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Exercise-based cardiac rehabilitation vs. percutaneous coronary intervention for chronic coronary syndrome: impact on morbidity and mortality.

Exercise-based cardiac rehabilitation versus percutaneous coronary intervention for chronic coronary syndrome: Impact on morbidity and mortality

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Funding/support

No funding to declare.

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Total wordcount 2728

Abstract

Background. Accumulating evidence questions the clinical value of percutaneous coronary intervention (PCI) for patients with chronic coronary syndrome (CCS).

Aim. To compare the impact of exercise-based cardiac rehabilitation (CR) *versus* PCI in patients with CCS on 18-month mortality and morbidity, and evaluate the effects of combining PCI with exercise-based CR.

Methods. A retrospective cohort study was conducted in March 2021. An online, real-world dataset of CCS patients was acquired, utilising TriNetX, a global federated health research network. CCS patients who received PCI were first compared with patients who were prescribed exercise-based CR. Second, we compared patients who received both CR+PCI *versus* CR alone. For both comparisons, patients were propensity score matched by age, sex, race, co-morbidities, medications, and procedures. We ascertained 18-month incidence of all-cause mortality, rehospitalisation, and cardiovascular comorbidity (stroke, acute myocardial infarction, and new-onset heart failure).

Results. The initial cohort consisted of 18,383 CCS patients. Following propensity score matching, exercise-based CR was associated with significantly lower odds of all-cause mortality (0.37 (95%CI: 0.29-0.47)), rehospitalisation (0.29 (95%CI: 0.27-0.32)), and cardiovascular morbidities, compared to PCI. Subsequently, patients that received both CR+PCI did not have significantly different odds for all-cause mortality (1.00 (95%CI: 0.63-1.60)), rehospitalisation (1.00 (95%CI: 0.82-1.23)), acute myocardial infarction (1.11 (95%CI: 0.68-1.81)), and stroke (0.71 (95%CI: 0.39-1.31)), compared to CR only.

Conclusions. Compared to PCI, exercise-based CR is associated with lower odds of 18-month all-cause mortality, rehospitalisation, and cardiovascular morbidity in CCS patients, while combining PCI to exercise-based CR did not improve the associated benefits of exercise-based CR.

Word count: 249

Key words
Chronic Coronary Syndrome; Angina; Cardiac Rehabilitation; Exercise; Percutaneous Coronary Intervention; Secondary Prevention

Introduction

Coronary artery disease is highly common in the Western population[1], with chronic coronary syndrome (CCS) being a major public health concern [2]. Patients with CCS receive optimal medical treatment, usually followed by Percutaneous Coronary Intervention (PCI) to target the stenotic coronary artery. Accumulating evidence questions the clinical value of PCI for reducing mortality and cardiovascular events in patients with CCS [3-7], especially in the short term (1-2 years following PCI). This highlights the need to explore alternative treatment strategies for patients with CCS.

Physical inactivity plays a crucial role in the development and progression of cardiovascular disease, including CCS [8]. Previous work revealed that exercise-based cardiac rehabilitation (CR) increases exercise capacity, improves quality of life, and reduces morbidity and mortality in patients with cardiovascular disease [9, 10]. Such benefits may also apply to patients with CCS. Indeed, exercise-based CR following PCI is associated with improved event-free survival, and lower mortality compared to PCI alone [11]. Previous RCTs in patients with CCS suggested that exercise-based CR is associated with improved coronary collateral flow index, improved exercise capacity, and superior 1-year survival rates compared to PCI [12, 13]. In line with these findings, a recent Cochrane systematic review found a small increase in exercise capacity following CR, as compared to standard treatment, though it was highlighted that further research was needed to determine the impact on mortality and morbidity [14]. Nevertheless, exercise-based CR is currently not part of routine care for patients with CCS, either as a first choice option (i.e. instead of PCI) or in addition to PCI [15, 16].

The first aim of this study was to examine the association between exercise-based CR and 18-month all-cause mortality, rehospitalisation, and cardiovascular morbidity *versus* PCI alone in patients diagnosed with CCS. Second, we assessed the added value of combining exercise-based CR with PCI, compared to exercise-based CR alone, on these clinical outcome parameters. We hypothesised that exercise-based CR is associated with lower all-cause mortality, rehospitalisation, and cardiovascular morbidity in patients with CCS, with no added value of PCI for exercise-based CR.

