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Article

LVEF and Heart Failure: Evidence for Non-Linear Connection in a Secondary Analysis Based on a Cross-Sectional Study in Myocardial Infarction Patients Undergoing Percutaneous Coronary Intervention

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Abstract

Objective: To evaluate the relationship between ejection fraction (EF) and heart failure (HF) in patients with myocardial infarction (MI) after percutaneous coronary intervention (PCI). **Results**: After adjusting for confounding factors, it was found that the relationship between LVEF and HF was stable and consistent through different adjustment models. When LVEF was increased to >50%, the risk of heart failure was reduced by 31% compared to patients with LVEF <50%. There was a non-linear saturation effect between LVEF and HF, and the incidence of HF was gradually increased with the decrease of LVEF. On the left side of inflection 55%, LVEF was negatively correlated with HF, but the correlation was not statistically significant on the right side of inflection 55%. **Conclusion**: In patients with MI after PCI, LVEF and HF showed a non-linear relationship. When LVEF was less than 55%, LVEF was negatively correlated with HF, and the risk of HF occurrence was increased with the decrease of LVEF. Therefore, LVEF can be used as a major index to predict HF after PCI.

Keywords

atrial fibrillation; percutaneous coronary intervention; recurrence; myocardial infarction; heart failure

Introduction

Myocardial infarction (MI) is not only a severe type of coronary heart disease (CHD) but also a leading cause of death and physical disability, commonly occurring in the rapidly growing population of elderly persons [1].

Left ventricular ejection fraction (LVEF) refers to the percentage of left ventricular end-diastolic volume generated by each stroke. The ejection fraction (EF) is closely related to the contractible ability of the myocardium, with a stronger contractible ability of the myocardium indicating more stroke output and greater EF. Under normal circumstances, the LVEF is ≥50%. When the body is quiet, the LVEF is about 55%–65%, and the right ventricular ejection fraction is ≥40% [2].

As the most commonly used indicator of left ventricular systolic function, LVEF provides the main diagnostic basis for heart failure (HF). According to the 2016 European Society of Cardiology (ESC) guidelines, HF patients can be divided into three categories. Recently, HF has been classified into the following three subgroups based on the LVEF: HF with reduced LVEF (HFrEF; LVEF <40%), HF with mid-range LVEF (HFmrEF; 40% ≤ LVEF < 50%), and HF with preserved LVEF (HFpEF; LVEF ≥50%) [3]. Prior research has concentrated on HFrEF and HFpEF, and there is little research on HFmrEF, which remains a grey area of HF research [4]. However, as indicated by prior epidemiology, approximately 20.2%–21.8% of individuals have HFmrEF. The mortality rate of HFmrEF is comparable to that of HFpEF but lower than that of HFrEF; HFmrEF is more likely to be an intermediate condition of HFpEF and HFrEF. Additionally, its clinical features are also similar to those of HFrEF. It has been shown that improved description and analysis of HFmrEF are facilitated by more definitional clarity [5].

However, little is known about the association between LVEF and the risk of HF after percutaneous coronary intervention (PCI). Therefore, this study further analyzed the association between LVEF and the risk of HF in patients after PCI through a cross-sectional/observational cohort study based on the previous database.

Methods

Data Source

The data were acquired from the 'DATADRYAD' database situated at https://datadryad.org. Users can download the unprocessed data from this website at no cost. The

Dryad data package was utilized in this study in compliance with the Dryad terms of service. Dryad scientific data package [Hai-Mu Yao, You-Dong Wan, Xiao-Juan Zhang, De-Liang Shen, Jin-Ying Zhang, Ling Li, Luo-Sha Zhao, Tong-Wen Sun (2014)] [5] were cited with data from "A Long-term follow-up results in patients undergoing PCI with drug-eluting stents: results from a single high-volume PCI center" (Dryad Digital Repository: https://pubmed.ncbi.nlm.nih.gov/25113554/) [6].

The variables included in the database file were as follows: age, sex, body mass index, systolic blood pressure (SBP), diastolic blood pressure (DBP), prior PCI, prior coronary artery bypass graft, occlusion myocardial infarction (OMI), peripheral vascular disease, LVEF, hypertension, diabetes mellitus (DM), dyslipidemia, current smoker, renal insufficiency, presence shock, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), triglyceride (TG), and glycemia.

