
Sex, male	57.6	52.4	67.6	55.6	50.2	68.9	59.1	53.8	67.4
Race, white	55.0	83.6	80.0	60.6	87.5	83.9	51.9	81.8	78.4
Weight, kg	79.4 (66.8–94.0)	81.0 (68.0–96.0)	86.0 (73.0–100.0)	77.0 (64.0–91.0)	79.0 (66.3–93.2)	85.3 (72.7–99.9)	80.8 (68.0–95.3)	81.9 (69.0–97.5)	86.2 (73.1–101.0)
Medical history									
Diabetes mellitus	72.7	47.7	30.4	68.5	43.9	26.0	73.9	50.0	31.8
Dyslipidemia	73.7	70.6	62.1	60.9	62.3	56.8	76.6	72.6	62.6
Hypertension	94.5	88.2	73.2	90.6	84.2	67.0	95.1	89.3	74.6
Current/recent smoker	18.2	18.1	36.5	17.3	17.3	38.5	17.6	118.0	34.7
Prior MI	43.6	34.5	25.3	40.0	33.9	23.9	43.9	33.8	25.3
Prior PCI	41.3	30.9	25.5	33.3	26.4	22.4	45.8	33.3	26.7
Prior CABG	28.1	24.9	14.3	28.4	26.4	14.4	27.9	24.1	13.9
Prior HF	45.2	27.9	9.7	42.4	26.8	7.9	45.1	27.9	10.0
Prior stroke	18.6	13.7	6.7	19.0	14.0	6.2	17.8	13.2	6.7
Prior PAD	30.3	17.2	8.0	33.2	17.3	7.7	28.3	16.2	7.6
Atrial fib/flutter	14.9	14.3	6.9	12.4	12.7	6.1	15.9	15.5	7.5
Features on presentation									
Heart rate, bpm	90 (78–105)	86 (72–103)	82 (70–96)	90 (77–108)	86 (72–102)	80 (69–94)	90 (78–104)	86 (72–102)	82 (70–96)
Systolic BP, mmHg	144 (119–171)	144 (122–168)	150 (131–170)	141 (115–166)	141 (120–164)	145 (127–165)	146 (121–174)	147 (124–171)	152 (133–172)
Cardiogenic shock	3.3	3.0	0.9	2.8	2.3	0.7	2.7	2.6	0.8
Cardiac arrest	2.9	2.5	1.1	NA	NA	NA	3.1	2.4	1.1
ECG findings									
New/presumed new ST depression	22.6	21.6	19.0	28.1	28.2	25.2	20.0	18.9	16.7
New/presumed new T-wave inversion	12.9	12.0	13.8	14.5	12.0	14.0	12.1	10.9	12.6
Transient ST-segment elevation	1.2	1.8	2.4	1.9	2.3	3.9	1.1	1.5	1.9
ACTION Registry–GWTG risk score for mortality	43 (37–50)	33 (27–40)	26 (20–31)	45 (38–51)	35 (28–41)	26 (21–32)	43 (36–49)	33 (26–40)	25 (20–31)
ACTION Registry–GWTG risk score for bleeding	42 (38–46)	31 (26–36)	23 (18–28)	42 (38–46)	31 (26–36)	23 (19–28)	42 (38–46)	30 (25–35)	23 (18–27)

ACTION Registry–GWTG indicates Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines; BP, blood pressure; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HF, heart failure; NSTEMI, non–ST-segment–elevation myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; MI, myocardial infarction; NA, not available.

Table 5. Medical and Invasive Therapy Among Patients With NSTEMI Stratified by Degree of CKD