Methods

Study Design and Participants

A retrospective observational study was conducted using anonymized data within TriNetX, a global federated health research network with access to electronical medical records (EMRs) from participating healthcare organisations including academic medical centres, specialty physician practices, and community hospitals, predominantly in the United States [17]. CCS was identified from International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM, ICD-10-CM) codes in patient EMRs: I20 (Angina pectoris), excluding I20.0 (Unstable angina pectoris). Cardiac rehabilitation was identified from ICD-10-CM codes Z71.82 (Exercise counselling), Healthcare Common Procedure Coding System (HCPCS) codes G0422 (Intensive CR; with or without continuous ECG), S9472 (CR program, non-physician provider, per diem), or Current Procedural Terminology (CPT) codes 93797/93798 (Physician or other qualified healthcare professional services for outpatient CR with/without ECG) and 1013171 (Physician or other qualified health care professional services for outpatient CR). PCI was identified from ICD-10-CM codes 92928 (Percutaneous transcatheter placement of intracoronary stent(s), with coronary angioplasty when performed; single major coronary artery or branch) and 92941 (Percutaneous transluminal revascularization of acute total/subtotal occlusion during acute myocardial infarction, coronary artery, or coronary artery bypass graft, any combination of intracoronary stent, atherectomy, angioplasty, including aspiration thrombectomy when performed, single vessel) and HCPCS codes C1725 (Catheter, transluminal angioplasty, non-laser (may include guidance, infusion/perfusion capability) and C600 (Percutaneous transcatheter placement of drug eluting intracoronary stent(s), with coronary angioplasty when performed; single major coronary artery or branch). This study is reported as per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[18] As a federated network, research studies using the TriNetX research network do not require ethical approvals as no patient identifiable identification is received.

Data Collection

The TriNetX network was searched on 29th March 2021 and an online real-world dataset of patients with CCS was acquired [17]. All cohorts were aged ≥18 years with exercise-based CR and/or PCI recorded in EMRs within 6-months of an CCS diagnosis. For both the exercise-based CR and PCI cohorts, patients with CCS were identified in EMRs from at least 18-months prior to the search date to ensure a minimum follow-up of 18-months from CCS diagnosis or 12-months from CR/PCI. At the time of the search, 45 participating healthcare organisations had data available for patients who met the study inclusion criteria.

Statistical Analysis

All statistical analyses were completed on the TriNetX online platform. Baseline characteristics were compared using chi-squared tests for categorical variables and independent-sample t-tests for continuous variables. Current exercise-based CR provision is typically reserved for cardiovascular patients following an acute coronary syndrome, heart failure, or those undergoing a revascularisation procedure (coronary artery bypass graft or planned percutaneous coronary intervention). Thus, propensity score matching (PSM) was used to control for these differences in the two cohorts. The exercise-based CR and PCI cohorts were 1:1 PSM using logistic regression for age at CCS diagnosis, sex, race, hypertensive diseases, ischaemic heart diseases, cerebrovascular diseases, diabetes mellitus, chronic kidney disease, HF, cardiovascular procedures (e.g. cardiography, echocardiography, cardiac catheterisation, cardiac devices, electrophysiological procedures), and cardiovascular medications (e.g. beta-blockers, antiarrhythmics, diuretics, antilipemic agents, antianginals, calcium channel blockers, ACE inhibitors). These variables were chosen because they are established cardiovascular disease risk factors and/or were significantly different between the two cohorts. The TriNetX platform uses 'greedy nearest-neighbour matching' with a calliper of 0.1 pooled standard deviations. Following PSM, logistic regressions produced odds ratios with 95% confidence intervals (CIs) for 18-month incidence of all-cause mortality, rehospitalisation, stroke, AMI, and new-onset HF. These outcomes were first compared between exercise-based CR and PCI and second between exercise-based CR and CR+PCI. Statistical significance was set at $P<0.05$.

Results

The initial cohort consisted of 18,383 patients with CCS with at least 18-months follow-up. Of this study population, 12,676 patients had a history of PCI treatment alone, 4,368 patients received exercise-based CR within 6-months following CCS diagnosis, and 1,339 patients had a history of CR+PCI following CCS diagnosis (Table 1). The cohort of CCS patients that received exercise-based CR only were younger, had a lower proportion of white ethnicity, a higher proportion of unknown ethnicity, and had higher proportions of health conditions, cardiovascular procedures, and medications than the PCI group (Table 1). Following 1:1 PSM, although some variables were significantly different between the cohorts (white and Asian ethnicity and cardiovascular medications), the cohorts were considered well matched (n=4,357, Table 1). For our second research question, the cohort that underwent CR+PCI had more people identified as white ethnicity, less people identified as unknown ethnicity, less patients with HF and cerebrovascular diseases, and more patients with ischemic heart disease, cardiovascular procedures and medications compared to the CR group. Following 1:1 PSM, the two groups of n=1,337 showed no statistically different characteristics (Table 2).

