Second drug-eluting stent implantation versus coronary artery bypass grafting in treatment of young patients with left main and/or multivessel coronary disease

Xue Chen

Capital Medical University Affiliated Anzhen Hospital

Xuehui Zhang

Capital Medical University Affiliated Anzhen Hospital

Yunfeng Yan

Capital Medical University Affiliated Anzhen Hospital

Xin Zhao

Capital Medical University Affiliated Anzhen Hospital

Maoxiao Nie

Capital Medical University Affiliated Anzhen Hospital

Tingting Feng

Capital Medical University Affiliated Anzhen Hospital

Zhe Liang

Capital Medical University Affiliated Anzhen Hospital

Quanming Zhao (✉ zhaoquanming1@sina.com)

Capital Medical University Affiliated Anzhen Hospital <https://orcid.org/0000-0003-3457-4953>

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Abstract

Background Many studies have compared outcomes of coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) for complex coronary artery disease (CAD). However, no trials have focused on young patients (< 45 years) with complex CAD. We conducted a retrospective evaluation to compare the outcomes of a 2nd drug-eluting stent and CABG in young patients with LM or three-vessel disease.

Methods and results In the young patients with complex CAD who underwent PCI or CABG, Kaplan-Meier analysis and Cox regression before and after propensity-score matching were used to compare major adverse cardiac and cerebrovascular events (MACCE), including myocardial infarction (MI), stroke, death and repeat revascularization. During the follow-up, MACCE occurred in 20.5% of patients in the PCI group and 8.6% in the CABG group (hazard ratio [HR]: 3.263, 95% confidence interval [CI]: 1.379 to 7.722, $p=0.007$). Repeat revascularization occurred more frequently in the PCI group (18.9% vs. 3.7% respectively, HR: 6.968, 95% CI: 2.036 to 23.842, $p=0.002$). There were no significant differences in other endpoints. After propensity-score matching, no conclusions were changed.

Conclusions In young patients with LM or three-vessel disease, PCI showed a higher incidence of MACCE, which was mainly driven by repeat revascularization. However that did not translate into hard endpoints differences. Therefore, PCI is an alternative treatment to CABG in young patients with complex CAD.

Background

The left main (LM) disease and three-vessel disease are complex coronary artery disease (CAD), whose treatment is more difficult. Coronary artery bypass graft (CABG), as an effective treatment for CAD, has introduced more than 50 years which, is currently the preferred modality to treat complex CAD (1–3). However, over the last twenty years, there have been significant advances in percutaneous coronary intervention (PCI), from the era of balloon angioplasty and subsequently bare-metal stents to drug-eluting stents (DESs) (4–6). With improving technology and technique of PCI, such as adjunctive antithrombotic drugs, periprocedural management and the experience of interventional cardiologists, research has increasingly focused on more complex diseases, such as disease and multivessel disease.

The latest European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS) guidelines(7) recommend CABG (class I, level A) for complex CAD both LM disease and three-vessel disease regardless of anatomic complexities of coronary arteries. However, PCI is an alternative in the case of LM disease and three-vessel disease if the SYNTAX score is ≤ 22 (class I, level A); if the SYNTAX is >22 , it would be inferior for LM disease and three-vessel disease (class II or III, level A or B). Even so, along with the rapidly progressing technology, an increasing number of patients and cardiologists prefer PCI over CABG, according to many trials. Several trials have reported that PCI is noninferior to CABG in patients with LM disease (8) or multivessel disease (9). On the other hand, many trials have suggested CABG might provide better clinical outcomes than PCI (10–12).

In view of the younger characteristics of CAD patients and the likelihood of graft failure, and considering that 62% of patients will have recurrent ischemia by 15 years postoperatively (13), it is essential to consider the risk/benefit ratio of PCI and CABG for LM and three-vessel disease, weighing procedural invasiveness and the associated short-term complications against long-term event rates of death, myocardial infarction (MI), stroke, and repeat revascularization, and improvements in health-related quality of life (14). Therefore, we hypothesize that PCI should be performed at an early age if possible to alleviate symptoms to provide another choice for advanced illness. We conducted a retrospective evaluation to compare real world outcomes between CABG and PCI using second-generation DESs in young patients with LM disease or three-vessel disease.

