



# Ad hoc percutaneous coronary intervention in patients with stable coronary artery disease: A report from the National Cardiovascular Data Registry CathPCI Registry

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**Background** Percutaneous coronary intervention (PCI) may be performed in the same procedure as diagnostic coronary angiography (ad hoc PCI). This study aimed to evaluate current rates of ad hoc PCI use and associated risks of adverse outcomes in patients with stable coronary artery disease (CAD).

**Methods** We identified 550,742 patients with stable CAD who underwent PCI in the National Cardiovascular Data Registry CathPCI Registry from 2009 to 2017. We compared in-hospital bleeding, acute kidney injury (AKI), and mortality between patients receiving ad hoc versus non-ad hoc PCI using logistic regression with inverse probability weighted propensity adjustment.

**Results** Between 2009 and 2017, 82.9% of patients underwent ad hoc PCI. Patients who did not undergo ad hoc PCI had higher prevalence of peripheral vascular disease, heart failure, chronic kidney disease, and coronary artery bypass graft. Ad hoc PCI was associated with lower bleeding risk (adjusted odds ratio [aOR] 0.83, 95% CI 0.79-0.87) but no differences in risks of AKI (aOR 0.95, 95% CI 0.90-1.00) or mortality (aOR 1.09, 95% CI 0.97-1.23) compared with non-ad hoc PCI. Ad hoc PCI was associated with AKI risk in patients with glomerular filtration rate <30 mL/min (interaction  $P < .001$ ), mortality risk in multivessel PCI (interaction  $P = .031$ ), and risks of AKI and mortality in PCI of chronic total occlusions (interaction  $P = .045$  and  $.002$ , respectively).

**Conclusions** Ad hoc PCI is extremely common among US patients with stable CAD and is associated with lower bleeding risk but no differences in risks of AKI or mortality compared with non-ad hoc PCI. (*Am Heart J* 2019;216:53-61.)

In patients who undergo elective cardiac catheterization that demonstrates obstructive coronary artery disease (CAD), a choice must be made whether to do percutaneous coronary intervention (PCI) in the same session immediately after diagnostic coronary angiography (ad hoc PCI) or to delay PCI to a separate session (non-ad hoc). In the early PCI era, ad hoc PCI was relatively uncommon due to less advanced imaging systems requiring more contrast and greater need for surgery support. Over time, patient convenience and a desire to reduce hospital length of stay have made ad hoc PCI more attractive.<sup>1-3</sup> However, use of ad hoc PCI in patients with stable CAD has been questioned due to

potential disadvantages such as greater intravenous contrast load and less thorough consideration of patient preferences and alternative therapies to PCI.<sup>4,5</sup> Although these trade-offs are acknowledged by cardiologists, trends in utilization and short-term outcomes for ad hoc PCI compared with non-ad hoc PCI in the current era are not well understood.

In this study, we used the American College of Cardiology (ACC) National Cardiovascular Data Registry (NCDR) CathPCI registry to evaluate rates of ad hoc PCI use over time as well as clinical and hospital characteristics associated with ad hoc and non-ad hoc PCI use. We also compared risks of in-hospital bleeding, acute kidney injury (AKI), and mortality following ad hoc versus non-ad hoc PCI.

## Methods

### Study population

The NCDR CathPCI Registry is a national registry that collects consecutive PCI procedures performed at hospitals across the United States.<sup>6</sup> CathPCI registry hospitals required institutional review board approval or waiver of the need for review to participate in this quality

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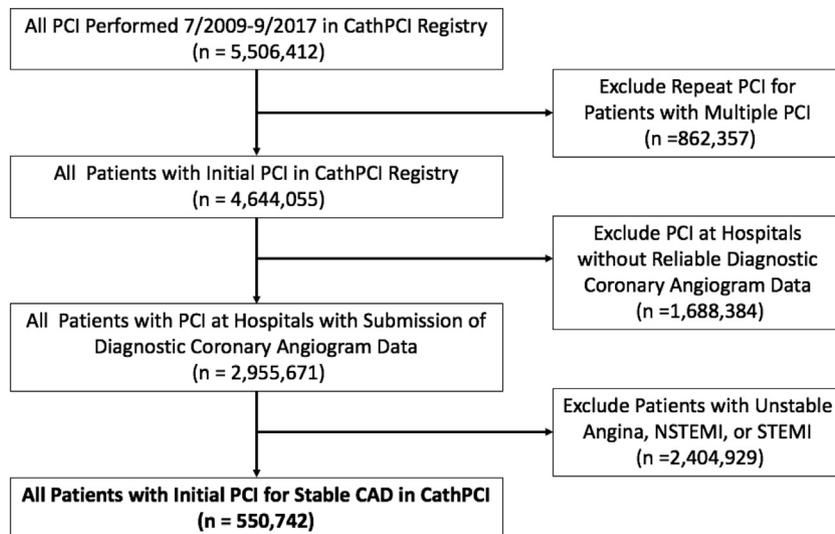
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Figure 1



