Revascularization Rates and Associated Costs in Patients With Stable Ischemic Heart Disease Initiating Ranolazine Versus Traditional Antianginals as Add-on Therapy

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To assess the frequency and costs of revascularization procedures in patients with stable ischemic heart disease (SIHD) initiating ranolazine versus traditional antianginals. Adults (≥18 years) with a diagnosis of SIHD who initiated ranolazine or a traditional antianginal (beta-blocker [BB], calcium channel blocker [CCB], or long-acting nitrate [LAN]) as second or third line therapy between 2008 and 2016, were selected from the IBM MarketScan Databases. Inverse probability weighting based on propensity score was employed to balance the ranolazine and traditional antianginals cohorts on patient clinical characteristics. Outcomes assessed were frequency and total cost of revascularization procedures over a 12-month follow-up. A total of 108,741 patients with SIHD were included. Of these, 18% initiated treatment with ranolazine, 21% received BBs, 24% received CCBs, and 37% were treated with LANs. Revascularization rates were significantly lower in ranolazine patients (11%) than in BB (16%) and LAN (14%) patients (both p <0.001), and more comparable to CCB patients (10%; p = 0.007). Compared with BB and LAN, those in the ranolazine cohort were less likely to have a revascularization procedure during hospitalization and had a shorter length of stay if hospitalized (all p <0.001). The mean healthcare costs associated with revascularization were lower in ranolazine patients ($2,933) than in BB ($4,465) and LAN ($3,609) patients (p <0.001), but similar to CCB patients ($2,753; p = 0.29). In conclusion, ranolazine treatment in patients with SIHD was associated with fewer revascularization procedures and lower associated healthcare costs compared with patients initiating BB or LAN, and comparable to patients initiating CCBs. **(Am J Cardiol 2019;123:1602−1609)**

In 8.7 million patients with stable ischemic heart disease (SIHD),[1] chronic angina is often initially treated with medical therapy, with 1 or more antianginal (AA) therapies such as a long-acting nitrate (LAN), beta-blocker (BB), calcium channel blocker (CCB), or ranolazine.[2] BBs have been the recommended first-line AA.[2] However, recent studies have raised concerns about their efficacy at improving mortality especially in patients without prior myocardial infarction.[3-5] Alternative AAs such as CCB, LAN, and ranolazine can be added if angina remains uncontrolled with BB, or used as monotherapy if BBs are contraindicated or results in unacceptable side effects. If symptoms are inadequately controlled with medical therapy, guidelines recommend considering coronary revascularization which may improve angina burden but are a major driver of healthcare costs in patients with SIHD.[6−8] Previous research has shown that use of ranolazine, as compared with traditional AAs, was associated with lower healthcare costs and fewer hospitalizations in patients with chronic stable angina.[9-11] Real-world data are limited on healthcare resource utilization for revascularization procedures and associated healthcare costs for patients treated with ranolazine versus traditional AAs. The purpose of this study is to describe the frequency and costs of revascularization procedures in a large real-world population of patients with SIHD after initiating ranolazine or traditional AAs as add-on therapy.

Methods

A retrospective, inverse probability of treatment-weighted matched cohort design was used to compare the revascularization rates and associated costs between patients with SIHD treated with ranolazine, BBs, CCBs, or LANs as second or third line therapy (Figure 1). This analysis was performed using patient-level administrative claims data extracted from the MarketScan Commercial Claims and Encounters Database and the MarketScan Medicare Supplemental and Coordination of Benefits database covering January 1, 2007 to June 30, 2017 The Commercial Claims and Encounters Database contains inpatient, outpatient, and outpatient prescription drug experience of approximately 137.6 million employees and their dependents covered under both fee-for-service and managed care health plans. The Medicare Supplemental and Coordination