Authors of the original study have waived all copyright and related ownership of these data. Therefore, we could use these data for secondary analysis without infringing on the author's rights.

Study Population

Yao *et al*. [5] completed the entire study. This document provides a concise overview of the study's procedures to enhance your understanding of the whole research process and the precise particulars are outlined in the original document by Hai-Mu Yao and colleagues [5]. An observational cohort study was carried out in a single high-volume PCI center in a hospital in Henan province, China from July 2009 to August 2011. The study exclusively included persons who received treatment with a minimum of one Drug-eluting stent (DES) and completed long-term follow-up assessments. Coronary angiographic evaluations were conducted using established methods, including both quantitative and qualitative approaches. The PCI procedure followed the standard protocols. Before coronary intervention, all patients received loading doses of 300 mg of aspirin and 300 mg of clopidogrel, whether or not they had previously received antiplatelet medication. The surgeon was granted full authority over the treatment strategy, stenting techniques, selection of stent type, and administration of intravascular ultrasonography or glycoprotein IIb/IIIa receptor inhibitors. All patients received a daily dose of aspirin 100 mg for life and clopidogrel 75 mg daily for the first 12 months after the procedure.

Measurement of Covariants

The measurement and evaluation of LVEF, HF, and other covariates were comprehensively described in the original document. Clinical risk factors for cardiovascular disease were evaluated upon hospital admission. Patients with a smoking history were defined as those who had smoked within the past decade. A patient was diagnosed with diabetes mellitus if his hemoglobin A1c level was above 6.5%, fasting plasma glucose concentration exceeded 6.1 mmol/L, or they were receiving insulin or another oral hypoglycemic drug. A patient with a DBP of 90 mmHg or above or the use of antihypertensive medication was classified as having hypertension. Dyslipidaemia was diagnosed in patients with HDL-C concentration below 40 mg/dL, LDL-C concentration above 140 mg/dL, or lipid-lowering medication.

Statistical Analysis

Quantitative data were represented as the mean ± standard deviation for a normal distribution or the median (quartile) for a skewed distribution. Categorical data were represented either as frequency or as a percentage. The statistical evaluation of the means and proportions of the groups was conducted using the one-way analysis of variance (ANOVA) for normal distribution, the Kruscal Whallis H test for skewed distribution, and the Chi-square tests for categorical data. The link between LVEF and HF was evaluated using a univariate linear regression model. Furthermore, the publication enumerates the unadjusted model and the multivariate correction model. Consistent with the guidelines of the STROBE statement, we also presented the findings of unadjusted, minimal-adjusted, and fully-adjusted analyses. The adjustment of covariances was based on the assumption that they must have altered the matched odds ratio by a minimum of 10% when included in this model [7]. Furthermore, the non-linear relationship was determined using the generalized additive model (GAM). After that, the threshold effect of the HF and LVEF on the smoothing plot was calculated using a two-piecewise linear regression model. By analyzing the ratio of LVEF to HF in the smoothed curve, the recursive approach may automatically identify the inflection point where the maximum model likelihood is applied [8]. Stratified linear regression models were employed for the subgroup analysis. A likelihood ratio test was conducted to analyze the modification and interaction within the subgroup. All analyses were conducted using the statistical software application packages EmpowerStats (version 2.0 Windows https://www.empowerstats.net/en/, X&Y Solutions, Inc., Boston, MA, USA) and R (http://www.R-project.org, The R Foundation, Vienna, Austria). A two-sided p-value of less than 0.05 indicated a statistically significant level.

Results

The Selection of Participants

Among the total 2533 participants, 933 individuals were not included in this study as they were eliminated due

to missing LVEF values, resulting in 1600 subjects available for data analysis.

Baseline Characteristics of Participants

The average age of the participants was 59.95 $\pm$ 11.08 years old. Approximately 68.06% of the participants were male. Baseline characteristics are listed in Table 1.

There was no statistically significant difference in heart rate, SBP, DBP, uric acid, HDL-C, LDL-C, TC, sex, smoking, DM history, COPD, third-degree AVB, stroke, peripheral vascular disease, AMI, recurrent angina, number of diseased vessels among different LVEF groups. Compared with patients in the high-level LVEF group, patients in the other three groups showed a significantly lower age, but notably higher atrial fibrillation and OMI.

Univariate Analysis

The results of the univariate analysis are shown in Table 2.

