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ORIGINAL ARTICLE

Association Between Coronary Assessment in Heart Failure and Clinical Outcomes Within a Safety-Net Setting Using a Target Trial Emulation Observational Design

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BACKGROUND: Ischemic cardiomyopathy is the leading cause of heart failure (HF). Most patients do not undergo coronary assessment after HF diagnosis. There are no randomized clinical trials of coronary assessment after HF diagnosis.

METHODS: Using an electronic health record cohort of all individuals with HF within the San Francisco Health Network from 2001 to 2019, we identified factors associated with coronary assessment. Then, we studied the association of coronary assessment within 30 days of HF diagnosis with all-cause mortality and a composite of mortality and emergent angiography using a target trial emulation observational comparative-effectiveness approach. Target trial emulation is an approach to causal inference based on creating a hypothetical randomized clinical trial protocol and using observational data to emulate the protocol. We used propensity scores for covariate adjustment. We used national death records to improve the ascertainment of mortality and included falsification end points for the cause of death.

RESULTS: Among 14 829 individuals with HF (median, 62 years old; 5855 [40%] women), 3987 (26.9%) ever completed coronary assessment, with 2467/13 301 (18.5%) with unknown coronary artery disease status at HF diagnosis assessed. Women, older individuals, and people without stable housing were less likely to complete coronary assessment. Among 5972 eligible persons of whom 627 underwent early elective coronary assessment, coronary assessment was associated with lower mortality (hazard ratio, 0.84 [95% CI, 0.72–0.97]; P=0.025), reduced risk of the composite outcome (hazard ratio, 0.86 [95% CI, 0.73–1.00]), higher rates of revascularization (odds ratio, 7.6 [95% CI, 5.4–10.6]), and higher use of medical therapy (odds ratio, 2.5 [95% CI, 1.7–3.6]), but not the falsification end points.

CONCLUSIONS: In a safety-net population, disparities in coronary assessment after HF diagnosis are not fully explained by coronary artery disease risk factors. Early coronary assessment is associated with improved HF outcomes possibly related to higher rates of revascularization and guideline-directed medical therapy but with low certainty that this finding is not attributable to unmeasured confounding.

Key Words: angiography ■ coronary artery disease ■ disparities ■ heart failure ■ mortality

Editorial by Russo and Danaei

Heart failure (HF) is a major cause of morbidity and mortality with >1 000 000 new cases per year in the United States[1] and disproportionately affects those who identify as Black or African American.[2] Ischemic cardiomyopathy attributable to obstructive coronary artery disease (CAD) accounts for 60% to 70% of HF cases.[3,4]

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For Sources of Funding and Disclosures, see page 537.

WHAT IS KNOWN

- A low proportion of individuals undergo coronary assessment after heart failure diagnosis.
- Coronary assessment is associated with improved outcomes in observational studies but has not been studied in a randomized controlled trial.

WHAT THE STUDY ADDS

- Within a safety-net population, there are significant disparities in who completes coronary assessment after heart failure diagnosis that are not explained by risk factors for ischemic cardiomyopathy.
- In our observational study, early coronary assessment was associated with improved survival, revascularization, and higher rates of prior guideline-directed medical therapy use.
- Although we used rigorous causal inference methods, answers to this important clinical question remain inconclusive without a randomized clinical trial.

Nonstandard Abbreviations and Acronyms

ACE	angiotensin-converting enzyme
ARB	angiotensin receptor blocker
ARNI	angiotensin receptor/neprilysin inhibitor
CABG	coronary artery bypass graft
CAD	coronary artery disease
GDMT	guideline-directed medical therapy
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HR	hazard ratio
LVEF	left ventricular ejection fraction
OR	odds ratio
SGLT2i	sodium glucose cotransporter-2 inhibitor

According to the 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America Guideline for the Management of HF, "in patients with HF, an evaluation for possible ischemic heart disease can be useful to identify the cause and guide management" (level 2a recommendation).[5] Importantly, the recommendation applies to both HF with a reduced ejection fraction (HFrEF) and HF with a preserved ejection fraction (HFpEF), which is also commonly caused by CAD, despite strong evidence to support this recommendation. This is partly based on the 10-year follow-up of the STICH (Surgical Treatment for Ischemic Heart Failure) trial (STICHES), which found that coronary artery bypass graft (CABG) surgery added to medical therapy had a mortality benefit for patients with HFrEF due to ischemic cardiomyopathy. REVIVED-BCIS2 (Study of Efficacy and Safety of Percutaneous Coronary Intervention to Improve Survival in Heart Failure), which randomized patients with ischemic HFrEF and evidence of viability to revascularization with percutaneous coronary intervention, did not find an intermediate-term benefit.[6] This has led some cardiologists to question routine coronary assessment for patients with HF.

To our knowledge, there are no randomized clinical trials of coronary assessment strategies among patients with HF. Observational studies suggest that coronary assessment during HF hospitalization or within 30 days of diagnosis is associated with higher use of medical therapy and revascularization and with reduced mortality and rehospitalization.[7–9] Despite the guidelines and observational evidence, most commercially insured patients with HF do not undergo coronary assessment within 90 days, with disparities by county, patient demographics, and comanagement by a cardiologist.[10] Women and persons of Black race are less likely to be referred for coronary assessment in other settings.[11] None of the published studies have examined coronary assessment in a safety-net setting, and most do not adequately account for selection effects for coronary assessment, exclude patients with acute coronary syndromes (ACSs), or align timing and eligibility to minimize selection bias, confounding and immortal time, three potent threats to observational comparative-effectiveness research.

We therefore designed this study to examine whether there are differences in who undergoes coronary assessment among those with HF within a safety-net setting and second whether elective coronary assessment early after HF diagnosis among those without known CAD is associated with clinical outcomes. We hypothesized that there would be disparities in coronary assessment by patient demographics not explained by CAD risk factors. Our second hypothesis was that early coronary assessment would be associated with lower mortality and lower risk of subsequent emergent angiography among those without prior coronary assessment or indication for emergent coronary angiography.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Participants

We developed an electronic health record cohort of all individuals with HF by *ICD-9* or *ICD-10* code who received care within San Francisco's municipal health system, the San Francisco Health Network, from 2001 to 2019. HF was defined as *ICD-9* codes: 428, 428.0, 428.1, 428.2X, 428.3X, 428.4, 428.9, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93 and *ICD-10* codes: I50.1, I50.20, I50.21, I50.22, I50.23,

I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.9, I11.0 coded during an outpatient or inpatient health care encounter. Patients were included from January 1, 2001 to August 1, 2019, and last follow-up was December 31, 2019.

Exposures

Left heart catheterization with invasive coronary angiography, exercise and pharmacologic nuclear stress tests, and coronary computed tomographic angiography were considered coronary assessments. For those with coronary assessments and echocardiograms, full texts of reports were extracted, including a look back period to 1999. We categorized the results using structured text extraction with a manual review for refining the structured test extraction and verifying quality control. After extraction, all reports were manually reviewed for accuracy by the first author. For the outcomes assessment, the coronary assessment was considered early if it occurred within 30 days of the index HF diagnosis.

