**Prognostic Implications of Diastolic Dysfunction Change in Patients With Coronary Artery Disease Undergoing Percutaneous Coronary Intervention**

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**Background:** The association between a change in diastolic function (DF) and long-term clinical outcomes in patients undergoing percutaneous coronary intervention (PCI) is unknown. The aim of this study was to investigate the prognostic effect of changes in diastolic dysfunction in patients undergoing PCI.

**Methods and Results:** Consecutive patients who underwent PCI and echocardiography before and after revascularization were prospectively included. Major adverse cardiac event (MACE) was defined as a composite of cardiac death, myocardial infarction, and repeat revascularization. A total of 1,235 patients were identified. Baseline diastolic dysfunction was present in 1,033 patients (83.6%). At follow-up echocardiography, DF had worsened in 219 (17.8%) patients and was unchanged in 623 patients (50.4%). The risk of MACE was significantly higher in the worsened DF group compared with the unchanged DF group (adjusted hazard ratio [aHR]: 2.15; 95% confidence interval [CI]: 1.59 to 2.90; P<0.001) and the improved or normal DF group (aHR: 2.20; 95% CI, 1.49 to 3.27; P<0.001). Patients with worsened DF consistently had a higher risk of MACE in various subgroups, especially irrespective of left ventricular systolic function.

**Conclusions:** Aggravation of DF was independently associated with an increased risk of MACE in patients undergoing PCI. Evaluating changes in DF after PCI is a simple but useful method for predicting long-term clinical outcomes.

**Key Words:** Coronary artery disease; Diastolic dysfunction; Percutaneous coronary intervention

Left ventricular (LV) systolic function is a well-known prognostic factor in patients with coronary artery disease (CAD); however, it is normal or preserved in most patients undergoing percutaneous coronary intervention (PCI) in the modern era. Therefore, the effects of revascularization cannot be fully determined, based on changes in LV systolic function alone. Because myocardial ischemia causes diastolic dysfunction earlier than systolic dysfunction, diastolic function (DF) might be a more sensitive measure of the effects of revascularization compared with systolic function.

Diastolic dysfunction of the LV is an independent predictor of all-cause death in outpatients with normal LV systolic function. It is also associated with adverse outcomes in patients with CAD or acute myocardial infarction (MI). Moreover, in patients with a normal baseline LV ejection fraction (EF) according to outpatient echocardiography, worsening of DF is an independent predictor of death. However, data on the prognostic implications of changes in DF after revascularization are very limited. A few studies have reported that diastolic dysfunction improves after revascularization in patients with acute MI or ischemic cardiomyopathy. However, those studies had small sample sizes, and they also did not investigate the prognostic implications of an improvement in diastolic dysfunction with respect to long-term clinical outcomes. Thus, no study to date has looked into how DF changes after revascularization in a sufficiently large population that includes patients with preserved LV systolic function. Moreover, it
is unknown whether a change in DF is associated with long-term clinical outcomes after revascularization. Considering that most patients undergoing PCI have preserved LV systolic function and impaired DF, investigating the prognostic implications of changes in DF on long-term clinical outcomes in patients undergoing PCI is considered to have great clinical importance. Therefore, in the present study, we investigated changes in DF and their association with long-term clinical outcomes in a broad spectrum of patients undergoing PCI.

**Methods**

**Study Design and Patients**

The study cohort consisted of consecutive patients undergoing PCI with drug-eluting stents (DES) between June 1, 2003 and June 30, 2014 and who had echocardiography data from before the index procedure and during follow-up within 12 months of the index procedure. We excluded patients who had MI or repeat revascularization before follow-up echocardiography, patients with severe valvular heart disease, and patients with a history of prior valvular surgery. Additionally, we excluded patients for whom DF could not be assessed because of arrhythmia or a poor acoustic window (Figure 1).

Clinical, angiographic, and procedural findings and clinical outcome data were prospectively collected in our PCI registry by research coordinators. Patients were routinely followed at 1, 6, and 12 months after the index procedure and annually thereafter. Further information was collected by telephone contact or medical records if necessary. For validation, information about vital status was obtained through December 31, 2014 from the National Population Registry of the Korea National Statistical Office using a unique personal identification number. The Samsung Medical Center Institutional Review Board approved this study and waived the requirement for written informed consent for access to the institutional PCI registry.