CR versus PCI: mortality, rehospitalisation and morbidity

After propensity score matching, 18-month mortality was 2.0% in CCS patients receiving CR (*n*=86, of 4,346 patients) and 5.2% in patients undergoing PCI (*n*=225, of 4,327 patients, $p<0.0001$), resulting in 63% lower odds of all-cause mortality in the CR cohort (OR 0.37, 95%CI: 0.29-0.47) compared to PCI.

Rehospitalisation rate was significantly lower in CCS patients receiving CR (16.5%, *n*=717 of 4,357 patients) compared to PCI (40.2%, *n*=1,751 of 4,357 patients, *p*<0.0001). Logistic regression models showed 71% lower odds of rehospitalisation (OR 0.29, 95%CI: 0.27-0.32) after CR compared to PCI. The CR cohort also showed significantly lower odds for morbidity compared to PCI only: AMI (OR 0.72, 95%CI: 0.57-0.90), and stroke (OR 0.58, 95%CI: 0.43-0.79). CR was not significantly associated with lower odds of new onset HF (OR 0.88, 95%CI: 0.74-1.05) (Figure 1).

CR + PCI versus CR: mortality, rehospitalisation and morbidity

18-month mortality was 2.7% in the CR+PCI cohort (*n*=36, of 1,334 patients) and 2.7% in the CR cohort (*n*=36, of 1,332 patients, *p*=0.995). There was no significant difference in odds for all-cause mortality between CR+PCI and CR alone (OR 1.00, 95%CI: 0.63-1.60). The CR+PCI cohort revealed no significant differences in 18-month rehospitalisation (16.8%, *n*=224 of 1,337 patients) compared to CR alone (16.8%, *n*=224 of 1,337 patients). Logistic regression models showed no differences in odds for rehospitalisation between the two groups (OR 1.00, 95%CI: 0.82-1.23). The CR+PCI cohort showed no significant differences for 18-month occurrence of AMI (OR 1.11, 95%CI: 0.68-1.81), and stroke (OR 0.71, 95%CI: 0.39-1.31), compared to CR alone. The CR cohort showed significantly higher odds for new onset of HF compared to CR+PCI (OR 1.61, 95%CI: 1.15-2.25) (Figure 2).

Discussion

The aim of this study was to evaluate the potential role of exercise-based CR in patients with CCS, either compared to PCI alone or in addition to PCI. First, we found that prescription of exercise-based CR in CCS patients, compared to traditional referral for PCI, was associated with significantly lower odds for all-cause mortality, rehospitalisation and cardiovascular morbidity at 18 months from diagnosis. Second, when CCS patients receive PCI in addition to exercise-based CR, we found that exercise-based CR following PCI did not alter the benefits of exercise-based CR on all-cause mortality, rehospitalization, AMI, or stroke in patients with CCS. These observations highlight the potential for exercise-based CR to play a central role in management of patients with CCS, which associates with improved clinical outcomes compared to current, invasive strategies like PCI.

Given the large sample size, long-term follow-up, and PSM cohorts, this study provides promising evidence that exercise-based CR is associated with superior clinical outcomes at 18-months compared to PCI alone. In the past decade, several studies have explored the clinical treatment of patients with CCS. Recently, both the COURAGE trial and the ISCHEMIA trial revealed limited impact of routine invasive strategy, when added to optimal medical treatment, in patients with CCS on the 4-year risk for ischemic cardiovascular events or all-cause mortality [6, 7]. Indeed, the 1-year analyses revealed a significantly higher event rate in CCS patients who underwent the routine invasive strategy compared to optimal medical treatment [6]. When comparing the 1-year post-PCI mortality rates from previous work (1-4%) [19, 20], including the ISCHEMIA-trial (1.7%) [21], we observed a somewhat higher mortality rate (5%), perhaps explained by the design of these previous studies, which excluded high-risk patients and co-morbidity, subsequently underestimating the mortality rate in the real-world population of patients with CCS. Indeed, recent studies focussing on a real-world population report relatively high mortality rates (11.3%, 4.7 years follow-up) [11]. This therefore highlights that the data from our study is actually data from the real-world population. More importantly, our data reinforces the observations of the ISCHEMIA trial pertaining to the short-term effects of invasive strategies in patients with CCS, there is the high risk for mortality and morbidity following PCI.