Study population criteria. *NSTEMI*, non–ST-elevation myocardial infarction; *STEMI*, ST-elevation myocardial infarction.

improvement registry; as data are collected anonymously, individual informed consent was not required. We identified all PCI procedures from July 1, 2009, to September 30, 2017 ( $n = 5,506,412$  at 1,730 hospitals). For patients with multiple PCI procedures, we examined their first PCI procedure to avoid double counting, excluding 862,357 repeat PCI procedures. Although CathPCI registry participation mandated data collection for all PCI procedures, we limited our analysis to hospitals that submitted data on at least 50 diagnostic angiograms (and at least double the volume of diagnostic angiograms to PCIs reported), as has been done in previous studies, to ensure that our analysis population consisted of hospitals that submitted both diagnostic angiogram and PCI procedures (779 hospitals excluded,  $n = 1,688,384$ ).<sup>7</sup> Patients undergoing PCI for unstable angina, non–ST-elevation myocardial infarction, or ST-elevation myocardial infarction ( $n = 2,404,929$ ) were excluded. The final study cohort included 550,742 patients undergoing PCI at 1,355 hospitals (Figure 1).

#### Data definitions

CathPCI Registry hospitals abstracted demographic, clinical, anatomic, and procedural data using uniform data definitions.<sup>8</sup> Patients who underwent both diagnostic catheterization and PCI procedure during a single laboratory visit were defined as undergoing ad hoc PCI. All other patients who underwent PCI in a laboratory visit separate from the diagnostic angiogram were designated as having had non–ad hoc PCI.

The primary clinical outcomes of interest in this study were post-PCI bleeding, AKI, and mortality. *Bleeding* was defined as any bleeding event within 72 hours post-PCI,

including arterial access site external bleeding or hematoma, retroperitoneal bleeding, gastrointestinal bleeding, genitourinary bleeding, intracranial hemorrhage, cardiac tamponade, hemoglobin decrease of  $\geq 3$  mg/dL for patients with preprocedure hemoglobin  $\geq 16$  mg/dL, or postprocedure blood transfusion for patients with preprocedure hemoglobin  $\geq 8$  mg/dL. *AKI* was defined based on Acute Kidney Injury Network criteria as change in preprocedural to postprocedural creatinine by an in-hospital absolute increase of  $\geq 0.3$  mg/dL or a relative increase of  $\geq 50\%$ . *Mortality* was defined as any in-hospital death occurring post-PCI.

#### Statistical analysis

Data are reported as means (SD) for continuous variables and as percentages for categorical variables. Univariate comparisons between patient characteristics in the ad hoc and non–ad hoc PCI groups were performed using Wilcoxon rank sum tests for continuous variables and  $\chi^2$  tests for categorical variables. Absolute standardized differences were derived to determine significant differences in characteristics; by convention, a standardized difference  $>10\%$  is considered significant. For analyses comparing ad hoc and non–ad hoc PCI, adjusted odds ratios (ORs) for outcomes were estimated using logistic regression models with inverse probability weights to adjust for confounding and account for clustering within hospitals.<sup>9</sup> Weights were calculated by fitting a propensity score model comparing ad hoc and non–ad hoc PCI.<sup>10</sup> Variables in the propensity model included available demographic, clinical, procedural, and hospital characteristics (Supplementary Table I). Unweighted and weighted balance of covariates between groups was evaluated using