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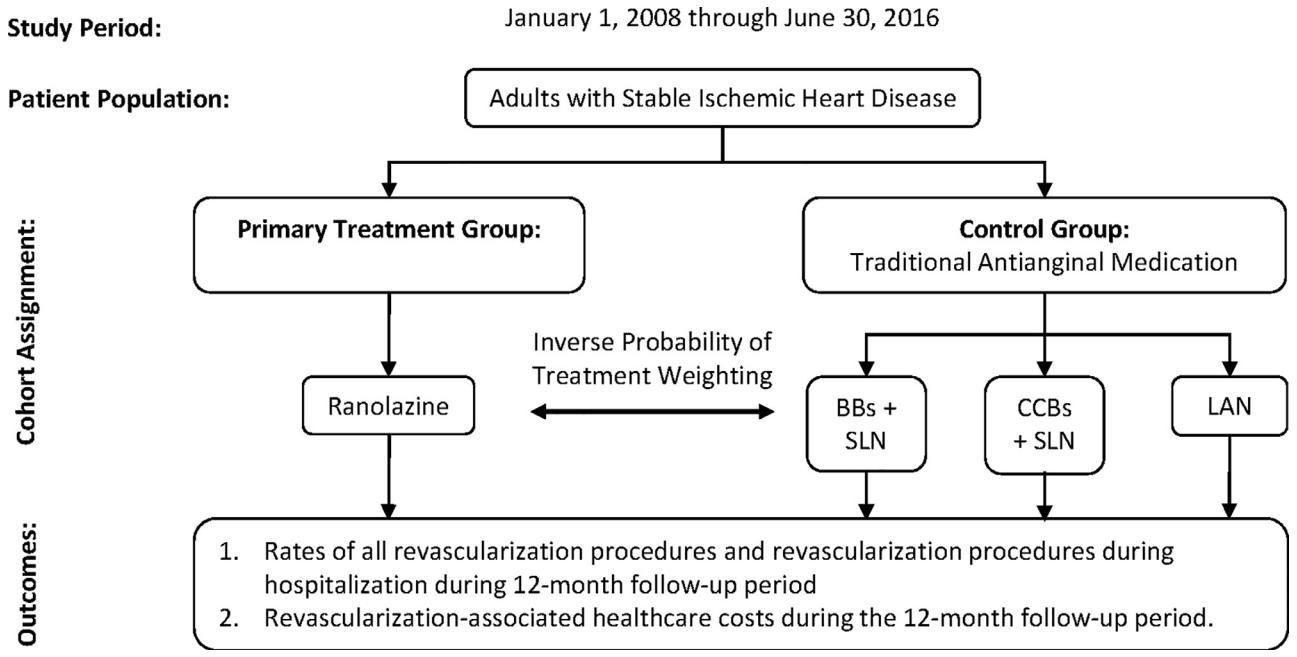

Figure 1. Study design. Abbreviations: BB = beta-blocker; CCB = calcium channel blocker; LAN = long-acting nitrate; SLN = sublingual nitroglycerin.

Benefits Database contain medical and prescription data on approximately 10.2 million retirees with Medicare supplemental insurance paid for by employers. These data spanned 1995 to 2017 and enrollees were covered by a geographically diverse group of self-insured employers and private insurance plans across the United States.

Potential SIHD patients were first identified based on their use of AA therapy. Patients were included in the study if they had ≥2 outpatient pharmacy claims ≥30 days apart for ranolazine or a traditional AA between January 1, 2008 and June 30, 2016. Since the objective of the study was to evaluate the effect of ranolazine versus addition of an alternative AA on downstream revascularization rates, the index date was defined as the date of the first ranolazine prescription or first prescription for a second or third line traditional AA. Patients were assigned to 1 of 4 mutually exclusive study cohorts (the primary treatment cohort [ranolazine] and the 3 control cohorts [BB, CCB, and LAN]) as follows. Patients in the ranolazine cohort were required to have ≥1 and <3 AA classes during the baseline period. All patients with ≥2 qualifying claims for ranolazine were assigned to the ranolazine cohort, and the remaining patients were assigned to 1 of the 3 control cohorts based on which traditional AA was initiated as a second- or third-line agent.