The results of the current study suggest that exercise-based CR is associated with significantly lower odds for all-cause mortality, rehospitalisation, and cardiovascular morbidity, compared to matched patients who receive PCI. These observations are in line with a previous, small-sized RCT (n=101) performed by Hambrecht *et al.* in which the effects of exercise-based CR were compared against PCI in patients with CCS across 1-year follow-up. This previous study showed improved exercise capacity and superior event-free survival in CCS patients that received exercise-based CR, although the coronary artery stenosis remained present in patients with CCS [12]. In a recent Cochrane systematic review and meta-analysis (seven trials with n=581 CCS patients), it was deemed that CR conveyed a small improvement in exercise capacity for patients with CCS, though further research was needed to determine the impact on mortality and morbidity.[14] Another study showed that exercise-based CR improved myocardial perfusion through collateralization and enhanced coronary endothelial function in CCS patients [13]. These direct effects of exercise-based CR on coronary artery function and structure may explain the significantly lower 1-year event rate observed by these authors [22, 23]. To our knowledge, our PSM-based comparison between patients with CCS who underwent either exercise-based CR (n=4,368) *or* PCI (n=12,676), represents the first large-scale real-world evidence reinforcing the observations from Hambrecht *et al*. This highlights the need to further explore the clinical impact of exercise-based CR in patients with CCS adopting prospective research powered to investigate the effects on long-term clinical outcomes.

Despite the observations from the COURAGE and ISCHEMIA-trials and the absence of a reliable evidence base, invasive procedures have become routine care in cardiology for patients with CCS. Accordingly, our study explored the association of prescription to PCI in addition to exercise-based CR compared to exercise-based CR alone. A first, somewhat surprising observation, was that only ~1 in 10 patients that underwent PCI were prescribed additional exercise-based CR (1,339 versus 12,676, respectively). This clearly demonstrates that exercise-based CR is not routinely prescribed following PCI. Subsequently we evaluated the potential benefits of combining exercise-based CR with PCI, but found that this combination of therapeutic strategies does not outperform the clinical benefits of exercise-based CR alone. Since groups were well matched for important cardiovascular risk factors, our observations support the relevance of prescribing exercise-based CR in real-world CCS populations, with exercise-based CR being associated with providing systemic benefit to the entire arterial system [9, 10, 12, 13]. Combining PCI with exercise-based CR showed a small, but significantly lower proportion of new-onset of HF. Nonetheless, this did not translate to differences in odds between both therapeutics for all-cause mortality, rehospitalisation, stroke, and AMI. Although PCI improves coronary perfusion allowing increased cardiac output, [6, 12] these benefits may not outweigh the potential risks of PCI for patients with CCS as found in the ISCHEMIA trial [6].

Limitations.

Several limitations must be acknowledged. Although our study is based on a comprehensive database of EMRs from multiple healthcare organisations, some co-morbidities may be under-reported, and details of certain characteristics were not available. Important information that is unavailable from EMRs include the type of exercise incorporated in the CR programmes (i.e., frequency, intensity, type, duration), intervention adherence, and type/intensity of medical support. Other important under-reported variables include coronary status and baseline status of CCS, which is important as it prevented insight into the impact of disease severity. Therefore, we cannot exclude the presence of selection bias for the CR vs PCI cohort comparisons. This is important to consider when interpreting these results. Similarly, we could not control for some potential confounding (e.g., left ventricular function, the extent of myocardial ischemia, lifestyle and socioeconomic status), and we were unable to fully control for ethnicity. Whilst this difference in ethnicity cannot be ignored, the small difference unlikely explains our primary finding. In addition, medication use was lower in the exercise-based CR group compared to the PCI group, which is in agreement with a recent study [11]. At least, given the established cardioprotective effects of these drugs the lower medication use unlikely explains all of the lower mortality and morbidity in the exercise-based CR group. These limitations highlight the need for subsequent prospective trials to confirm the findings suggested in the present study.

Conclusions.