**Table I.** Baseline patient characteristics\*

Characteristic	Ad hoc PCI (n = 456,402), No. (%)	Non-ad hoc PCI (n = 94,340), No. (%)	Standardized difference (%)
Age, y (mean, SD)	66.9, 10.8	68.1, 11.0	11.64
Age ≥ 7years	189,313 (41.5)	43,937 (46.6)	-10.27
Male sex	317,255 (69.5)	64,363 (68.2)	-2.78
Race/ethnicity			7.96
White	403,252 (88.4)	83,274 (88.3)	
African American	33,979 (7.4)	7856 (8.3)	
Asian	12,043 (2.6)	2022 (2.1)	
Hispanic	24,096 (5.3)	4160 (4.4)	
Other	4557 (1.0)	878 (0.9)	
Current/recent smoker	86,778 (19.0)	18,869 (20.0)	2.55
Hypertension	392,034 (85.9)	82,896 (88.0)	6.10
GFR			18.29
<30 or on dialysis	19,974 (4.4)	5162 (5.5)	
30-59	97,157 (21.3)	23,790 (25.2)	
60-89	206,720 (45.3)	39,479 (41.8)	
≥90	111,448 (24.4)	21,041 (22.3)	
Hemoglobin, mg/dL (median, IQR)	13.7 (12.5-14.8)	13.3 (11.9-14.5)	23.42
Diabetes	181,793 (39.8)	39,416 (41.8)	3.99
Peripheral vascular disease	63,050 (13.8)	16,615 (17.6)	10.50
Cerebrovascular disease	59,382 (13.0)	14,759 (15.7)	7.56
Chronic lung disease	69,347 (15.2)	16,433 (17.4)	6.07
Prior PCI	155,641 (34.1)	31,203 (33.1)	-2.16
Prior CABG	84,803 (18.6)	21,529 (22.8)	10.48
Prior MI	117,158 (25.7)	27,593 (29.3)	8.04
Heart failure (within 2 wk pre-PCI)			7.11
No	399,034 (87.4)	80,559 (85.4)	
Yes; NYHA Class I/II	22,023 (4.8)	4577 (4.9)	
Yes; NYHA Class III/IV	35,249 (7.7)	9175 (9.7)	
LVEF <40	44,423 (12.3)	10,479 (17.7)	15.16
Antianginal medications			12.66
β-Blockers	280,131 (61.4)	63,277 (67.1)	
Calcium channel blockers	91,508 (20.0)	20,398 (21.6)	
Nitrates	59,262 (13.0)	16,622 (17.6)	

MI, Myocardial infarction; LVEF, left ventricular ejection fraction.

\*All values presented are percentages except for age and hemoglobin.

Cramer  $\Phi$  for categorical variables and  $R^2$  for continuous variables (Supplemental Figure).

Prespecified subgroup analyses were conducted based on hypotheses that outcomes may be worse in patients with certain high-risk features, including age (>70 vs ≤70 years), glomerular filtration rate (GFR; <30, 30-59, ≥60 mL/min), and heart failure severity at the time of admission (New York Heart Association [NYHA] class III/IV vs I/II or no heart failure), or in patients undergoing more complex procedures such as multivessel PCI or PCI of a chronic total occlusion (CTO). We performed interaction analyses to assess whether the relationship between ad hoc PCI and each outcome of interest differed based on stratified subgroups. For the outcome of AKI, we also tested for a significant interaction based on contrast volume received as a continuous variable. Adjusted OR and 95% CIs were determined for each subgroup using the inverse probability weighted propensity adjusted logistic regression models described above.

Two-sided  $P$  values < .05 were considered statistically significant, and all statistical analyses were performed using SAS version 9.4 (SAS Inc, Cary, NC). All analyses were conducted at the Duke Clinical Research Institute (Durham, NC).

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## Results

### Utilization rates of ad hoc PCI

We evaluated a total of 550,742 patients who underwent PCI for stable CAD from July 1, 2009, to September 30, 2017. The mean age of this population was 67.1 years