**Coronary Angiography and Intervention**

Coronary angiography and stent implantation were performed using standard interventional techniques based on the practice guidelines established by the Korean Society of Interventional Cardiology. Pre- and postprocedure coronary angiograms were reviewed and analyzed quantitatively at the angiographic core laboratory (Heart Vascular Stroke Institute, Samsung Medical Center, Seoul, Korea) using standard definitions with an automated edge-detection system (Centricity CA 1000, GE, Waukesha, WI, USA). To calculate the Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) score, each coronary lesion with ≥50% diameter stenosis in vessels ≥1.5 mm was scored using an algorithm described elsewhere. A residual SYNTAX score was determined for the remaining lesions after completion of PCI.

**DF Measurement and Analysis**

Comprehensive transthoracic echocardiography was performed with commercially available equipment (Vivid 7, GE Medical Systems, Milwaukee, WI, USA; Acuson 512, Siemens Medical Solution, Mountain View, CA, USA; or Sonos 5500, Philips Medical System, Andover, MA, USA). Standard 2D, color, and tissue Doppler imaging was performed with positional change. The LVEF was assessed by biplane Simpson’s rule using manual tracing of digital images. The pulse-wave Doppler transmural inflow velocity was

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**Figure 1.** Study design and population. DF, diastolic function; MI, myocardial infarction; PCI, percutaneous coronary intervention; TTE, transthoracic echocardiography.
obtained from an apical 4-chamber view for assessment of DF in accordance with current guidelines using a combination of echocardiographic variables, mitral inflow velocity of the early phase (E) and late phase (A) during diastole, deceleration time, and pulsed-wave Doppler-derived mitral annular velocity imaging in the septal wall ($e'$). DF was categorized as: (1) normal ($e'>0.08\text{ m/s}$, LAVI <34 mL/m$^2$), E/A $\geq0.8$ and <1.5, deceleration time $>160\text{ ms}$, mean E/e' $\leq8$); (2) Grade 1, impaired relaxation (E/A $<$0.8, deceleration time $>200\text{ ms}$, mean E/e' $\leq8$); (3) Grade 2, pseudonormal pattern (E/A $\geq0.8$ and $<1.5$, deceleration time of 160–200ms, mean E/e'=$9–12$); or (4) Grade 3, restrictive pattern (E/A $\geq1.5$, deceleration time $<160\text{ ms}$, mean E/e' $\geq13$). The presence of diastolic dysfunction was confirmed by decreased mitral annulus velocity (septal $e'$ $<0.08\text{ m/s}$) and enlarged left atrial (LA) volume (LAV index $>34\text{ mL/m}^2$). Improvement of diastolic dysfunction was defined categorically as an improvement of at least 1 DF class. Aggravation of DF was defined as progression of at least 1 DF class. We classified patients into 3 groups according to the change in DF class before and after PCI: worsening DF group; unchanged DF group; and improved/normal DF group. LA enlargement was defined as an indexed volume $>34\text{ mL/m}^2$.

**Clinical Outcomes and Definitions**

The primary outcome of this study was major adverse cardiac event (MACE), which was defined as a composite of cardiac death, MI, and any repeat revascularization over 5 years after the initial follow-up echocardiography. Secondary endpoints included the individual components of the primary endpoint, all-cause death, and cardiac death or MI. All deaths were considered to be of cardiac cause unless a definite non-cardiac cause could be established. MI was defined as either elevated cardiac enzyme levels, such as troponin I or the myocardial band fraction of creatine kinase, greater than the upper limit of the normal range with either ischemic symptoms or ECG changes implicating ischemia or MI at readmission requiring subsequent hospitalization (defined as an emergency admission with a principal diagnosis of MI). We defined repeat revascularization as any repeat PCI or surgical bypass of any segment of a target or non-target vessel.

