Journal of the American Heart Association

ORIGINAL RESEARCH

Clinical and Vessel Characteristics Associated With Hard Outcomes After PCI and Their Combined Prognostic Implications

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BACKGROUND: Cardiac death or myocardial infarction still occurs in patients undergoing contemporary percutaneous coronary intervention (PCI). We aimed to identify adverse clinical and vessel characteristics related to hard outcomes after PCI and to investigate their individual and combined prognostic implications.

METHODS AND RESULTS: From an individual patient data meta-analysis of 17 cohorts of patients who underwent post-PCI fractional flow reserve measurement after drug-eluting stent implantation, 2081 patients with available clinical and vessel characteristics were analyzed. The primary outcome was cardiac death or target-vessel myocardial infarction at 2 years. The mean age of patients was 64.2±10.2 years, and the mean angiographic percent diameter stenosis was 63.9%±14.3%. Among 11 clinical and 8 vessel features, 4 adverse clinical characteristics (age ≥65 years, diabetes, chronic kidney disease, and left ventricular ejection fraction <50%) and 2 adverse vessel characteristics (post-PCI fractional flow reserve ≤0.80 and total stent length ≥54 mm) were identified to independently predict the primary outcome (all $P<0.05$). The number of adverse vessel characteristics had additive predictability for the primary end point to that of adverse clinical characteristics (area under the curve 0.72 versus 0.78; $P=0.03$) and vice versa (area under the curve 0.68 versus 0.78; $P=0.03$). The cumulative event rate increased in the order of none, either, and both of adverse clinical characteristics ≥2 and adverse vessel characteristics ≥1 (0.3%, 2.4%, and 5.3%; P for trend <0.01).

CONCLUSIONS: In patients undergoing drug-eluting stent implantation, adverse clinical and vessel characteristics were associated with the risk of cardiac death or target-vessel myocardial infarction. Because these characteristics showed independent and additive prognostic value, their integrative assessment can optimize post-PCI risk stratification.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04684043. www.crd.york.ac.uk/prospero/. Unique Identifier: CRD42021234748.

Key Words: drug-eluting stent ■ fractional flow reserve ■ risk stratification

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This manuscript was sent to Saket Girotra, MD, SM, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.123.030572

For Sources of Funding and Disclosures, see page 10.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Adverse clinical and vessel characteristics (age ≥65 years, diabetes, chronic kidney disease, and left ventricular ejection fraction <50%, post–percutaneous coronary intervention fractional flow reserve ≤0.80 and total stent length ≥54 mm) were independent predictors of cardiac death or myocardial infarction at 2 years after drug-eluting stent implantation.
- There was additive prognostic value between adverse clinical and vessel characteristics, and the risk of hard outcomes was the highest in patients who had both adverse clinical characteristics ≥2 and adverse vessel characteristics ≥1.

What Are the Clinical Implications?

- A comprehensive assessment to identify adverse clinical and vessel characteristics can help an optimized risk prediction for hard outcomes after percutaneous coronary intervention.
- Future study is needed to prove the prognostic impact of reducing adverse vessel characteristics with incorporation of information on physiologic focal/diffuse disease in patients with and without adverse clinical characteristics.

Nonstandard Abbreviations and Acronyms

ACCs	adverse clinical characteristics
AVCs	adverse vessel characteristics
FFR	fractional flow reserve
GRACE	Global Registry of Coronary Events
LASSO	least absolute shrinkage and selection operator
POST-PCI FLOW	Prognostic Implications of Physiologic Investigation After Revascularization With Stent
TVMI	target-vessel myocardial infarction

Clinical outcomes after percutaneous coronary intervention (PCI) have improved with advances in stents, procedural techniques, and medical therapy in recent decades. However, hard clinical end points such as cardiac death or myocardial infarction (MI) still occur in patients undergoing contemporary PCI.[1–3] Multiple studies have reported risk prediction models for death after PCI by combining angiographic parameters and patient characteristics,[4–6] and current guidelines recommend individual risk stratification and secondary prevention according to various clinical characteristics among patients undergoing PCI.[7,8] Meanwhile, residual ischemia after PCI, which can be evaluated by a pressure wire–based index such as post-PCI fractional flow reserve (FFR), is associated with a risk of hard outcomes after PCI.[9] Given that about one-fourth of cases with angiographically successful PCI have residual ischemia, post-PCI physiologic assessment can provide prognostic information not captured by angiography alone.[10–13] Therefore, an integrative assessment incorporating clinical risk factors as well as angiographic and physiologic vessel characteristics is a reasonable approach for risk prediction for hard outcomes after PCI. In this regard, we aimed to identify adverse clinical and vessel characteristics associated with hard outcomes after PCI and to investigate their individual and combined prognostic implications.

METHODS

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

The study population was from the POST-PCI FLOW (Prognostic Implications of Physiologic Investigation After Revascularization With Stent; clinicaltrials.gov identifier NCT04684043; PROSPERO Registration ID: CRD42021234748) study, which was a systematic review and individual patient-level meta-analysis of previous studies related to post-PCI FFR from inception to June 18, 2022. The study protocol was approved by the ethics committee of Seoul National University Hospital and performed following the principles of the Declaration of Helsinki. The study protocol was described in detail previously.[9] Briefly, a manual search for relevant articles was performed in the MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials. The prespecified inclusion criteria were as follows: (1) PCI with drug-eluting stents; (2) post-PCI FFR measured after stent implantation; (3) minimum follow-up duration of 6 months for tracking clinical outcomes; (4) available clinical outcomes including all-cause death, cardiac death, target-vessel myocardial infarction (TVMI), or target-vessel revascularization. After the systematic review, 29 studies met the inclusion criteria, and principal investigators of 28 studies from 17 cohorts across 16 countries agreed to share anonymized data for the individual patient-level meta-analysis. Among a total of 5277 patients from the POST-PCI FLOW study, 2081 patients with fully available data for 19 clinical and vessel characteristics were included

in the current study. All patients in the current study received PCI with second-generation drug-eluting stents. The requirement for informed consent was waived because all data were collected in a deidentified form.