The results of the univariate analysis showed that atrial fibrillation, third-degree AVB, stroke, AMI, and age were correlated with HF. However, heart rate, SBP, DBP, uric acid, HDL-C, LDL-C, TC, sex, smoking, DM history, COPD, stroke, peripheral vascular disease, recurrent angina, LM, LAD, LCX, RCA, number of diseased vessels, and OMI were not associated with HF.

The Results of the Relationship between LVEF and HF

A univariate linear regression model was used to evaluate the association between LVEF and HF. Meanwhile, the non-adjusted and adjusted models are shown in Table 3.

The crude model demonstrated a positive connection between long-term LVEF and HF $\beta = 0.95$, 95% confidence interval (CI): 0.91 to 1.00, $p = 0.0361$]. When corrected for age and sex, the results in the minimum adjusted model showed no significant differences ($\beta = 0.95$, 95% CI: 0.91 to 1.00, $p = 0.0331$). Furthermore, we were unable to identify any changes in the fully adjusted model ($\beta = 0.93$, 95% CI: 0.89 to 0.98, $p = 0.0103$). Moreover, sensitivity analysis was conducted and LVEF was treated as a categorical variable (Quartile). It was discovered that the same pattern was evident (all $p > 0.05$).

The Analyses of Non-Linear Relationship

As LVEF was a continuous variable, the analysis of non-linear relationship is necessary. In the present study (Fig. 1), it was found that the relationship between LVEF and HF was non-linear (after adjusting age, SBP, DBP, uric acid, TG, TC, HDL-C, LDL-C, sex, smoking, heart rate, hypertension history, DM history, atrial fibrillation, cardiac shock, OMI, COPD, third-degree AVB, stroke, peripheral vascular disease, AMI, recurrent angina, and number of diseased vessel).

The inflection point was determined as 55 using a two-piecewise linear regression model. For the left side of the inflection point, $\beta = 0.89$, 95% CI: 0.85 to 0.92, and $p < 0.0001$, respectively. Nevertheless, no correlation between LVEF and HF on the right side of the inflection point ($\beta = 1.00$, 95% CI: 0.96 to 1.04, $p = 0.8976$) was observed (Table 4).

Discussion

A secondary analysis was conducted in this study based on observational cohort data and the association between LVEF and HF was investigated in patients with MI after PCI. The relationship between LVEF and HF was explored using the GAM model. Three categories of HF patients were stated in the introduction section: HFrEF, HFmrEF, and HFpEF. It's evident that the link between LVEF and HF was not strictly linear. Therefore, we cannot employ only a linear regression model and assume a linear connection when examining the association between LVEF and HF [9]. A higher LVEF does not necessarily translate into a lower risk of HF. Additionally, this study is appropriate for GAM and has a sizable sample size. In addition to capturing the intricate non-linear connection, the smoothing function allows for visual representation, which is useful for model comprehension [10].

First, it was found that the relationship between LVEF and HF was stable and consistent through different adjustment models. When LVEF was increased to >50%, the risk of heart failure was reduced by 31% compared to patients with LVEF <50%. Secondly, we observed that there was a non-linear saturation effect between LVEF and HF, and the incidence of HF was gradually increased with the decrease of LVEF. On the left side of inflection 55%, LVEF was significantly negatively correlated with HF, but the correlation was not statistically significant on the right side of inflection 55%. A previous study has demonstrated that the risk of HF does not increase even if LVEF increases again [11].

As can be seen from Table 1, there were 16 patients with HF in the LVEF <40% group, accounting for 57% of the total patients. The results showed that HFrEF increased the proportion of HF after PCI, with more decrease in LVEF indicating a higher proportion of HF, and these two were positively correlated. The number of patients with HF in the LVEF 40–50% HFmrEF group was 25, accounting for 23% of the total number. Additionally, there were not a small number of patients with HF in the intermediate range of LVEF, and LVEF was positively correlated with HF. However, when LVEF was 50–60% or more than 60%, the number of patients with HF was significantly reduced. All these indicate that EF is not only a marker of cardiac function, but can also reflect prognosis-related information [12]. As a result, EF has become an essential component of clinical treatment regimens, as well as inclusion criteria and alternative endpoints for clinical trials [13]. EF is not a static

Table 1. Baseline characteristics of participants.