In addition, eligible patients needed to be ≥18 years old on the index date, have continuous enrollment with medical and pharmacy benefits for ≥12 months before (baseline) and ≥12 months after (follow-up) the index date, and have ≥1 inpatient or nondiagnostic outpatient claim of stable angina, history of unstable angina, previous myocardial infarction, history of percutaneous coronary intervention, or history of coronary artery bypass graft during the baseline period. Additionally, patients in the BB and CCB cohorts were required to have ≥1 outpatient pharmacy claim for sublingual nitroglycerin during the baseline or follow-up period to help identify utilization for an angina indication.

Baseline demographic characteristics, including age, age categories (18-29, 30-39, 40-49, 50-59, 60-69, 70-74, 75-79, 80+), gender, geographic region (Northeast, North Central, South, West), payer (commercial or Medicare), and index year (2008 to 2015), were measured on the index date. Clinical characteristics were measured during the baseline period. Clinical characteristics included Deyo-Charlson co-morbidity index, common co-morbidities of SIHD (angina, diabetes, dyslipidemia, hypertension, myocardial infarction, heart failure, atrial or ventricular arrhythmia, obesity, long-term kidney disease, smoking, acute coronary syndrome, and peripheral vascular disease), AA utilization in baseline period (ranolazine, BB, CCB, LAN, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, diuretics, statins, and anticoagulants), as well as select measures of baseline health resource utilization and costs (number of admissions, number of emergency room visits, and total healthcare costs).

Healthcare costs were based on paid amounts of adjudicated claims, including insurer and health plan payments as well as patient cost sharing in the form of copayment, deductible, and coinsurance. The costs for services provided under capitated arrangements were estimated using payment proxies that were computed based on paid claims at the procedure level using the *MarketScan Commercial and Medicare Supplemental Databases*. All dollar estimates were inflated to 2016 dollars using the Medical Care Component of the Consumer Price Index.[12]

The following revascularization-related outcomes were examined for the primary treatment cohort and all 3 control cohorts for the 12-month follow-up period: (1) the number patients with ≥1 claim for a revascularization procedure; (2) the number of patients with ≥1 claim for a revascularization procedure during hospitalization; (3) the number of hospitalizations per patient with revascularization; (4) the hospital length of stay in days; and (5) the cost of

revascularization procedures. For this study, revascularization procedures included percutaneous coronary intervention, or coronary artery bypass graft. A list of eligible Current Procedural Terminology, Healthcare Common Procedure Coding System, and International Classification of Diseases ninth and tenth Edition Clinical Modification codes can be found in Supplementary File 1.

After cohort assignment and application of eligibility criteria, inverse probability of treatment weighting was used to adjust for differences in baseline SIHD patient characteristics between the 3 control cohorts and the primary treatment cohort. Multinomial logistic regression modeling was performed to calculate a generalized propensity score which indicated the conditional probability of receiving BB, CCB, LAN, or ranolazine as a second- or third-line treatment. The weighting factors included the following baseline characteristics: age, age categories, gender, index year, co-morbid diagnosis of diabetes, dyslipidemia, hypertension, myocardial infarction, heart failure, atrial or ventricular arrhythmia, obesity, long-term kidney disease, smoking, acute coronary syndrome, or peripheral vascular disease, preindex use of 1 or 2 AA classes, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, diuretics, statins, or anticoagulants, as well as baseline total healthcare costs, number of inpatient admissions, and number of emergency room visits. After weighting, the standardized difference between cohorts was calculated for each covariate and factors with standardized difference values of ≤ 0.1 were considered well balanced.[13]

Continuous measures are presented as means and standard deviations. Categorical measures are presented as counts and percentages. Statistical tests of significance were conducted using Chi-square tests for dichotomous or categorical variables and dependent *t* tests for continuous variables. An a priori 2-tailed p value <0.05 was set as the threshold for statistical significance.