Methods

This was a single-center retrospective study comparing PCI with 2nd DES and CABG in young patients with LM and three-vessel disease. We performed a review of all young patients who underwent diagnostic coronary angiography, and PCI or CABG at Beijing Anzhen Hospital from January 2015 to December 2016. We screened these patients and enrolled them if they had LM and/or three-vessel disease and underwent PCI with a 2nd-generation DES or CABG. The patients who had previously undergone PCI were also included in our study. Patients were excluded if: 1) they did not suffer from LM or three-vessel disease; 2) they had acute myocardial infarction (MI), either ST segment elevation or non-ST segment elevation; 3) they underwent concomitant valvular or aortic surgery; 4) they had previous CABG surgery; and 5) patients were unable to receive both procedures or did not want to.

In our trial, the revascularization strategy was determined by physicians' and/or patients' preferences, on the basis of hemodynamic conditions, anatomic factors, vessel size, the presence of comorbidities and quality of arterial and/or venous conduits grafts fit.

All PCI procedures were performed according to current standard interventional guidelines. Antiplatelet therapy and periprocedural anticoagulation followed standard regimens. All patients received 300 mg of loading dose aspirin and/or clopidogrel (or 180 ticagrelor) before the procedure. After PCI, all patients were recommended 100 mg/day aspirin indefinitely and 75 mg/day clopidogrel or ticagrelor 90 mg twice daily for at least 1 year. There was no restriction on the second-generation DESs.

The bypass graft revascularization was performed with standard bypass techniques. A normal midline sternotomy incision was used to expose the heart and both on-pump and off-pump surgeries were performed at the preference of the surgeon. The internal thoracic artery was preferred for bypass of the left anterior descending artery. After CABG, medications were given according to the guidelines or the preference of the surgeon.

Patient data on demographics, comorbid conditions, laboratory echocardiography, procedure and so on were collected via chart review. The ethics committee at our hospital (Beijing Anzhen Hospital) reviewed our study protocol and approved the use of clinical data for the study. Because of the retrospective nature of our trial, the need for patient informed consent was waived. Follow-up and information on the clinical status were achieved by clinical visits and telephone interviews.

The primary endpoint in our trial was major adverse cardiac or cerebrovascular events (MACCE), a composite of all-cause death, stroke, myocardial infarction (MI), and repeated revascularization. Secondary endpoints were the individual occurrence of all-cause death, stroke, MI and repeat revascularization. Deaths were considered cardiac unless unequivocally noncardiac. Stroke was defined as a focal neurological deficit of central origin lasting >24 h, confirmed by a neurologist and computed tomography or magnetic resonance imaging. MI was defined as a creatine-kinase-MB level >50 ng/ml or the appearance of new Q-waves or ST segment elevation >2 mm, on the electrocardiogram which were confirmed by a veteran cardiologist. Repeated revascularization in our trial was any revascularization that was performed on any vessel by PCI or CABG.

Young patients were defined as < 45 years old according the World Health Organization (WHO). The lesion of each vessel, including its main branches (diameter ≥ 1.5 mm) was defined as $\geq 50\%$ stenosis. Multivessel disease or three-vessel disease was $\geq 50\%$ stenosis in all three epicardial coronary arteries, consisting of the left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA) or their main branches. Other definitions, such as hypertension (HT) and diabetes mellitus, were based on the basis of international guidelines or medication management.

Baseline and outcome data for individual patients were pooled. Continuous variables are expressed as mean $\pm$ standard deviation (SD) and were compared using Student's T-test. Categorical variables are presented as frequencies and proportions and comparisons were performed using the chi-square test or Fisher's exact test, as appropriate.

The rate of cumulative events and incidence curves for clinical outcome were estimated using the Kaplan-Meier method. A Cox proportional hazard regression was performed to determine independent predictors of MACCE, MI, stroke, death and

repeat revascularization in univariate and multivariate analyses. The analyses were used to determine the noninferiority of PCI and to find the adjusted hazards. Adjusted covariates included operation strategy (PCI/CABG), age, sex (male/female), smoking (yes/no), alcohol (yes/no), body mass index (BMI), HT (yes/no), DM (yes/no), hypercholesterolemia (HC, yes/no), family history (yes/no), creatinine clearance rate (CCR), uric acid (UA), C-reactive protein (CRP), blood group (A,B,AB, O), left ventricular ejection fraction (LVEF), prior MI (yes/no), prior heart failure (HF, yes/no), prior stroke (yes/no), prior stent (yes/no), collateral circulation (yes/no), lesion type (LM or three-vessel disease) and Gensini score. Multivariable predictors of outcomes were identified using forward stepwise selection with a significance level of <0.05 for entry and exit criteria. Finally, the significant factors and several clinically important factors entered subsequent analysis. The results are reported as hazard ratio (HR) and 95% confidence interval (CI).