LVEF group	<40	≥40, <50	≥50, <60	≥60	*p*-value
N	28	108	340	1124	
Age (years, mean ± SD)	60.68 ± 11.25	62.57 ± 10.07	61.36 ± 10.71	59.67 ± 10.92	0.008
Heart rate (mean ± SD)	71.85 ± 13.34	71.47 ± 13.00	72.44 ± 11.69	72.02 ± 10.97	0.882
SBP (mmHg, mean ± SD)	103.14 ± 27.52	97.70 ± 29.17	99.96 ± 27.91	103.33 ± 28.89	0.091
DBP (mmHg, mean ± SD)	78.04 ± 9.47	77.91 ± 11.77	77.11 ± 11.85	77.12 ± 11.76	0.897
LVEF (%)	34.14 ± 4.20	44.75 ± 2.96	56.18 ± 2.69	64.52 ± 3.60	<0.001
Uric acid (mg/dL, mean ± SD)	289.60 ± 118.72	323.49 ± 103.13	301.52 ± 86.29	302.43 ± 93.18	0.13
TG (mmol/L, mean ± SD)	1.33 ± 0.66	1.64 ± 0.82	1.89 ± 1.72	1.97 ± 1.37	0.024
TC (mmol/L, mean ± SD)	3.84 ± 0.94	4.16 ± 1.01	4.23 ± 1.13	4.28 ± 1.04	0.152
HDL-C (mmol/L, mean ± SD)	1.02 ± 0.29	1.01 ± 0.31	1.05 ± 0.31	1.08 ± 0.31	0.063
LDL-C (mmol/L, mean ± SD)	2.58 ± 0.97	2.62 ± 0.86	2.60 ± 0.92	2.67 ± 0.93	0.617
HF (n, %)					<0.001
No	12 (42.86%)	83 (76.85%)	300 (88.24%)	990 (88.24%)	
Yes	16 (57.14%)	25 (23.15%)	40 (11.76%)	132 (11.76%)	
Sex (n, %)					0.654
Female	7 (25.00%)	34 (31.48%)	102 (30.00%)	369 (32.83%)	
Male	21 (75.00%)	74 (68.52%)	238 (70.00%)	755 (67.17%)	
Smoking (n, %)					0.917
No	17 (60.71%)	69 (63.89%)	225 (66.18%)	740 (65.84%)	
Yes	11 (39.29%)	39 (36.11%)	115 (33.82%)	384 (34.16%)	
Hypertension history (n, %)					<0.001
No	20 (71.43%)	67 (62.04%)	179 (52.80%)	515 (45.82%)	
Yes	8 (28.57%)	41 (37.96%)	160 (47.20%)	609 (54.18%)	
DM history (n, %)					0.681
No	21 (75.00%)	83 (76.85%)	259 (76.18%)	887 (78.98%)	
Yes	7 (25.00%)	25 (23.15%)	81 (23.82%)	236 (21.02%)	
Atrial fibrillation (n, %)					<0.001
No	24 (85.71%)	106 (98.15%)	334 (98.24%)	1100 (97.86%)	
Yes	4 (14.29%)	2 (1.85%)	6 (1.76%)	24 (2.14%)	
Cardiac shock (n, %)					0.003
No	28 (100.00%)	107 (99.07%)	340 (100.00%)	1124 (100.00%)	
Yes	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	
OMI (n, %)					<0.001
No	21 (75.00%)	83 (76.85%)	285 (83.82%)	1050 (93.42%)	
Yes	7 (25.00%)	25 (23.15%)	55 (16.18%)	74 (6.58%)	
COPD (n, %)					0.724
No	28 (100.00%)	106 (98.15%)	336 (98.82%)	1114 (99.11%)	
Yes	0 (0.00%)	2 (1.85%)	4 (1.18%)	10 (0.89%)	
Third-degree AVB (n, %)					0.295
No	28 (100.00%)	108 (100.00%)	339 (99.71%)	1124 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	1 (0.29%)	0 (0.00%)	
Stroke (n, %)					0.143
No	26 (92.86%)	98 (90.74%)	319 (93.82%)	1073 (95.46%)	
Yes	2 (7.14%)	10 (9.26%)	21 (6.18%)	51 (4.54%)	
Peripheral vascular disease (n, %)					0.944
No	28 (100.00%)	108 (100.00%)	339 (99.71%)	1121 (99.73%)	
Yes	0 (0.00%)	0 (0.00%)	1 (0.29%)	3 (0.27%)	
AMI (n, %)					0.756
No	26 (92.86%)	104 (96.30%)	327 (96.18%)	1070 (95.20%)	
Yes	2 (7.14%)	4 (3.70%)	13 (3.82%)	54 (4.80%)	
Recurrent angina (n, %)					0.695
No	26 (92.86%)	97 (89.81%)	296 (87.06%)	997 (88.70%)	
Yes	2 (7.14%)	11 (10.19%)	44 (12.94%)	127 (11.30%)	

Table 1. Continued.