Outcomes

The two primary outcomes were all-cause mortality and a composite outcome of all-cause mortality and emergent coronary angiography for acute myocardial infarction including ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI) cardiogenic shock, ventricular arrhythmias, and cardiac arrest ascertained by a manual review of all cardiac catheterization reports by the first author. Emergent angiography performed at other sites was not included. Patients were linked with Social Security Death Index/National Death Index (SSDI/NDI) records for all-cause mortality by name, birth date, and social security number (if available). For patients who could not be linked, vital status and date of death if deceased were abstracted from the medical records.

Additional Variables

We extracted past medical history at the time of HF diagnosis using ICD codes. Psychiatric comorbidities were not measured. Using the first available echocardiogram concurrent with HF, we classified as HFrEF those with left ventricular ejection fraction (LVEF) <40%; if LVEF was not reported (as was common in earlier years of the study), we classified those with at least moderately reduced left ventricular function on qualitative assessment as HFrEF; we classified those with LVEF≥41% if reported or mild-to-moderate left ventricular systolic dysfunction or less on qualitative assessment if quantitative left ventricle was not reported as HFpEF. Medical records were manually reviewed for all individuals with a cardiac catheterization report with obstructive CAD (one or more major vessels [left anterior descending, left circumflex, right coronary artery] ≥80% or left main ≥50%) to ascertain revascularization outcomes. Among those hospitalized for HF, we extracted ambulatory prescription records before and after the index hospitalization and subsequent hospitalizations.

Statistical Analysis: Factors Associated With Coronary Assessment

We estimated the association between ever undergoing coronary assessment and baseline variables with adjustment for age, sex, race/ethnicity, documented unstable housing, diabetes, hypertension, chronic kidney disease, HIV, tobacco, and other substance use, having completed an echocardiogram, HFrEF, and presence of regional wall motion abnormalities using logistic regression.

Approach to Estimate Associations of Early Coronary Assessment With Outcomes

To estimate the effect of coronary assessment on the two outcomes, we designed a target trial emulation of a hypothetical randomized clinical trial.[12,13] We took advantage of variations in practice, and we did not actually randomize any patients or conduct a clinical trial. We included patients aged <80 years old with incident HF starting in the second year of the study period (2002), so we could exclude those with prevalent HF during the first year of the study (2001). We also excluded those with prior coronary assessment/known CAD (with a 3-year look back period to 1999), metastatic cancer, advanced cirrhosis, and initial presentation with an ACS (STEMI or NSTEMI), ventricular arrhythmias, cardiac arrest, and those with concurrent endocarditis, severe aortic stenosis or regurgitation, and severe mitral stenosis, and those who did not complete an echocardiogram.

Alignment of Eligibility and Follow-Up Time

We allowed a 30-day grace period for coronary assessment after diagnosis with HF to minimize immortal time bias. We set the start of follow-up and eligibility to the date of HF diagnosis. Patients were censored at death using the Social Security Death Index/National Death Index date of death, at the end of the social security death index/National Death Index search for those matched and alive (December 31, 2018 [n=267] or December 31, 2019 [n=1396]), and electronic health record last contact date and vital status for those who could not be matched (n=1647).

Propensity Score Model

We generated a logistic propensity score model for coronary assessment including the restricted cubic spline of age, sex, race/ethnicity, unstable housing, medical history, substance use, hospitalization at the time of diagnosis with HF, EF category concurrent or preceding HF, and diagnosis year, all of which are variables known before the treatment assignment. We assessed the proportion tested by propensity score quintile, the balance of covariates across propensity score quintiles and using standardized mean differences, and goodness-of-fit using the Hosmer-Lemshow test.

Statistical Analysis

We used Cox proportional hazards models to estimate the hazard ratio (HR) for mortality and the composite outcome by coronary assessment status adjusted for age, sex, the restricted cubic spline of the propensity score for testing coronary assessment, and HF hospitalization at the time of diagnosis. Because the proportional hazards assumption was violated with nonparallel log-log plots of survival and test of the scaled Schoenfeld residuals, we incorporated sex-by-age interaction terms and conducted sensitivity analyses with truncated follow-up times (Figure S1).

We conducted subgroup analyses considering differences by sex, HFrEF versus HFpEF, HF hospitalization at diagnosis,

and the study period dichotomized into 2002 to 2012 and 2013 to 2019 by introducing interaction terms. To consider possible mechanisms for improvement in mortality among those who underwent coronary assessment, we classified participants based on the results of the testing and conducted an exploratory analysis considering the use of goal-directed medical therapy among hospitalized patients for whom prescription records were available. We also considered the role of revascularization, including the number of vessels and whether or not revascularization was performed as a time-varying exposure.

To check the robustness of our findings to our analytic choices, we conducted sensitivity analyses examining the role of censoring time on our findings and using inverse probability of treatment weighting with dropping the most extreme 5% of weights (those who were tested despite very low propensity score, which suggests that unmeasured factors may be playing a role in the decision to refer the patient) as an alternative analytic strategy. We used the inverse probability of treatment weighting results to estimate the average treatment effect on mortality at 4 years and overall. As another alternative approach, we used propensity matching with 2:1 (untested: tested) nearest neighbor matching based on the Mahalanobis distance again to estimate the average treatment effect on mortality at 4 years and overall, which we report in the Results in the Supplemental Material.

Finally, we tested several falsification end points,[14] namely specific causes of death that we did not expect to be substantially affected by coronary assessment including both traumatic (homicide/suicide and motor vehicle accident) and nontraumatic diagnoses that we did hypothesize would not be impacted by coronary assessment (cirrhosis and pneumonia/sepsis). For these outcomes, we reported the number and proportion with a death certificate by group and then reproduced the primary Cox proportional hazards models using the specific cause of death as the primary outcome.

Although our primary interest was the estimated hazard ratios and CIs, we considered $P<0.05$ significant for the two primary outcomes, $P<0.001$ significant for univariate analyses, and $P<0.10$ significant for interactions. Analyses were performed using STATA version 17.1. IRB approval was granted by the University of California with a waiver of informed consent. Results are reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[15]

RESULTS

Description of Cohort and Coronary Assessment

The cohort included 14 829 individuals with HF who received care within San Francisco Health Network from 2001 to 2019. The median age at diagnosis was 62 (interquartile range, 53–75). There were 5855 women (40%), and a high proportion of Black, Asian, and Hispanic/Latino individuals (Table 1). Among those with HF (both HFrEF and HFpEF), 3987 (26.9%) completed at least one coronary assessment, mostly invasive coronary angiography, with about one-third within 30 days of index HF diagnosis (Table 2). For comparison, 11 172 (75.4%) ever completed an echocardiogram.

Excluding those with prior coronary assessment (n=1447), only 2467/13 301 (18.5%) of individuals with unknown CAD status at the time of HF diagnosis underwent coronary assessment concurrent with or after HF diagnosis, with a decreasing trend over time (Figure 1; $P<0.001$). Among those with HFrEF, 1082/3204 (33.8%) underwent coronary assessment concurrent with or after HF diagnosis.