Results

Within the study period of January 1, 2008 through June 30, 2016, of the 108,741 eligible patients with SIHD, 18% were treated with ranolazine, 21% with BBs, 24% with CCBs, and 37% with LANs (Figure 2). After inverse probability treatment weighting, baseline demographic, and clinical characteristics were well balanced between the treatment cohort and the controls (Tables 1 and 2). Study patients had a mean age of 67 years, more than half were male, and they were most likely to live in the southern United States.

The mean baseline Deyo-Charlson Co-morbidity Index was 2.1, and the most common co-morbidities were hypertension, dyslipidemia, and diabetes (Table 2). Use of non-AA heart disease medication was common across all cohorts with 73% to 77% of patients receiving diuretics, 68% to 70% receiving statins, and 47% receiving angiotensin-converting enzyme inhibitors. Over the 1-year preindex period, patients had on average 0.78 to 0.92 inpatient admissions and 2.42 to 3.01 emergency room visits. The mean total cost of inpatient, outpatient and outpatient pharmacy pre-index healthcare expenditures ranged from $35,542 to $41,530.

In the baseline period, 84% to 85% of patients were treated with AA agents from only 1 class, and 15% to 16% of the patients were treated with AA agents from 2 classes.

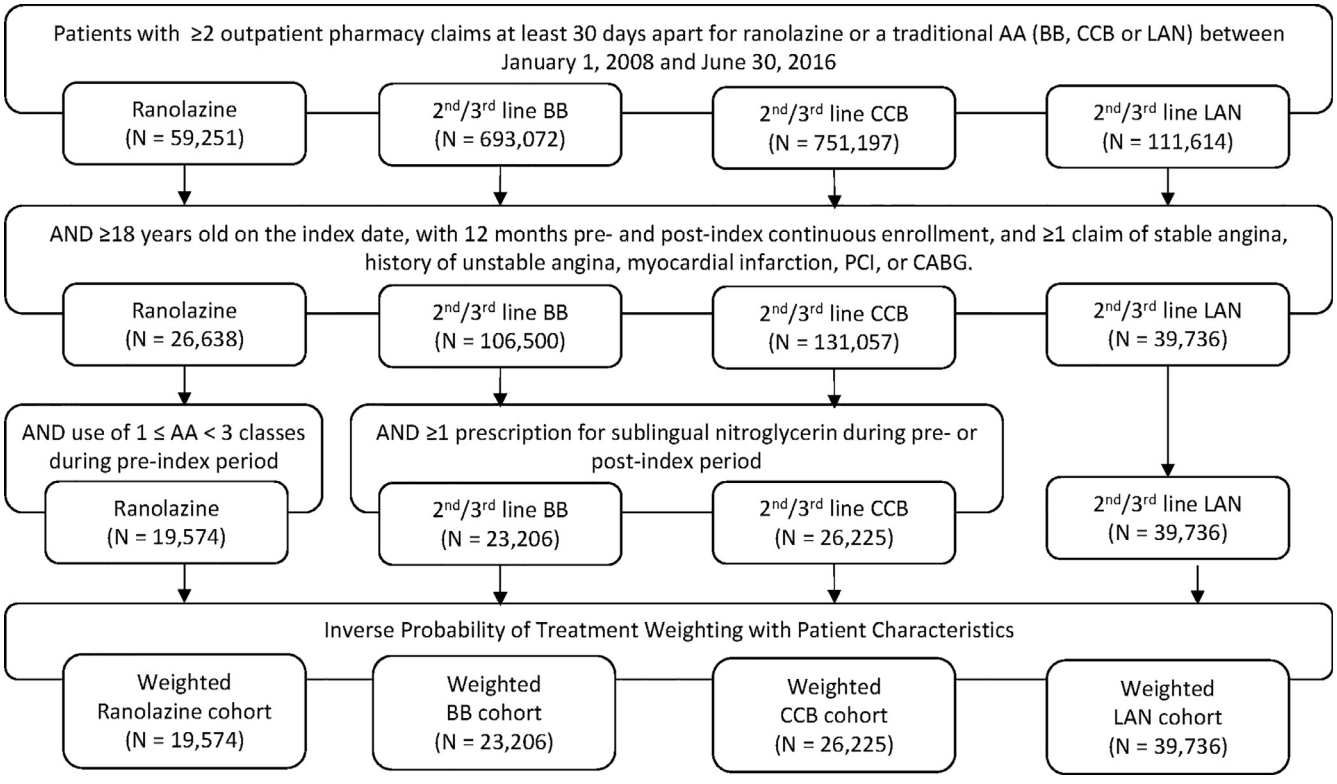

Figure 2. Patient selection. Abbreviations: AA = antianginal; BB = beta-blocker; CABG = coronary artery bypass graft; CCB = calcium channel blocker; LAN = long-acting nitrate; PCI = percutaneous coronary intervention; SIHD = stable ischemic heart disease.

Table 1
Patient demographics

Variable	Ranolazine (N = 19,574)	Beta blocker (N = 23,206)	SDiff*	Calcium channel blocker (N = 26,225)	SDiff	Long-acting nitrates (N = 39,736)	SDiff
Age† (years, mean ± SD)	66.5 ± 12.5	67.1 ± 12.5	0.047	66.9 ± 12.3	0.031	67.0 ± 12.9	0.037