**Table II.** Procedural and hospital characteristics\*

	Ad hoc PCI (n = 456,402)	Non-ad hoc PCI (n = 94,340)	Standardized difference (%)
Procedural characteristics			
PCI indication	No (%)	No (%)	
No angina or other symptoms	102,163 (22.4)	28,203 (29.9)	17.40
Atypical chest pain	57,446 (12.6)	7030 (7.5)	
Stable angina	296,537 (65.0)	59,012 (62.6)	
Lesion length, mm (mean, SD)	19.0, 11.2	20.2, 13.2	9.84
Lesion diameter <2 mm	12,988 (3.0)	3767 (4.3)	7.01
Preprocedure TIMI 0 or 1 flow	64,412 (14.2)	13,889 (14.8)	1.71
ACC/AHA type C Lesion	212,659 (46.7)	48,970 (52.0)	10.61
Lesion in graft			5.40
Not in graft	432,639 (94.8)	88,676 (94.0)	
Vein	21,351 (4.7)	4785 (5.1)	
LIMA	1567 (0.3)	463 (0.5)	
Other artery	845 (0.2)	416 (0.4)	
Bifurcation lesion	47,541 (10.4)	11,676 (12.4)	6.17
Multivessel PCI performed	66,507 (14.6)	20,148 (21.4)	17.74
PCI of CTO	16,290 (3.6)	5726 (6.1)	11.69
More than 1 stent implanted	150,755 (33.0)	39,203 (41.6)	17.70
Femoral access	353,598 (77.5)	78,533 (83.2)	14.56
Hospital characteristics, n (%)			
Annual PCI volume (median, IQR)	592.7 (362.5-925.3)	725.7 (454.7-1119.5)	30.50
Region			14.95
West	75,960 (16.6)	9090 (9.6)	
Northeast	68,339 (15.0)	14,195 (15.0)	
Midwest	124,841 (27.4)	26,427 (28.0)	
South	187,248 (41.0)	44,621 (47.3)	
Teaching hospital	217,764 (47.7)	45,189 (47.9)	0.37
Location/community			2.22
Rural	57,998 (12.7)	10,374 (11.0)	
Suburban	148,914 (32.6)	31,743 (33.6)	
Urban	249,490 (54.7)	52,223 (55.4)	
No. of hospital beds (median, IQR)	371.0 (250.0-534.0)	362.0 (240.0-542.0)	-1.27

AHA, American Heart Association; LIMA, left internal mammary artery.

\*All data presented are percentages unless otherwise specified.

(SD = 10.8), and 30.7% were women. *Ad hoc PCI*, defined as both the diagnostic angiogram and the PCI performed during the same laboratory visit, was performed in 456,402 (82.9%) of these patients. Over the course of our study, the proportion of patients who underwent *ad hoc PCI* increased from a low of 78.2% in 2009 quarter 3 to 84.7% in 2017 quarter 3.

#### Univariate comparisons of *ad hoc* and non-*ad hoc* PCI

As shown in [Table I](#), patients who underwent PCI as a separate, later procedure were older and had higher rates chronic kidney disease with GFR <60 mL/min, peripheral vascular disease, prior coronary artery bypass graft (CABG) surgery, and reduced left ventricular ejection fraction. Non-*ad hoc* PCI patients were also more likely to have femoral access, multivessel disease, longer lesion length, and complex coronary anatomy, and ultimately were more likely to undergo multivessel PCI or have more than 1 stent implanted ([Table II](#)). There was little variation across hospitals in the frequency of *ad hoc* PCI;

**Table III.** Clinical outcomes after *ad hoc* versus non-*ad hoc* PCI

A. Unadjusted rates of adverse outcomes in *ad hoc* and non-*ad hoc* PCI (%)

	Ad hoc PCI	Non-ad hoc PCI	P value
Bleeding	2.4	3.4	<.001
AKI	7.4	8.5	<.001
Mortality	0.4	0.4	.007

B. Adjusted risk\* of adverse outcomes in *ad hoc* versus non-*ad hoc* PCI

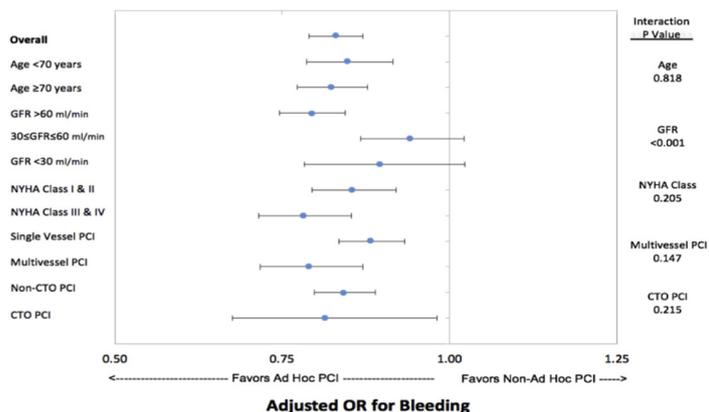
	Adjusted OR (95% CI)	P value
Bleeding	0.83 (0.79-0.87)	<.001
AKI	0.95 (0.90-1.00)	.055
Mortality	1.09 (0.97-1.23)	.149

\*Adjustment performed using inverse probability weighted propensities using patient, procedural, and hospital characteristics.

