

Dyspnea Among Patients With Chronic Total Occlusions Undergoing Percutaneous Coronary Intervention Prevalence and Predictors of Improvement

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Background—Dyspnea is a common angina equivalent that adversely affects quality of life, but its prevalence in patients with chronic total occlusions (CTOs) and predictors of its improvement after CTO percutaneous coronary intervention (PCI) are unknown. We examined the prevalence of dyspnea and predictors of its improvement among patients selected for CTO PCI.

Methods and Results—In the OPEN CTO registry (Outcomes, Patient health status, and Efficiency in Chronic Total Occlusion) of 12 US experienced centers, 987 patients undergoing CTO PCI (procedure success 82%) were assessed for dyspnea with the Rose Dyspnea Scale at baseline and 1 month after CTO PCI. Rose Dyspnea Scale scores range from 0 to 4 with higher scores indicating more dyspnea with common activities. A total of 800 (81%) reported some dyspnea at baseline with a mean (\pm SD) Rose Dyspnea Scale of 2.8 ± 1.2 . Dyspnea improvement was defined as a ≥ 1 point decrease in Rose Dyspnea Scale from baseline to 1 month. Predictors of dyspnea improvement were examined with a modified Poisson regression model. Patients with dyspnea were more likely to be female, obese, smokers, and to have more comorbidities and angina. Among patients with baseline dyspnea, 70% reported less dyspnea at 1 month after CTO PCI. Successful CTO PCI was associated with more frequent dyspnea improvement than failure, even after adjustment for other clinical variables. Anemia, depression, and lung disease were associated with less dyspnea improvement after PCI.

Conclusions—Dyspnea is a common symptom among patients undergoing CTO PCI and improves significantly with successful PCI. Patients with other potentially noncardiac causes of dyspnea reported less dyspnea improvement after CTO PCI. (*Circ Cardiovasc Qual Outcomes*. 2017;10:e003665. DOI: 10.1161/CIRCOUTCOMES.117.003665.)

Key Words: anemia ■ dyspnea ■ lung diseases ■ percutaneous coronary intervention ■ quality of life

Dyspnea is one of the more challenging symptoms to assess and treat in patients with coronary artery disease (CAD) because it can arise from both cardiac ischemia and noncardiac causes.¹⁻³ Patients who present with dyspnea as their principal symptom of ischemic heart disease are less likely to be recognized as having CAD, less likely to receive evidence-based treatments, and more likely to experience poor in-hospital and long-term outcomes.^{1,4,5} Although the assessment of dyspnea as an angina equivalent is always challenging, this may be even more difficult in patients with chronic total occlusions (CTOs). CTOs are commonly encountered complex lesions⁶ and are often associated with typical angina symptoms; however, patients also may complain of a wide

range of less specific symptoms because they have adapted to chronic myocardial ischemia.⁷

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Successful percutaneous coronary intervention (PCI) of a CTO has been shown to improve angina and disease-specific quality of life.⁸ However, its effect on dyspnea remains poorly defined. Because the principal indication for CTO PCI in a patient with stable CAD is symptom relief, it is important to understand how CTO PCI impacts dyspnea so as to define one of the potential benefits of the procedure. To address this gap in knowledge, we leveraged a US multicenter registry of patients undergoing CTO PCI to examine the burden of dyspnea in

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WHAT IS KNOWN

- Successful chronic total occlusion percutaneous coronary intervention has been shown to improve angina and disease-specific quality of life.
- However, it is unknown whether successful chronic total occlusion percutaneous coronary intervention improves dyspnea.

WHAT THE STUDY ADDS

- Dyspnea is a common symptom among patients undergoing chronic total occlusion percutaneous coronary intervention and it occurs in 81% of patients.
- Successful chronic total occlusion percutaneous coronary intervention improves dyspnea significantly.

patients presenting for the procedure, the effect of PCI on dyspnea, and factors associated with dyspnea improvement after attempted CTO PCI.