	Overall 2007–2015			2007–2008			2014–2015		
	ESRD on Dialysis (n=17 104)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=174 543)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=315 229)	ESRD on Dialysis (n=1512)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=20 790)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=31 950)	ESRD on Dialysis (n=6120)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=56 508)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=110 429)
Medications within 24 h									
Aspirin	94.9	96.4	98.2	94.0	95.8	97.6	95.9	97.1	98.4
$P2Y_{12}$ receptor inhibitor	47.9	48.9	58.9	45.8	48.2	61.0	49.3	49.1	58.5
β-Blocker	81.5	84.0	86.1	90.9	92.2	93.6	79.2	81.9	83.9
ACEi	28.9	32.9	40.4	43.4	44.1	47.9	23.7	28.0	36.7
ARB	10.5	11.2	8.2	13.2	12.5	7.5	10.2	11.3	9.0
Statin	59.3	60.8	66.7	53.8	56.9	62.4	61.6	64.5	70.0
Glycoprotein IIb/IIIa inhibitor	5.1	14.4	24.1	17.3	33.1	51.0	2.8	8.0	14.1
Any anticoagulant	84.6	89.7	94.4	83.8	89.5	93.5	86.3	90.5	94.8
Bivalirudin	20.1	20.7	28.7	12.5	11.5	15.1	22.1	23.1	30.8
Invasive procedures									
Coronary angiography	71.3	69.6	90.5	63.8	64.6	88.9	76.9	73.8	91.5
PCI*	54.5	56.0	62.8	48.5	53.8	62.2	58.6	57.7	63.8
DES (among stented PCI patients)	77.0	75.9	78.9	61.0	61.0	63.3	85.1	84.0	86.6
CABG*	10.5	12.4	13.0	12.4	14.1	14.5	9.5	11.9	12.3
Medications at hospital discharge									
Aspirin	96.5	97.2	98.1	95.8	96.6	98.0	96.8	97.5	98.2
Any $P2Y_{12}$ inhibitor	70.8	68.6	76.2	60.5	61.8	73.1	76.5	73.1	79.2
Clopidogrel	65.8	62.8	61.7	68.6	69.6	78.2	64.2	58.2	53.8
Prasugrel	5.9	6.6	13.6	…	…	…	6.0	6.5	12.6
Ticagrelor	7.1	9.1	13.1	…	…	…	7.7	9.7	14.0
β-Blocker	96.3	96.6	96.5	94.8	95.9	95.8	97.1	97.1	97.0
ACEi/ARB	65.0	67.9	70.5	71.9	70.5	71.5	61.4	66.2	69.7
Aldosterone blocker	2.1	5.9	3.8	3.2	6.1	3.4	2.2	5.9	4.1
Statin	89.1	90.9	94.1	79.2	83.5	89.5	93.4	94.5	96.1

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; DES, drug-eluting stent; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention.
*Among patients undergoing angiography.

remains prevalent among MI patients, with ≈25% of STEMI patients and 40% of NSTEMI patients having CKD. Second, although remaining significantly lower compared with STEMI patients with preserved renal function, the use of $P2Y_{12}$ receptor inhibitors within 24 hours and at hospital discharge, coronary angiography, and primary PCI and the percentage of patients within the guideline-recommended D2B goal have increased over the past decade among STEMI patients with CKD. Nevertheless, despite this increased use of evidence-based therapies and decreased in-hospital bleeding over time, in-hospital mortality rates were unchanged. Third, similar to patients with STEMI, the use of in-hospital coronary

Table 6. In-Hospital Outcomes Among Patients With NSTEMI Stratified by Degree of CKD

	Overall 2007–2015			2007–2008			2014–2015		
	ESRD on Dialysis (n=17 104)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=174 543)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=315 229)	ESRD on Dialysis (n=1512)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=20 790)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=31 950)	ESRD on Dialysis (n=6120)	CKD (eGFR <60 mL/min per 1.73 m^2) (n=56 508)	No CKD (eGFR ≥60 mL/min per 1.73 m^2) (n=110 429)
Death	8.1	6.6	1.5	10.1	7.3	1.8	7.8	6.1	1.4
Major bleeding	14.2	11.1	4.3	19.3	15.5	6.1	11.0	8.5	3.3
AKI									
No	…	74.5	88.5	…	73.3	88.5	…	76.1	89.5
Mild	…	7.9	6.2	…	9.0	6.2	…	7.3	5.6
Moderate	…	9.5	3.5	…	10.1	3.6	…	8.7	3.2
Severe	…	8.1	1.8	…	7.6	1.7	…	7.9	1.7

AKI indicates acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction.

angiography and PCI also increased over time among NSTEMI patients with CKD; however, unlike STEMI patients, in addition to in-hospital bleeding, in-hospital mortality was lower over time in NSTEMI patients regardless of presence or degree of CKD.