To reduce selection bias and any other related potential confounding factors, we performed a baseline characteristic adjustment for patients using propensity score. The propensity scores were estimated using a multiple logistic regression model. A full nonparsimonious model was developed that included all variables listed in Tables 1 and 2. Patients who underwent PCI and patients who underwent CABG were then matched at a 1:1 ratio by propensity score using a nearest-neighbor matching algorithm with a caliper of 0.01. The absolute standardized differences of variables included in the calculation of propensity score were compared before and after propensity-score matching. Standardized differences <10% for these included variables indicated a relatively better balance. The baseline characteristics and outcomes between the two propensity-score-matched subsets were recompared.

Subgroup analyses, including sex, HT, DM, prior MI, prior HF, lesion type and Gensini score, were run using the Cox proportional hazard model. The variables included in the model were significant and were proved in the model design or were clinically relevant. Tests for interaction were performed to assess the heterogeneity of the treatment effect among subgroups.

A two-side p value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were carried out using SPSS software version 20.0 (IBM Corporation) or Stata version 14.0 (StataCorp, College Station, TX, USA).

Results

Between January 2015 and December 2016, a total of 1964 patients underwent angiography and PCI or CABG in our hospital. However, 1751 patients were removed from our trial by the inclusion and exclusion criteria, leaving 213 patients who entered the study, including 81 CABG and 132 PCI with 2nd DESs (Figure 1).

Baseline demographic characteristics are listed in Table 1. In the overall population, the incidence of smoking (72.7% vs. 56.8%, $p = 0.017$), hyperlipidemia (22% vs. 8.6%, $p = 0.012$), and several physical and biochemical indexes such as BMI (28.05 ± 3.75 vs. 26.80 ± 3.18 , $p = 0.013$), CCR (130.00 ± 32.08 vs. 121.34 ± 27.41 , $p = 0.045$), and UA (390.03 ± 90.05 vs. 347.56 ± 97.86 , $p = 0.001$) were higher in patients in the PCI group, whereas the Gensini score (69.80 ± 35.10 vs. 86.64 ± 36.77 , $P = 0.001$) showed the opposite difference. The antiplatelet drug P₂Y₁₂ inhibitor (99.2% vs. 91.4%, $p = 0.005$) was significantly more common in patients in the PCI group compared with those in the CABG group. There were no differences between treatment groups in terms of age, sex, HT, DM, LVEF, prior MI, prior HF, lesion type or other factors.

The median duration of follow-up among all patients was 38 months (interquartile range: 36 to 41 months). The cumulative incidences of clinical outcomes of all patients are described in Table 2 and Figure 2. Between the follow-ups, the incidence of MACCE was 20.5% in the PCI group and 8.6% in the CABG group (unadjusted HR: 2.508, 95% CI: 1.091 to 5.762, $p = 0.03$; adjusted HR: 3.263, 95% CI: 1.379 to 7.722, $p = 0.007$). The incidence of repeat revascularization was 18.9% in the PCI group and 3.7% in the CABG group (unadjusted HR: 5.435, 95% CI: 1.64 to 18.011, $p = 0.006$; adjusted HR: 6.968, 95% CI: 2.036 to 23.842, $p = 0.002$). There were no significant differences in other endpoints, such as MI, stroke or death, before or after adjusting for multiple variables and clinical background (1.5% vs. 2.5%, $p = 0.86$; 0 vs. 2.5%, $p = 0.881$; 0 vs. 2.5%, $p = 0.939$, after adjustment, respectively).