Primary Outcome

The primary outcome was a composite of cardiac death or TVMI. All deaths were considered cardiac in origin unless a noncardiac cause was specified. TVMI was defined as an MI that occurred by any lesion in the same target vessel. Among 2081 patients, 128 patients had 2 target vessels, 13 had 3 target vessels, and the remaining 1940 had 1 target vessel, and the vessel with the lowest post-PCI FFR value was chosen for the target vessel of the patient in patients who had ≥2 target vessels. The definitions of clinical outcomes followed the Academic Research Consortium.[14]

Selection of Adverse Clinical and Vessel Characteristics

Among 19 variables with 11 clinical characteristics (age, sex, clinical diagnosis at index procedure, diabetes, hypertension, dyslipidemia, smoking history, chronic kidney disease [CKD], prior MI, left ventricular ejection fraction [LVEF], and multiple target vessels) and 8 vessel characteristics (target vessel, reference vessel diameter, percent diameter stenosis, minimum lumen diameter, post-PCI percent diameter stenosis, post-PCI minimum lumen diameter, total stent length in the target vessel, and post-PCI FFR), adverse clinical and adverse vessel characteristics related to the primary outcome were selected by the least absolute shrinkage and selection operator (LASSO) Cox regression model.[15,16] All 19 variables with non-0 coefficients were included in the regression model. The LASSO model reduced the dimension of a prediction model by introducing a tuning parameter (lambda) to penalize the coefficient of variables, and the absolute values of variable coefficients were reduced toward 0 with an increment of the tuning parameter to select fewer variables. A 10-fold cross validation was performed during the process for selection of the optimal lambda, which was determined by choosing the most regularized model with minimum mean square error.[15]

Statistical Analysis

Categorical variables were presented as numbers (percentages) and continuous variables as means±SDs. All analyses were performed on a per-patient basis. Among selected features by the LASSO model, the continuous variables were converted into binary variables using the established cutoff or the optimal cutoff value on the basis of the maximal log-rank statistics. The cumulative event of the primary outcome was estimated using Kaplan–Meier estimates, and the log-rank test was used to compare the survival curves between groups. Hazard ratios (HRs) and 95% CIs were derived from Cox proportional hazard regression. The assumption on the Cox proportional hazard regression was estimated by Schoenfeld residuals. In multivariable analysis, variables with $P<0.05$ in the univariable analysis were included to identify independent predictors for the primary outcome. The predictive value for the primary outcome was evaluated by Harrell's concordance statistic. All P values <0.05 were considered statistically significant. The software package R version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis.

RESULTS

Baseline Characteristics

Baseline clinical and vessel characteristics are presented in Table 1. Among a total of 2081 patients

Table 1. Baseline Characteristics

	Total (N=2081)
Clinical characteristics	
Age, y	64.2±10.2
Sex, male, n (%)	1600 (76.9)
Clinical diagnosis, n (%)	
Stable ischemic heart disease	1107 (53.2)
Acute coronary syndrome	974 (46.8)
Diabetes, n (%)	764 (36.7)
Hypertension, n (%)	1402 (67.4)
Dyslipidemia, n (%)	1111 (53.4)
Current smoking, n (%)	608 (29.2)
Chronic kidney disease, n (%)	124 (6.0)
Prior myocardial infarction, n (%)	250 (12.0)
Left ventricular ejection fraction, %	61.8±8.8
Vessel characteristics	
Target-vessel location, n (%)	
Left anterior descending artery	1536 (73.8)
Left circumflex artery	212 (10.2)
Right coronary artery	333 (16.0)
Reference vessel diameter, mm	2.9±0.5
% diameter stenosis	63.9±14.3
MLD, mm	1.0±0.5
Post-PCI % diameter stenosis	9.5±7.4
Post-PCI MLD, mm	2.8±0.5
Total stent length, mm	35.4±21.1
Post-PCI FFR	0.88±0.07

FFR indicates fractional flow reserve; MLD, minimum lumen diameter; and PCI, percutaneous coronary intervention.