Consistent with prior reports,[1,9,21–24] CKD remains prevalent among patients with MI and is associated with a graded increase in adverse in-hospital outcomes, both mortality and bleeding, with worsening kidney function. Despite this increased risk for adverse outcomes, compared with patients with preserved renal function, CKD patients receive fewer evidence-based therapies. Several reasons have been postulated for this apparent undertreatment of this high-risk population. Patients with CKD, particularly those requiring renal replacement therapy, are typically excluded from clinical trials, and evidence pertaining to improved outcomes with standard evidence-based therapies for MI have been scarce in these patients. Treatment may be discouraged further by the potential for excess toxicities with certain therapies and a high prevalence of comorbidities that may be perceived as contraindications. However, recent studies suggest that, at least among carefully selected patients, certain treatment benefits appear to outweigh the risks. Data from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry

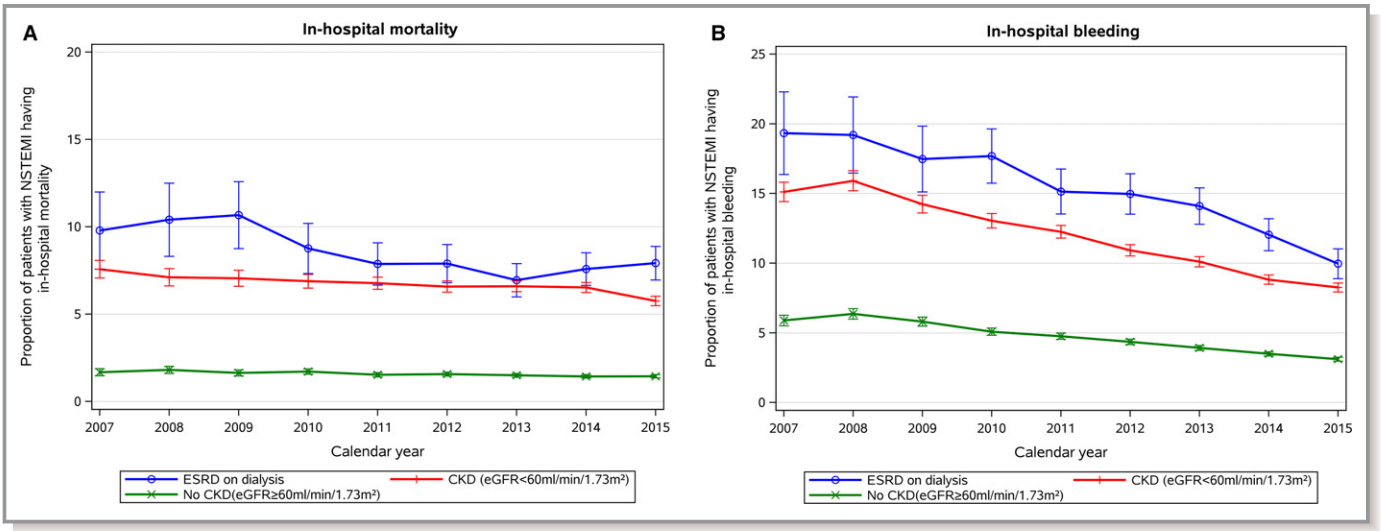

Figure 2. Temporal trends in (**A**) in-hospital mortality and (**B**) in-hospital bleeding by degree of CKD among patients with NSTEMI. CKD indicates chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction.

showed that a 1-year mortality benefit of early revascularization over medical therapy was seen in NSTEMI patients with estimated GFR >30 mL/min, with no benefit seen in patients with estimated GFR <30 mL/min.[5] The benefit of early revascularization on the composite end point of death, MI, and revascularization in patients with creatinine clearance of 30 to 60 mL/min was also noted in a subgroup analysis of the TACTICS-TIMI 18 (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction 18) trial.[25] Although contrast-induced AKI is important, its risk needs to be balanced against the marked cardiovascular morbidity and mortality of CKD patients. A retrospective study of >33 000 patients with MI showed that the overall incidence of AKI declined from 26.6% in 2000 to 19.7% in 2008 despite the aging population and rising prevalence of risk factors for acute renal failure, including CKD.[26] This decline in AKI has been postulated to be caused by improved efforts to prevent contrast-induced AKI.

Aspirin and β-blockers after MI have been shown to improve outcomes in patients with underlying kidney disease.[3,27] In a meta-analysis of 27 139 patients with CKD who participated in 50 randomized trials of antiplatelet agents (mostly aspirin), antiplatelet therapy significantly reduced the incidence of fatal or nonfatal MI compared with either placebo or no therapy. Antiplatelet therapy had no effect on mortality or stroke, and increased rates of major bleeding.[28] Post hoc and meta-analyses have noted improvements in cardiovascular outcomes with statin therapy in patients with mild to moderate renal dysfunction, with attenuated or no effects in patients with ESRD on dialysis.[29–31] Consistent reductions in ischemic end points have been noted with potent $P2Y_{12}$ receptor inhibitors ticagrelor and prasugrel compared with clopidogrel among PCI-treated acute coronary syndrome patients with CKD,[14,32] with no increase in major or fatal bleeding observed with ticagrelor compared with clopidogrel among patients with CKD. Although controlled data for evidence-based MI therapies has grown for patients with mild to moderate CKD, dialysis patients remain understudied. Nevertheless, the National Kidney Foundation guidelines recommend that all dialysis patients presenting with acute MI should be treated as nondialysis patients, with the exception of specific attention to drugs that have altered clearances in kidney failure.[33.]