Disparities in Coronary Assessment

Consistent with univariate analysis, in models adjusted for age, sex, race/ethnicity, housing status, medical history, substance use, hospitalization for HF, and ever having an echocardiogram, there were lower odds of completing coronary assessment among those with older age, female sex, and unstable housing (Table 1). Compared with White individuals, Asian and Hispanic/Latino individuals had higher odds of ever completing coronary assessment, but no difference in concurrent assessment. Black individuals, although not less likely to ever have coronary assessment, were much less likely to have their coronaries assessed concurrent with HF diagnosis (odds ratio [OR], 0.28 [95% CI, 0.11–0.74]), with no differences among Hispanic/Latino and Asian individuals compared to White individuals in concurrent coronary assessment. Hypertension and tobacco use were associated with higher odds of coronary assessment, but diabetes, chronic kidney disease, HIV, and methamphetamine use were associated with lower odds of completing coronary assessment. Ever completing an echocardiogram, a crude surrogate measure for completing cardiac testing, was associated with much higher odds of completing coronary assessment; among those who completed an echocardiogram, having HFrEF or regional wall motion abnormalities was associated with higher odds of testing. As expected, presentation with an ACS was associated with much higher odds of coronary assessment.

Findings on Coronary Assessment

Among 3987 individuals who ever underwent coronary assessment, on their first test, 1429 (36.1%) had no CAD or a negative stress test, 855 (21.6%) had nonobstructive CAD, 1269 (32%) had obstructive CAD or a positive stress test, 322 (8.1%) had evidence of prior revascularization, and 89 (2.3%) had possible ischemia or a nondiagnostic test. Among those who underwent nuclear stress (n=1359), 1029 (75.7%) were negative, 91 (6.7%) had possible ischemia, 160 (11.8%) were positive for ischemia, and 79 (5.8%) were nondiagnostic. Among those who underwent invasive coronary angiography (n=3190), 602 (18.9%) had no CAD, 956 (30.0%) had nonobstructive CAD, 469 (14.7%) had single-vessel obstructive CAD, 814 (25.5%)

Table 1. Participant Characteristics by Coronary Assessment and Adjusted Odds of Coronary Assessment

Characteristic/finding	Coronary assessment (n=3987)	No coronary assessment (n=10842)	Adjusted odds ratio (95% CI)	Interpretation (concordance or discordance with expected risk/benefit)
Age*	60.3 (52.4–68.7)	63.2 (53.1–77.4)	0.87 per decade (0.84–0.89)	Discordant with ischemic risk, but possibly concordant with perceived risk/benefit
Female*†	1390 (35.0%)	4465 (41.7%)	0.82 (0.76–0.90)	May reflect sexism
Race/ethnicity*				
White	843 (21.1%)	3164 (29.2%)	Reference	The implications and generalizability of these differences by race and ethnicity are uncertain and may represent structural differences in access to care, acculturation related to immigration, differences in physician perceptions of risk and interest in coronary assessment, or other societal or structural factors
Black	1096 (27.5%)	3034 (28.0%)	1.06 (0.94–1.19)	
Asian	933 (23.4%)	2243 (20.7%)	1.53 (1.36–1.73)	
American Indian/Alaskan Native	46 (1.2%)	112 (1.0%)	1.39 (0.95–2.02)	
Native Hawaiian/ Pacific Islander	12 (0.3%)	35 (0.3%)	0.75 (0.38–1.50)	
Hispanic/Latino	957 (24.0%)	1851 (17.1%)	1.79 (1.58–2.02)	
Other/decline to state	100 (2.5%)	403 (3.7%)	1.79 (1.29–2.25)	
Documented unstable housing*	96 (2.4%)	565 (5.2%)	0.41 (0.33–0.52)	May reflect concerns regarding follow-up as well as higher burden of substance use and psychiatric illness
Past medical history				
Hypertension*	3557 (89.2%)	8359 (77.1%)	1.85 (1.64–2.09)	Concordant
Diabetes	313 (7.9%)	934 (8.6%)	0.75 (0.65–0.87)	Discordant
Chronic kidney disease	582 (14.6%)	1621 (15.0%)	0.86 (0.77–0.97)	Discordant with risk of CAD, but concordant with expected risk of testing and benefit of revascularization
HIV	221 (5.5%)	685 (6.3%)	0.78 (0.67–0.93)	Discordant
Cirrhosis*	8 (0.2%)	68 (0.6%)	0.32 (0.15–0.68)	Concordant
Documented substance use				
Alcohol*	945 (23.7%)	2222 (20.5%)	0.84 (0.75–0.93)	Concordant
Tobacco*	2057 (51.6%)	4046 (37.3%)	1.38 (1.26–1.51)	Concordant
Cocaine*	629 (15.8%)	1462 (13.5%)	1.05 (0.92–1.21)	N/A
Methamphetamine	461 (11.6%)	1301 (12.0%)	0.79 (0.68–0.91)	Controversial
Opioid	398 (10.0%)	1188 (10.9%)	0.75 (0.65–0.86)	Controversial
HF hospitalization (ever)*	563 (14%)	1076 (9.9%)	1.14 (1.02–1.29)	Concordant
Echocardiographic parameters				
Ever had an echocardiogram*	3874 (97.2%)	7298 (67.4%)	13.0 (10.7–15.9)	Concordant
Echocardiogram within 30 d of HF diagnosis*	2132 (53.5%)	4157 (38.3%)		
LVEF as measured >30 d before diagnosis, %*	48±13	51±12		
LVEF measured within 30 d of HF diagnosis, %*	38±15	43±16		
HFrEF*,‡,‖	1567 (40.4%)	2123 (29.1%)	1.80 (1.64–1.97)	Controversial, but probably concordant with strength of evidence for revascularization
Regional wall motion abnormalities*‖	661 (46.5%)	433 (24.2%)	2.78 (2.36–3.27)	Concordant
Severe pulmonary hypertension‖	66 (3.1%)	117 (2.8%)		
Estimated pulmonary artery systolic pressure‖	36±15	37±15		
Severe aortic stenosis‖	15 (0.7%)	13 (0.3%)		
Severe aortic regurgitation*‖	24 (1.1%)	16 (0.4%)		
Severe mitral stenosis‖	6 (0.3%)	5 (0.1%)		
Severe mitral regurgitation*‖	188 (8.8%)	253 (6.1%)		
Severe tricuspid regurgitation*‖	144 (6.8%)	402 (9.7%)		

(*Continued*)

Table 1. Continued

Characteristic/finding	Coronary assessment (n=3987)	No coronary assessment (n=10842)	Adjusted odds ratio (95% CI)	Interpretation (concordance or discordance with expected risk/benefit)
Troponin I >0.04 ng/mL*#	326 (57.9%)	441 (41.0%)	2.24 (1.78–2.82)	Concordant
ST elevation myocardial infarction*	433 (10.9%)	15 (0.1%)	100 (58–173)	Concordant
Non-ST elevation myocardial infarction*	188 (4.7%)	1 (0.01%)	479 (67–3436)	Concordant

Patient characteristics at the time of index heart failure diagnosis by whether or not they ever underwent coronary assessment. *P* values were estimated using χ^2 test for categorical variables and *t*-tests for continuous variables. HF indicates heart failure; HFrEF, heart failure with reduced ejection fraction; LV, left ventricle; and LVEF, left ventricular ejection fraction.

*Signifies unadjusted *P*<0.001.

†One hundred thirty-seven individuals did not report sex as male or female.

‡HFrEF was defined as LVEF<40% or moderate or qualitative moderate or greater LV systolic dysfunction based on the concurrent echocardiogram or the worst LVEF from a prior echocardiogram for those missing concurrent echocardiograms.

‖Denominator for echocardiographic parameters percentages are those who had an echo within 30 d of HF diagnosis. We found significant differences in who completed coronary assessment by age, sex, race/ethnicity, past medical history, substance use, and other clinical parameters.