Methods

Study Design and Population

The OPEN CTO (Outcomes, Patient health status, and Efficiency in Chronic Total Occlusion hybrid procedures) is a prospective, single-arm registry that enrolled patients with CTOs who underwent attempted CTO PCI at 12 US sites. The methods of OPEN CTO registry were published earlier.⁹ Briefly, eligible patients were >18 years of age and had symptoms suggestive of ischemic heart disease. Patients with acute myocardial infarction within 72 hours of enrollment, active gastrointestinal bleeding within 3 months, expected survival <1 year, or planned PCI procedure within 30 days of enrollment were excluded from the study. CTO PCI operators had to have performed at least 100 CTO PCI procedures for a minimum of 2 years before participating in OPEN CTO. Technical success of the procedure was defined as <50% residual stenosis and Thrombolysis In Myocardial Infarction 2 or 3 flow without any side branch occlusion. Procedural success was defined as technical success with no procedural complications (ie, perforation, pericardial effusion, tamponade). Complete revascularization was defined by the operators as successful treatment of all physiologically significant lesions. Each participating site obtained institutional research board approval, and all patients provided informed consent.

Assessment of Angina and Dyspnea

Angina and dyspnea were assessed at baseline and at 1 month after CTO PCI with the Seattle Angina Questionnaire (SAQ) and Rose Dyspnea Scale (RDS), respectively. The SAQ is a 19-item questionnaire with a 4-week recall period that measures 5 domains of health in patients with CAD: angina frequency (SAQ AF), angina stability, quality of life, physical limitation, and treatment satisfaction.^{10,11} Domain scores range from 0 to 100, with higher scores indicating fewer symptoms and better quality of life. The SAQ has undergone extensive reliability and validity testing^{11,12} and is associated with long-term survival, hospitalization for acute coronary syndromes, and healthcare use among patients with chronic CAD.¹³ The frequency of angina from the patients' perspective was captured with the SAQ AF domain, which has been shown to correlate closely with daily angina diaries.¹⁴ Congruent with prior work, angina was categorized as none (SAQ AF score=100) or any (SAQ AF score <100).¹⁵

The RDS is a 4-item questionnaire with a 1-month recall period that assesses patients' level of dyspnea with common activities (Table 1).¹⁶ For each patient, the highest limitation associated with

Table 1. Distribution of Patients Across Different Rose Dyspnea Scale Scores at Baseline

Dyspnea Score	Interpretation of Score	Percentage of Cohort
0	No dyspnea	19.0%
1	Dyspnea only when hurrying or walking up a hill	17.2%
2	Dyspnea when walking with people of similar age on level ground	14.4%
3	Dyspnea when walking at own pace on level ground	19.2%
4	Dyspnea when washing or dressing	30.3%

dyspnea was designated as the RDS score, such that RDS scores range from 0 to 4, with 0 indicating no dyspnea and 4 indicating dyspnea with ordinary activities of washing and dressing (similar to the New York Heart Association class scoring for heart failure). The RDS has been validated in patients with CAD and shown to be associated with quality of life, rehospitalization, and long-term survival in patients with CAD.⁵ Dyspnea improvement was defined as a ≥ 1 point decrease in RDS from baseline to 1 month.

Statistical Methods

Demographic and clinical characteristics were compared between patients who reported any dyspnea versus no dyspnea at baseline using independent *t* tests for continuous variables and χ^2 tests for categorical variables. To explore the effect of successful CTO PCI on dyspnea improvement, we first examined the change in RDS from baseline to 1 month using an ordinal hierarchical logistic regression model (with site as a random effect) with procedural success as the independent variable. As an exploratory analysis, we tested the interaction of procedure success \times baseline angina (yes/no) in this model to examine whether the presence or absence of concurrent angina at baseline significantly modified the effect of successful PCI on dyspnea. Next, we constructed a modified Poisson regression model to examine factors associated with dyspnea improvement at 1 month after CTO PCI. As dyspnea improvement commonly occurred, this method allowed us to estimate relative risks directly and avoid overestimating the effect size.^{17,18} To take into account the different levels of change in RDS score at 1 month, we additionally performed (as a sensitivity analysis) multivariable linear models with the outcomes of RDS score at 1 month (on a continuous scale). Variables included in these models were selected a priori based on literature review and clinical judgment (balanced against concerns of overfitting) and included the following: age, sex, body mass index, smoking status, baseline RDS scores, baseline SAQ AF scores, 8-item Patient Health Questionnaire scores (higher scores=more depressive symptoms, scores ≥ 10 indicate a high likelihood of clinical depression),¹⁹ diabetes mellitus, prior myocardial infarction, chronic heart failure, chronic lung disease (including chronic obstructive pulmonary disease, obstructive sleep apnea, and emphysema), left ventricular ejection fraction, hemoglobin, procedural success, and completeness of revascularization. All baseline data elements (past medical history, patient demographics, and other baseline variables) were complete for the 987 patients in the analytic cohort. As a sensitivity analysis, we used multiple imputations to estimate 1-month RDS scores on patients who were alive but missing data. The results were consistent with the primary analysis, and so only the primary results are shown. All statistical analyses were performed with SAS, version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Patient Characteristics