After propensity-score matching was performed, there were 46 matched pairs of patients in the two groups. The baseline characteristics of patients after propensity-score matching are described in Table 3, and no significant differences were found between the two groups with more variables showing standardized differences less than 10% (additional file 1). Compared with the CABG group, the PCI group had a higher prevalence of MACCE (32.6% vs. 10.9%, HR: 4.496, 95% CI: 1.592 to 12.695, $p = 0.005$) and repeat revascularization (30.4% vs. 4.3%, HR: 11.6, 95% CI: 2.449 to 55.51, $p = 0.002$) after adjustment. However, as in the overall population, there were no significant differences in the incidence of MI (2.2% vs. 2.2%, $p = 0.55$), stroke (0 vs. 4.3%, $p = 0.658$) or death (0 vs. 2.2%, $p = 0.876$) (Table 4, Figure 3).

Subgroup analyses were performed based on important baseline characteristics. There were no significant interactions between any treatment effects of PCI versus CABG in the rate of MACCE except for the prior MI (p for interaction = 0.031). PCI was associated with an increased risk of MACCE in other subgroups. However, the patients who had ever suffered MI experienced a lower rate of MACCE in the PCI group than in the CABG group (HR: 0.652, 95% CI: 0.125 to 3.397) (Figure 4).

In the multivariate Cox regression analysis, age (HR: 1.147, 95% CI: 1.004 to 1.312, $p = 0.044$), CRP (HR: 1.011, 95% CI: 1.005 to 1.016, $p = 0.00$), Gensini score (HR: 1.013, 95% CI: 1.004 to 1.022, $p = 0.006$) and operation strategy (HR: 3.263, 95% CI: 1.379 to 7.722, $p = 0.007$) were found to be predictors of MACCE.

Predictors of repeat revascularization were CRP (HR: 1.011, 95% CI: 1.005 to 1.016, $p = 0.00$), Gensini score (HR: 1.012, 95% CI: 1.002 to 1.022, $p = 0.018$) and operation strategy (HR: 6.968, 95% CI: 2.036 to 23.842, $p = 0.002$). There were no significant predictors of other endpoints.

Discussion

In this retrospective study, CABG was shown to be superior to PCI with 2nd-generation DESs in young patients with LM and/or three-vessel disease in terms of the incidence of MACCE, which was driven mainly by repeat revascularization. There were no significant differences in the hard endpoints death, MI and stroke in line with the outcomes of the recent EXCLE trial (8). After adjustment by propensity-score matching to minimize selection bias, the conclusion was the same as in the overall population. Although this study was limited by its observational design, this is the first report specifically addressing the issue of LM and three-vessel disease in young patients, and it evaluated the potential noninferiority of PCI over CABG. Therefore, our results would be helpful when making a clinical decision in real-world practice, especially for young CAD patients.

It is a good thing that young patients have better baseline characteristics along with fewer and milder complications, so it is essential to consider the broad indications and long-term prognosis. In our study, there were no obvious differences between the two groups in baseline characteristics, except the CABG group had more complex coronary anatomy and lower usage of dual antiplatelets. However, the PCI group showed a higher incidence of MACCE and repeat revascularization.

As in some previous studies, we found that CABG was better than PCI for the composite endpoint of MACCE and repeat revascularization both in LM(6) and three-vessel disease(3, 12, 15). One of the reasons is that after PCI, progressive atherosclerosis can lead to new, severe stenosis and plaque rupture that may cause ischemia and repeat revascularization, and CABG offers better protection by bypassing a large proportion of obstructive lesions or vulnerable plaques, minimizing the impact of progressive disease in the entire upstream proximal vessel (16). Moreover, there was more incomplete revascularization in the PCI group that needed more than one intervention operation, whereas patients achieving complete revascularization showed similar outcomes between PCI and CABG (17). In addition, more routine angiographic follow-up was performed to detect early in-stent restenosis in patients treated with PCI rather than those with CABG. Many patients with PCI receive repeat revascularization that is angiographically rather than clinically driven. Thus, the rate of repeat revascularization might be underestimated for those patients undergoing CABG. We must recognize that with the introduction of high-pressure deployment, use of intravascular ultrasound, and improved stent design, restenosis of drug-eluting stent has diminished over time (10, 18).

Some studies proved that the PCI group had higher rates of MI (19, 20), whereas other studies (21, 22) supported our finding that there were similar rates of MI between the PCI and CABG groups. The main advantage of CABG might be the bypassing of long lesion segments by grafting, which protects, to a great extent, against target lesion MI and proximal de-novo lesion MI (10, 11). The small population and short follow-up time may be two of the reasons that caused the absence of significant differences in MI rates.