Age Categories† (years)							
18-29	11 (0.1%)	15 (0.1%)	0.004	17 (0.1%)	0.004	45 (0.1%)	0.020
30-39	175 (0.9%)	219 (0.9%)	0.005	254 (1.0%)	0.008	447 (1.1%)	0.023
40-49	1,425 (7.3%)	1,508 (6.5%)	0.031	1,667 (6.4%)	0.037	2,776 (7.0%)	0.011
50-59	4,552 (23.3%)	5,030 (21.7%)	0.038	5,819 (22.2%)	0.025	8,890 (22.4%)	0.021
60-69	3,322 (17.0%)	3,924 (16.9%)	0.002	4,378 (16.7%)	0.007	6,346 (16.0%)	0.027
70-74	4,364 (22.3%)	5,186 (22.3%)	0.001	6,107 (23.3%)	0.024	8,676 (21.8%)	0.011
75-79	2,227 (11.4%)	2,814 (12.1%)	0.023	3,237 (12.3%)	0.030	4,549 (11.4%)	0.002
80+	3,499 (17.9%)	4,509 (19.4%)	0.040	4,746 (18.1%)	0.006	8,006 (20.1%)	0.058
Male†	11,594 (59.2%)	13,398 (57.7%)	0.030	15,479 (59.0%)	0.004	23,472 (59.1%)	0.003
Payer, medicare	10,400 (53.1%)	12,811 (55.2%)	0.042	14,365 (54.8%)	0.033	21,877 (55.1%)	0.039
Geographic region							
Northeast	3,330 (17.0%)	3,048 (13.1%)	0.109	4,044 (15.4%)	0.043	6,105 (15.4%)	0.045
North Central	5,655 (28.9%)	7,838 (33.8%)	0.105	8,702 (33.2%)	0.093	14,272 (35.9%)	0.151
South	8,829 (45.1%)	9,078 (39.1%)	0.122	9,636 (36.7%)	0.171	14,595 (36.7%)	0.171
West	1,653 (8.4%)	3,095 (13.3%)	0.157	3,700 (14.1%)	0.180	4,504 (11.3%)	0.097
Unknown	106 (0.5%)	147 (0.6%)	0.012	143 (0.5%)	0.001	260 (0.7%)	0.015
Index year†							
2008	2,713 (13.9%)	3,739 (16.1%)	0.063	4,045 (15.4%)	0.044	6,123 (15.4%)	0.044
2009	2,819 (14.4%)	3,573 (15.4%)	0.028	4,030 (15.4%)	0.027	6,090 (15.3%)	0.026
2010	3,134 (16.0%)	3,664 (15.8%)	0.006	4,061 (15.5%)	0.014	6,134 (15.4%)	0.016
2011	2,961 (15.1%)	3,351 (14.4%)	0.019	3,860 (14.7%)	0.011	5,839 (14.7%)	0.012
2012	2,897 (14.8%)	3,212 (13.8%)	0.027	3,747 (14.3%)	0.015	5,686 (14.3%)	0.014
2013	2,481 (12.7%)	2,834 (12.2%)	0.014	3,181 (12.1%)	0.017	4,926 (12.4%)	0.008
2014	1,931 (9.9%)	2,200 (9.5%)	0.013	2,519 (9.6%)	0.009	3,782 (9.5%)	0.012
2015	637 (3.3%)	635 (2.7%)	0.031	781 (3.0%)	0.016	1,157 (2.9%)	0.020