Of 1000 patients enrolled in OPEN CTO, 987 patients (99%) had RDS scores at baseline, which comprised the analytic

cohort (Figure 1). Mean age of patients was 65 years, 80% were men, and 90% were white. Cardiac and noncardiac comorbidities were common, with prior myocardial infarction in 48%, prior PCI in 66%, prior bypass graft surgery in 36%, diabetes mellitus in 41%, and chronic lung disease in 14%. The majority of patients presenting for CTO PCI reported some degree of dyspnea at baseline (800; 81%) with a mean (\pm SD) RDS score of 2.8 ± 1.2 , indicating that the average patient had shortness of breath when walking at his own pace on level ground (Table 1). Most patients with dyspnea also reported angina, with only 190 patients (19%) reported only dyspnea as their ischemic symptom before PCI. Compared with patients who reported no limitations because of dyspnea, patients with dyspnea were more likely to be female, current smokers; have a diagnosis of heart failure, chronic lung disease, or diabetes mellitus; have higher body mass indices; and report more depressive symptoms (Table 2). Similar trends were observed among patients with increasing burdens of dyspnea (Table I in the [Data Supplement](#)).

Change in Dyspnea After CTO PCI

Among the 800 patients who reported dyspnea at baseline, 730 (91%) had 1-month RDS scores available. Among these patients, 509 (70%) had improvement in their dyspnea after CTO PCI, 163 (22%) had no change in dyspnea, and 58 (8%) reported worse dyspnea (Table II in the [Data Supplement](#)). On average, RDS scores improved by 1.4 ± 1.5 points from baseline to 1 month after CTO PCI.

Although dyspnea improved in the majority of patients with baseline dyspnea regardless of the success of the PCI, patients with a successful CTO PCI were more likely to have dyspnea improvement than those with failed PCI (Figure 2; $P<0.001$). For example, 42% of patients with successful CTO PCI reported no dyspnea at 1 month compared with 25% of patients with failed CTO PCI. In exploratory analysis, there was no significant difference in dyspnea improvement by success of PCI between those with and without concurrent angina ($n=458$

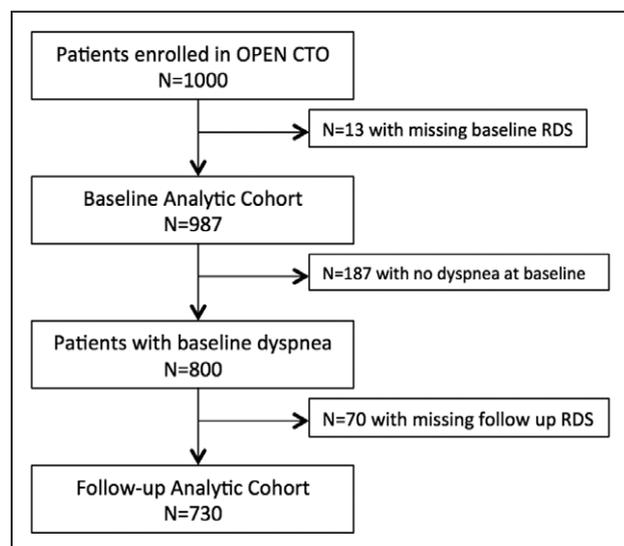


Figure 1. Flow chart of analytic population. OPEN CTO indicates Outcomes, Patient health status, and Efficiency in Chronic Total Occlusion; and RDS, Rose Dyspnea Scale.

