



Nationwide trends and outcomes of percutaneous coronary intervention for stable ischemic heart disease in end-stage kidney disease: a longitudinal study

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Background: Patients with end-stage kidney disease (ESKD) are at high risk for coronary artery disease. We investigate the trends and outcomes of percutaneous coronary intervention (PCI) for stable ischemic heart disease (SIHD) in patients with ESKD.

Methods: We utilized the United States Renal Data System [2010–2018] to include adult patients with ESKD on dialysis for at least 3 months who underwent PCI for SIHD. Patients with myocardial infarction during index hospitalization, history of coronary artery bypass graft or renal transplantation and without Medicare AB coverage were excluded. Trends and related outcomes, including mortality and revascularization rate, were studied.

Results: The mean age was 65.1 years with 57.5% male and a majority White (64.5%). The dialysis duration was ≤ 5 years in 83.3% patients. Hypertension (97.6%) and diabetes mellitus (76.8%) were the most common comorbidities. PCI procedures per 1,000 ESKD patients dropped from 6.2 in 2010 to 2.6 in 2018 ($P < 0.001$) while the index hospitalization mortality increased from 0.9% to 3.0% ($P < 0.001$). The 30-day and 1-year mortality also significantly increased from 3.2% to 6.1% and 26.5% to 31.9%, respectively. However, 1-year repeat revascularization rates dropped from 19.8% to 17.0% between 2010–2018 ($P < 0.001$). A significant increase in comorbidity burden was also noted.

Conclusions: We demonstrate a consistent decrease in PCI rates for SIHD in ESKD patients. However, the in-hospital mortality has increased significantly, in part, due to an increasing high-risk profile of these patients. Our results call for individualized clinical decision-making when exploring revascularization options in ESRD patients with SIHD.

Keywords: Renal disease; coronary; revascularization; trend; outcomes

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Introduction

Patients with end-stage kidney disease (ESKD) are at an increased risk for coronary artery disease (CAD), or ischemic heart disease (IHD), with an incidence of

up to 38% in patients initiating dialysis, and thus, are vulnerable to CAD-related morbidity and mortality (1-3). Revascularization is especially challenging in this subset of patients given their high likelihood of diffuse multivessel

involvement, calcification and plaque burden (2,4). While there are no randomized prospective trials, retrospective studies have compared coronary artery bypass graft (CABG) to percutaneous coronary intervention (PCI) in ESKD patients with CAD (5-8). These studies show that while CABG has a higher short-term mortality than PCI, the longer-term mortality and risk of repeat revascularization was either comparable or lower. However, in both groups, the overall mortality remains high in this population.

There is strong evidence that in patients with stable ischemic heart disease (SIHD), there is no benefit in clinical cardiovascular outcomes or mortality from an early revascularization approach compared to medical therapy (9-12). Likely due to this strong evidence base, there has been a significant reduction in use of PCI for SIHD in the general population in the last decade (13,14). However, patients with advanced kidney failure or those on dialysis were mostly excluded from these clinical trials. The study of comparative health effectiveness with medical and invasive approaches – Chronic Kidney Disease (ISCHEMIA-CKD trial) is the only trial that compared early revascularization to medical therapy in SIHD patients with advanced kidney disease and found no benefit of an early revascularization strategy in terms of reduction in mortality or risk of myocardial infarction (MI) (15). However, this study was limited to a total recruitment of 415 ESKD patients.

Thus, there is paucity of data on PCI use and outcomes

in patients with ESKD and SIHD. We, therefore, conducted a longitudinal study using the United States Renal Data System (USRDS) to study the temporal trends and outcomes of PCI in ESKD patients with SIHD. We present this article in accordance with the STROBE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-24-85/rc>).

Methods

Study design and population

This is a longitudinal study. We analyzed the USRDS between January 1st 2010 and December 31st 2018. This dataset provides comprehensive administrative records for about 95% of ESKD patients in the United States (16). Patients ≥ 18 years with ESKD on dialysis for at least 3 months who underwent PCI were included. We excluded all patients with a history of renal transplant, MI during index hospitalization, and any history of CABG or undergoing CABG during the index hospitalization. We also excluded patients who did not have both Medicare Part A and Part B coverage during their index hospitalization as the primary payer to ensure that we had continuous comorbidity and outcomes assessment for the study period. *Figure 1* shows derivation of the final study population. The relevant International Classification of Diseases, 9th and 10th Edition, diagnostic and procedure codes (ICD-9/10), and the Center for Medicare and Medicaid Services (CMS) Form 2728 were used to identify specific conditions and procedures (*Table S1*).