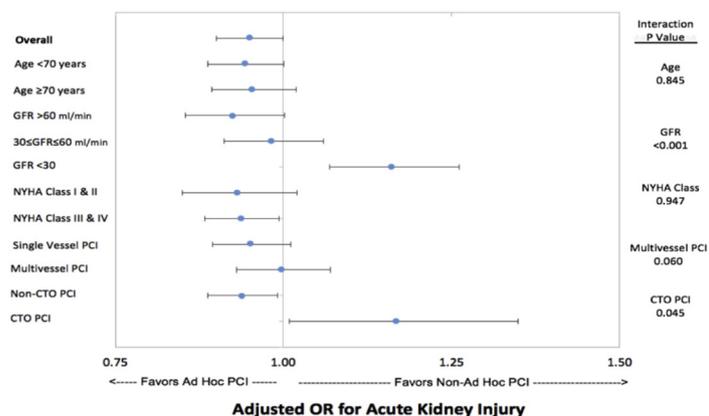
the median rate of *ad hoc* PCI in stable CAD patients was 91.1% (25th-75th percentiles: 81.0%-97.5%). *Ad hoc* PCI was more commonly performed at hospitals with lower PCI volumes ([Table II](#)).

**Figure 2**

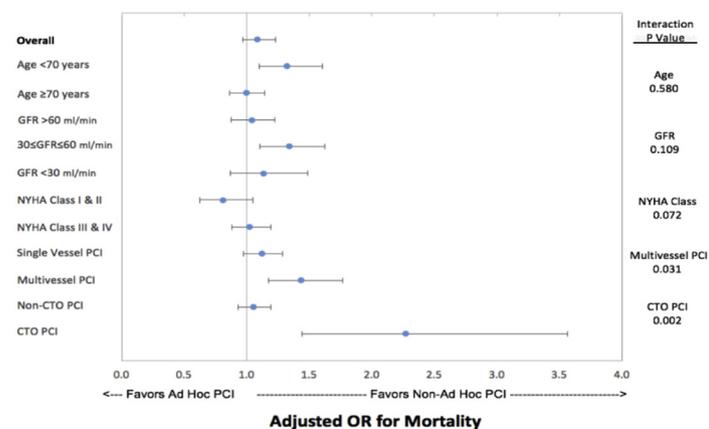
**A. Bleeding**



**B. Acute Kidney Injury**



**C. Mortality**



Outcomes for ad hoc versus non-ad hoc PCI by clinical subgroup. \*\*Number (n) of patients in each group: overall (550,742), age <70 years (317,492), age ≥70 years (233,250), GFR >60 mL/min (378,688), 30 ≤ GFR ≤ 60 mL/min (120,947), GFR <30 mL/min (25,136), NYHA Class I and II (26,600), NYHA Class III and IV (44,424), single-vessel PCI (464,087), multivessel PCI (86,655), non-CTO PCI (528,726), CTO PCI (22,016).

### Comparisons of in-hospital adverse outcomes

Unadjusted rates of bleeding, AKI, and death were lower for patients who underwent ad hoc PCI compared with non-ad hoc PCI (Table III, A). After multivariable inverse probability weighted propensity adjustment, ad hoc PCI was associated only with lower risk of bleeding when compared with non-ad hoc PCI (Table III, B). There were no differences in the adjusted risks of in-hospital AKI or death between the 2 groups.

Outcomes for subgroups stratified by patient risk factors (age, GFR, and NYHA class at the time of presentation) as well as PCI complexity (multi- vs single-vessel PCI and PCI of a CTO vs non-CTO lesion) are shown in Figure 2 and Supplementary Table II. Ad hoc PCI continued to be associated with lower bleeding risk in most patient subgroups with a significant interaction term *P* value only for GFR. There was no difference in bleeding between ad hoc and non-ad hoc PCI for patients with GFR  $\leq 60$ . For the outcome of AKI, the interaction terms were significant for GFR and CTO PCI. For patients with GFR  $< 30$  mL/min as well as those who underwent PCI of a CTO lesion, ad hoc PCI was associated with a significantly higher risk of AKI. Patients who underwent ad hoc PCI had significantly higher risk of mortality than patients who underwent non-ad hoc PCI when lesions in multiple vessels were treated, or the treated lesion was chronically occluded. There was no significant interaction between ad hoc status of PCI and contrast volume on risk of AKI, evaluated per 10-mL increase in contrast received during the PCI procedure (interaction *P* value = .626).