Table 2. Demographic and Clinical Characteristics of Patients With or Without Dyspnea at Baseline

	Any Dyspnea n=800	No Dyspnea n=187	P Value
Age, y	65.3 \pm 10.3	65.6 \pm 10.2	0.665
Male	627 (78.4%)	166 (88.8%)	0.001
White race	718 (89.8%)	172 (92.0%)	0.356
Body mass index, kg/m ²	30.8 \pm 6.1	28.9 \pm 5.4	<0.001
Hypertension	695 (86.9%)	151 (80.7%)	0.031
Prior myocardial infarction	391 (48.9%)	83 (44.4%)	0.268
Prior coronary stenting	517 (64.7%)	131 (70.1%)	0.165
Prior coronary bypass graft surgery	299 (37.4%)	60 (32.1%)	0.175
Chronic heart failure	199 (24.9%)	28 (15.0%)	0.003
Left ventricular dysfunction	144 (19.5%)	27 (16.5%)	0.367
Chronic lung disease	130 (16.3%)	12 (6.4%)	<0.001
Sleep apnea	151 (18.9%)	22 (11.8%)	0.021
Current smoker	115 (14.5%)	15 (8.2%)	0.022
Diabetes mellitus	349 (43.6%)	55 (29.4)	<0.001
On ≥ 2 antianginal medications	138 (17.3%)	18 (9.6%)	0.010
SAQ angina frequency	68.0 \pm 26.7	82.1 \pm 24.3	<0.001
SAQ physical limitations	60.0 \pm 25.2	87.0 \pm 17.8	<0.001
SAQ quality of life	44.6 \pm 25.8	68.3 \pm 24.6	<0.001
PHQ-8 score	7.2 \pm 5.7	3.1 \pm 3.8	<0.001
Hemoglobin, g/dL	13.5 \pm 1.7	13.9 \pm 1.5	0.015
Serum creatinine, mg/dL	1.2 \pm 1.0	1.2 \pm 1.1	0.641
Complete revascularization	607 (76.3%)	140 (74.9%)	0.688
CTO in LAD territory	153 (19.1%)	53 (28.3%)	0.005
Antianginal medications			
β -Blockers	683 (85.4%)	152 (81.3%)	0.162
Calcium channel blockers	198 (24.8%)	37 (19.8%)	0.151
Long acting nitrates	350 (43.8%)	58 (31.0%)	0.001
Ranolazine	127 (15.9%)	18 (9.6%)	0.029
Ticagrelor use			
At baseline	1.6%	2.2%	0.544
At discharge	2.5%	4.3%	0.187

CTO indicates chronic total occlusion; LAD, left anterior descending artery; PHQ-8, Personal Health Questionnaire Depression Scale; and SAQ, Seattle Angina Questionnaire.

and 150, respectively; Figure I in the [Data Supplement](#)). The interaction between the procedure success and the presence of angina at baseline was not significant ($P=0.12$), indicating that concurrent angina before CTO PCI did not modulate the effect of a successful procedure on dyspnea.

Factors Associated With Dyspnea Improvement

In the modified Poisson regression model that included demographic and clinical characteristics (including severity

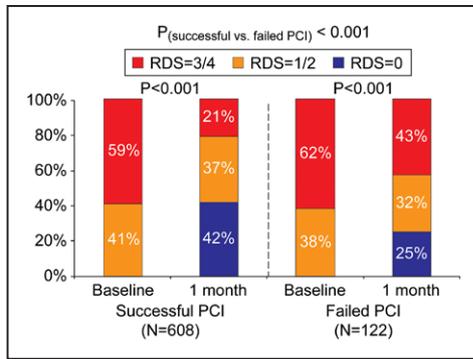


Figure 2. Dyspnea at baseline and 1 mo after chronic total occlusion (CTO) percutaneous coronary intervention (PCI) among patients with dyspnea at baseline, stratified by success of CTO PCI. The degree of improvement in dyspnea after successful vs failed PCI is compared using an ordinal logistic regression model. RDS indicates Rose Dyspnea Scale.

of angina), successful CTO PCI was associated with 28% higher rates of dyspnea improvement (relative risk, 1.28; 95% confidence interval, 1.11–1.49; $P < 0.001$; Table 3). Lower hemoglobin levels at baseline, greater depressive symptoms, and lung disease were associated with a lower likelihood of dyspnea improvement after CTO PCI. Patients who reported worse dyspnea at baseline were more likely to have improvement in dyspnea after CTO PCI. When taken into account the different level of change in RDS at 1 month, by modeling 1-month RDS on a continuous scale (instead of dyspnea improvement) using multivariable linear model, we report comparable results to our previous model with the exception that complete revascularization was associated with less dyspnea at 1 month (Table III in the [Data Supplement](#)).