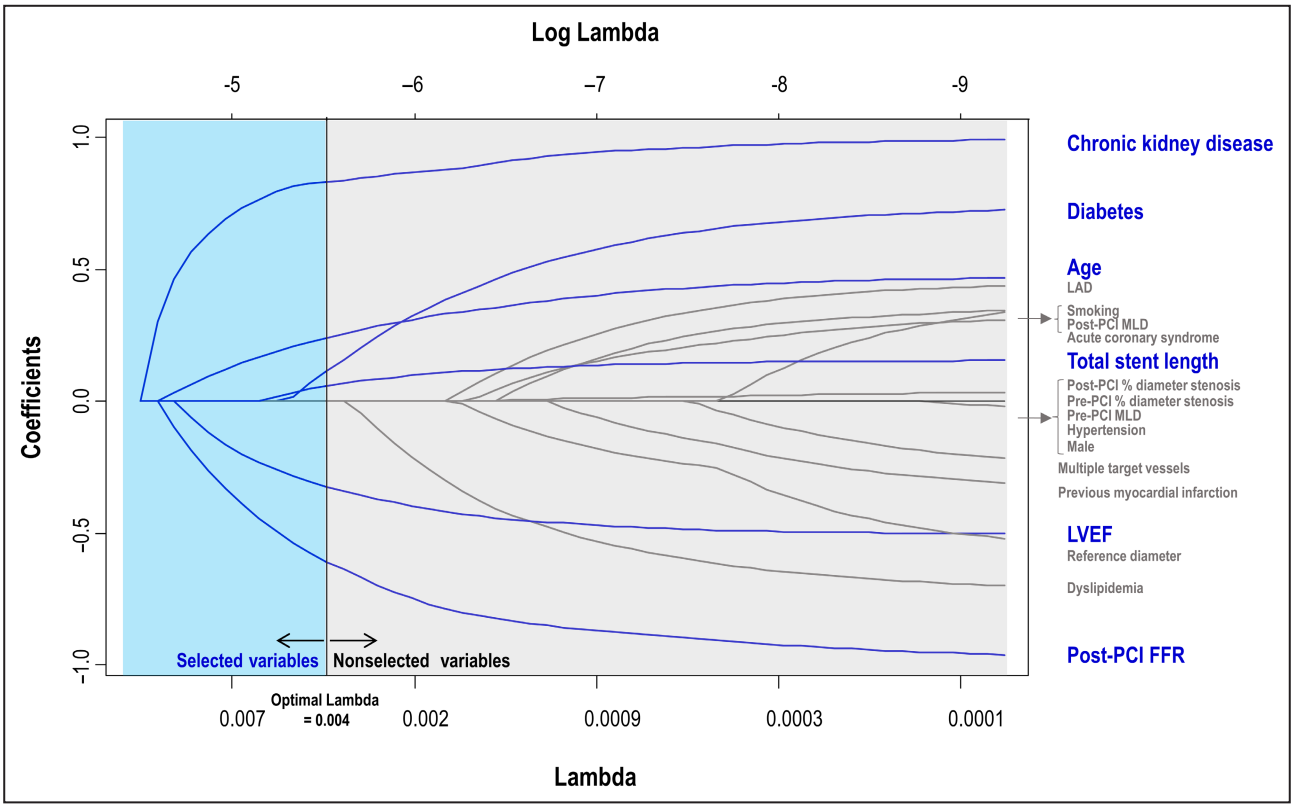

Figure 1. Identification of clinical and vessel characteristics related to cardiac death or TVMI by the LASSO–Cox regression model.

Among 19 clinical and vessel characteristics, 6 relevant features (4 clinical characteristics and 2 vessel characteristics) for cardiac death or TVMI were identified by the LASSO model. FFR indicates fractional flow reserve; LAD, left anterior descending artery; LASSO, least absolute shrinkage and selection operator; LVEF, left ventricular ejection fraction; MLD, minimum lumen diameter; PCI, percutaneous coronary intervention; and TVMI, target-vessel myocardial infarction.

(mean age, 64.2±10.2 years; 76.9% men), 974 (46.8%) presented with acute coronary syndrome; diabetes was present in 764 (36.7%) patients and CKD in 124 (6.0%); and the mean LVEF was 61.8%±8.8%. The target vessel was the left anterior descending artery in 1536 (73.8%) patients, the mean angiographic percent diameter stenosis was 63.9±14.3%, and the mean post-PCI FFR was 0.88±0.07. During the median follow-up duration of 2.0 years, the primary outcome occurred in 27 (cumulative event rate, 1.6%) patients with 18 cardiac deaths and 10 TVMIs.

Clinical and Vessel Characteristics Predictive of Cardiac Death or TVMI

The LASSO regression model identified predictors for cardiac death or TVMI (Figure 1). From the model with the minimum mean square error by the optimal lambda (Figure S1), 4 clinical characteristics (age, diabetes, CKD, and LVEF) and 2 vessel characteristics (total stent length and post-PCI FFR) were associated with the occurrence of cardiac death or TVMI (Figure 1). According to the lambda value, CKD was the most important factor to predict cardiac death or TVMI among clinical characteristics and post-PCI FFR among vessel characteristics. Using the established or best cutoff values for risk factors, adverse clinical characteristics (ACCs) were defined as age ≥65 years, diabetes, CKD, and LVEF <50%, and adverse vessel characteristics (AVCs) were defined as post-PCI FFR ≤0.80 and total stent length ≥54 mm.

The cumulative event of cardiac death or TVMI at 2 years according to the presence of ACCs and AVCs is presented in Figure 2. The risk was significantly higher in patients with age ≥65 years (HR, 3.33 [95% CI, 1.34–8.25]; *P*=0.009), diabetes (HR, 2.62 [95% CI, 1.22–5.65]; *P*=0.014), CKD (HR, 5.95 [95% CI, 2.52–14.1]; *P*<0.001), LVEF <50% (HR, 2.91 [95% CI, 1.17–7.20]; *P*=0.021), post-PCI FFR ≤0.80 (HR, 3.79 [95% CI, 1.73–8.28]; *P*<0.001), and total stent length ≥54 mm (HR, 2.42 [95% CI, 1.08–5.39]; *P*=0.031). This result was consistent in the competing risk analysis with treating noncardiac death as a competing event (Table S1). In multivariable analysis, all ACCs and AVCs were independent predictors for cardiac death or TVMI (Table 2).