**Statistical Analysis**

Baseline demographic data and clinical variables were summarized with continuous variables and expressed as mean±standard deviation or median with interquartile range. Categorical data are presented as a percentage and the number of events. Continuous variables were analyzed using ANOVA or the Kruskal-Wallis nonparametric tests as appropriate, and categorical variables were analyzed using Pearson $\chi^2$ test or Fisher’s exact test. In order to compare the worsened DF group and unchanged or improved DF group, we used t-tests or Wilcoxon rank sum tests when applicable to compare continuous variables and $\chi^2$ tests for categorical data. A Cox-proportional hazards model was used to compare the risks of adverse cardiac events between the worsened and unchanged or improved DF groups, respectively. We included in multivariate models covariates that were significant on univariate analysis and those that were
Results

Baseline and Procedural Characteristics

A total of 1,235 patients undergoing PCI with complete data sets consisting of both baseline and follow-up assessment of LV systolic and diastolic function were analyzed (age, 64.3±11.3 years; 72.1% male). The median interval from preprocedural to follow-up echocardiography was 7.0 (3.3–11.7) months. Baseline diastolic dysfunction was present in 1,033 patients (83.6%), with Grade 1 being the most prevalent (64.6%). At follow-up echocardiography, DF had worsened in 219 (17.8%) patients and was unchanged in 623 patients (50.4%), while 393 patients (31.8%) had improved or normal DF. Compared with the baseline echocardiographic evaluation, clinically relevant. Covariates were sex, hypertension, type of DES, and follow-up LVEF for comparison between the worsened and unchanged groups. Comparison of the worsened DF group and the improved/normal DF group included age, sex, smoking, chronic kidney disease, hypertension, previous cerebrovascular accident, presence of multivessel disease, type of DES, number of stents inserted, total stent length, and follow-up LVEF. Survival rates were compared between groups using Kaplan-Meier curves, and the significance of differences was calculated using log-rank tests.

All analysis was conducted with SPSS software version 17.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was concluded at a 2-sided significance level of 0.05 for all analyses.

Table 1. Baseline Characteristics of the Study Patients With CAD Undergoing PCI

|                         | Worsened DF (n=219) | Unchanged DF (n=623) | Improved DF (n=393) | P value      | Worsened DF vs. Unchanged DF | Worsened DF vs. Improved DF |
|-------------------------|---------------------|----------------------|---------------------|--------------|------------------------------|-----------------------------|
| Male                    | 155 (70.8)          | 414 (66.5)           | 321 (81.7)          | <0.001       | 0.240                        | 0.002                       |
| Age, years              | 67.0 (59.0–74.0)    | 60.0 (51.0–80.0)     | 58.0 (51.0–80.0)    | <0.001       | 0.184                        | <0.001                      |
| BMI                     | 24.2 (22.2–26.3)    | 24.2 (22.3–26.2)     | 24.5 (22.5–26.4)    | 0.430        | 0.355                        | 0.831                       |
| Smoker                  | 62 (28.3)           | 158 (25.4)           | 153 (38.9)          | <0.001       | 0.393                        | 0.008                       |
| CKD                     | 34 (15.5)           | 85 (13.6)            | 38 (9.7)            | 0.070        | 0.492                        | 0.031                       |
| Dyslipidemia            | 61 (27.9)           | 203 (32.6)           | 129 (32.8)          | 0.379        | 0.194                        | 0.203                       |
| Diabetes                | 113 (51.6)          | 313 (50.2)           | 184 (46.8)          | 0.439        | 0.730                        | 0.257                       |
| Hypertension            | 135 (61.6)          | 442 (70.9)           | 204 (51.9)          | <0.001       | 0.011                        | 0.020                       |
| History of PCI          | 25 (11.4)           | 94 (15.1)            | 44 (11.2)           | 0.140        | 0.180                        | 0.934                       |
| History of CVA          | 26 (11.9)           | 52 (8.3)             | 19 (4.8)            | 0.007        | 0.122                        | 0.001                       |
| ACS                     | 92 (42.0)           | 234 (37.6)           | 155 (39.4)          | 0.495        | 0.245                        | 0.535                       |
| Previous MI             | 49 (22.4)           | 117 (18.8)           | 75 (19.1)           | 0.496        | 0.250                        | 0.332                       |