In conclusion, the present study was designed to evaluate the potential role of exercise-based CR in CCS patients, and the added value of PCI for exercise-based CR, compared to exercise-based CR alone. Exercise-based CR was associated with a significantly lower odds of 18-month all-cause mortality, rehospitalisation, and cardiovascular morbidity in CCS patients, while addition of PCI did not improve the benefits of exercise-based CR in patients with CCS. This suggests that exercise-based CR is a promising alternative treatment strategy for patients with CCS, and warrants prospective investigation.

Acknowledgements

Funding/support

No funding to declare.

Data availability statement

To gain access to the data in the TriNetX research network, a request can be made to TriNetX (https://live.trinetx.com), but costs may be incurred, a data sharing agreement would be necessary, and no patient identifiable information can be obtained.

Disclosures

Benjamin JR Buckley has received funding from Bristol-Myers Squibb (BMS)/Pfizer. Stephanie L Harrison has received funding from BMS. Elnara Fazio-Eynullayeva and Paula Underhill are employees of TriNetX LLC. Gregory YH Lip: consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo and speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally.

Conflict of interest

The Authors declares that there is no conflict of interest.

Authorship

BB: corresponding author, conceptualization, analysis, data interpretation, writing draft and review and editing; IK: data interpretation, visualisation and writing original draft; SH: review and editing; EF: data curation; PU: data curation; HK: conceptualization, review and editing; GL: conceptualization, review and editing; and DT: conceptualization, review and editing, all authors have read and approved the manuscript.

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Figure Titles and Legends

Figure 1

Title: Odds of all-cause mortality, rehospitalisation and morbidity in patients receiving CR *versus* PCI.

Legend: All-cause mortality, rehospitalisation, and cardiovascular morbidities at 18-month follow-up from CCS diagnosis; comparing CCS patients who received CR (n=4,357) to CCS patients who received PCI (n=4,357). CI; confidence interval, CR; cardiac rehabilitation, n; number of patients, PCI; percutaneous coronary intervention.

Figure 2

Title: Odds of all-cause mortality, rehospitalisation and morbidity in patients receiving CR only *versus* CR and PCI combined.

Legend: All-cause mortality, rehospitalisation, and cardiovascular morbidities at 18-month follow-up from CCS diagnosis; comparing CCS patients who received CR only (n=1,337) to CCS patients who received both CR and PCI (n=1,337). CI; confidence interval, CR; cardiac rehabilitation, n; number of patients, PCI; percutaneous coronary intervention.

Table 1. **Patient Characteristics % (n) of the chronic coronary syndrome populations with percutaneous coronary intervention only or with cardiac rehabilitation only, before and after propensity score matching.**

	Initial populations			**Propensity score matched populations**		
	CCS with PCI only (n=12,676)	CCS with CR only (n=4,368)	*p*-value	CCS with PCI only (n=4,357)	CCS with CR only (n=4,357)	*p*-value
Age (years) at diagnoses; mean (SD)	65.3 (11.4)	64.2 (11.6)	<0.0001	64.7 (11.1)	64.2 (11.6)	0.0592
Sex						
Male	68.3 (8,656)	66.9 (2,924)	0.1004	66.6 (2,903)	67.0 (2,918)	0.7329
Female	31.7 (4,019)	33.1 (1,444)	0.0984	33.3 (1,453)	33.0 (1,439)	0.7501
Ethnicity[a]						
White	82.5 (10,460)	77.6 (3,388)	<0.0001	80.3 (3,498)	77.8 (3,388)	0.0038
Black or African	10.5 (1,325)	11.2 (491)	0.1455	10.3 (450)	11.3 (491)	0.1570
Asian	1.5 (193)	1.8 (80)	0.1607	1.3 (57)	1.8 (80)	0.0476
Unknown	5.1 (647)	9.2 (400)	<0.0001	8.0 (350)	8.9 (389)	0.1337
Ischemic heart diseases	84.1 (10,658)	96.7 (4,222)	<0.0001	96.9 (4,220)	96.6 (4,211)	0.5865
Hypertensive diseases	68.2 (8,643)	78.1 (3,413)	<0.0001	79.6 (3,469)	78.1 (3,402)	0.0788
Diabetes Mellitus	32.6 (4,134)	35.9 (1,566)	<0.0001	36.3 (1,580)	35.9 (1,565)	0.7379
Heart Failure	19.0 (2,408)	27.2 (1,190)	<0.0001	26.1 (1,137)	27.1 (1,182)	0.2754
Cerebrovascular diseases	12.8 (1,622)	16.9 (738)	<0.0001	16.8 (734)	16.8 (733)	0.9772
Chronic Kidney Disease	14.6 (1,853)	14.9 (651)	0.6456	14.3 (624)	14.9 (651)	0.4131
Cardiovascular Procedures[b]	77.4 (9,806)	89.1 (3,891)	<0.0001	88.7 (3,865)	89.1 (3,880)	0.6093
Cardiovascular Medications[c]	74.0 (9,380)	85.2 (3,720)	<0.0001	88.2 (3,842)	85.1 (3,709)	<0.0001