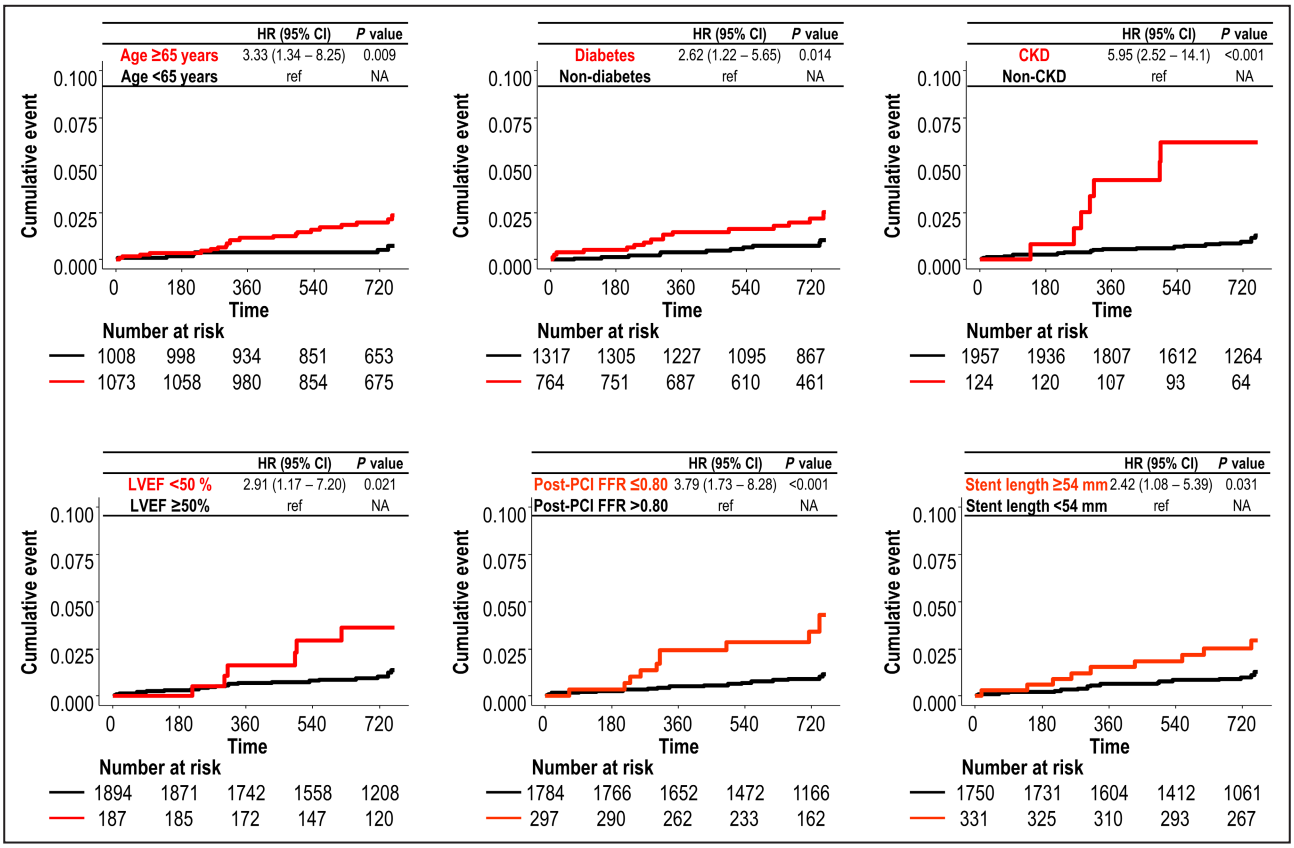

Figure 2. Prognostic value of adverse clinical and vessel characteristics for predicting cardiac death or TVMI.
The cumulative event of cardiac death or TVMI at 2 years according to adverse clinical and vessel characteristics is presented. Adverse clinical characteristics are age ≥65 years, diabetes, CKD, and LVEF <50%. Adverse vessel characteristics are post-PCI FFR ≤0.80 and total stent length ≥54 mm. CKD indicates chronic kidney disease; FFR, fractional flow reserve; HR, hazard ratio; LVEF, left ventricular ejection fraction; NA, not applicable; PCI, percutaneous coronary intervention; and TVMI, target-vessel myocardial infarction.

Additive Prognostic Value Between Adverse Clinical and Vessel Characteristics

When ACCs were combined, the cumulative event of cardiac death or TVMI proportionally increased in the order of 0, 1, and ≥2 of ACCs (0.3%, 1.5%, and 3.1%, respectively; *P* for trend <0.001). This relationship was consistent after adjustment for the number of AVCs (Table 3). Similarly, the cumulative event of cardiac death or TVMI was 0.8%, 3.2%, and 5.3% in patients with 0, 1, and 2 of AVCs (*P* for trend <0.001), of which the trend was similar after adjustment for ACCs (Table 3). Figure 3 represents the predictive value for cardiac death or TVMI based on the number of ACCs and AVCs. While there was no difference in area under the curve (AUC) between the 2 (AUC 0.68 versus 0.72; *P*=0.55), the combined number of adverse clinical and vessel characteristics had a higher AUC than that of the number of ACCs (AUC 0.78 versus 0.72; *P*=0.03) or that of the number of AVCs (AUC 0.78 versus 0.68; *P*=0.03) (Figure 3).