Lesion location

|                         |                         |                       |                       |             |                             |                             |
|-------------------------|-------------------------|-----------------------|-----------------------|--------------|------------------------------|------------------------------|
| LM                      | 16 (7.3)                | 36 (5.8)              | 26 (6.6)              | 0.695        | 0.419                        | 0.746                        |
| LAD                     | 143 (65.3)              | 417 (66.9)            | 240 (61.1)            | 0.160        | 0.659                        | 0.300                        |
| LCX                     | 94 (42.9)               | 257 (41.3)            | 153 (38.9)            | 0.598        | 0.666                        | 0.335                        |
| RCA                     | 100 (45.7)              | 290 (46.5)            | 180 (45.8)            | 0.961        | 0.821                        | 0.974                        |
| Multivessel disease     | 152 (69.4)              | 422 (67.7)            | 235 (59.8)            | 0.014        | 0.648                        | 0.018                        |
| CTO                     | 59 (26.9)               | 165 (26.5)            | 102 (26.0)            | 0.963        | 0.896                        | 0.790                        |
| Type of DES             |                         |                       |                       |              |                             |                             |
| 1st-generation          | 78 (35.6)               | 180 (28.9)            | 90 (22.9)             |              |                             |                             |
| 2nd-generation          | 141 (64.4)              | 443 (71.1)            | 303 (77.1)            |              |                             |                             |
| Stent number            | 1 (1–3)                 | 1 (1–3)               | 1 (1–2)               | 0.006        | 0.234                        | 0.003                        |
| Total stent length, mm  | 34.0 (23.0–56.0)        | 32.0 (23.0–56.0)      | 28.0 (20.0–46.0)      | 0.006        | 0.129                        | 0.002                        |
| Maximal stent diameter, | 3.0 (2.75–3.25)         | 3.0 (2.75–3.25)       | 3.0 (2.75–3.5)        | 0.274        | 0.876                        | 0.204                        |
| SYNTAX score            | 16.0 (8.9–23.0)         | 14.0 (9.0–21.4)       | 12.0 (7.0–21.5)       | 0.028        | 0.197                        | 0.013                        |
| Residual SYNTAX score   | 4.0 (0–10.0)            | 4.0 (0–10.0)          | 2.0 (0–8.0)           | 0.044        | 0.602                        | 0.153                        |

Medications at discharge

|                         |                         |                       |                       |             |                             |                             |
|-------------------------|-------------------------|-----------------------|-----------------------|--------------|------------------------------|------------------------------|
| Aspirin                 | 215 (98.2)              | 614 (98.6)            | 391 (99.5)            | 0.274        | 0.751                        | 0.194                        |
| Clopidogrel             | 207 (94.5)              | 596 (95.7)            | 363 (92.4)            | 0.083        | 0.488                        | 0.312                        |
| Statin                  | 164 (74.9)              | 476 (78.7)            | 289 (73.5)            | 0.508        | 0.582                        | 0.715                        |
| ACEI/ARB                | 133 (60.7)              | 368 (59.1)            | 220 (56.0)            | 0.460        | 0.687                        | 0.254                        |
| β-blocker               | 116 (53.0)              | 332 (53.3)            | 200 (50.9)            | 0.747        | 0.934                        | 0.622                        |
| Diuretics               | 42 (19.2)               | 128 (20.6)            | 60 (15.3)             | 0.106        | 0.665                        | 0.213                        |

Values are mean±standard deviation or n (%). ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker; ACS, acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; CTO, chronic total obstruction; CVA, cerebrovascular accident; DES, drug-eluting stent; LAD, left anterior descending coronary artery; LCX, left circumflex artery; LM, left main coronary artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.
Table 2. Baseline and Follow-up Echocardiographic Findings