#Only includes individuals who were hospitalized with HF (n=1639).

had multivessel obstructive CAD including 329 with obstructive left main disease (≥50%) and 468 with 3 or more vessels with obstructive disease (≥80% as reported visually in angiography report or left main and obstructive right CAD), and 349 (10.9%) had evidence of prior revascularization. Results were similar among those who underwent coronary assessment after HF diagnosis (Results in the Supplemental Material).

Associations With Mortality and Composite of Emergent Revascularization and Mortality

Among 14829 individuals included in the cohort, 5972 were included in the analysis of the effect of early coronary assessment within 30 days of HF diagnosis (age<80, no prior coronary assessment, no urgent/emergent indication for coronary angiography, and no metastatic cancer or cirrhosis, and completed echocardiogram) including 627 who underwent testing and 5345 who did not (Figure 2). Patient characteristics were well-balanced after propensity adjustment (Table 3; Table S1). At the end of follow-up (median, 3.8 years), 201 (32.1%) who underwent early coronary assessment had died compared to 2008 (37.6%) among those who did not (unadjusted *P*=0.007). For the primary composite outcome, 219 (34.9%) and 2071 (38.8%), respectively, had died or underwent emergent coronary angiography (unadjusted *P*=0.06). Of eligible participants who did not undergo early coronary assessment, 639 (12%) crossed over and underwent coronary assessment at a median of 380 days (interquartile range, 116–1090) after HF diagnosis.

Among eligible patients, early elective coronary artery assessment at the time of HF diagnosis was associated with a 16% lower risk of all-cause mortality over the entire study period (hazard ratio [HR], 0.84 [95% CI, 0.72–0.98]; *P*=0.025; Figure 3). Early coronary assessment was associated with a 14% lower risk for the composite outcome: HR, 0.86 ([95% CI, 0.73–0.995]; *P*=0.04). Results were similar in sensitivity analyses including additional potential confounders and different censoring intervals (Results in the Supplemental Material; Table S2).

Cause-Specific Mortality and Falsification End Points

Among those with death certificates (n=1432), we used the underlying cause of death to explore cause-specific mortality including falsification end points (Table 4). The cardiovascular disease cause-specific hazard ratios were <1, consistent with the hypothesis that early coronary assessment would be associated with a lower risk of cardiovascular mortality. The falsification end points were uncommon in both groups, but the point estimates for the effect estimates were ≈1 as expected. The falsification end points suggest that the primary result was not purely the result of residual confounding and, thus, supports the internal validity of the primary outcome.

Table 2. Type and Timing of Initial Coronary Assessment (n=3987)

Test type	Testing completed >30 d before HF diagnosis	Testing completed within 30 d of HF diagnosis	Testing completed >30 d after HF diagnosis	Total
Invasive coronary angiography	682 (58.6%)	1051 (89.9%)	1107 (66.9%)	2840 (71.2%)
Nuclear stress	477 (41.0%)	114 (9.8%)	532 (32.2%)	1123 (28.2%)
CCTA	4 (0.3%)	4 (0.3%)	16 (1.0%)	24 (0.6%)
Total	1163 (29.2%)	1169 (29.3%)	1655 (41.5%)	3987

Number and percentage who underwent each type of testing by test timing category (column percentage except total row which is row percentage). CCTA indicates coronary computed tomographic angiography; and HF, heart failure.

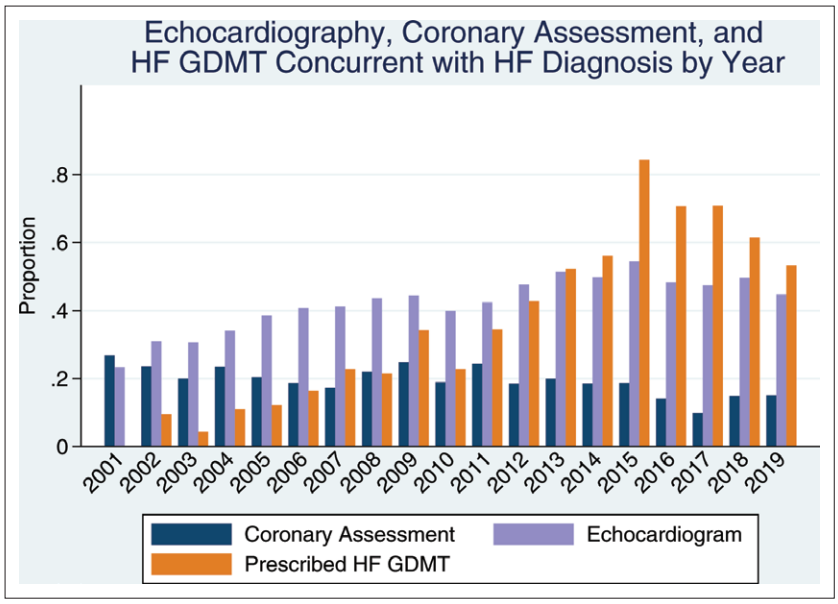

Figure 1. Trends in echocardiography and coronary assessment by year. The proportion of individuals with incident heart failure who completed coronary assessment (navy) and echocardiogram (lavender) within 30 days of diagnosis and the proportion hospitalized with heart failure with reduced ejection fraction at the time of diagnosis prescribed outpatient guideline-directed medical therapy (GDMT) at hospital discharge (orange) by year. There was a statistically significant trend for less coronary assessment completed over time and much higher rates of GDMT prescription in the more recent years of the study. HF indicates heart failure.

Specific Subgroups of Interest: Female Patients, Hospitalized Patients, HFrEF, Chronic Kidney Disease, and Those Found to Have Obstructive CAD

The effect estimates for coronary assessment on mortality did not vary by sex, with hazard ratios of 0.85 (95% CI, 0.59–1.12) for women and 0.84 (95% CI, 0.71–1.00) for men ($P_{interaction}$=0.86). Although not statistically significant, the effect estimates were stronger among those hospitalized at HF diagnosis (HR, 0.72 [95% CI, 0.55–0.93]) compared to those not hospitalized (HR, 0.92 [95% CI, 0.76–1.11]; $P_{interaction}$=0.12). There was no difference by HFrEF (LVEF<40%) versus HFpEF: HR, 0.84 in HFrEF (95% CI, 0.69–1.01) versus HR, 0.86 in HFpEF (0.66–1.11; $P_{interaction}$=0.89) or by regional wall motion abnormalities on the concurrent echocardiogram ($P_{interaction}$=0.41). Patients with chronic kidney disease did not have evidence of the benefit of early coronary assessment (HR, 1.13 [95% CI, 0.79–1.64]; $P_{interaction}$=0.10). Among those who completed early coronary assessment, compared to no evidence of CAD or negative stress test, obstructive CAD was associated with higher risk (HR, 1.30 [95% CI, 1.01–1.67]). Among those who underwent coronary angiography, only multivessel CAD was associated with higher risk (HR, 1.47 [95% CI, 1.06–2.04]).