### Discussion

The vast majority of PCI procedures in contemporary United States practice were performed in an ad hoc fashion for patients with stable coronary artery disease. Patients for whom PCI procedures were deferred to a later, separate procedure were older and more likely to have comorbidities and complex coronary anatomy than ad hoc PCI patients. After multivariable adjustment, ad hoc PCI was associated with lower risk of in-hospital bleeding. There was no difference in adjusted risks of postprocedural AKI or mortality between patients who underwent ad hoc and non-ad hoc PCI. Subgroup analyses suggest that ad hoc PCI may be associated with a higher risk of AKI in patients with GFR  $< 30$  mL/min as well as higher risk of mortality in patients who undergo PCI on multiple vessels or a CTO lesion.

Ad hoc PCI offers several benefits over non-ad hoc PCI including single vascular site access, shorter hospital stay, lower cost, and improved patient satisfaction.<sup>3,11,12</sup> The 2011 ACC and American Heart Association guidelines do not provide specific recommendations for or against the use of ad hoc PCI in patients with stable CAD, and the

Society for Cardiovascular Angiography and Interventions 2013 consensus statement recommends an individualized approach to selection of ad hoc PCI.<sup>3,13</sup> In comparison to a prior analysis of 2001-2003 NCDR data showing a usage rate of 61% for ad hoc PCI, our study shows that ad hoc PCI has essentially become the default pathway for patients with stable CAD in the United States with rates currently up to 84% and minimal variation in practice across hospitals.<sup>1</sup> Ad hoc PCI is much more common in the United States than in Japan (24.8%)<sup>14</sup> but comparable to Korea (75.2%).<sup>15</sup> There may be disadvantages to this trend, however, including a limited process of informed consent and potentially limited consideration of other treatment options such as CABG or intensification of medical management.<sup>3,5,16-19</sup> Other concerns with ad hoc PCI have included self-referral bias and lack of adequate preparation or expertise for complex cases.<sup>3,4</sup>

Older retrospective studies found that patients undergoing ad hoc PCI were generally healthier with fewer comorbidities and better renal function.<sup>1,2,20,21</sup> Contemporary data mirror these practice patterns. Non-ad hoc PCI is more commonly performed in older patients who may not be able to tolerate prolonged procedures, patients with peripheral arterial disease whose vascular access site may need to be changed to proceed with PCI, patients with renal insufficiency to avoid contrast nephropathy, or patients with prior CABG who may have more complicated anatomy and treatment decision making. We also showed that ad hoc PCI procedures are more likely to involve uncomplicated coronary anatomy with lower rates of multiple stents or multivessel PCI.

Our study showed lower rates of postprocedural bleeding among patients who received ad hoc PCI when compared with patients who required 2 or more procedures. This relationship persisted after multivariable adjustment and was consistent across subgroups, suggesting a potential benefit to considering PCI immediately following coronary angiogram. Lower rates of vascular injury have also been observed previously with ad hoc PCI.<sup>21</sup> One possible explanation for this may be that a second PCI procedure requires repeat vascular access which may increase bleeding risk. This may be especially significant in US practice, where femoral access remains prevalent (78.5% of patients in our cohort); risks of bleeding in practice elsewhere may differ if radial access is used more frequently. Another possible reason for the lower risk of bleeding seen with ad hoc PCI may be that patients who undergo a separate PCI procedure have more complicated coronary anatomy that requires longer duration of intravenous anticoagulation and vascular site manipulation which predispose to bleeding.

Although deferring an additional contrast load may be helpful in avoiding AKI in patients with chronic renal insufficiency, 2 previous large studies did not show a significant difference in renal failure with ad hoc PCI.<sup>1,21</sup>

After multivariable adjustment, we also found no difference in risk of acute kidney injury between patients with ad hoc versus non-ad hoc PCI. However, our large study cohort permitted us to observe a differing relationship between ad hoc PCI and risk of AKI among patients with varying degrees of chronic renal insufficiency; ad hoc PCI was associated with significantly higher AKI risk among patients with GFR <30 mL/min. These results are hypothesis generating, suggesting that patients with severe renal dysfunction should be considered for a staged procedural approach.