|                         | Worsened DF (n=219) | Unchanged DF (n=623) | Improved DF (n=393) | P value | Worsened DF vs. Unchanged DF | Worsening DF vs. Improved DF |
|-------------------------|---------------------|----------------------|---------------------|---------|------------------------------|------------------------------|
| **Pre-PCI echocardiography** |                     |                      |                     |         |                              |                              |
| E (m/s)                 | 0.6 (0.5–0.7)       | 0.6 (0.5–0.7)        | 0.7 (0.6–0.9)       | <0.001  | 0.295                        | <0.001                       |
| A (m/s)                 | 0.8 (0.6–0.9)       | 0.8 (0.7–1.0)        | 0.7 (0.5–0.8)       | <0.001  | 0.001                        | <0.001                       |
| EA ratio                | 0.7 (0.6–1.0)       | 0.7 (0.6–0.8)        | 1.1 (0.9–1.3)       | <0.001  | <0.001                       | <0.001                       |
| Deceleration time (ms)  | 229.0 (192.0–267.0) | 233.0 (199.0–276.0)  | 198.0 (173.0–231.0) | <0.001  | 0.228                        | <0.001                       |
| E’ (m/s)                | 0.06 (0.05–0.08)    | 0.05 (0.04–0.07)     | 0.07 (0.06–0.08)    | <0.001  | 0.001                        | <0.001                       |
| E/E’                   | 10.1 (8.4–12.3)     | 10.9 (8.9–14.3)      | 10.2 (7.8–13.4)     | 0.002   | 0.009                        | 0.783                        |
| LA volume index (mL/m²) | 30.4 (25.4–38.5)    | 31.4 (25.6–39.4)     | 31.6 (25.4–39.8)    | 0.621   | 0.330                        | 0.542                        |
| Ejection fraction (%)   | 60.0 (53.0–67.0)    | 60.0 (50.0–66.0)     | 59.0 (50.0–66.0)    | 0.506   | 0.440                        | 0.242                        |
| **Post-PCI echocardiography** |                     |                      |                     |         |                              |                              |
| E (m/s)                 | 0.7 (0.6–0.9)       | 0.6 (0.5–0.7)        | 0.6 (0.5–0.7)       | <0.001  | <0.001                       | <0.001                       |
| A (m/s)                 | 0.7 (0.6–0.9)       | 0.8 (0.7–1.0)        | 0.7 (0.6–0.8)       | <0.001  | <0.001                       | 0.034                        |
| EA ratio                | 1.0 (0.8–1.2)       | 0.7 (0.6–0.9)        | 0.9 (0.7–1.2)       | <0.001  | <0.001                       | 0.086                        |
| Deceleration time (ms)  | 203.5 (173.8–245.3) | 236.0 (220.3–279.0)  | 215.0 (191.0–249.5) | <0.001  | <0.001                       | 0.001                        |
| E’ (m/s)                | 0.06 (0.05–0.07)    | 0.05 (0.04–0.06)     | 0.07 (0.06–0.09)    | <0.001  | 0.005                        | <0.001                       |
| E/E’                   | 12.3 (10.0–15.8)    | 11.2 (8.8–14.3)      | 8.7 (7.4–10.9)      | <0.001  | <0.001                       | <0.001                       |
| LA volume index (mL/m²) | 35.0 (27.0–44.0)    | 32.0 (26.8–41.5)     | 30.4 (25.0–36.8)    | <0.001  | 0.180                        | <0.001                       |
| Ejection fraction (%)   | 60.0 (47.5–65.0)    | 61.0 (53.0–67.0)     | 61.0 (55.0–66.5)    | 0.011   | 0.011                        | 0.003                        |

Values are mean±standard deviation or n (%). DF, diastolic function; LA, left atrium; PCI, percutaneous coronary intervention.

differ among the 3 groups. On follow-up echocardiography, patients with aggravated DF demonstrated significantly higher filling pressure, which was expressed by E/e’, followed by those with unchanged and improved DF, respectively.

Clinical Outcomes

The median follow-up duration was 44 months (interquartile range: 21–73 months). Over the 5-year period after follow-up echocardiography, MACE occurred in 74 patients (42.2%) in the worsened DF group, 107 patients (22.9%) in the unchanged DF group, and 48 patients (14.8%) in the improved DF group. The risk of MACE was significantly higher in the worsened DF group compared with the unchanged DF group (adjusted hazard ratio [aHR]: 2.15; 95% confidence interval [CI]: 1.59 to 2.90; P<0.001) and improved DF group (aHR: 2.20; 95% CI: 1.49 to 3.27; P<0.001) (Figure 3A). Each component of the primary end point was also significantly higher in patients with worsening DF compared with the unchanged DF and improved/normal DF group (Table 3, Figure 3B-D). The association of DF change and clinical outcomes was more potent in patients with a relatively short interval of follow-up echocardiography (Supplementary Tables 1–6).
KIM EK et al. and the association with long-term clinical outcomes in patients undergoing PCI. Although DF remained unchanged in approximately half of the study patients, it improved or was aggravated in the remaining half following revascularization. Patients with aggravated DF had a significantly higher risk of MACE compared with those with unchanged or improved DF during long-term follow-up. The association between DF change after PCI and long-term clinical outcome was consistent among the various subgroups.