The optimal cutoff value for the number of ACCs was ≥2, and for the number of AVCs was ≥1. The risk of cardiac death or TVMI was higher in patients with ACCs ≥2 (HR, 3.35 [95% CI, 1.57–7.15]; *P*=0.002) or with AVCs ≥1 (HR, 4.20 [95% CI, 1.92–9.19]; *P*<0.001) (Figure S2). Figure 4 shows the cumulative event of cardiac death or TVMI in 4 groups divided by ACCs ≥2 and AVCs ≥1, with the risk being highest in patients with both ACCs ≥2 and AVCs ≥1 than in those who had none or either of ACCs ≥2 and AVCs ≥1. Individual outcomes showed a similar trend according to ACCs ≥2 and AVCs ≥1 (Table S2).

DISCUSSION

The current study identified ACCs and AVCs associated with the occurrence of cardiac death or TVMI after PCI and investigated their individual and combined prognostic implications. The main findings of the study were as follows: (1) ACCs were age ≥65 years, diabetes, CKD, and LVEF <50%, and AVCs were post-PCI FFR ≤0.80 and total stent length ≥54 mm; (2) all ACCs and AVCs were independent predictors for cardiac death or TVMI; (3) there was additive predictive value for cardiac death or TVMI between the number of ACCs and AVCs, and the risk of cardiac death/TVMI

Table 2. Independent Predictors for Cardiac Death or TVMI

	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Clinical characteristics				
Age, per 1-y increase	1.10 (1.05–1.15)	<0.001	1.09 (1.04–1.14)*	<0.001
Male	1.06 (0.43–2.62)	0.906	…	…
Acute coronary syndrome	1.13 (0.53–2.42)	0.745	…	…
Diabetes	2.62 (1.22–5.65)	0.014	2.27 (1.05–4.90)*	0.037
Hypertension	1.38 (0.58–3.26)	0.466	…	…
Dyslipidemia	0.71 (0.33–1.52)	0.380	…	…
Current smoking	1.00 (0.44–2.27)	0.991	…	…
Chronic kidney disease	5.95 (2.52–14.1)	<0.001	3.04 (1.25–7.36)*	0.014
Prior myocardial infarction	1.24 (0.43–3.60)	0.687	…	…
Left ventricular ejection fraction, per 1% increase	0.95 (0.92–0.97)	<0.001	0.95 (0.92–0.98)*	<0.001
Vessel characteristics				
Left anterior descending artery	2.94 (0.88–9.76)	0.079	…	…
Reference vessel diameter, per 1-mm increase	0.60 (0.28–1.30)	0.198	…	…
% diameter stenosis, per 1% increase	1.00 (0.97–1.02)	0.880	…	…
MLD, per 1-mm increase	0.82 (0.36–1.88)	0.636	…	…
Post-PCI % diameter stenosis, per 1% increase	1.02 (0.97–1.07)	0.455	…	…
Post-PCI MLD, per 1-mm increase	0.72 (0.32–1.60)	0.416	…	…
Total stent length, per 10-mm increase	1.15 (1.01–1.30)	0.032	1.18 (1.04–1.35)†	0.011
Post-PCI FFR, per 0.1 increase	0.39 (0.25–0.61)	<0.001	0.37 (0.23–0.58)†	<0.001

FFR indicates fractional flow reserve; HR, hazard ratio; MLD, minimum lumen diameter; PCI, percutaneous coronary intervention; and TVMI, target-vessel myocardial infarction.

*Adjusted for variables with $P<0.05$ in univariable analysis (age, diabetes, chronic kidney disease, and left ventricular ejection fraction) among clinical characteristics.

†Adjusted for variables with $P<0.05$ in univariable analysis (total stent length, and post-PCI FFR) among vessel characteristics.

increased in the order of none, either, and both of ACCs ≥2 and AVCs ≥1.

Risk Prediction of Hard Outcomes After PCI

While clinical outcomes after PCI have improved along with the evolution of PCI techniques and optimization of adjunctive pharmacotherapy, a significant proportion of patients still experience death or MI after PCI.[1–3] In the pooled analysis of 21 randomized clinical trials with >30 000 patients, the 5-year mortality rate after PCI was about 10%, and half of those cases were attributable to cardiovascular causes.[1] In addition, spontaneous MI occurring after PCI was associated with >7 times higher risk of subsequent

Table 3. Independent Prognostic Significance of Adverse Clinical and Vessel Characteristics

	Cumulative event of 2-y cardiac death or TVMI, %	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Number of ACCs					
0 (n=624)	0.3	…	…	…	…
1 (n=877)	1.5	7.99 (1.03–61.9)	0.047	8.15 (1.05–63.1)*	0.044
≥2 (n=580)	3.1	16.9 (2.23–127)	0.006	17.2 (2.28–131)*	0.006
Number of AVCs					
0 (n=1493)	0.8	…	…	…	…
1 (n=548)	3.2	3.97 (1.78–8.83)	<0.001	3.71 (1.66–8.30)†	0.001
2 (n=40)	5.3	7.65 (1.67–34.9)	0.009	5.78 (1.26–26.6)†	0.024

ACCs are age ≥65 years, diabetes, CKD, and LVEF <50%. AVCs are post-PCI FFR ≤0.80 and total stent length ≥54 mm. ACCs indicates adverse clinical characteristics; AVCs, adverse vessel characteristics; CI, confidence interval; CKD, chronic kidney disease; FFR, fractional flow reserve; HR, hazard ratio; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; and TVMI, target-vessel myocardial infarction.