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was originally reviewed and approved by the Institutional Review Board (IRB) of the University of Kansas Medical Center Human Research Protection Program on 11/23/2021 (No. STUDY00148033) and individual consent for this retrospective analysis was not required in accordance with local/national guidelines. USRDS has approved the data/study to be published.

Outcomes and statistical analysis

We studied the trends for the number of PCI procedures performed per 1,000 ESKD patients during the study period and the associated in-hospital mortality as our primary outcome. Additional outcomes included 30-day mortality (death during index hospitalization and up to 30 days after

Highlight box

Key findings

- A consistent decrease in percutaneous coronary intervention (PCI) rates for stable ischemic heart disease (SIHD) in end-stage kidney disease (ESKD) patients over the past decade with a concurrent increase in in-hospital mortality.
- The comorbidity burden in this population has also increased.

What is known and what is new?

- Patients with ESKD are at high risk for coronary artery disease-related morbidity and optimal revascularization strategy, including PCI, remains unclear in this population.
- Utilization of PCI for SIHD in ESKD patients over the past decade has been declining with an associated increase in in-hospital mortality, which could partly be attributed to a parallel increase in the comorbidity burden.

What is the implication, and what should change now?

- Our results call for caution and individualized clinical decision-making when exploring revascularization options for ESKD patients with SIHD.

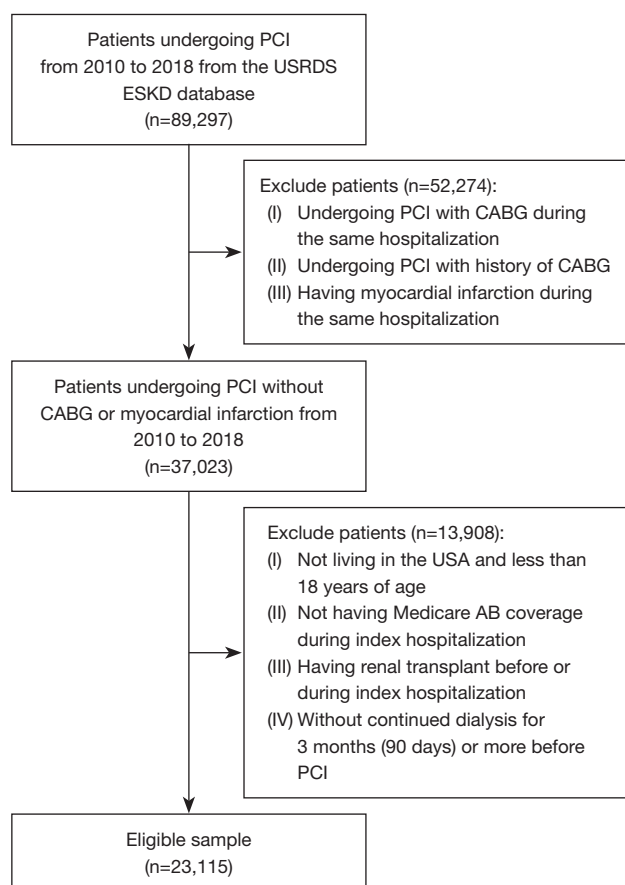


Figure 1 Derivation of the study population. CABG, coronary artery bypass graft; ESKD, end-stage kidney disease; PCI, percutaneous coronary intervention.

PCI) and 1-year mortality. We also investigated the rates of repeat revascularization (surgical or percutaneous) at one year following discharge after initial PCI. The long-term survival was estimated using the Kaplan-Meier method. The follow-up period for assessing long-term mortality was until death, end of Medicare AB coverage, or study end-date of December 31st, 2019, whichever was earlier. The Cochran-Armitage test was utilized for trend analysis of the number of PCI procedures and the length of the index hospitalization stay. Logistic regression was performed to identify trends in in-hospital mortality, 30-day mortality, 1-year mortality, and 1-year repeat revascularization rates, adjusting for comorbidities such as age, congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, dysrhythmias, liver disease, and cancer. All reported P values are two-sided. Statistical analyses were performed using the SAS 9.4 (SAS Institute Inc, Cary, NC, USA) software.

Disclaimer

The data reported here have been supplied by the USRDS. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government.