Although the prognostic effect of recovery of regional or global systolic function after revascularization is well established, little attention has been paid to the effects of changes in DF. Indeed, while diastolic dysfunction can be improved by revascularization, it might also be unchanged or even aggravated by residual or newly developed ischemia. Therefore, diastolic dysfunction per se, as well as the change in DF after revascularization, can be an indepen-

Subgroup Analysis
To investigate whether there was an association between the change in DF after PCI and clinical outcomes across the various subgroups, we performed post-hoc subgroup analyses. Patients with worsened DF consistently had a higher risk of MACE compared with those with unchanged or improved DF in the various subgroups. Especially, aggravation of DF at follow-up echocardiography was consistently associated with adverse cardiac outcomes irrespective of the presence of LV systolic dysfunction (Figure 4). However, there was significant interaction between the prognostic implications of DF change and follow-up duration of echocardiography or type of stent inserted.

Discussion
In this observational study, we investigated changes in DF and the association with long-term clinical outcomes in patients undergoing PCI. Although DF remained unchanged in approximately half of the study patients, it improved or was aggravated in the remaining half following revascularization. Patients with aggravated DF had a significantly higher risk of MACE compared with those with unchanged or improved DF during long-term follow-up. The association between DF change after PCI and long-term clinical outcome was consistent among the various subgroups.

Although the prognostic effect of recovery of regional or global systolic function after revascularization is well established, little attention has been paid to the effects of changes in DF. Indeed, while diastolic dysfunction can be improved by revascularization, it might also be unchanged or even aggravated by residual or newly developed ischemia. Therefore, diastolic dysfunction per se, as well as the change in DF after revascularization, can be an indepen-
With a broad spectrum of CAD strengthens our results patients following revascularization and was aggravated in LV diastolic dysfunction was unchanged in half of the patients (83.6%) with CAD in the present study had diastolic dysfunction only at baseline,\textsuperscript{23} most of the previous studies supporting this idea evaluated myocardial relaxation after PCI,\textsuperscript{9} are several possible explanations for this finding.\textsuperscript{8,28,30} First, diastolic dysfunction might not have improved in some patients because of residual ischemia resulting from incomplete revascularization, development of new ischemia from restenosis of treated lesions, or progression of atherosclerosis in non-culprit lesions.\textsuperscript{31} Differences in residual SYNTAX scores among the 3 groups evaluated in the present study also supported this possibility.

A second explanation is that procedural complications, including distal embolization of microemboli or a lack of reflow during PCI, might have resulted in persistently impaired DF. Importantly, both distal embolization and lack of reflow during PCI are associated with adverse outcomes.\textsuperscript{32} In our analysis, we identified that patients with an increased number of treated segments were independently associated with aggravation of DF after PCI. A complex procedure to treat multiple lesions might cause myocardial injury along the index territory,\textsuperscript{33} which subsequently may result in DF aggravation after PCI. In patients with extensive CAD, PCI is associated with a higher rate of MACE than coronary artery bypass grafting surgery.\textsuperscript{34} A third explanation for the results of our study was that several risk factors including age, hypertension, diabetes, obesity, and fluid overload with elevated filling pressures are associated with DF. Although PCI lessens ischemia, DF caused by factors other than ischemia cannot be fully recovered or improved by PCI alone. Taken together, a change in DF can reflect myocardial ischemia and the control status of risk factors and, in doing so, can serve as an independent predictor of long-term clinical outcomes after PCI. Our data suggested that monitoring diastolic dysfunction before and after revascularization is an important method of predicting long-term clinical outcomes and selecting patients who require more intensive risk factor modification. However, serial echocardiography at baseline and follow-up was performed in only 15.9% of consecutive

### Diastolic Function and CAD

| Compared With Unchanged DF group (n=842) | Worsened DF group (n=219) | Comparison group\textsuperscript{a} | Unadjusted | Adjusted\textsuperscript{b} |
|-----------------------------------------|--------------------------|----------------------------------|------------|--------------------------|
|                                         | HR (95% CI)  | P value | HR (95% CI)  | P value |
| MACE\textsuperscript{c}               | 42.2%        | 22.9%   | 2.19 (1.63–2.95) | <0.001 | 2.15 (1.59–2.90) | <0.001 |
| All-cause death                        | 29.5%        | 16.8%   | 2.00 (1.44–2.78) | <0.001 | 2.06 (1.48–2.87) | <0.001 |
| Cardiac death                          | 17.5%        | 9.2%    | 2.34 (1.42–3.84) | 0.001  | 2.37 (1.44–3.92) | 0.001  |
| MI                                      | 7.7%         | 3.1%    | 2.75 (1.33–5.69) | 0.007  | 2.75 (1.32–5.73) | 0.007  |
| Cardiac death or MI                    | 22.3%        | 11.3%   | 2.39 (1.55–3.69) | <0.001 | 2.39 (1.54–3.69) | <0.001 |
| Any revascularization                  | 28.8%        | 15.2%   | 1.95 (1.36–2.80) | <0.001 | 1.93 (1.34–2.78) | <0.001 |