*Adjusted for number of AVCs.

†adjusted for number of ACCs.

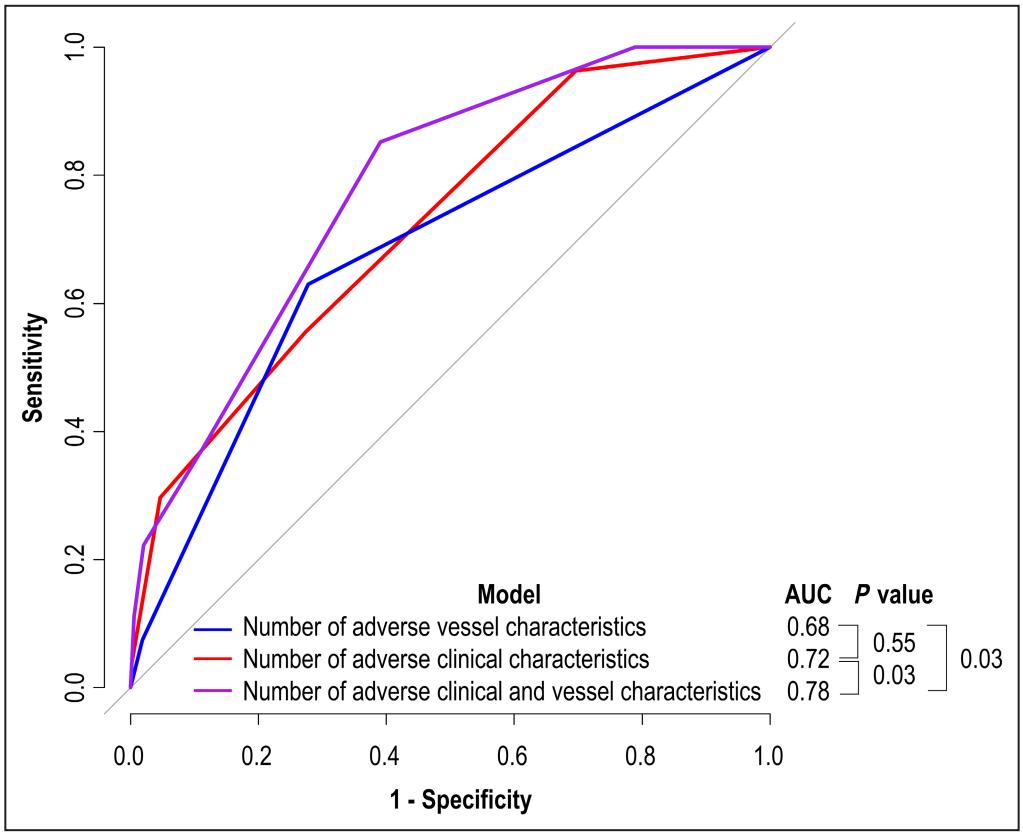

Figure 3. Additive prognostic value of adverse clinical and vessel characteristics.
In the ROC curve analysis, AUC for cardiac death or TVMI was compared among the number of ACCs, AVCs, and adverse clinical and vessel characteristics. ACCs are age ≥65 years, diabetes, CKD, and LVEF <50%. AVCs are post-PCI FFR ≤0.80 and total stent length ≥54 mm. ACCs indicates adverse clinical characteristics; AVCs, adverse vessel characteristics; AUC, area under the curve; CKD, chronic kidney disease; FFR, fractional flow reserve; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; ROC, receiver-operating characteristic; and TVMI, target-vessel myocardial infarction.

post-PCI death,[17] which necessitates risk prediction for hard outcomes among patients undergoing PCI. Several risk models for adverse events after PCI have been proposed and validated by combining several clinical risk factors[4,18,19] and anatomic vessel characteristics.[5,6,20,21] Thus, current guidelines recommend an individual approach for secondary prevention according to disease severity or clinical risk score.[7,8] In the interim, a growing body of evidence has reported that physiologic indexes measured after PCI are independent prognostic indicators.[22] A higher risk of death was predicted by low post-PCI FFR,[10,23] and a recent individual patient-level meta-analysis demonstrated the risk continuum of post-PCI FFR value for cardiac death or TVMI.[9] Nonetheless, the previously proposed risk models did not incorporate post-stent physiologic data, and relative and combined prognostic implications of clinical, angiographic, and physiologic characteristics for hard outcomes after PCI have not been established.

Adverse Clinical and Vessel Characteristics for Hard Outcomes After PCI

In the current analysis conducted from the largest registry that included patients who underwent post-PCI FFR measurement, the LASSO–Cox method was applied to reduce collinearity among 19 various clinical and pre- and post-PCI vessel characteristics and to identify the best predictors for cardiac death or TVMI. As for clinical characteristics, age ≥65 years, diabetes, CKD, and LVEF <50% were selected and were all independent predictors, which is supported by the well-established relationship of ACCs with short-term and long-term death after cardiac surgery or PCI.[5,24] In addition to clinical risk factors, 2 vessel characteristics, total stent length and post-PCI FFR, were selected from the LASSO model and independently predicted hard outcomes. This result was supported by the individual prognostic significance of lesion length or physiologic