Results

Patient characteristics

A total of 23,115 ESKD patients underwent PCI for SIHD over the study duration. The mean age was 65.1 years with 57.5% of the study population being male and 64.5% White. Most patients had been on dialysis for 5 years or less (83.3%) with hemodialysis being the most common mode of dialysis (92.0%). The most common comorbidities in this population included hypertension (97.6%), diabetes mellitus (76.8%) and congestive heart failure (58.8%). The overall patient demographics and characteristics are shown in *Table 1*. The mean age and comorbidity burden were noted to rise over the years (*Table 2*) with increasing prevalence of congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, dysrhythmias and liver disease. The Elixhauser Comorbidity Index (ECI) increased from 4.0 in 2010 to 6.0 in 2018. The follow-up time did not have a normal distribution with a median follow-up time of 1.96 years and a mean follow-up time of 2.66 years.

Patient outcomes

As shown in *Figure 2*, the number of PCI procedures declined from 6.2 procedures per 1,000 ESKD patients in 2010 to 2.6 procedures per 1,000 ESKD patients in 2018 ($P<0.001$). The in-hospital mortality increased from 0.9% in 2010 to 3.0% in 2018 ($P<0.001$). During this time period, the 30-day and 1-year mortality also increased from 3.2% to 6.1% and 26.5% to 31.9% respectively ($P<0.001$) respectively. There was a decline in the 1-year repeat revascularization rate (from 19.8% in 2010 to 17.0% in 2018, $P<0.001$). These trends remained statistically significant after adjusting for age and other key comorbidities. *Figure 3* presents these trends in mortality and repeat revascularization outcomes over the study duration. In addition, the length of the index hospitalization stay increased from 3 days in 2010 to 4 days in 2018 ($P<0.001$).

A survival analysis showed dismal survival rates of 71.2%, 54.0%, and 24.7% at 1-, 2- and 5-year, respectively (*Figure 4*).

Table 1 Baseline demographic characteristics and comorbid conditions of ESKD patients undergoing PCI for SIHD

Overall characteristics	Values (N=23,115)
Male sex	13,288 (57.5)
Race	
White	14,904 (64.5)
Black	6,815 (29.5)
Asian/other	1,396 (6.0)
Age (years)	65.1±11.6
Age groups (years)	
<50	2,374 (10.3)
50–64	8,653 (37.4)
65–79	9,789 (42.3)
≥80	2,299 (9.9)
Dialysis duration (years)	3.5±3.1
Dialysis duration groups (years)	
<2	9,171 (39.7)
2–5	10,067 (43.6)
6–10	3,178 (13.7)
≥11	699 (3.0)
Dialysis modality	
Hemodialysis	21,276 (92.0)
Peritoneal dialysis	1,839 (8.0)
Comorbid conditions	
CHF	13,603 (58.8)
COPD	3,315 (14.3)
CVA/TIA	2,805 (12.1)
Cancer	1,392 (6.0)
Diabetes mellitus	17,744 (76.8)
Dysrhythmia	6,488 (28.1)
Hypertension	22,569 (97.6)
Liver disease	600 (2.6)
PVD	6,865 (29.7)
Elixhauser comorbidity index	5.2±1.9

Data are presented as mean ± SD or n (%). CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ESKD, end-stage kidney disease; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SIHD, stable ischemic heart disease; SD, standard deviation; TIA, transient ischemic attack.

Discussion

The main findings of this nationwide study are that there has been a consistent decline over the past decade in the number of PCI performed for SIHD in ESKD patients on dialysis and that there has been a significant increase in the in-hospital and 1-year mortality in these patients after having undergone PCI.

In the general population, without chronic kidney disease (CKD), recent studies have documented an overall decrease in the number of elective PCI procedures performed. A recent analysis from 4 states (Florida, Michigan, Maryland and New York) between 2010 and 2017 found a 23% decrease in annual elective PCI procedures (14). Similarly, a study from Washington state from 2005 to 2017 also found an overall decrease in elective PCI procedures (17). In both these studies, the drop was mostly until 2013 after which the decline halted or started to rise some. This reduction in elective PCI may in part be attributed to the publication of several landmark randomized clinical trials that have compared early revascularization strategies to medical therapy in patients with SIHD. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, a randomized trial of therapies for type 2 diabetes and coronary artery disease (BARI2D) and the Initial Invasive or Conservative Strategy for Stable Coronary Disease (ISCHEMIA) trial—all demonstrated no benefit of early revascularization strategies in SIHD compared to a more conservative approach (9,11,12).