Discussion

In a large, multicenter study of patients with chronic CAD undergoing CTO PCI, we found that dyspnea was common, with the average patient reporting shortness of breath when walking on level ground with similarly aged people. However, 70% of patients with dyspnea at baseline reported less dyspnea by 1 month after CTO PCI. Dyspnea improvement

Table 3. Factors Significantly Associated With Improvement in Dyspnea at 1-Month Post-CTO PCI

	Relative Risk (95% CI)	P Value
Baseline dyspnea score (per +1 point)	1.12 (1.08–1.16)	<0.001
Procedural success*	1.28 (1.11–1.49)	<0.001
PHQ-8 (per +5 points)	0.74 (0.64–0.86)	<0.001
Chronic lung disease	1.12 (1.08–1.16)	<0.001
Hemoglobin (per +1 mg/dL)	1.28 (1.11–1.49)	<0.001

Other variables included in the model but were not statistically significant: age, sex, body mass index, current smoking, baseline Seattle Angina Questionnaire Angina Frequency domain score, diabetes mellitus, chronic heart failure, prior myocardial infarction, ejection fraction, and complete revascularization. CI indicates confidence interval; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; and PHQ-8, Personal Health Questionnaire Depression Scale.

*Defined as technical success without major adverse cardiac event.

was more common after successful CTO PCI in patients with a greater burden of dyspnea at baseline and in those without other comorbidities that themselves are associated with dyspnea (eg, obesity, lung disease). Taken together, these findings suggest that dyspnea that arises from ischemic heart disease is often improved with CTO PCI.

Prior Studies

Although several studies have shown that dyspnea can be an atypical symptom of ischemia, few studies have examined the effects of anti-ischemic interventions (medications or revascularization) on dyspnea.^{7,20,21} One of the largest studies to examine the effect of revascularization on dyspnea was the FREEDOM trial (Future REvascularization Evaluation in patients with Diabetes mellitus: optimal management of Multivessel disease), which randomized patients with diabetes mellitus and multivessel CAD to bypass graft surgery or multivessel PCI with drug-eluting stents.²⁰ Interestingly, in this study of patients with complex CAD, the burden of dyspnea was lower at baseline than in our study, with only 70% reporting any dyspnea and an average RDS score of 1.6. At 1 month after revascularization with PCI, 67% of patients were free of dyspnea, a level of improvement comparable to that observed in our study. In a study of 147 patients who underwent CTO PCI who were propensity-score matched with 1616 patients who underwent non-CTO PCI, dyspnea improvement was also similar between groups.⁷ Our current study extends on these prior studies by demonstrating the substantial burden of dyspnea in patients who present for CTO PCI, documenting the improvement of dyspnea in the majority of patients after CTO PCI (similar to non-CTO PCI), and also exploring predictors of dyspnea improvement.

Clinical Implications

We think that our findings highlight the importance of ensuring dyspnea is related to ischemia to maximize the benefits of CTO PCI, particularly in the absence of typical angina. It is well established that dyspnea alone can be a sign of myocardial ischemia and is the most common ischemic symptom reported after chest pain.^{4,22} However, dyspnea is a nonspecific symptom and can be challenging to interpret with respect to its relationship with ischemia and its predicted response to anti-ischemic treatment. Although prior studies have shown that ≈ 1 in 3 patients who present for ischemic evaluation with dyspnea alone had ischemia on stress testing, this rate is lower than that observed in patients who present with typical angina²³ or a combination of chest pain and dyspnea, which had the highest specificity for ischemia.²⁴ As the primary goal of PCI in stable CAD is symptom relief, understanding whether a patient's dyspnea is related to ischemia is key to knowing whether or not the patient will benefit from revascularization. This is particularly important in procedures with higher risk and healthcare use, such as CTO PCI, as compared with noncomplex PCI. As such, a careful investigation is recommended before CTO PCI in patients with only dyspnea as their symptom of ischemia, especially when other comorbidities are present that may be contributing to dyspnea, such as obesity, anemia, heart failure, and chronic lung disease.