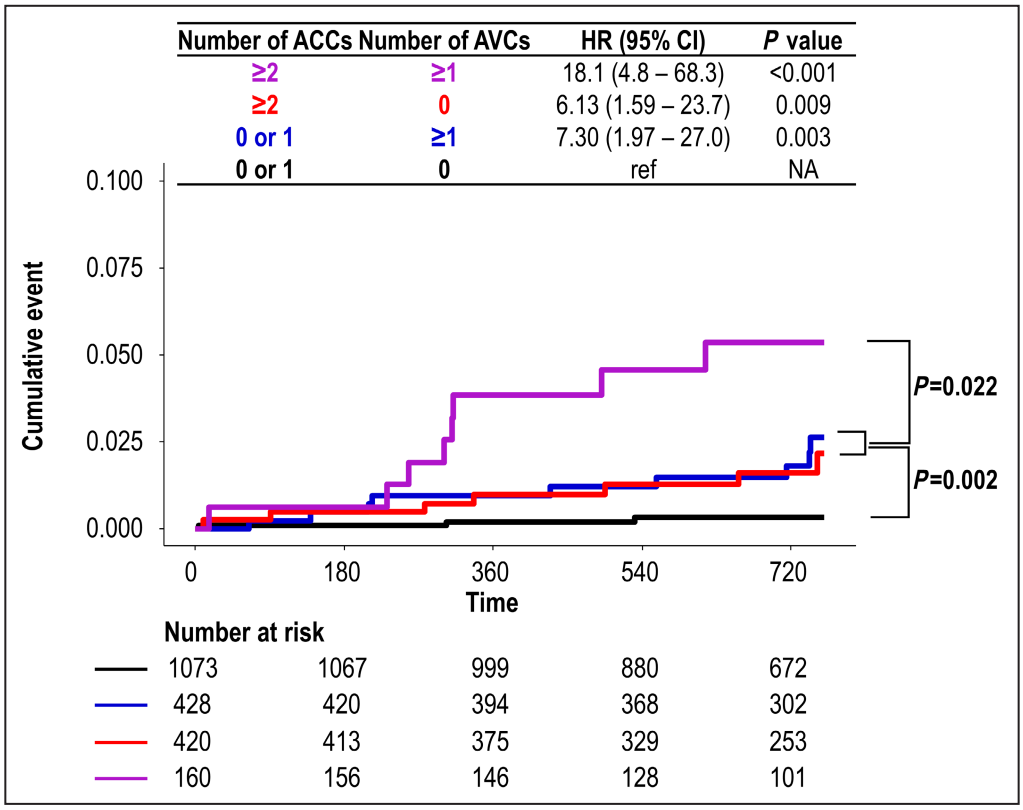

Figure 4. Risk stratification according to a high number of ACCs and AVCs.
The cumulative event of cardiac death or TVMI at 2 years in the 4 groups divided by ACCs ≥2 and AVCs ≥1 is presented. ACCs are age ≥65 years, diabetes, CKD, and LVEF <50%. AVCs are post-PCI FFR ≤0.80 and total stent length ≥54 mm. ACCs indicates adverse clinical characteristics; AVCs, adverse vessel characteristics; CI, confidence interval; CKD, chronic kidney disease; FFR, fractional flow reserve; HR, hazard ratio; LVEF, left ventricular ejection fraction; NA, not applicable; PCI, percutaneous coronary intervention; and TVMI, target-vessel myocardial infarction.

index on adverse clinical events after PCI[9,25–27] and further implies that vessel-level risk factors, as well as patient-level clinical risk profile, can be determinants of hard outcomes in patients undergoing PCI. Moreover, it is interesting to note that pre- and post-PCI angiographic parameters, other than total stent length and post-PCI FFR, were not considered as AVCs in the current risk model. This finding is associated with the relationship of lesion length with total atherosclerotic burden[28] and the nature of post-PCI physiologic properties that cannot be predicted by pre- or post-stent angiographic parameters.[29,30] Within various vessel characteristics, simultaneous selection of total stent length and post-PCI FFR as AVCs indicate the complex prognostic contribution of disease extent and residual ischemia on hard outcomes after PCI, which is in line with the study demonstrating that residual functional synergy between PCI with taxus and cardiac surgery scores had a higher discrimination ability for clinical outcomes after PCI than 3-vessel FFR or residual synergy between PCI with taxus and cardiac surgery scores.[31] Moreover, the event rate was highest in patients with both low post-PCI FFR and long stent length followed by either or none of them, and this finding implies a worse prognosis of physiologic diffuse lesions. Therefore, not only clinical risk factors but also the disease extent and physiologic status represented by stent length and post-PCI physiologic index need to be considered in prediction of hard outcomes following revascularization.

Incremental Prognostic Relevance of Adverse Vessel and Clinical Characteristics

In patients with established atherosclerotic cardiovascular disease, clinical risk factors are main determinants of recurrent adverse events.[18,19] The prognostic importance of clinical risk factors over vessel characteristics has also been reported. While clinical and procedural risks were predictive of post-PCI major adverse cardiac and cerebrovascular events at 3 years, clinical risk factors had a greater impact on outcomes in patients undergoing PCI,[32] and this finding was