LVEF group	<40	≥40, <50	≥50, <60	≥60	*p*-value
LM (n, %)					0.838
No	27 (96.43%)	104 (96.30%)	326 (95.88%)	1089 (96.89%)	
Yes	1 (3.57%)	4 (3.70%)	14 (4.12%)	35 (3.11%)	
LAD (n, %)					0.111
No	2 (7.14%)	11 (10.19%)	55 (16.18%)	199 (17.70%)	
Yes	26 (92.86%)	97 (89.81%)	285 (83.82%)	925 (82.30%)	
LCX (n, %)					0.893
No	14 (50.00%)	58 (53.70%)	169 (49.71%)	578 (51.42%)	
Yes	14 (50.00%)	50 (46.30%)	171 (50.29%)	546 (48.58%)	
RCA (n, %)					0.101
No	13 (46.43%)	48 (44.44%)	164 (48.24%)	605 (53.83%)	
Yes	15 (53.57%)	60 (55.56%)	176 (51.76%)	519 (46.17%)	
Number of diseased vessel (n, %)					0.167
0	7 (25.00%)	42 (38.89%)	133 (39.12%)	404 (35.94%)	
1	10 (35.71%)	35 (32.41%)	120 (35.29%)	470 (41.81%)	
3	11 (39.29%)	30 (27.78%)	85 (25.00%)	241 (21.44%)	
4	0 (0.00%)	1 (0.93%)	2 (0.59%)	9 (0.80%)	

SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; OMI, occlusion myocardial infarction; AVB, atrioventricular block; COPD, chronic obstructive pulmonary disease; TC, total cholesterol; TG, triglyceride; AMI, acute myocardial infarction; LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery; HF, heart failure; DM, diabetes mellitus; LM, left main stem.

measure, instead, it increases or decreases over time, requiring reclassification and prognosis assessment [14–16]. Even small changes in LVEF in any direction can significantly affect prognosis.

A big data study from Australia, presented at the recent European Society of Cardiology Virtual Conference on Heart Failure Discovery, has demonstrated a J-shaped relationship between LVEF and the risk of all-cause and cardiovascular death; the risk of all-cause and cardiovascular death was lowest when the LVEF was in a range from 65% to 69.9% [7,17,18]. However, once you get out of that sweet spot, there are clear gender differences. After adjustment for body mass index, age, heart rate, valvular heart disease, E-peak velocity, and other potential confounding factors, men with LVEF of 45%–64.9% did not have an increased risk of cardiovascular death, compared with men with LVEF of 65%–69.9%. The risk of cardiovascular death began to increase only when the LVEF was below 45% [8]. In contrast, women with LVEF of 45%–55% had twice the risk of cardiovascular death compared with women with LVEF of 45%–65%, who also tended to have an increased risk of cardiovascular death. Additionally, the risk of death also began to increase for women when the LVEF was greater than 70% [19]. Our study showed consistent findings. In short, patients with HFrEF and HFmrEF after PCI had an increased risk of HF, and patients with LVEF of above 55% had a notably reduced risk of HF. Therefore, in clinical work, the LVEF index should be observed more frequently, and the LVEF of patients with HFrEF and HFmrEF should be improved as much as possible. Since this study is a cross-sectional study, we cannot better distinguish the causal relationship between the two. Therefore, there may be missed diagnoses in HFpEF patients [20]. Overall, these data suggest that it is necessary to conduct a randomized study to dynamically observe HF in patients after PCI and future interventions for all HF categories after PCI. In different HF types, PCI patients need to pay attention to the time change of EF during postoperative follow-up, and there are many reasons. Data from smaller cohorts suggest that HFmrEF may switch between HFpEF and HFrEF, and some postoperative complications may be important mediators of EF deterioration [21]. Additionally, a recent study has shown that HF patients with EF recovery have a better prognosis than HFrEF and HFpEF patients without EF changes.