*Values are % (n) unless otherwise stated.

Baseline characteristics were compared using a chi-squared test for categorical variables and an independent-sample t-test for continuous variables. [a]Data are taken from structured fields in the electronic medical record systems of the participating healthcare organizations, therefore, there may be regional or country-specific differences in how race categories are defined. [b]Cardiovascular procedures include cardiography, echocardiography, catheterization, cardiac devices, electrophysiological procedures. [c]Cardiovascular medications include beta-blockers, antiarrhythmics, diuretics, lipid lowering agents, antianginals, calcium channel blockers, ACE inhibitors.

Table 2. **Patient Characteristics % (n) of the chronic coronary syndrome populations with cardiac rehabilitation only or with both cardiac rehabilitation and percutaneous coronary intervention, before and after propensity score matching.**

	Initial populations			**Propensity score matched populations**		
	CCS with CR only (n=4,368)	CCS with CR+PCI (n=1,339)	*p*-value	CCS with CR only (n=1,337)	CCS with CR+PCI (n=1,337)	*p*-value
Age (years) at diagnoses; mean (SD)	64.2 (11.6)	65.3 (11.1)	0.0023	65.2 (11.1)	65.3 (11.1)	0.7672
Sex						
Male	66.9 (2,924)	71.0 (951)	0.0051	71.7 (958)	71.0 (949)	0.7004
Female	33.1 (1,444)	29.0 (388)	0.0051	28.3 (379)	29.0 (388)	0.7004
Ethnicity[a]						
White	77.6 (3,388)	83.3 (1,116)	<0.0001	84.9 (1,135)	83.4 (1,115)	0.2897
Black or African	11.2 (491)	10.4 (139)	0.3797	8.5 (114)	10.4 (139)	0.0986
Asian	1.8 (80)	1.7 (23)	0.7843	1.7 (23)	1.7 (23)	1.000
Unknown	9.2 (400)	4.3 (57)	<0.0001	4.8 (64)	4.3 (57)	0.5149
Ischemic heart diseases	96.7 (4,222)	99.8 (1,336)	<0.0001	99.9 (1,335)	99.8 (1,334)	0.6544
Hypertensive diseases	78.1 (3,413)	79.5 (1,064)	0.3020	80.0 (1,070)	79.5 (1,063)	0.7361
Diabetes Mellitus	35.9 (1,566)	35.5 (476)	0.8398	35.7 (477)	35.6 (476)	0.9678
Heart Failure	27.2 (1,190)	21.1 (282)	<0.0001	20.1 (269)	21.1 (282)	0.5342
Cerebrovascular diseases	16.9 (738)	12.2 (164)	<0.0001	12.0 (161)	12.3 (164)	0.8591
Chronic Kidney Disease	14.9 (651)	13.6 (182)	0.2343	12.8 (171)	13.6 (182)	0.5297
Cardiovascular Procedures[b]	89.1 (3,891)	98.4 (1,317)	<0.0001	98.5 (1,317)	98.4 (1,315)	0.7558
Cardiovascular Medications[c]	85.2 (3,720)	94.5 (1,266)	<0.0001	94.1 (1,258)	94.5 (1,264)	0.6163

*Values are % (n) unless otherwise stated.

Baseline characteristics were compared using a chi-squared test for categorical variables and an independent-sample t-test for continuous variables. [a]Data are taken from structured fields in the electronic medical record systems of the participating healthcare organizations, therefore, there may be regional or country-specific differences in how race categories are defined. [b]Cardiovascular procedures include cardiography, echocardiography, catheterization, cardiac devices, electrophysiological procedures. [c]Cardiovascular medications include beta-blockers, antiarrhythmics, diuretics, lipid lowering agents, antianginals, calcium channel blockers, ACE inhibitors.