Limitations

Our study findings should be interpreted in light of the following potential limitations. First, this is a single-arm registry, and all patients underwent a revascularization attempt. As such, the observed effects of CTO PCI on dyspnea may also be related, in part, to a placebo effect. However, because CTO PCI was not always successful, we were able to use patients with failed procedure as a reference group, albeit an unblinded one, to document greater improvement with a successful CTO PCI. Second, the RDS is a rather coarse scale for measuring dyspnea and may not have captured smaller changes. However, it is the only dyspnea scale that has been validated in patients with CAD⁵ and was able to detect changes in the majority of patients. Finally, our data only show short-term improvement in dyspnea after CTO PCI. It is not known whether these results are durable over time, which is also important to demonstrate as prior analysis in the FREEDOM study did show a small, gradual increase in dyspnea over time in the PCI arm.²⁰

Conclusions

We found that dyspnea was exceedingly common among patients selected for CTO PCI, reported by 81% of patients before PCI. Among patients with dyspnea before PCI, dyspnea improved in 70% of patients by 1 month—rates that were higher after successful CTO PCI. Anemia, depression, and lung disease were associated with less dyspnea improvement after CTO PCI. Further studies are needed to understand how to better select patients with dyspnea for CTO PCI to maximize health status improvement after PCI, particularly among patients who report dyspnea without concurrent chest pain.

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Disclosures

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References

- Abidov A, Rozanski A, Hachamovitch R, Hayes SW, Aboul-Enein F, Cohen I, Friedman JD, Germano G, Berman DS. Prognostic significance of dyspnea in patients referred for cardiac stress testing. *N Engl J Med*. 2005;353:1889–1898. doi: 10.1056/NEJMoa042741.
- Cook DG, Shaper AG. Breathlessness, lung function and the risk of heart attack. *Eur Heart J*. 1988;9:1215–1222.
- Wiklund I, Herlitz J, Hjalmarson A. Quality of life five years after myocardial infarction. *Eur Heart J*. 1989;10:464–472.
- Brieger D, Eagle KA, Goodman SG, Steg PG, Budaj A, White K, Montalescot G; GRACE Investigators. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. *Chest*. 2004;126:461–469. doi: 10.1378/chest.126.2.461.
- Arnold SV, Spertus JA, Jones PG, Xiao L, Cohen DJ. The impact of dyspnea on health-related quality of life in patients with coronary artery disease: results from the PREMIER registry. *Am Heart J*. 2009;157:1042–1049.e1. doi: 10.1016/j.ahj.2009.03.021.
- Christofferson RD, Lehmann KG, Martin GV, Every N, Caldwell JH, Kapadia SR. Effect of chronic total coronary occlusion on treatment strategy. *Am J Cardiol*. 2005;95:1088–1091. doi: 10.1016/j.amjcard.2004.12.065.
- Safley DM, Grantham JA, Hatch J, Jones PG, Spertus JA. Quality of life benefits of percutaneous coronary intervention for chronic occlusions. *Catheter Cardiovasc Interv*. 2014;84:629–634. doi: 10.1002/ccd.25303.
- Grantham JA, Jones PG, Cannon L, Spertus JA. Quantifying the early health status benefits of successful chronic total occlusion recanalization: results from the FlowCardia's Approach to Chronic Total Occlusion Recanalization (FACTOR) Trial. *Circ Cardiovasc Qual Outcomes*. 2010;3:284–290. doi: 10.1161/CIRCOUTCOMES.108.825760.
- Sapontis J, Marso SP, Cohen DJ, Lombardi W, Karpaliotis D, Moses J, Nicholson WJ, Pershad A, Wyman RM, Spaedy A, Cook S, Doshi P, Federici R, Thompson CR, Nugent K, Gosch K, Spertus JA, Grantham JA; OPEN CTO Study Group. The Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures registry: rationale and design. *Coron Artery Dis*. 2017;28:110–119. doi: 10.1097/MCA.0000000000000439.
- Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Fihn SD. Monitoring the quality of life in patients with coronary artery disease. *Am J Cardiol*. 1994;74:1240–1244.
- Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonnell M, Fihn SD. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. *J Am Coll Cardiol*. 1995;25:333–341.
- Babaliaros V, Devireddy C, Lerakis S, Leonardi R, Iturra SA, Mavromatis K, Leshnowar BG, Guyton RA, Kanitkar M, Keegan P, Simone A, Stewart JP, Ghasemzadeh N, Block P, Thourani VH. Comparison of transfemoral transcatheter aortic valve replacement performed in the catheterization laboratory (minimalist approach) versus hybrid operating room (standard approach): outcomes and cost analysis. *JACC Cardiovasc Interv*. 2014;7:898–904. doi: 10.1016/j.jcin.2014.04.005.
- Arnold SV, Morrow DA, Lei Y, Cohen DJ, Mahoney EM, Braunwald E, Chan PS. Economic impact of angina after an acute coronary syndrome: insights from the MERLIN-TIMI 36 trial. *Circ Cardiovasc Qual Outcomes*. 2009;2:344–353. doi: 10.1161/CIRCOUTCOMES.108.829523.
- Arnold SV, Kosiborod M, Li Y, Jones PG, Yue P, Belardinelli L, Spertus JA. Comparison of the Seattle Angina Questionnaire with daily angina diary in the TERISA clinical trial. *Circ Cardiovasc Qual Outcomes*. 2014;7:844–850. doi: 10.1161/CIRCOUTCOMES.113.000752.
- Spertus JA, Salisbury AC, Jones PG, Conway DG, Thompson RC. Predictors of quality-of-life benefit after percutaneous coronary intervention. *Circulation*. 2004;110:3789–3794. doi: 10.1161/01.CIR.0000150392.70749.C7.
- Rose GA, Blackburn H. Cardiovascular survey methods. *Monogr Ser World Health Organ*. 1968;56:1–188.
- Greenland S. Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. *Am J Epidemiol*. 2004;160:301–305. doi: 10.1093/aje/kwh221.
- Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159:702–706.
- McManus D, Pipkin SS, Whooley MA. Screening for depression in patients with coronary heart disease (data from the Heart and Soul Study). *Am J Cardiol*. 2005;96:1076–1081. doi: 10.1016/j.amjcard.2005.06.037.
- Abdallah MS, Wang K, Magnuson EA, Spertus JA, Farkouh ME, Fuster V, Cohen DJ; FREEDOM Trial Investigators. Quality of life after PCI vs CABG among patients with diabetes and multivessel coronary artery disease: a randomized clinical trial. *JAMA*. 2013;310:1581–1590. doi: 10.1001/jama.2013.279208.