Abbreviation: SD = standard deviation.
* The standardized difference (SDiff) versus ranolazine; For weighted characteristics, SDIff values ≤ 0.100 were interpreted as indicating good balance.
† Characteristics used in inverse probability of treatment weighting.

For patients in the ranolazine, CCB, and LAN cohorts, over 3 quarters of patients took BBs as either their first- or second-line AA during the baseline period. For patients in the BB cohort, over 80% of patients took CCBs as a first - or second-line agent in the baseline period.

During follow-up, revascularization rates were significantly lower in ranolazine patients (11%) than in BB (16%) and LAN (14%) patients (both p <0.001) and more comparable to CCB patients (10%, p = 0.007) (Figure 3). Additionally, compared with BB and LAN patients, patients in the ranolazine cohort were less likely to have a revascularization procedure during hospitalization and had a shorter length of stay if hospitalized (all p values <0.001) (Table 3). Over a follow-up of 1 year, healthcare costs associated with revascularization were significantly lower in ranolazine patients ($2,933 ± $17,281) than BB ($4,465 ± $18,210) and LAN ($3,609 ± $16,543) patients (both p <0.001). Whereas CCB and ranolazine patients had similar healthcare costs ($2,753 ± $18,307), and ($2,933 ±$17,281, p = 0.285) respectively (Figure 4).

Discussion

In this retrospective analysis of real-world data from 108,741 patients with SIHD, we found that patients receiving ranolazine as a second- or third-line agent were less likely to undergo a revascularization procedure in the year following treatment initiation than those on BBs or LANs as a second- or third-line agent. Additionally, revascularization-associated healthcare costs were higher for patients in the BB and LAN cohorts than ranolazine cohort. Revascularization rates for the ranolazine cohort were more similar to those patients on CCBs, and revascularization-associated healthcare costs were comparable between patients in the ranolazine and CCB cohorts.

The primary indication of percutaneous coronary intervention in SIHD is for the relief of angina not responsive to medical therapy.[6] Specifically, percutaneous coronary intervention does not appear to reduce the risk of recurrent myocardial infarction or improve survival in this setting.[14,15] The use of percutaneous coronary intervention increases inpatient costs by a mean of $20,146 with a 3.8% risk of procedural complications including a 1.3% risk of any bleeding complication and a 0.2% risk of inpatient mortality.[16,17] Additionally, a follow-up to the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial found that delaying revascularization through treatment with medical therapy was not associated with irreversible ischemic events or increased 1-year mortality and that the primary drivers for subsequent revascularization were continued angina and patient dissatisfaction with their current treatment regimen.[18] These findings suggest that, for many patients, initial management of SIHD should focus on optimizing medical therapy for