Our study found no difference in unadjusted and adjusted mortality risks between patients who underwent ad hoc versus non-ad hoc PCI. This is not particularly surprising given the low overall post-PCI mortality rates in a contemporary stable CAD population.<sup>22,23</sup> The choice between an ad hoc and non-ad hoc procedure is unlikely to have life-threatening implications among the vast majority of these patients. However, patients undergoing CTO PCI had higher AKI and mortality risks with an ad hoc approach, which was used for 74.0% of these patients. CTO procedures in particular require careful assessment of risk versus benefit, alternative treatment options such as CABG or medical optimization, informed shared decision making with patients, experienced operators, and preprocedural planning.<sup>24</sup> For patients undergoing CTO PCI for stable CAD, the association of an ad hoc approach with higher risk of AKI may be due to cumulative contrast exposure. The more concerning association with mortality risk needs to be validated in other studies but lends caution against the routine use of ad hoc CTO PCI to allow for more prudent planning with appropriate equipment and expertise. The higher mortality risk associated observed with ad hoc procedures for multivessel PCI similarly casts doubt on regular use of this approach, particularly when CABG may offer better long-term outcomes for many patients with multivessel disease.<sup>5,25,26</sup> However, these findings also need to be confirmed with future investigations.

This study has several limitations. This was a retrospective study and cannot fully account for unmeasured confounders when comparing outcomes between patients who underwent ad hoc and non-ad hoc PCI despite multivariable propensity-weighted adjustment. It is therefore possible that observed differences in outcomes were driven by operator selection and unmeasured patient characteristics rather than timing of PCI. Variables such as coronary artery complexity as well as bleeding and AKI outcomes were reported by operators and staff at participating sites without independent adjudication. Although the NCDR conducts annual random audits to ensure data accuracy, we cannot exclude the possible influence of operator experience and/or reporter bias when describing angiographic characteristics in the medical record. Because the CathPCI Registry does not mandate collection of diag-

nostic angiogram data, details on the timing of PCI after the diagnostic angiogram as well as the specific operators involved in both procedures could not be described for all non-ad hoc PCI patients, as this information was voluntarily reported in only 22% of patients. In addition, only outcomes following the initial PCI were included for patients who received multiple PCI over the study period, and therefore it is uncertain how events from subsequent PCI procedures would have affected our findings. Finally, we evaluated only in-hospital outcomes and could not include outcomes following discharge.

## Conclusions

Most patients with stable coronary artery disease treated with PCI in the United States undergo an ad hoc PCI procedure immediately following the diagnostic angiogram. Ad hoc PCI is associated with lower post-PCI bleeding, suggesting a possible risk with a second vascular access in clinical practice. There were no significant differences in risks of AKI or mortality when comparing ad hoc versus non-ad hoc PCI. However, certain populations such as those with baseline CKD or who undergo multivessel or CTO PCI may have risk of harm with ad hoc PCI. Interventional cardiologists should carefully consider patient characteristics and clinical anatomy at the time of coronary angiography before proceeding with ad hoc PCI.

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## Declarations of interest

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## Author contributions

All authors have reviewed and approved the manuscript. Specific contributions are detailed below.

**K. F. Faridi:** Dr Faridi contributed to the conception and design of the study, the supervision, data acquisition, analysis and interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr Faridi has approved the version of the manuscript being submitted.

**J. A. Rymer:** Dr Rymer contributed to conception and design of the study, the supervision, analysis and interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr Rymer has approved the version of the manuscript being submitted.

**S. V. Rao:** Dr Rao contributed to the conception and design of the study, the supervision, analysis and interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr Rao has approved the version of the manuscript being submitted.

**D. Dai:** Dr Dai contributed to the conception and design of the study, data acquisition, analysis and interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr Dai has approved the version of the manuscript being submitted.

**D. Wojdyla:** Mr Wojdyla contributed to the conception and design of the study, data acquisition, analysis and interpretation, the manuscript drafting, and the critical revision of the manuscript. Mr Wojdyla has approved the version of the manuscript being submitted.

**R. W. Yeh:** Dr Yeh contributed to the conception and design of the study, analysis and interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr Yeh has approved the version of the manuscript being submitted.

**T. Y. Wang:** Dr Wang contributed to conception and design of the study, the supervision, data acquisition, analysis and interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr. Wang has approved the version of the manuscript being submitted.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ahj.2019.07.004>.

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