Role of Revascularization, GDMT, and Outpatient Follow-up

We were able to ascertain revascularization records for 294/321 (92%) with obstructive CAD. Early coronary evaluation was associated with much higher odds of undergoing revascularization (11.2% versus 1.6%; P<0.001; adjusted OR, 6.7 [95% CI, 4.7–9.7]). Among those revascularized, revascularization strategies were not significantly different between those who did or did not undergo early coronary assessment; 49% versus 40% received CABG (P=0.31) and 56 versus 62% received PCI (P=0.44), respectively. About half in each group with multivessel disease received revascularization (43% versus 53%; P=0.16) including 55% with left main disease and 50% with 3 or more obstructed vessels.

The median time from HF diagnosis to revascularization was 19 days compared to 1145 days (3.1 years) among those who did not undergo early coronary assessment (P<0.0001). Those who completed early coronary assessment were much less likely to subsequently be revascularized in the setting of an ACS (11% versus 90%; P<0.001). Acknowledging confounding from referral bias and the benefit of revascularization in the setting of ACS, revascularization was associated with improved mortality in both groups (HR, 0.58 [95% CI, 0.39–0.87]; $P_{interaction}$=0.47).

Only 9% with known coronary anatomy had 3-vessel disease; accounting for revascularization only minimally attenuated the overall effect estimate (HR, 0.88 [95% CI, 0.75–1.03]). Compared to a reference of no CAD (all of whom did not undergo revascularization), having multivessel CAD without revascularization was associated with higher risk (HR, 2.27 [95% CI, 1.54–3.35]) accounting for revascularization as a time-varying exposure. This risk was mitigated in revascularized multivessel CAD (HR, 0.94 [95% CI, 0.61–1.45]; Table S3), regardless of revascularization strategy with CABG or PCI, perhaps due to differences in statin use (HR, 1.25 [95% CI, 0.52–2.98], accounting for statin use). The extent to which the observed benefit is attributable to revascularization versus selection effects cannot be determined from our data, but the magnitude of the apparent benefit suggests unmeasured confounding.

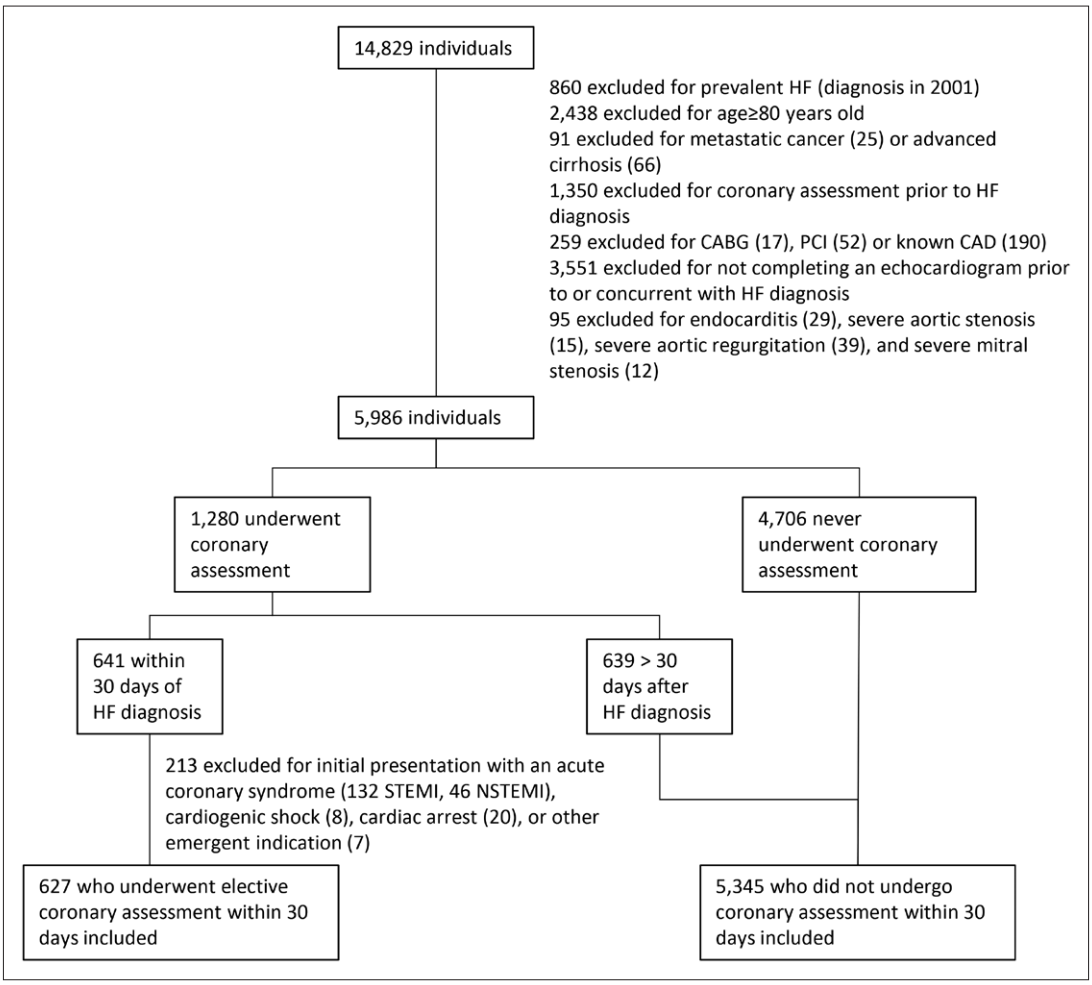

Figure 2. Consort diagram for target trial of elective coronary assessment at the time of heart failure (HF) diagnosis. To make good use of our observational data, we emulated a randomized controlled trial of elective coronary assessment at the time of heart failure diagnosis by creating a hypothetical trial of individuals "assigned" to early coronary assessment compared to those assigned to not undergo coronary assessment. This figure shows how we excluded individuals prevalent heart failure, with known coronary artery disease (CAD), competing diagnoses (cirrhosis/cancer), then by timing of coronary assessment, and finally excluding those whose initial presentation necessitated emergent coronary angiography (who would be more likely to benefit). CABG indicates coronary artery bypass graft; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST elevation myocardial infarction.

Among those who were hospitalized for whom we had medication records, we considered whether ambulatory guideline-directed medical therapy (GDMT) for HF and CAD could explain the apparent benefit of coronary assessment on mortality. To do this, we restricted our analysis to those hospitalized at the time of HF diagnosis for whom we had data on medical therapy and timing. For HF GDMT (beta-blocker, ACE [angiotensin-converting enzyme]-inhibitor/angiotensin receptor blocker, and mineralocorticoid receptor antagonist), we only included those with HFrEF (n=791; 196 who underwent early coronary assessment), but for aspirin and statin, we did not restrict by HF type (n=1104; 230 who underwent early coronary assessment).

A much higher proportion who underwent coronary assessment were prescribed each class of medical therapy before hospitalization compared to those who did not undergo coronary assessment ($P<0.01$ for each medication class; Table 5). Fewer than 10% of eligible individuals not already on therapy were initiated on each class of GDMT after hospitalization with no differences between groups. Prescriptions for aspirin, statin, ACE inhibitor/angiotensin receptor blocker, beta-blocker, and mineralocorticoid receptor antagonist were each associated with lower hazard for mortality. Notably, early coronary assessment was associated with statin prescription (adjusted OR, 2.2 [95% CI, 1.6–2.9]), but this did not attenuate the association between coronary assessment and mortality ($P_{interaction}=0.33$).