similar in prediction of 2-year hard outcomes in patients undergoing PCI for bifurcation lesions.[15] In this context, in the cardiac catheterization laboratory, it is important to understand whether clinical risk profile alone should drive overall prognosis or whether vessel-level features have additional prognostic significance in predicting hard outcomes after PCI. In the current study, the number of AVCs significantly enhanced the predictive value for cardiac death or TVMI in addition to the number of ACCs and vice versa. In particular, the event rate of cardiac death or TVMI at 2 years was the highest in patients who had both ACCs ≥2 and AVCs ≥1 (5.3%) as compared with none (0.3%) or either (2.4%) of them, which implies a possible incremental prognostic impact between them. This finding aligns with prior risk models demonstrating that combined synergy between PCI with taxus and cardiac surgery scores and clinical risk factors such as age, creatinine clearance, and LVEF showed better discrimination ability to predict death or ischemic events after PCI than synergy between PCI with taxus and cardiac surgery scores or GRACE (Global Registry of Coronary Events) score alone,[5,6,33] or a machine learning–based risk prediction model showing that the incorporation of clinical, anatomic, and physiologic factors could help predict target-vessel failure.[34] In addition to prior evidence, we proposed that the combined ACCs and AVCs can better predict post-PCI hard outcomes than individual assessment alone. In the aspect of risk modification, ACCs such as diabetes, CKD, or LVEF <50% are risk factors that can be modified to some extent by only optimal medical therapy, and whether AVCs can be modulated in a catheterization laboratory still remains unclear. Although recent studies have shown that post-PCI FFR-based optimization can significantly improve post-PCI FFR values,[35,36] AVCs might not be fully adjusted by PCI because low post-PCI FFR and long stent length indicates residual diffuse disease. Moreover, clinical outcomes of untreated diffuse disease with remained low post-PCI FFR versus long stented lesions that achieved high post-PCI FFR need to be further defined. Because pullback pressure tracings can provide information on residual physiologic focal or diffuse disease, future studies are warranted to incorporate information on physiologic focal/diffuse disease into AVCs and to prove the prognostic impact of reducing AVCs on hard outcomes in patients with and without ACCs.

Limitations

The current study has several limitations. Not all patients had full information on 19 vessel and patient characteristics in the original individual patient-level meta-analysis, and this substudy only included those patients for whom complete information was available. The study population represented those who underwent post-PCI FFR among patients undergoing PCI, which might have caused a potential selection bias. Information on medical therapy or intravascular imaging was not included in the analysis. Pressure pullback data were not available in most studies, so the location of residual pressure gradients in and out of stents and physiologic diffuse lesions were not assessed. Information on other vessels that did not receive post-PCI FFR measurements was not available. Due to a small number of events, various confounders could not be fully adjusted for in the multivariable analysis.

CONCLUSIONS

In patients who underwent drug-eluting stent implantation, adverse clinical and vessel characteristics were associated with the risk of cardiac death or MI. Because these adverse characteristics have independent and additive prognostic implications, performing a comprehensive assessment to identify them can inform an optimized risk prediction model for hard outcomes after PCI.

ARTICLE INFORMATION

Received April 12, 2023; accepted July 31, 2023.

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Acknowledgments

The statistical part of this work was supported by Medical Research Collaboration Center in Seoul National University Hospital Biomedical Research Institute, Seoul, Korea. Drs Bon-Kwon Koo and Doyeon Hwang had full access to all data in the study and took responsibility for the integrity of the data and the accuracy of data analysis. The data were available to all investigators upon request, and the publication committee assumed final responsibility for the decision to submit the manuscript for publication.

Sources of Funding

None.

Disclosures

Dr Lee received a research grant from St. Jude Medical (Abbott Vascular) and Philips Volcano. Dr Doh received a research grant from Philips Volcano. Dr Chen is a consultant for Microport and Boston Scientific International and received a grant from the National Natural Scientific Foundation of China. Dr Toth receives consultancy fees and unrestricted research grants from Abbott, Medtronic, and Terumo. Dr Johnson has received institutional research support from Volcano/Philips (DEFINE-FLOW [Combined Pressure and Flow Measurements to Guide Treatment of Coronary Stenoses], clinicaltrials.gov NCT02328820), Abiomed (for study of Impella-related coronary physiology), and St. Jude Medical (CONTRAST [Can Contrast Injection Better Approximate FFR Compared to Pure Resting Physiology?], clinicaltrials.gov NCT02184117); has an institutional licensing agreement with Boston Scientific for the smart-minimum FFR algorithm commercialized under 510(k) K191008; and has pending patents on diagnostic methods for quantifying aortic stenosis and transcatheter aortic valve implantation physiology, and also algorithms to correct pressure tracings from fluid-filled catheters. Dr Azzalini received honoraria from Teleflex, Abiomed, GE Healthcare, Asahi Intecc, Philips, Abbott Vascular, and Cardiovascular System, Inc. Dr Massoud Leesar received an institutional research grant from ACIST. Dr Diletti reports an institutional research grant to Erasmus University Medical Center and consultancy to ACIST Medical Systems. Dr Collison has received consultancy/speaker fees from Abbott. Dr Daemen received institutional grant/research support from Astra Zeneca, Abbott Vascular, Boston Scientific, ACIST Medical, Medtronic, Microport, Pie Medical, and ReCor medical, and consultancy and speaker fees from Abbott Vascular, Abiomed, ACIST Medical, Boston Scientific, Cardialysis BV, CardiacBooster, Kaminari Medical, ReCor Medical, PulseCath, Pie Medical, Sanofi, Siemens Health Care, and Medtronic. Dr Koo received an institutional research grant from St. Jude Medical (Abbott Vascular) and Philips Volcano. The remaining authors have no disclosures to report.

Supplemental Material

Tables S1–S2
Figures S1–S2

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