While some other studies showed that CABG resulted in significantly higher rates of stroke compared with PCI for LM or multivessel disease (5, 23), we found that the difference in rates was indistinctive. The mechanisms underlying the increased risk of stroke with CABG are likely multifactorial. First, CABG performed on-pump with cannulation and clamping of the aorta increases the rates of stroke, which may be reduced by an off-pump procedure (24). Furthermore, stroke may be less common after PCI due to the routine use of dual antiplatelets after stent implantation. However, in the present study, the CABG group also had higher usage of aspirin and clopidogrel or ticagrelor.

Partly different from Head's study (25), we and Park et al. shared the same outcome in terms of death to a certain extent (4), i.e., that there was no significant difference in the rate of death between the PCI and CABG groups. The low mortality after treatment in both groups showed that modern revascularization techniques and adjunctive therapy can lead to excellent survival in young patients with LM and three-vessel disease. All these low incidences of MI, stroke and death might relate to the young characteristics of the patients enrolled in our study.

In the subgroup analysis, we found that CABG might lead to higher rates of MACCE in patients who had previously suffered MI, whereas in the opposite patients, PCI caused more MACCE. No relevant studies support this discovery, so it will be important to conduct further studies to see if this finding is generalizable.

In contrast to previous reports involving multivessel or LM disease in part, we found that, along with operation strategy, the predictors of MACCE and repeat revascularization were age, CRP and Gensini score. It is possible that, the inflammation condition and coronary anatomy play an important role in the long-term curative effect, which has been verified by other studies. Kosmoudou et al. (26) found that elevated baseline CRP level was strongly associated with subsequent death, MI and stroke. Misumida et al. (27) detected that SYNTAX score 2 was correlated with mortality. However, some predictors such as diabetes mellitus (28), heart failure (29), chronic renal failure (30) and so on, which proved related to MACCE in other studies, were not included in our finding. From a clinical viewpoint, using these relevant variables that were considered potential predictors of MACCE in young patients with LM and three-vessel disease, represents a first step to implementing further preventive measures and tailored therapies.

Considering the discussion above, patients in the PCI group with a 2nd DES had higher rates of repeat revascularization, which did not translate into a higher incidence of the hard endpoints of MI, stroke and death. A recent meta-analysis and the PRECOMBAT study also supports our results (6, 31). The young age of our patients could explain this result, but it is important to select appropriate operations for long-term survival. The relative benefits of CABG versus PCI with stents in terms of outcomes are highly debated, particularly with each advancement in stent design. Now, the state-of-the-art stent is the second-generation DES, which is thinner and is coated with a more biocompatible polymer and new 'limus' drugs that allow less inflammation and a lower rate of restenosis compared with first-generation DESs (12, 32, 33). PCI may also be preferred because of its improved early safety profile.

The internal mammary arteries have been widely used as conduits to the left anterior descending artery due to their long-term patency, and the advantage of CABG may be partially due to the completeness of revascularization (34). Although high long-term patency of the internal mammary artery is expected, some vein graft degeneration can be expected beyond 5 years (10). Multiple arterial grafting is associated with improved survival and a reduced requirement of reintervention compared with grafting of a single internal thoracic artery plus the saphenous vein (35). In the current era, routine use of the right internal mammary artery has not been widely adopted despite its identical histological features to the left internal

mammary artery due to technical difficulties and concerns about a potential increase in rates of bleeding and wound complication(20).

Saphenous vein grafts are routinely used in CABG surgery as additional conduits to artery grafts. However, saphenous vein grafts typically present accelerated atherosclerosis resulting in a high rate of stenosis or occlusion of the graft, which contributes to higher morbidity and mortality (36). In the case of graft failure, repeat revascularization after either PCI or CABG is necessary in a certain number of patients, if appropriate. Nevertheless, in addition to an increased operation difficulty, patients undergoing re-CABG have a 2- to 4-fold higher mortality than they do in the first operation, whereas PCI in patients previously treated with CABG is associated with worse acute and long-term outcomes compared with native artery PCI (37, 38).

Our study had some limitations. First, it was a nonrandomized, retrospective study, although we performed propensity-score matching to minimize the potential selection bias and ascertainment bias. Second, the follow-up duration and number of enrolled patients might not be sufficient to evaluate the long-term outcomes of revascularization. Third, this was a single-center study that only included Chinese, and more ethnicities are required in further trials. Fourth, because the treatment choice was left to the physician or patients, selection bias was inevitable. Moreover, some patients who underwent CABG, had the angiography done in outside hospitals rather than our hospital, which affected our evaluation of the lesion. Finally, we used the prevalent SYNTAX score with the Gensini score to estimate the anatomic complexity due to practical considerations.