Similar to that seen in the general population, the results from our study in ESKD patients also show a consistent and significant decrease in PCI procedures performed for SIHD. This is surprising given that the previously mentioned studies essentially excluded patients with advanced kidney disease. The more recently published ISCHEMIA-CKD is the only study that has evaluated revascularization strategies in SIHD in patients with advanced kidney disease (15). It randomized 777 patients with advanced kidney disease [estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m² of body surface area] and SIHD with moderate to severe ischemia to early revascularization or conservative therapy. There was no difference in the outcome of death or MI. This study, however, had only about 400 patients with ESKD. The reduced use of PCI seen in our study may also have been influenced by the recognition of higher adverse events and in hospital mortality in patients with advanced kidney disease undergoing PCI (18).

Our study results showed a concerning increase in

Table 2 Trends for age and comorbidities in patients with ESKD undergoing PCI for SIHD

Characteristic	2010	2011	2012	2013	2014	2015	2016	2017	2018	P value [†]
Age (years)	64.8±11.6	64.8±11.8	65.4±11.9	64.6±11.6	65.3±11.6	65.4±11.4	65.6±11.6	65.5±11.5	65.3±11.3	<0.001
Age groups (years)										0.16
<50	424 (10.8)	367 (11.0)	301 (10.5)	273 (10.7)	214 (9.7)	195 (9.8)	187 (9.5)	204 (9.6)	209 (9.7)	
50–64	1,500 (38.3)	1,268 (38.2)	1,042 (36.3)	980 (38.4)	815 (36.8)	747 (37.6)	737 (37.4)	769 (36.2)	795 (36.9)	
65–79	1,642 (41.9)	1,360 (40.9)	1,216 (42.4)	1,078 (42.2)	947 (42.8)	852 (42.8)	829 (42.1)	922 (43.4)	943 (43.8)	
≥80	353 (9.0)	328 (9.9)	309 (10.8)	221 (8.7)	237 (10.7)	195 (9.8)	218 (11.1)	231 (10.9)	207 (9.6)	
Dialysis duration (years)	3.3±2.8	3.4±3.0	3.3±3.1	3.5±3.1	3.5±3.2	3.5±3.1	3.7±3.3	3.8±3.2	3.7±3.2	<0.001
Comorbid conditions										
CHF	2,052 (52.4)	1,868 (56.2)	1,617 (56.4)	1,440 (56.4)	1,360 (61.5)	1,244 (62.5)	1,187 (60.2)	1,400 (65.9)	1,435 (66.6)	<0.001
COPD	363 (9.3)	382 (11.5)	326 (11.4)	292 (11.4)	273 (12.3)	270 (13.6)	446 (22.6)	489 (23.0)	474 (22.0)	<0.001
CVA/TIA	457 (11.7)	424 (12.8)	366 (12.8)	289 (11.3)	265 (12.0)	241 (12.1)	252 (12.8)	250 (11.8)	261 (12.1)	0.98
Cancer	186 (4.7)	204 (6.1)	175 (6.1)	152 (6.0)	168 (7.6)	105 (5.3)	118 (6.0)	134 (6.3)	150 (7.0)	0.005
Diabetes mellitus	2,788 (71.1)	2,546 (76.6)	2,205 (76.9)	1,965 (77.0)	1,711 (77.3)	1,575 (79.2)	1,555 (78.9)	1,668 (78.5)	1,731 (80.4)	<0.001
Dysrhythmia	726 (18.5)	843 (25.4)	745 (26.0)	697 (27.3)	697 (31.5)	667 (33.5)	652 (33.1)	722 (34.0)	739 (34.3)	<0.001
Hypertension	3,862 (98.5)	3,273 (98.5)	2,833 (98.8)	2,518 (98.7)	2,194 (99.1)	1,939 (97.5)	1,815 (92.1)	2,041 (96.0)	2,094 (97.2)	<0.001
Liver disease	32 (0.8)	53 (1.6)	56 (2.0)	74 (2.9)	65 (2.9)	66 (3.3)	63 (3.2)	86 (4.0)	105 (4.9)	<0.001
PVD	974 (24.9)	1,057 (31.8)	863 (30.1)	763 (29.9)	699 (31.6)	661 (33.2)	676 (34.3)	631 (29.7)	541 (25.1)	0.04
Elixhauser comorbidity index	4.0±1.2	5.1±1.8	5.1±1.9	5.2±1.9	5.6±1.9	5.8±1.9	5.8±1.9	5.9±1.9	6.0±1.9	<0.001

Data are presented as mean ± SD or n (%). [†], P value for trend between years 2010 and 2018. CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ESKD, end-stage kidney disease; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SIHD, stable ischemic heart disease; SD, standard deviation; TIA, transient ischemic attack.