Table 2
Baseline clinical characteristics

Variable	Ranolazine (N = 19,574)	Beta blocker (N = 23,206)	SDiff*	Calcium channel blocker (N = 26,225)	SDiff	Long-acting nitrates (N = 39,736)	SDiff
Deyo-Charlson Comorbidity Index† (Mean ± SD)	2.1 ± 2.1	2.0 ± 2.1	0.032	2.1 ± 2.1	0.013	2.1 ± 2.1	0.002
Comorbid conditions							
Stable angina	19,405 (99.1%)	22,649 (97.6%)	0.122	25,592 (97.6%)	0.122	38,804 (97.7%)	0.118
Diabetes†,‡	7,852 (40.1%)	9,111 (39.3%)	0.017	10,378 (39.6%)	0.011	15,831 (39.8%)	0.006
Dyslipidemia†	10,556 (53.9%)	12,243 (52.8%)	0.024	13,801 (52.6%)	0.026	20,901 (52.6%)	0.027
Hypertension†	14,423 (73.7%)	16,812 (72.4%)	0.028	19,049 (72.6%)	0.024	29,316 (73.8%)	0.002
Myocardial infarction†	5,056 (25.8%)	5,275 (22.7%)	0.072	6,496 (24.8%)	0.024	10,155 (25.6%)	0.006
Heart failure†	4,225 (21.6%)	4,721 (20.3%)	0.031	5,462 (20.8%)	0.019	8,160 (20.5%)	0.026
Atrial or ventricular arrhythmia†	6,255 (32.0%)	7,430 (32.0%)	0.001	8,441 (32.2%)	0.005	12,550 (31.6%)	0.008
Obesity†	1,579 (8.1%)	1,735 (7.5%)	0.022	2,069 (7.9%)	0.007	3,109 (7.8%)	0.009
Chronic kidney disease†	2,354 (12.0%)	2,606 (11.2%)	0.025	2,922 (11.1%)	0.028	4,590 (11.6%)	0.015
Cigarette smoker†,‡	1,987 (10.1%)	2,214 (9.5%)	0.020	2,556 (9.7%)	0.013	3,926 (9.9%)	0.009
Acute coronary syndrome†	7,127 (36.4%)	7,884 (34.0%)	0.051	9,458 (36.1%)	0.007	14,220 (35.8%)	0.013
Peripheral vascular disease†	2,285 (11.7%)	2,832 (12.2%)	0.016	3,105 (11.8%)	0.005	4,644 (11.7%)	0
Proportion of patients with the following antianginals							
Ranolazine	n/a	86 (0.4%)	n/a	148 (0.6%)	n/a	214 (0.5%)	n/a
Beta blockers	15,242 (77.9%)	n/a	n/a	25,144 (95.9%)	0.553	34,793 (87.6%)	0.258
Calcium channel blockers	3,355 (17.1%)	19,053 (82.1%)	1.709	n/a	n/a	10,562 (26.6%)	0.230
Long-acting nitrates	3,946 (20.2%)	7,795 (33.6%)	0.306	5,066 (19.3%)	0.021	n/a	n/a
Patients with 1 additional AA class† (index on 2nd line therapy)	16,604 (84.8%)	19,564 (84.3%)	0.014	22,241 (84.8%)	0.001	34,117 (85.9%)	0.029
Patients with 2 additional AA classes† (index on 3rd line of therapy)	2,970 (15.2%)	3,642 (15.7%)	0.014	3,984 (15.2%)	0.001	5,619 (14.1%)	0.029
Proportion of patients with the following medications							
Angiotensin converting enzyme inhibitors†	9,103 (46.5%)	10,762 (46.4%)	0.003	12,374 (47.2%)	0.014	18,883 (47.5%)	0.020
Angiotensin II receptor blockers†	5,220 (26.7%)	6,055 (26.1%)	0.013	6,798 (25.9%)	0.017	10,572 (26.6%)	0.001
Diuretics†	14,258 (72.8%)	17,776 (76.6%)	0.087	19,570 (74.6%)	0.041	28,916 (72.8%)	0.002
Statins†	13,305 (68.0%)	16,249 (70.0%)	0.044	18,141 (69.2%)	0.026	27,244 (68.6%)	0.013
Anticoagulants†	2,231 (11.4%)	2,868 (12.4%)	0.030	3,164 (12.1%)	0.021	4,718 (11.9%)	0.015
Selected baseline all-cause healthcare utilization and costs (Mean ± SD)							
Number of admissions†	0.8 ± 1.1	0.9 ± 0.9	0.001	0.8 ± 1.0	0	0.9 ± 1.1	0
Number of emergency room visits†	3.0 ± 7.4	2.4 ± 6.6	0	2.8 ± 6.5	0	2.9 ± 6.7	0.011
Total cost† (mean ± SD)	$41,530 ± $53,239	$38,286 ± $50,219	0	$35,542 ± $57,459	0	$39,880 ± $60,081	0.001