Among those with HFrEF hospitalized for HF, undergoing early coronary assessment was associated with higher odds of ever being prescribed HF GDMT (59% versus 43%; adjusted OR, 2.5 [95% CI, 1.7–3.6]), but not with greater initiation of HF GDMT (11.1% versus 7.9%; adjusted OR, 1.4 [95% CI, 0.8–2.5]). Being on at least one class of GDMT was associated with

Table 3. Patient Characteristics for Those Included in the Target Trial Emulation and Standardized Mean Differences Before and After Propensity Adjustment

	Coronary assessment within 30 d of HF diagnosis (n=627)	No coronary assessment within 30 d of HF diagnosis (n=5345)	Unadjusted standardized mean difference	Standardized mean difference after propensity adjustment
Age	56.3 (11.1)	57.9 (12.3)	−0.103	0.001
Female	161 (25.8%)	1899 (35.7%)	−0.153	0.002
Race/ethnicity				
White	135 (21.5%)	1390 (26.0%)	−0.074	−0.009
Black	149 (23.8%)	1741 (32.6%)	−0.139	−0.011
Hispanic/Latino	162 (25.8%)	1027 (19.2%)	0.126	0.015
Asian	165 (26.3%)	1011 (18.9%)	−0.019	0.000
American Indian/Alaskan Native	6 (1.0%)	66 (1.2%)	−0.019	0.000
Native Hawaiian/Pacific Islander	2 (0.3%)	26 (0.5%)	0.112	0.010
Other/decline to state	8 (1.3%)	84 (1.6%)	−0.018	−0.008
Documented unstable housing	16 (2.6%)	353 (6.6%)	−0.138	0.000
Past medical history				
Hypertension	527 (84.1%)	4421 (82.7%)	0.025	0.011
Diabetes	54 (8.6%)	529 (9.9%)	−0.031	0.000
Chronic kidney disease	73 (11.6%)	933 (17.5%)	−0.117	−0.003
HIV	39 (6.2%)	475 (8.9%)	−0.071	−0.004
Substance use				
Alcohol	158 (25.2%)	1507 (28.2%)	−0.048	−0.007
Tobacco	341 (54.4%)	2753 (51.5%)	0.041	0.002
Cocaine	104 (16.6%)	1094 (20.5%)	−0.071	−0.007
Methamphetamine	97 (15.5%)	938 (17.5%)	−0.040	−0.003
Opioid	60 (9.6%)	826 (15.5%)	−0.126	−0.003
HF hospitalization	241 (35.5%)	880 (16.3%)	0.347	0.044
Echocardiographic findings				
Ejection fraction concurrent HF, mean (SD)	33.5 (13.1)	41.5 (15.8)	−0.392	0.017
Regional wall motion abnormalities	33 (30.3%)	392 (23.6%)	0.510	0.180
Severe pulmonary hypertension	18 (3.2%)	96 (2.7%)	0.019	0.012
Estimated pulmonary artery systolic pressure, mm Hg	38.1 (16.1)	35.9 (14.9)	0.103	0.105
Severe mitral regurgitation	68 (12.0%)	230 (6.5%)	0.135	0.104
Severe tricuspid regurgitation	44 (7.7%)	265 (7.5%)	0.007	−0.030

Patient characteristics among individuals included in the assessment of the association of early coronary assessment with outcomes. Standardized mean differences are small (<0.10) after propensity adjustment suggesting that the propensity score balances these measured covariates, with the exception of regional wall motion abnormalities (which we explored in a sensitivity analysis with an interaction term), estimated pulmonary artery systolic pressure, and severe mitral regurgitation (which we explored by excluding those with severe mitral regurgitation and severe pulmonary hypertension with similar results reported in Results in the Supplemental Material). HF indicates heart failure.

a 57% lower hazard for mortality (HR, 0.43 [95% CI, 0.33–0.57]). Accounting for the number of GDMT classes prescribed attenuated the association of early coronary assessment with mortality (HR, 0.87 accounting for GDMT [95% CI, 0.60–1.27] versus 0.71 among those hospitalized with medication records [95% CI, 0.55–0.92]; $P_{interaction}$=0.88). Because GDMT was prescribed at much higher rates from 2013 onward (74% versus 26%; P<0.001), we subsequently restricted the analysis to only those diagnosed in 2013 and later. Among those diagnosed in 2013 and later, there was no benefit of elective coronary assessment (HR, 1.02 [95% CI, 0.75–1.39]), but the median follow-up time was only 2 years for this subset as compared to 7 years among those diagnosed 2002 to 2012, and the interaction term was not statistically significant ($P_{interaction}$=0.15). Accounting for the annual proportion of hospitalized HFrEF receiving outpatient GDMT did not attenuate the overall benefit (HR, 0.84 [95% CI, 0.72–0.98]).

Among those admitted with HF at the time of diagnosis, completing coronary assessment was associated

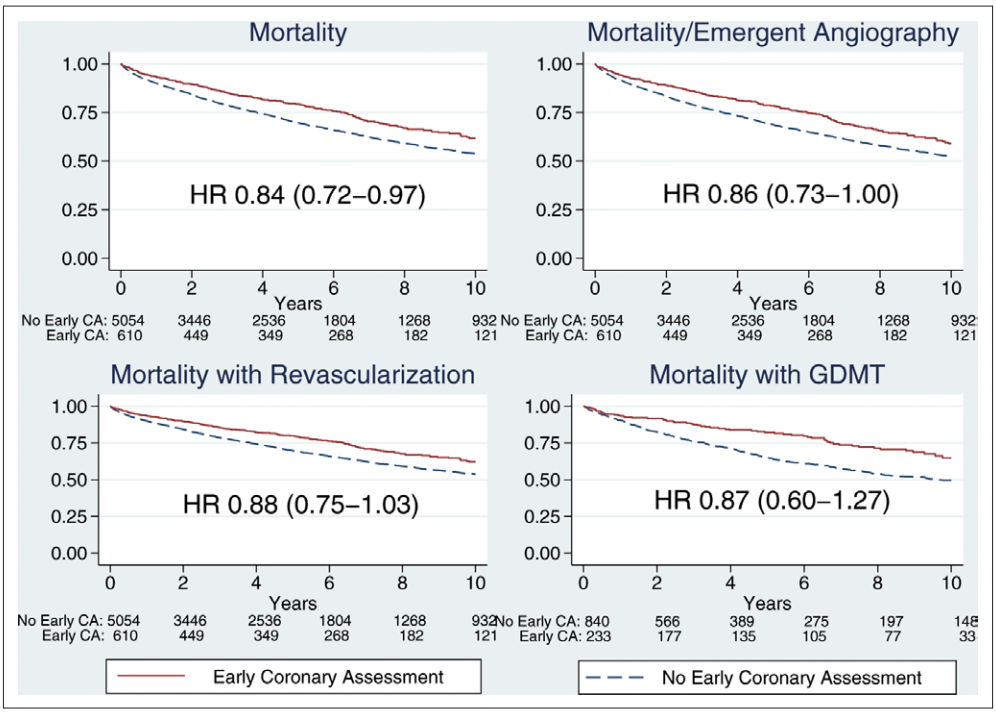

Figure 3. Association of early coronary assessment in heart failure (HF) with outcomes.
After defining the target trial, we adjusted for age, sex, propensity for coronary assessment as a restricted cubic spline, and HF hospitalization before testing and show the adjusted survival curves by concurrent coronary assessment. Hazard ratios (HRs) are comparing those who completed early coronary assessment to those who did not, with the bottom two additionally adjusting for revascularization (**bottom left**) and use of guideline-directed medical therapy (GDMT) among hospitalized patients with heart failure with reduced ejection fraction (**bottom right**). At-risk tables are shown below each. CA indicates coronary assessment.

with higher odds of attending outpatient follow-up within 30 days (83% versus 63%; $P<0.001$), which was in turn associated with lower mortality (HR, 0.81 [95% CI, 0.68–0.95]), but there was no effect modification of outpatient follow-up status on the benefit of completing coronary assessment ($P_{interaction}=0.91$).