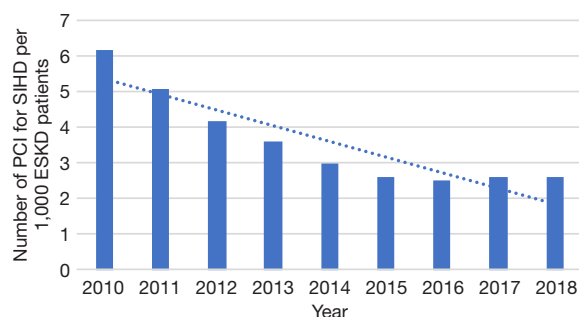


Figure 2 A declining trend of PCI procedures for SIHD in patients with ESKD over the study duration. ESKD, end-stage kidney disease; PCI, percutaneous coronary intervention; SIHD, stable ischemic heart disease.

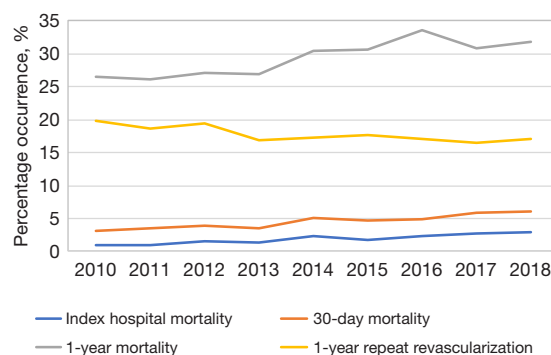


Figure 3 Trends for in-hospital, 30-day, 1-year mortality and 1-year repeat revascularization rates in ESKD patients with SIHD undergoing PCI over the years 2010–2018. ESKD, end-stage kidney disease; PCI, percutaneous coronary intervention; SIHD, stable ischemic heart disease.

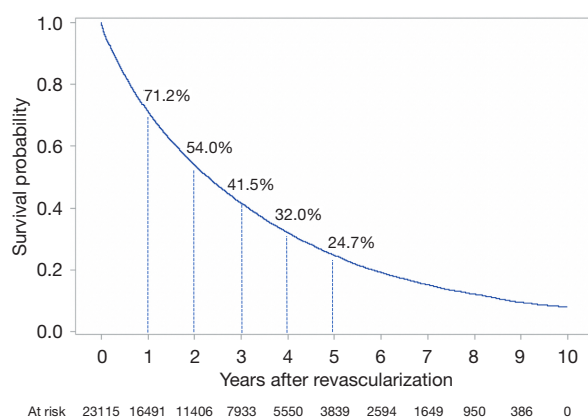


Figure 4 Survival curve for end-stage kidney disease patients with stable ischemic heart disease who underwent percutaneous coronary intervention.

in-hospital, 30-day and 1-year mortality over the study duration. There are several possible reasons for this finding. The most likely reason is that with passing years, the population has significantly more major comorbidity burden with a higher prevalence of congestive heart failure, peripheral arterial disease, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, dysrhythmia and liver disease. This has likely contributed to worse short and long-term mortality. This trend of increasing comorbidities in PCI population has also been described in the general population in several national- and state-level studies (13,17,19). A modest increase in PCI mortality in elective or non-MI procedures has also been reported in some studies. In an analysis of the national inpatient sample, Alkhouli *et al.* (13) reported a modest increase in risk-adjusted in-hospital mortality (0.8% to 1.0%, $P < 0.001$ for trend) between 2003 and 2016. A study of all PCI and CABG done in Washington State [2005–2017] also reported an increase in all PCI unadjusted in-hospital mortality (1.5–2.3%, $P < 0.0001$) and after adjustment for baseline national cardiovascular data registry (NCDR) CathPCI mortality score and PCI characteristics, the ratio of observed to expected deaths increased as well (0.98–1.19, $P < 0.0001$) (17). Another reason for the increased mortality may be a shift from CABG to PCI of patients with a higher risk profile. A recent publication from our group reporting trends of coronary bypass surgery for SIHD in the ESKD population shows declining trends of bypass surgery over the years 2009–2017 with an associated decline in post-procedural mortality (20). This trend could indicate that providers are now more selective in referring ESKD patients for