| Compared With Improved DF group (n=612) | MACE\textsuperscript{c} | All-cause death | Cardiac death | MI | Cardiac death or MI | Any revascularization |
|----------------------------------------|--------------------------|----------------|-------------|-----|---------------------|----------------------|
|                                         | HR (95% CI)  | P value | HR (95% CI)  | P value | HR (95% CI)  | P value |
| MACE\textsuperscript{c}               | 42.2%        | 14.8%   | 2.97 (2.07–4.27) | <0.001 | 2.20 (1.49–3.27) | <0.001 |
| All-cause death                        | 29.5%        | 7.8%    | 3.35 (2.18–5.15) | <0.001 | 1.86 (1.18–2.94) | 0.010  |
| Cardiac death                          | 17.5%        | 3.1%    | 4.97 (2.41–10.22) | <0.001 | 2.33 (1.10–4.96) | 0.028  |
| MI                                      | 7.7%         | 1.8%    | 4.21 (1.62–10.96) | 0.003  | 2.59 (0.94–7.15) | 0.066  |
| Cardiac death or MI                    | 22.0%        | 4.7%    | 4.47 (2.46–8.15) | <0.001 | 2.38 (1.26–4.48) | 0.010  |
| Any revascularization                  | 28.8%        | 11.0%   | 2.53 (1.64–3.90) | <0.001 | 2.31 (1.44–3.69) | <0.001 |

Values are mean ± standard deviation or n (%). \textsuperscript{a}n=623 for the unchanged DF group and 393 for the improved DF group. \textsuperscript{b}For comparison with unchanged group, adjusted for sex, hypertension, type of stent and follow-up ejection fraction. For comparison with the improved DF group, adjusted for age, sex, smoking, CKD, hypertension, previous cerebrovascular accident, multivessel disease, type of stent, number of inserted stent, total stent length and follow-up ejection fraction. \textsuperscript{c}Major adverse cardiac events included cardiac death, MI and repeat revascularization. Abbreviations as in Figures 1, 2.
Figure 4. Subgroup analysis. (A) Comparative unadjusted hazard ratios of cardiac death, MI, or revascularization for subgroups of the overall population between patients with worsened and unchanged DF. (B) Comparative unadjusted hazard ratios of cardiac death, MI, or revascularization for subgroups of the overall population between patients with worsened and improved DF. ACS, acute coronary syndrome; CI, confidence interval; CKD, chronic kidney disease; EF, ejection fraction; LAD, left anterior descending coronary artery; MACE, major adverse cardiac event. Other abbreviations as in Figure 1.
patients undergoing PCI in our study. Thus, echocardiography after PCI during follow-up seems to be underused, despite previous data showing that the use of echocardiography lowers the risk of death among patients with CAD.36

**Study Limitations**

First, this was a single-center observational study and thus our results might be subject to unrecognized confounding factors. Although we performed multivariate analysis and adjusted for several potential confounding factors, we could not correct for unmeasured or unobserved variables. A second limitation was that we did not utilize a uniform follow-up time interval between pre- and post-echocardiography. However, most patients (>90% of enrolled patients) underwent follow-up echocardiography >1 month after revascularization, which is considered a sufficient length of time for long-term recovery of DF after revascularization.38 Lastly, there might have been error in interpreting and classifying the DF grade despite the use of current generalized criteria. However, because we also measured LAV and performed tissue Doppler imaging in addition to other echocardiographic variables, such potential errors were expected to be minimal.

In conclusion, regardless of LV systolic function and other clinical factors, LV diastolic dysfunction change has prognostic implication in patients who have undergone PCI. Assessment of both systolic and diastolic dysfunction in CAD patients before and after revascularization should be considered in order to better predict long-term clinical outcomes and to determine the need for more intensive management.

**Disclosure**

None.

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**Supplementary Files**

Please find supplementary file(s):

http://dx.doi.org/10.1253/circj.CJ-19-0237