DISCUSSION

In this study of nearly 15 000 individuals with HF from 2001 to 2019 who received care in the municipal safety-net system in San Francisco, we found significant differences in who received coronary artery assessment that

Table 4. Cause-Specific Mortality including Falsification End Points

	Coronary assessment (n=144)	No coronary assessment (n=1288)	Unadjusted *P* value for association between coronary assessment and specific cause of death	Estimate of effect of coronary assessment on cause-specific mortality
Cardiac causes reported as underlying cause of death				
Cardiovascular disease and risk factors	71 (49%)	573 (45%)	0.29	0.82 (0.63–1.06)
Acute myocardial infarction	5 (3.47%)	51 (3.96%)	1.00	0.60 (0.66–1.56)
Heart failure	38 (26.39%)	292 (22.67%)	0.35	0.76 (0.54–1.08)
Falsification end points reported as underlying cause of death				
Homicide or suicide	1 (0.69%)	10 (0.78%)	1.00	1.08 (0.13–8.90)
Motor vehicle accident	0 (0%)	9 (0.70%)	0.61	Cannot estimate
Cirrhosis*	4 (2.78%)	34 (2.64%)	1.00	1.03 (0.35–3.06)
Pneumonia/sepsis†	4 (2.78%)	40 (3.11%)	0.81	1.06 (0.37–3.08)

We report the number and proportion of deaths (number with specific underlying cause of death/total with death certificates linked) for the falsification end points, unadjusted *P* values based on Fisher exact test, and the hazard ratios and 95% CI for the effect of coronary assessment on the falsification end points (cause-specific death vs survival).

*Because we excluded individuals with known cirrhosis at the time of heart failure diagnosis from the target trial, we considered it as a possible falsification end point.

†Finally, because pneumonia and sepsis are typically acute illnesses that we would not expect coronary assessment to prevent or treat we included it as an additional falsification end point. Hazard ratios below 1 for cardiac causes of death and ≈1 for the falsification end points are consistent with our primary findings.

Table 5. Medical Therapy Among Those Hospitalized for Heart Failure By Coronary Assessment

	Timing	Coronary assessment	No coronary assessment	Unadjusted *P* value	Adjusted HR for mortality
ACE inhibitor/angiotensin receptor blocker	Prehospitalization	94 (48.0%)	207 (34.8%)	<0.001	
	Started	13 (6.6%)	27 (4.5%)		
	Ever	107 (55.0%)	234 (39.3%)	<0.001	0.40 (0.30–0.53)
Beta-blocker	Prehospitalization	97 (49.5%)	210 (35.3%)	0.001	
	Started	12 (6.1%)	32 (5.4%)		
	Ever	109 (55.6%)	242 (40.7%)	<0.001	0.39 (0.30–0.52)
Mineralocorticoid receptor antagonist	Prehospitalization	46 (23.5%)	91 (15.3%)	0.009	
	Started	6 (3.1%)	13 (2.2%)		
	Ever	52 (26.5%)	104 (17.5%)	0.006	0.52 (0.35–0.78)
Aspirin	Prehospitalization	78 (33.9%)	197 (22.5%)	<0.001	
	Started	20 (8.7%)	63 (7.2%)		
	Ever	98 (42.6%)	260 (29.7%)	<0.001	0.48 (0.38–0.61)
Statin	Prehospitalization	87 (37.8%)	194 (22.2%)	<0.001	
	Started	16 (7.0%)	42 (4.8%)		
	Ever	103 (44.8%)	236 (27.0%)	<0.001	0.45 (0.35–0.58)

Individuals with HFrEF hospitalized prior to coronary assessment were included for the beta-blocker, ACE/ARB, and mineralocorticoid receptor antagonist analysis (n=791; 196 who underwent coronary assessment at time of HF diagnosis and 595 who did not). Individuals hospitalized at the time of diagnosis prior to coronary assessment regardless of HFrEF were included for the aspirin/statin analyses (n=1104; 230 who underwent coronary assessment and 874 who did not). Adjusted cox proportional hazards models include age, sex, hypertension, diabetes, chronic kidney disease, coronary assessment, cubic spline for propensity for testing, and each individual class of medical therapy. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; HF, heart failure; HFrEF, Heart failure with reduced ejection fraction; and HR, hazard ratio.

did not align with the risk of CAD or risks of coronary assessment. Our second question was whether this matters for clinical outcomes including mortality and a composite of mortality and emergent coronary angiography. Our findings suggest that early coronary assessment after HF diagnosis is associated with reduced mortality, although the causal pathway remains uncertain. Individuals who received early coronary assessment were much more likely to be revascularized but also had higher rates of GDMT prescription before testing. Although there is a meaningful risk of residual confounding from our use of observational, electronic health record–collected data, our findings using current best practices of comparative-effectiveness research suggest that early coronary assessment may be beneficial and does not suggest major harm.

Patterns in Coronary Artery Assessment

Within a safety-net setting, fewer than one in five had coronary assessment concurrent with or after HF diagnosis. We found that women, older individuals, and those with documented unstable housing were less likely to complete coronary assessment, as well as differences by race and ethnicity, past medical history, and substance use. These patterns were not explained by coronary risk: for example, diabetes and HIV were associated with lower odds of testing even accounting for chronic kidney disease. Our findings are similar to several recent studies that have found a low proportion of individuals who underwent coronary assessment among individuals with incident HF without known CAD ranging from 16% to 40% across a range of practice settings in the United States and Europe.[9,16–18] Similarly, another study found that among those with incident HF in the United States, 35% underwent coronary assessment within 90 days of HF diagnosis, with similar patterns as found in our study, with younger, male, hospitalized patients, with a lower ejection fraction more likely to have a coronary assessment.[10] These patterns, particularly lower testing among women even accounting for differences in risk by age, race and ethnicity, and ejection fraction may be attributable to biases in referral (provider-level sexism and racism), differences in resources available to complete testing (structural sexism and racism), or differences in acceptability of testing (patient-physician trust and patient preferences). Not surprisingly, those referred for early coronary assessment were much more likely to ever undergo revascularization and went revascularization sooner after HF diagnosis, with similar rates of CABG and PCI.