The present study offers several advantages. First, a generalized linear model was employed to assess the linear correlation between LVEF and HF. Additionally, the generalized additive model was utilized to elucidate the non-linear correlation. GAM provides significant benefits for handling non-linear relationships, which are capable of nonparametric smoothing and fitting regression splines into data [22]. The application of GAM will enhance our ability to uncover the genuine correlation between exposure and outcomes. Furthermore, this investigation was an observational cohort study that incorporated inevitable confounding factors. Meticulous statistical modifications were employed to mitigate the interference of residual confounding factors. Although previous studies have investigated the risk factors for in-hospital HF events after PCI and long-

Table 2. Results of univariate analysis.

	Statistics	Effect size (β)	p
EF	60.88 ± 7.45	0.95 (0.93, 0.96)	<0.0001
Heart rate	72.16 ± 11.67	1.00 (0.99, 1.01)	0.617
SBP	103.26 ± 28.77	1.00 (1.00, 1.00)	0.8746
DBP	77.20 ± 12.02	1.00 (0.99, 1.01)	0.9156
Hypertension history			
No	1286 (50.79%)	ref	
Yes	1246 (49.21%)	1.01 (0.79, 1.29)	0.9349
DM history			
No	2010 (79.42%)	ref	
Yes	521 (20.58%)	1.31 (0.99, 1.74)	0.0633
Atrial fibrillation			
No	2483 (98.03%)	ref	
Yes	50 (1.97%)	2.18 (1.10, 4.30)	0.0249
Cardiac shock			
No	2529 (99.84%)	ref	
Yes	4 (0.16%)	5,979,481.87 (0.00, inf.)	0.9535
OMI			
No	2298 (90.72%)	ref	
Yes	235 (9.28%)	1.22 (0.82, 1.80)	0.3295
COPD			
No	2511 (99.13%)	ref	
Yes	22 (0.87%)	0.36 (0.05, 2.67)	0.3168
Third-degree AVB			
No	2525 (99.68%)	ref	
Yes	8 (0.32%)	7.66 (1.91, 30.79)	0.0041
Stroke			
No	2398 (94.67%)	ref	
Yes	135 (5.33%)	1.60 (1.00, 2.55)	0.0477
Peripheral vascular disease			
No	2527 (99.76%)	ref	
Yes	6 (0.24%)	0.00 (0.00, inf.)	0.9722
AMI			
No	2415 (95.34%)	ref	
Yes	118 (4.66%)	1.71 (1.05, 2.78)	0.0321
Recurrent angina			
No	2244 (88.59%)	ref	
Yes	289 (11.41%)	0.87 (0.58, 1.29)	0.4821
Uric acid	303.12 ± 93.12	1.00 (1.00, 1.00)	0.8922
TG	1.91 ± 1.35	0.99 (0.89, 1.09)	0.7632
TC	4.26 ± 1.06	0.89 (0.78, 1.01)	0.0645
HDL-C	1.06 ± 0.32	1.02 (0.68, 1.53)	0.9157
LDL-C	2.67 ± 0.94	0.89 (0.77, 1.03)	0.1086
Number of diseased vessels			
0	924 (36.48%)	ref	
1	1005 (39.68%)	0.74 (0.55, 0.98)	0.0363
2	1 (0.04%)	0.00 (0.00, inf.)	0.9739
3	582 (22.98%)	1.11 (0.82, 1.50)	0.5137
4	21 (0.83%)	1.16 (0.34, 3.99)	0.8163
Sex			
Female	809 (31.94%)	ref	
Male	1724 (68.06%)	0.64 (0.50, 0.82)	0.0004
Age	59.95 ± 11.08	1.02 (1.01, 1.04)	<0.0001

Table 2. Continued.

	Statistics	Effect size (β)	p
EF			
<40	28 (1.75%)	ref	
≥40, <45	52 (3.25%)	0.25 (0.09, 0.66)	0.0054
≥45, <50	56 (3.50%)	0.20 (0.08, 0.55)	0.0016
≥50, <55	83 (5.19%)	0.18 (0.07, 0.45)	0.0003
≥55, <60	257 (16.06%)	0.08 (0.03, 0.18)	<0.0001
≥60, <65	640 (40.00%)	0.11 (0.05, 0.23)	<0.0001
≥65, <70	396 (24.75%)	0.09 (0.04, 0.21)	<0.0001
≥70	88 (5.50%)	0.10 (0.04, 0.26)	<0.0001

EF, ejection fraction; DM, diabetes mellitus.