Conclusion

In our retrospective study evaluating PCI with second DESs versus CABG in young patients with LM and/or three-vessel disease in the real world, the PCI group suffered higher rates of MACCE compared with the CABG group, which was driven by repeat revascularization, but did not translate into a higher incidence of hard endpoints, such as MI, stroke and death. In our opinion, for these young patients, along with the technical development of second-generation DESs for PCI, higher use of intravascular ultrasound and fractional flow reserve and new imaging techniques, such as optimal coherence tomography, may be an alternative treatment strategy to CABG for long-term prognosis. Of course, further research and longer follow-up durations are indispensable.

Abbreviation

BMI: body mass index;

CABG: coronary artery bypass grafting;

CAD: coronary artery disease

PCI: percutaneous coronary intervention;

DES: drug eluting stent;

CCR: creatinine clearance rate;

UA: uric acid;

LVEF: left ventricular ejection fraction;

HF: heart failure;

MI: myocardial infarction;

CRP: C-reactive protein

MACCE: major adverse cardiovascular or cerebrovascular events which are the composite of all-cause death, stroke, MI, and ischemia-driven revascularization.

HT: hypertension;

DM: diabetes mellitus;

LM disease: left main coronary artery disease, which includes LM coronary artery disease in isolation and LM coronary artery disease with multivessel disease (three-vessel disease)

Declarations

Ethics approval and consent to participate

The ethics committee at our hospital (Beijing Anzhen Hospital) reviewed our study protocol and approved the use of clinical data for the study. Because of the retrospective nature of our trial, the need for patient informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XC, XZ, YY, XZ, MN, TF, ZL and QZ designed the study. XC, XZ and YY contributed the data collection. XC, YY and XZ did the data analysis. XC and MN constructed the tables and figures. XC, TF, ZL and QZ interpreted the data. XC wrote the first draft of the manuscript. All authors critically reviewed the manuscript and approved the final version and its submission.

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Authors' information

1 Beijing Anzhen Hospital, Affiliated to Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases. The Key Laboratory of Remodelling-related Cardiovascular Diseases, Department of Cardiology, 2 Anzhen Road, Chaoyang District, Beijing 100029, China.

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Tables

Table 1. Comparison of traditional echocardiographic parameters between control and MHD groups

	MHD (n=34)	Control (n=35)	P-value
Age (years)	52±9	49±10	0.327
Male gender (%)	52.9	48.6	
HD time (months)	23(10-36)		
Heart rate (beats/min)	76.79±9.63	72.34±10.50	0.071
BMI	22.18±2.11	21.29±2.14	0.086
SBP (mmHg)	144.65±17.00	121.40±6.49	<0.001
DBP (mmHg)	88.82±11.17	75.91±6.29	<0.001
CREA (umol/L)	855.41±191.36	55.86±9.92	<0.001
Cause of ESRD			
Glomerulonephritis (cases)	19 (55.8%)		
Diabetic Nephropathy (cases)	6 (17.6%)		
Hypertensive nephrosclerosis (cases)	5 (14.7%)		
Polycystic kidney (cases)	4 (11.8%)		

Data are expressed as mean ± SD. Bold number: P < 0.05

HD: hemodialysis; BMI: body mass index; BP: systolic blood pressure; DBP: diastolic blood pressure; CREA: serum creatinine; ESRD: end-stage renal disease.

Table 2. Comparison of traditional echocardiographic parameters between control and MHD groups

	MHD	Normal	P-value
LVIDD (mm)	52.56±6.13	46.06±3.07	<0.001
LVIDS (mm)	36.65±5.55	31.11±2.84	<0.001
IVST (mm)	11.56±1.62	8.86±1.38	<0.001
LVPWT (mm)	11.24±1.50	8.14±1.38	<0.001
LAD (mm)	42.38±5.29	34.86±3.12	<0.001
LVEF (%)	58.24±5.16	60.11±4.00	0.095
LVMI (g/m ²)	56.59±9.11	31.60±3.82	<0.001
E/A	0.99±0.15	1.15±0.19	<0.001
E/e'	7.97±1.67	7.08±1.36	0.019