The proportion of NSTEMI patients with ESRD on dialysis increased from 2007–2008 to 2014–2015. Several factors could explain this trend. Establishing an accurate diagnosis of NSTEMI in dialysis patients can be problematic because troponin increases, nonspecific ECG abnormalities are common, and typical symptoms of MI are less frequent,[12] but the prevalence of obstructive coronary artery disease is high. Consequently, differentiating type 1 versus type 2 MI can be difficult. Furthermore, increased use of higher sensitivity troponin contributes to the increased diagnostic coding of NSTEMI. We found increased use of in-hospital coronary angiography and PCI over time among NSTEMI patients with CKD, with the greatest increase among ESRD patients requiring dialysis. These findings suggest increased awareness and less therapeutic nihilism in providing CKD patients, particularly dialysis patients, with guideline-recommended MI treatment. We observed significant reduction in in-hospital bleeding over time, regardless of the presence or degree of CKD, likely because of increased awareness of the adverse prognostic implications of bleeding[34] and consequent implementation of bleeding-reduction strategies. In contrast to data from the US Renal Data System database, where in-hospital and 2-year cumulative probability of mortality did not decrease among NSTEMI dialysis patients between 1993 and 2008,[18] in-hospital mortality was lower in 2014–2015 compared with 2007–2008 among NSTEMI patients regardless of presence or degree of CKD.

Unlike NSTEMI, the proportion of STEMI patients with ESRD on dialysis remained constant over the past decade, likely because establishing a diagnosis relies on specific ECG criteria rather than simply on biomarker criteria. Increased use of $P2Y_{12}$ receptor inhibitors, coronary angiography, and primary PCI and achievement of D2B times within guideline recommendations among STEMI patients with CKD over the past decade have paralleled STEMI patients without CKD; however, despite this increase in use of invasive and medical therapies, there was no improvement in-hospital mortality. Our observations are similar to findings from the CathPCI registry®, in which, despite significant reductions in D2B time from 2005 to 2009, no reduction in in-hospital mortality was observed among STEMI patients undergoing primary PCI.[35] However, they contrast with data from the US Renal Data System database, in which in-hospital and 2-year cumulative probability of mortality decreased among STEMI dialysis patients between 1993 and 2008.[18] This absence of improvement in in-hospital mortality is not explained by temporal trends in underlying comorbidity, as the proportion of STEMI patients with CKD remained constant over time, as did the patient demographics and features on presentation in the overall cohort and in each group stratified by presence and degree of CKD. Possible explanations include reductions in D2B time that are too small to reduce infarct size, initiation of treatment that is too late, or follow-up that is too short to show improvement in survival.[36] In-hospital mortality after STEMI continues to remain extremely high at ≈1 in 5 ESRD patients on dialysis and 1 in 7 patients with CKD without dialysis, highlighting the need for additional measures to improve outcomes in this very high-risk population.

Limitations

The data source lacks precision regarding contraindications and reasons for not using individual medications and procedures. Ticagrelor and prasugrel were not available in 2007–2008. Only short-term in-hospital outcomes were evaluated. Whether increased angiography and faster reperfusion, greater use of drug-eluting stents and evidence-based medications, and lower rates of AKI and in-hospital bleeding translate into a longer term survival benefit for patients with CKD was not evaluated in this study. Data were extracted from hospitals with different creatinine assays and standards, and no standard central determination of kidney function was performed. The initial creatinine value is assumed to be at steady state, that is, representing chronic kidney function, not AKI. In addition, information on albuminuria and proteinuria was not available.

Conclusions

A progressive increase in uptake of evidence-based medical and invasive therapies has occurred over the past decade among MI patients with CKD, particularly ESRD patients on dialysis. These trends likely reflect a combination of accumulation of evidence supporting the benefit of these therapies in patients with CKD and increased awareness and less therapeutic nihilism on the part of practitioners. Despite increased uptake of these therapies, improvement of in-hospital mortality over time was observed only among NSTEMI patients, not STEMI patients. Although encouraging, persistent high residual early mortality rates demonstrate opportunities for further improvement of care for this high-risk population.

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