Coronary Assessment and Outcomes

There are no randomized controlled studies of coronary assessment in HF, and we reproduced the findings from earlier observational studies that suggested coronary assessment may be associated with improved outcomes. An analysis from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients

with Heart Failure) study, which found that coronary assessment was associated with greater use of GDMT and improved outcomes among those found to have significant CAD, did not account for the propensity for referral for coronary assessment and stratified based on nonischemic and ischemic cardiomyopathy which is unknown without coronary assessment.[7] Similarly, an observational study within the Veterans Affairs system found that ischemic evaluation was associated with reduced mortality and higher use of GDMT, but that study excluded those who did not survive >90 days, creating immortal time bias and excluding immediate harms from invasive coronary assessment.[18] Observational data from Ontario suggest that early invasive coronary angiography within 2 weeks of HF diagnosis is associated with 4× higher rates of revascularization within 90 days, 26% lower morality, and 16% lower HF readmissions at two years.[8] However, that study included those with known CAD and those presenting with ACSs who are much more likely to benefit from immediate invasive angiography. Not surprisingly, we also found that early coronary assessment was associated with higher GDMT prescriptions (even before coronary assessment) and a higher likelihood of revascularization.

The best study on this topic demonstrated that early coronary assessment after HF within 1 month of HF diagnosis was associated with a 7% reduction in mortality among Medicare beneficiaries (HR, 0.93 [95% CI, 0.91–0.96]).[9] Similar to our study, they found that early coronary assessment was associated with higher rates of revascularization and HF GDMT. They conducted a mediation analysis and found that ≈70% of the benefit was attributable to changes in CAD medical therapy with statins. Although coronary assessment was associated with statin prescription in our study, we did not find a statistically significant increase in statin prescription after testing, nor was our primary outcome attenuated when we accounted for statin prescription.

To our surprise, there was no heterogeneity by ejection fraction. Those found to have multivessel CAD had a higher risk of mortality which appeared to be attenuated by revascularization. Early coronary assessment among those with chronic kidney disease was associated with a higher risk of mortality, although the CIs cross 1. We interpret this to mean that those with chronic kidney disease are less likely to benefit and/or more likely to experience harm from early coronary assessment, which is concordant with the ISCHEMIA-CKD randomized clinical trial of coronary angiography and revascularization if appropriate for patients with chronic stable coronary disease in the setting of advanced chronic kidney disease.[19]

We used a rigorous approach to use observational data to answer a question not addressed with randomized clinical trial data. To do so, we thought carefully about inclusion and exclusion criteria to restrict inclusion to those with equipoise regarding coronary assessment, started follow-up time for all individuals at the time of incident HF diagnosis, limited coronary assessment to a 30-day grace period to minimize immortal time bias, used propensity scores to adjust for confounders measured at the time of study eligibility, tested falsification end points, and conducted extensive sensitivity analyses. Our results were robust to our analytic assumptions using alternative approaches. Including individuals who eventually underwent coronary assessment after 30 days in the no coronary assessment group is analogous to crossover in a randomized trial; crossover would tend to bias our results toward the null, but this approach is the best approximation to the intention-to-treat approach. None of the subgroups of interest met our specified criteria for statistical significance but there were nonsignificant trends toward greater benefit among those hospitalized at the time of their HF diagnosis, those with HFrEF, and those with regional wall motion abnormalities on echocardiogram, and less benefit among individuals with chronic kidney disease.

Future Directions

Our study and the study by Zheng et al[9] leave several important questions unanswered. First, does the benefit we found persist in an era of widespread use of contemporary GDMT for HF with angiotensin receptor blockers/neprilysin inhibitors, beta-blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors (SGLT2i)? Our study suggests that if there is a benefit, participants will need to be followed for longer than 2 years to have any potential benefit outweigh the upfront risks from coronary assessment and subsequent revascularization among those found to have multivessel CAD.

Second, the role of coronary assessment in HF is most often linked to identifying patients who may benefit from revascularization, and we found that early coronary assessment was associated with earlier revascularization and a much higher likelihood of ever undergoing revascularization. The STICHES trial demonstrated that surgical revascularization for ischemic cardiomyopathy is associated with improvements in long-term outcomes including mortality and rehospitalization at 10 years[20] but did not demonstrate a statistically significant result at 5 years in an earlier era of medical therapy. Results from two large randomized controlled trials, ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches)[21] (which excluded patients with LVEF<40%) and REVIVED-BCIS2 (which only included patients with LVEF<35%),[6] have called into question the role of revascularization in chronic stable angina and ischemic cardiomyopathy, respectively. Even with these studies (with only medium-term results reported to date), there are unanswered questions including whether percutaneous coronary intervention and CABG should be considered equivalent in this setting, the role of viability or functional testing, and most importantly whether revascularization improves HF symptoms, quality of life, and long-term mortality.

To our knowledge, there are no randomized trials on the role of coronary assessment in HF, and there is limited evidence to guide who should have their coronaries assessed after diagnosis with HF, the best strategies for initial test selection, and ultimately whether early elective coronary assessment among patients with new HF prospectively improves patient-centered outcomes. To definitively answer these questions requires a pragmatic randomized clinical trial embedded in routine clinical care, especially given the consistently low rates of referral for coronary assessment across the published studies.

Limitations

The first limitation is that this is an observational study based primarily on the use of electronic health records. The use of *ICD* codes to ascertain propensity for coronary assessment results in a meaningfully high risk of residual confounding, as many clinical and socioeconomic factors are not well-captured in the electronic records. Second, we were unable to use an intention-to-treat approach as we were not able to ascertain those referred for testing who did not complete it. Those who complete coronary artery testing are more likely to attend outpatient follow-up, take prescribed medications, and undergo revascularization; limiting our study population to those who had completed an echocardiogram only partially accounts for this selection bias. A third limitation is that we only included coronary assessment performed within San Francisco Health Network or ordered by San Francisco Health Network and performed at UCSF Health (nuclear stress), which would tend to bias the results toward the null, although we were able to ascertain revascularization outcomes across the major regional health systems due to electronic health record connectivity. Although we planned to estimate atherosclerotic cardiovascular risk using the pooled cohort equations as a proxy for who should be referred for coronary assessment, ultimately, we did not do this as hospital blood pressures may reflect acute illness and medication use, lipid panels were missing for many individuals, and we could not verify current versus past smoking. We also did not have access to time-varying covariates except outpatient prescription data which was only available for those who were hospitalized before and after hospitalization, limiting our ability to adjust for the time-varying nature of GDMT in the whole study population and even more importantly from including GDMT into our propensity model. Additionally, this study was conducted before the use of SGLT2i (sodium-glucose cotransporter-2 inhibitor) and widespread angiotensin receptor blockers/neprilysin inhibitor use. Two limitations to our approach to immortal time are (1) by classifying those for whom physicians intentionally deferred coronary assessment (for acute kidney injury, pneumonia, or gastrointestinal bleed, for example) in the no early coronary assessment group we may have biased that group to have worse outcomes, and (2) our approach does not account for those who hypothetically would have been randomized to early coronary assessment and then died before they completed it. Despite our best efforts, these issues make the interpretation of our findings less conclusive despite the robustness of our findings to our analytic assumptions.

Conclusions

Among individuals with HF in a safety-net setting, we found significant differences in who completed coronary assessments that are not explained by coronary risk factors. Our results suggest that early coronary assessment among patients with HF without another indication for urgent coronary assessment is associated with improved mortality, more revascularization, and higher use of HF GDMT in a safety-net population. The extent to which our findings reflect a true benefit from early coronary assessment rather than unmeasured confounding from selection effects or residual confounding remains uncertain, suggesting that this clinical question requires a randomized clinical trial to answer with confidence.

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Disclosures

None.

Supplemental Material

Supplemental Results
Figure S1
Tables S1–S3

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