Data are expressed as mean ± SD. Bold number: P < 0.05

LVIDD: left ventricular internal diameter at end-diastole; LVIDS: left ventricular internal diameter at end-systole; IVST: interventricular septal thickness at end-diastole; LVPWT: left ventricular posterior wall thickness at end-diastole; LAD: left atrial diameter; LVEF: left ventricular ejection fraction; LVMI: left ventricular mass index; E/A: peak early diastolic velocity of mitral orifice/peak late diastolic velocity of mitral orifice(by pulsed Doppler); E/e': peak early diastolic velocity of mitral orifice(by pulsed Doppler)/peak velocity during early diastolic of mitral annulus (by pulsed-wave tissue Doppler)

Table 3. Comparison of global and layer-specific LS and CS between control and MHD groups

Variable	Longitudinal strain (%)				Circumferential strain(%)			
	Sub-endocardial	Mid-myocardial	Sub-epicardial	Global	Sub-endocardial	Mid-myocardial	Subepicardial	Global
MHD	-17.04±4.09	-14.76±4.11	-13.50±2.99	-15.07±3.46	-24.70±4.68	-15.33±2.44	-9.20±1.67	-16.41±2.59
Normal	-23.41±3.58	-20.18±3.25	-18.07±2.75	-20.55±3.16	-27.40±3.51	-18.94±2.74	-12.36±2.52	-19.57±2.75
P-value	<0.001	<0.001	<0.001	<0.001	0.008	<0.001	<0.001	<0.001

Data are expressed as mean ± SD. Bold number: P < 0.05

Table 4. Comparison of horizontal layer-specific longitudinal strain between control and MHD groups

Segmental LV wall	Longitudinal strain (%)								
	Endocardial			Middle			Epicardial		
	MHD	Normal	P-value	MHD	Normal	P-value	MHD	Normal	P-value
basal segment	-12.47±4.23	-19.57±2.92	<0.001	-12.15±4.32	-18.66±2.58	<0.001	-12.15±3.53	-18.06±2.75	<0.001
middle segment	-16.56±4.42	-22.40±3.42	<0.001	-14.82±3.93	-19.83±3.28	<0.001	-14.38±3.14	-18.37±2.61	<0.001
apex segment	-22.09±5.37	-28.26±5.26	<0.001	-17.32±5.26	-22.06±4.54	<0.001	-13.65±4.12	-17.77±3.43	<0.001

Data are expressed as mean ± SD. Bold number: P < 0.05

Table 5. Comparison of horizontal layer-specific circumferential strain parameters between control and MHD patients

Segmental LV wall	Circumferential strain(%)								
	Sub-endocardial			Mid-myocardial			sub-epicardial		
	MHD	Normal	P-value	MHD	Normal	P-value	MHD	Normal	P-value
basal segment	-23.88±5.99	-27.46±5.37	0.011	-15.15±3.60	-19.09±4.18	<0.001	-9.47±2.62	-13.11±3.64	<0.001
middle segment	-23.79±5.40	-26.00±3.80	0.053	-14.44±3.52	-17.97±3.26	<0.001	-8.56±3.15	-12.43±3.17	<0.001
apex segment	-26.41±7.23	-28.74±5.25	0.131	-16.41±3.49	-19.77±4.03	<0.001	-9.56±3.41	-11.54±3.39	0.018

Data are expressed as mean ± SD. Bold number: P<0.05

Table 6. Comparison of time to peak longitudinal strain of LV 17 segments between control and MHD groups

variable	TTP (ms)		
	MHD	Normal	P-value
bas ANT-SEPT	415±93	375±55	0.032
bas ANT	424±85	375±53	0.006
bas LAT	451±73	383±57	<0.001
bas POST	405±54	379±51	0.045
bas INF	394±56	367±33	0.017
bas SEPT	389±71	376±52	0.669
mid ANT-SEPT	375±56	363±42	0.499
mid ANT	403±80	360±39	0.006
mid LAT	431±67	366±38	<0.001
mid POST	401±51	366±41	0.002
mid INF	381±48	360±30	0.028
mid SEPT	368±52	360±33	0.094
ap ANT	389±60	365±33	0.044
ap LAT	385±59	369±33	0.151
ap INF	397±61	358±28	0.001
ap SEPT	370±46	362±33	0.372
ap AP	383±46	364±28	0.047

Data are expressed as mean ± SD. Bold number: P < 0.05

Bas: basal segment; mid: middle segment; ap: apex segment; ANT-SEPT: anterior septum wall; ANT: anterior wall; LAT: lateral wall; POST: posterior wall;

INF: inferior wall; SEPT: septum wall; TTP: time to peak longitudinal strain.