21. Arnold SV, Morrow DA, Wang K, Lei Y, Mahoney EM, Scirica BM, Braunwald E, Cohen DJ; MERLIN-TIMI 36 Investigators. Effects of ranolazine on disease-specific health status and quality of life among patients with acute coronary syndromes: results from the MERLIN-TIMI 36 randomized trial. *Circ Cardiovasc Qual Outcomes*. 2008;1:107–115. doi: 10.1161/CIRCOUTCOMES.108.798009.
22. Phibbs B, Holmes RW, Lowe CR. Transient myocardial ischemia: the significance of dyspnea. *Am J Med Sci*. 1968;256:210–221.
23. Argulian E, Agarwal V, Bangalore S, Chatterjee S, Makani H, Rozanski A, Chaudhry FA. Meta-analysis of prognostic implications of dyspnea versus chest pain in patients referred for stress testing. *Am J Cardiol*. 2014;113:559–564. doi: 10.1016/j.amjcard.2013.10.019.
24. Bergeron S, Ommen SR, Bailey KR, Oh JK, McCully RB, Pellikka PA. Exercise echocardiographic findings and outcome of patients referred for evaluation of dyspnea. *J Am Coll Cardiol*. 2004;43:2242–2246. doi: 10.1016/j.jacc.2004.03.033.

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Supplemental material

Supplementary Table 1. Comparison of patients' characteristics in different Rose Dyspnea Scale score groups