Table 3. Relationship between LVEF and HF in different models.

Exposure	Non-adjusted	Adjust I	Adjust II
EF	0.95 (0.91, 1.00) 0.0361	0.95 (0.91, 1.00) 0.0331	0.93 (0.89, 0.98) 0.0103
LVEF group			
<40	1	1	1
≥40, <50	0.38 (0.14, 1.02) 0.0541	0.34 (0.12, 0.93) 0.0350	0.39 (0.12, 1.25) 0.1143
≥50, <60	0.29 (0.08, 1.06) 0.0606	0.27 (0.07, 1.00) 0.0506	0.33 (0.08, 1.44) 0.1391
≥60	0.44 (0.09, 2.10) 0.3004	0.42 (0.09, 2.06) 0.2855	0.62 (0.11, 3.68) 0.6016

Non-adjusted model: no covariates are adjusted.

Minimally-adjusted model: only sex and age are adjusted.

Fully-adjusted model: all covariates presented in Table 1 are adjusted.

Table 4. Non-linearity explanation of LVEF and HF using two-piecewise linear model.

Exposure	Effect size	95% CI	p-value
Fitting model using binary logistic regression	0.94	0.92, 0.96	<0.0001
Fitting model using two-piece wise linear mode			
Inflection point	55		
< Inflection point	0.89	0.85, 0.92	<0.0001
> Inflection point	1	0.96, 1.04	0.8976
p-value for Log likelihood ratio test			<0.001

The adjustment strategy was the same with a fully-adjusted model.

term HF after PCI, the present study adjusted for various confounding factors (such as sex, age, and medical history) and found an association between EF and HF. Third, we used the correlation between the measured LVEF and HF in patients after PCI and found that both HFrEF and HFmrEF would increase the risk of HF with the decrease of LVEF [23].

Of course, there are some limitations in this study. First, this study was an observational cohort study with a secondary analysis, and thus it may provide weak evidence between exposure and outcomes, making it difficult to distinguish the causation. Second, the study population only includes a single high-volume PCI center from one city in China, and we cannot generalize with other biography ethic groups. Third, limited by the original data, this study lacks more detection indicators reflecting HF (such as echocardiographic detection indicators, left ventricular end-diastolic diameter, left ventricular end-systolic diameter, and left ventricular stratified strain) and the analysis of whether they can be used as independent predictors of HF.

Strengths and Limitations of this Study

The current study has a number of benefits. To explain the non-linear association, we applied the generalised additive model. There are definite advantages to using the Geometric Approximation Method (GAM) when managing non-linear connections. This approach can be used to fit regression splines into data and perform nonparametric smoothing. Our capacity to identify the true relationship between exposure and results will be improved by the use of Generalised Additive Modelling (GAM). Moreover, this study was an observational cohort that had unavoidable