CABG. Subsequently, it is likely that high-surgical risk patients are referred for high-risk PCI, which could also explain the increasing post-PCI mortality trends in our current study. In the general population, the Washington State study [2005–2017] authors found that the mean NCDR CathPCI mortality score increased for PCI by 2.3 points and decreased for CABG patients by 0.1 points, with an absolute difference between the two groups of 3.3 points (95% confidence interval, 2.7–3.9) (17). This also corresponded with a significant increase in higher risk PCI procedures such as atherectomy (1.3% to 3.0%, $P < 0.0001$), left main intervention (1.6% to 4.3%, $P < 0.0001$) and PCI for chronic total occlusions (4.4% to 7.6%, $P < 0.0001$).

Current guidelines recommend CABG be preferred over PCI for ESKD patients with multivessel CAD if patients are otherwise suitable (21). However, these patients are overall high-risk and that may also result in a shift towards higher risk PCI in these patients. In the ISCHEMIA-CKD trial, in those randomized to the revascularization arm, 85% received PCI and only 15% underwent CABG even though a majority of patients had multivessel disease (15). This is a significantly higher percentage of PCI when compared to the ISCHEMIA trial (conducted in patients without advanced kidney disease) where 26% of patients underwent CABG (12). This also suggests an inclination of physicians to choose PCI more often for advanced kidney disease patients with multivessel disease.

In regard to repeat revascularization, PCI has been shown to have a high rate of needing repeat revascularization in patients with CKD. In a report from the state of New York, patients with CKD (only about 8% of these patients had ESKD) had a revascularization rate of 26% at a mean follow-up of 2.9 years (7). In our ESKD population, the 1-year revascularization rate was high though the trend was towards less repeat revascularization. This is likely related to use of newer generation stents and perhaps more focus on clinically—rather than ischemia-driven revascularization.

The survival for ESKD patients undergoing PCI for SIHD is low at the 1-year (71.2%), and especially drops at the 5-year assessment (24.7%). The ESKD patient population is an extremely high-risk group and our study data reflects this with a 2-year mortality of 46% and 5-year mortality of 75.5%. These rates are similar to the mortality rate of 54% at 2.9 years in ESKD patients post-PCI in a New York State study (7). These are also similar to the 2-year mortality of 47% and 5-year mortality of 76% reported in an older study from the USRDS [2004–2009] for all PCI, and not only for SIHD (6). The high mortality

rates for ESKD patients are not just related to CAD and acute coronary events. In fact, in the overall population of ESKD (not just those with CAD), the 5 year mortality is almost 60% (22). These mortality rates have not improved in the last decade (22). Some common non-CAD related causes of death include cardiac arrest and arrhythmia from myocardial scarring and left ventricular hypertrophy, electrolyte shifts from hemodialysis, and sympathetic system activation during hemodialysis especially from intra-dialysis hypotension and stroke (23,24).

An important limitation of our study is the administrative nature of the database. The USRDS remains susceptible to coding errors given that data extraction is performed using ICD-9/10 codes. Several unmeasured confounders and important clinical variables, such as the degree of chest pain and ischemia, left ventricular systolic function, the coronary anatomy, details of PCI performed such as the number and type of stents deployed, the patient's functional status and quality of life, cannot be accounted for or measured. The USRDS, however, remains an important data source to raise important queries for vulnerable population groups like those with ESKD. It is important to consider that the study results were limited to a patient population with Medicare AB coverage, somewhat limiting the generalizability. While we highlight key trends and outcomes, a clinical trial remains the gold-standard to address important queries that our study raises regarding the use of PCI in SIHD for ESKD patients.

Conclusions

This nationwide study shows a consistent decrease in PCI rates for SIHD in ESKD patients over the past decade. However, the in-hospital mortality has increased significantly, in part, due to an increasing high-risk profile of these patients. In view of the high overall mortality of ESKD patients and the uncertain benefit of PCI in ESKD, study results call for caution and patient specific clinical decision making when choosing PCI for ESKD patients with SIHD.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-24-85/rc>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-24-85/coif>). E.H. received payment for expert testimony on a 2023 case review. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the University of Kansas Medical Center Human Research Protection Program (No. STUDY00148033) and individual consent for this retrospective analysis was not required in accordance with local/national guidelines. United States Renal Data System (USRDS) has approved the data/study to be published.

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