	Rose Dyspnea Score at Baseline					P-value
	0 n=186	1 n=191	2 n=179	3 n=201	4 n=225	
Age (y)	65.6 ± 10.2	65.9 ± 10.6	65.1 ± 10.6	65.4 ± 10.0	64.9 ± 10.2	0.36
Male	166 (88.8%)	145 (85.3%)	116 (81.7%)	152 (80.4%)	214 (71.6%)	<0.001
White race	172 (92.0%)	151 (88.8%)	131 (92.3%)	168 (88.9%)	268 (89.6%)	0.47
Body mass index (kg/m ²)	28.9 ± 5.4	29.2 ± 5.2	30.8 ± 5.3	30.4 ± 6.3	32.0 ± 6.6	< 0.001
Prior myocardial infarction	83 (44.4%)	72 (42.4%)	64 (45.1%)	95 (50.3%)	160 (53.5%)	0.01
Prior coronary stenting	131 (70.1%)	98 (57.6%)	101 (71.1%)	119 (63.3%)	199 (66.6%)	0.92
Prior coronary bypass graft surgery	60 (32.1%)	52 (30.6%)	56 (39.4%)	79 (41.8%)	112 (37.5%)	0.06
Chronic heart failure	28 (15.0%)	33 (19.4%)	31 (21.8%)	49 (25.9%)	86 (28.8%)	< 0.001
Moderate/Severe left ventricular dysfunction	27 (16.5%)	23 (14.4%)	21 (15.9%)	35 (20.7%)	65 (23.5%)	0.01
Chronic lung disease	12 (6.4%)	19 (11.2%)	15 (10.6%)	27 (14.3%)	69 (23.1%)	< 0.001
Sleep apnea	22 (11.8%)	25 (14.7%)	26 (18.3%)	28 (14.8%)	72 (24.1%)	< 0.001
Current smoker	15 (8.2%)	17 (10.2%)	19 (13.6%)	23 (12.2%)	56 (18.9%)	< 0.001
Diabetes mellitus	55 (29.4%)	56 (32.9%)	66 (46.5%)	82 (43.4%)	145 (48.5%)	< 0.001
On ≥2 antianginal medications on arrival	18 (9.6%)	15 (8.8%)	27 (19.0%)	47 (24.9%)	49 (16.4%)	0.001
SAQ Angina Frequency	82.1 ± 24.3	80.2 ± 21.9	69.2 ± 25.6	64.9 ± 26.0	62.4 ± 27.9	< 0.001
SAQ Physical Limitations	87.0 ± 17.8	75.7 ± 18.9	63.3 ± 19.9	62.5 ± 21.7	46.9 ± 26.6	< 0.001
SAQ Quality of Life	68.3 ± 24.6	57.2 ± 24.9	47.8 ± 24.5	42.9 ± 25.0	37.0 ± 24.6	< 0.001
PHQ-8 Score	3.1 ± 3.8	4.5 ± 4.9	6.2 ± 5.3	6.7 ± 5.1	9.4 ± 5.9	< 0.001
Hemoglobin (g/dL)	13.9 ± 1.5	13.7 ± 1.5	13.8 ± 1.5	13.6 ± 1.8	13.3 ± 1.8	0.001

Supplementary Table 2. Rose Dyspnea Scale scores at 1 month compared to baseline.						
	1 month					
Baseline	0	1	2	3	4	Total
1	85	50	7	8	7	157
2	56	41	17	13	8	135
3	75	41	26	17	15	174
4	72	57	27	29	79	264
Total	288	189	77	67	109	730

Dark grey shading represent patients with worse dyspnea at follow up compared to baseline while the light grey represent patients with improved dyspnea.

Supplementary Table 3. Factors associated with level of dyspnea at 1 month after CTO PCI

	Estimate (95% CI)¹	P-value
Baseline Dyspnea score (per +1 point)	0.35 (0.29 to 0.42)	<0.001
Procedural success²	-0.32 (-0.57 to -0.07)	<0.001
Complete revascularization	-0.35 (-0.56 to -0.14)	<0.001
PHQ-8 depression score (per +5 points)	0.11 (0.02 to 0.19)	0.009
Chronic lung disease	0.44 (0.21 to 0.68)	<0.001
Hemoglobin (per +1 mg/dL)	-0.11 (-0.16 to -0.05)	<0.001

Other variables included in the model but were not significantly associated with 1 month RDS: age, sex, current smoking, baseline Seattle Angina Questionnaire Angina Frequency domain score, diabetes mellitus, prior myocardial infarction, ejection fraction, body mass index, and congestive heart failure.

¹Estimate is the difference in 1-month RDS score that is independently associated with that factor (i.e., patients with procedural success are estimated to have 0.32 lower RDS at 1 month compared with patients without procedural success)

²Defined as technical success without major adverse cardiac event

Supplementary Figure 1. Dyspnea at baseline and 1-month after CTO PCI among patients with dyspnea at baseline, stratified by success of PCI. A. Patients with

dyspnea and no angina at baseline. B. Patients with both dyspnea and angina at baseline.

The degree of improvement in dyspnea after successful vs. failed PCI did not

significantly differ according to the presence vs. absence of concurrent angina at baseline

(interaction of procedural success*baseline angina was not significant; p=0.22).

A.

B.