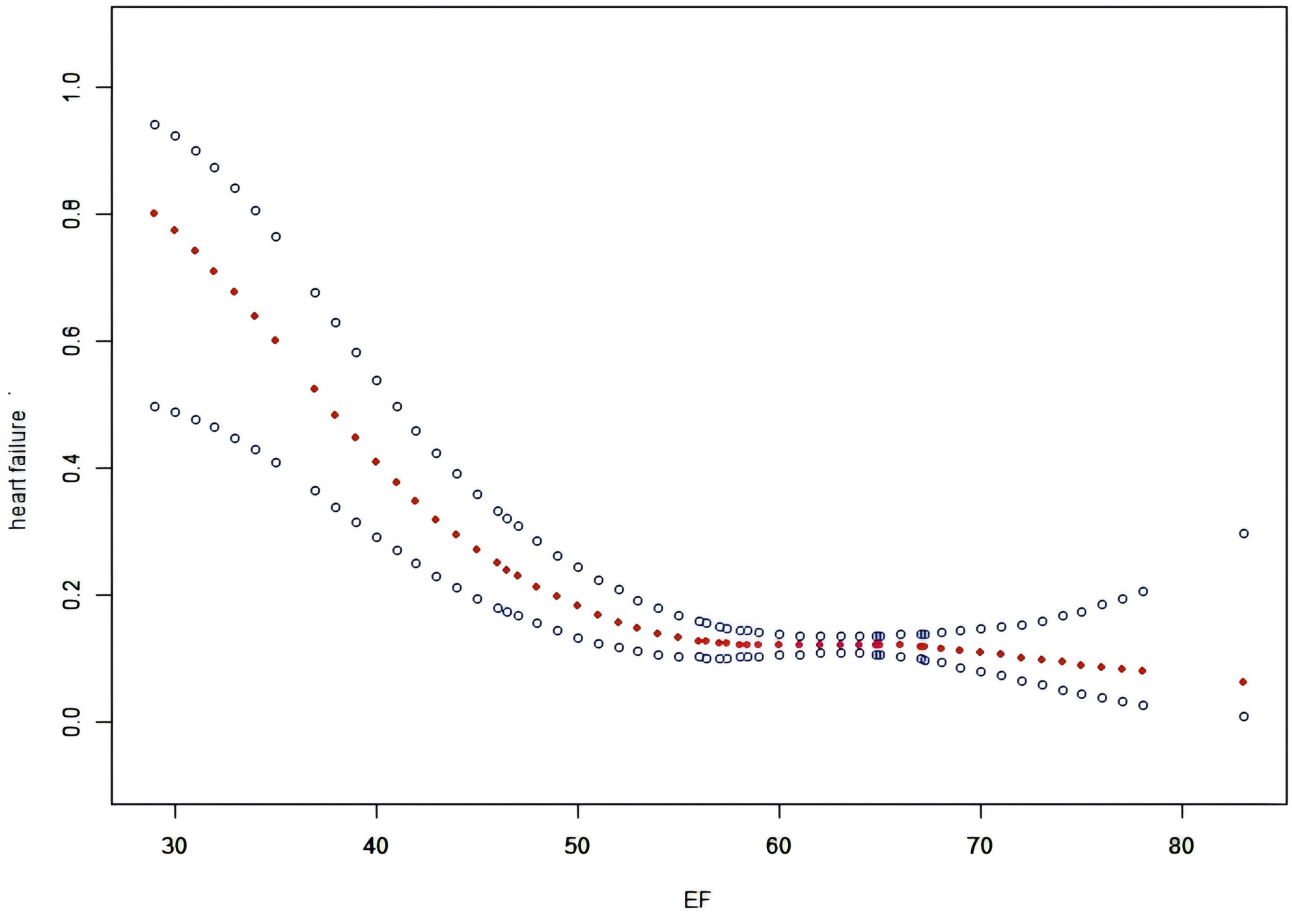

Fig. 1. The relationship between LVEF and HF. A non-linear relationship between LVEF and HF was detected after adjusting for age, SBP, DBP, uric acid, TG, TC, HDL-C, LDL-C, sex, smoking, heart rate, hypertension history, DM history, atrial fibrillation, cardiac shock, OMI, COPD, third-degree AVB, stroke, peripheral vascular disease, AMI, recurrent angina, and number of diseased vessel.

confounding variables. We used careful statistical adjustments to reduce the impact of residual confounding factors.

Naturally, there are certain restrictions on our study. First, because the study was an observational cohort study with secondary analysis, it was challenging to determine causality because it only offered shaky evidence linking exposure to outcomes. Second, we are unable to generalise with other biographical ethicgroups because the study sample solely consists of one high-volume PCI centre from a single Chinese metropolis. Thirdly, we do not have further detection signs showing HF because of the limitations of the original data.

Conclusion

In patients with MI after PCI, LVEF, and HF showed a non-linear relationship. When LVEF was less than 55%, LVEF was negatively correlated with HF, and the occurrence risk of HF was increased with the decrease of LVEF. Therefore, LVEF can be used as a major index to predict HF after PCI.

Availability of Data and Materials

Data are openly available in a public repository upon reasonable request. Additionally, some data presented in this study are openly available in Dryad at - (https://doi.org/10.1136/bmjopen-2014-004892).

Author Contributions

LZ and YZ contributed equally to this work and share frst authorship. LZ and YZ contributed to the design and conduct of work, including article writing. CL, YY, FH and HC collected the data. QH, WZ, AL and XW provided help and advice on the data analysis. SL summarized the data. BZ contributed significantly to the conception of the article design and its final approval. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors agree to be 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.

Ethics Approval and Consent to Participate

In the previously published article [5], Hai-Mu Yao, *et al*. has clearly stated that: the study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all Participants.

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Conflict of Interest

The authors declare no conflict of interest.

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