Bold number: P < 0.05.

Table 7. Comparison of LV PSD between control and MHD groups

Group	n	PSD
MHD	34	57.26±18.18
Normal	35	29.97±8.31
P-value		<0.001

Data are expressed as mean $\pm$ SD. PSD: peak strain dispersion. Bold number: $P < 0.05$

Table 8. Correlation between PSD and LV three-layer myocardial LS and GLS

	Longitudinal strain (%)			
	Endocardial	Middle	Epicardial	Global
r-value	0.467	0.513	0.236	0.463
p-value	0.005	0.002	0.179	0.006

Bold number: $P < 0.05$

Table 9. ROC curve analysis of accuracy of LV three-layer myocardial LS and CS in MHD patients

Parameters	AUC	95%CI	Cut-off Value (%)	Sensitivity (%)	Specificity(%)	Youden index
LS sub-endocardial	0.894	0.796-0.955	-21.15	85.3	82.9	0.6521
LS mid-myocardial	0.852	0.746-0.926	-18.33	73.5	80.0	0.5353
LS sub-epicardial	0.870	0.767-0.939	-17.08	82.4	77.1	0.6244
CS sub-endocardial	0.669	0.545-0.778	-24.33	50.0	80.0	0.3000
CS mid-myocardial	0.837	0.728-0.915	-17.86	73.5	82.9	0.5639
CS sub-epicardial	0.852	0.746-0.926	-11.65	82.4	74.3	0.5664

AUC: area under the curve; 95% CI: 95% confidence interval; LS: longitudinal strain; CS: circumferential strain.

Table 10. Evaluation of intra-observer and inter-observer variability

	Intra-observer		Inter-observer	
	ICC	95%CI	ICC	95%CI
LS sub-endocardial	0.90	0.76-0.96	0.87	0.69-0.94
LS mid-myocardial	0.89	0.76-0.96	0.79	0.55-0.91
LS sub-epicardial	0.87	0.70-0.95	0.88	0.72-0.95
GLS	0.89	0.75-0.96	0.87	0.71-0.95
CS sub-endocardial	0.89	0.74-0.95	0.87	0.71-0.93
CS mid-myocardial	0.77	0.51-0.90	0.82	0.60-0.92
CS sub-epicardial	0.86	0.69-0.94	0.80	0.57-0.92
GCS	0.84	0.63-0.93	0.83	0.62-0.93
PSD	0.96	0.90-0.98	0.95	0.88-0.98

ICC: intra-class correlation coefficients; 95% CI: 95% confidence interval; LS: longitudinal strain; GLS: global longitudinal strain; CS: circumferential strain; GCS: global circumferential strain; PSD: peak strain dispersion.

Figures

Figure 1

Flow chart of enrolled patients. PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; STEMI: ST-segment-elevation myocardial infarction; NSTEMI: non-ST-segment-elevation myocardial infarction; LM disease: left main coronary artery disease.

Figure 2

Kaplan-Meier cumulative event curves of MACCE and secondary end points before propensity-score matching. The adjusted risk of PCI relative to CABG is shown. PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; MI: myocardial infarction.

Figure 3

Kaplan-Meier cumulative event curves of MACCE and secondary end points after propensity-score matching. The adjusted risk of PCI relative to CABG is shown. PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; MI: myocardial infarction.

Figure 4

Subgroup analysis based on sex, HT, DM, prior MI, prior HF, LM disease and Gensini score. HT: hypertension; DM: diabetes mellitus; MI: myocardial infarction; HF: heart failure; LM disease: left main coronary artery disease, which includes LM coronary artery disease in isolation and LM coronary artery disease with multivessel disease (three-vessel disease); ✱: because the data point is outside the axis limits. Additional file 1: Standardized differences before and after propensity-score matching. An absolute standardized difference of less than 10% indicates a good match. Abbreviations as in Table 1.

Supplementary Files

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