Abbreviations: AA = antianginal; DCCI = Deyo-Charlson comorbidity index; ER = emergency room; SD = standard deviation.

* The standardized difference (SDiff) versus ranolazine. For weighted characteristics, SDIff values ≤ 0.100 are generally acknowledged as indicating good balance.

† Characteristics used in inverse probability of treatment weighting.

‡ Diagnosis or condition-related treatment.

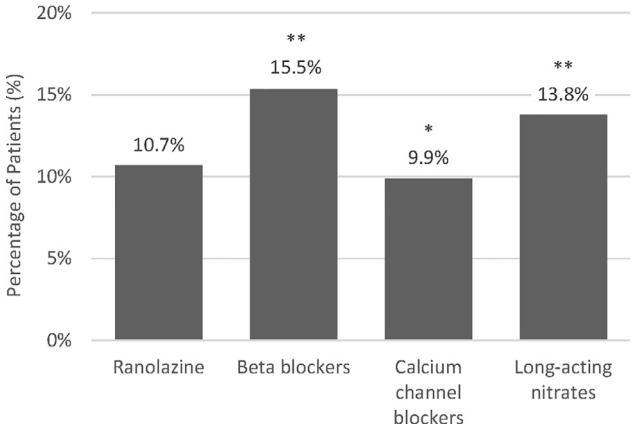

Figure 3. Revascularization rates during follow-up. Notes: *indicates p <0.01. ** indicates p <0.001.

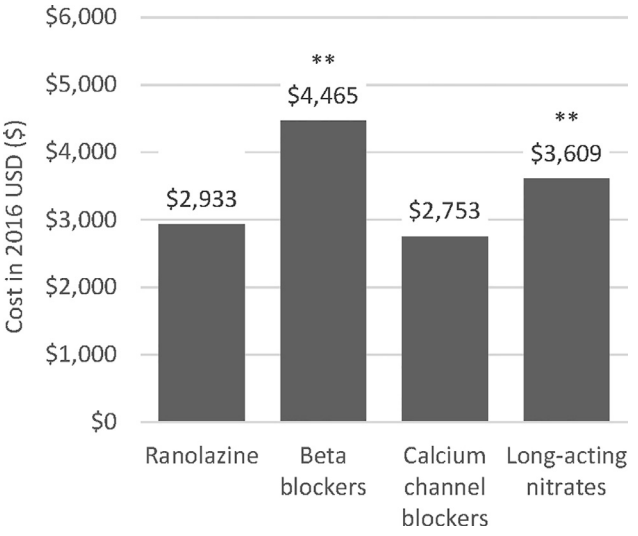

Figure 4. Revascularization-associated healthcare costs during the 12-month follow-up period. Abbreviations: USD = United States dollar. Notes: ** indicates p <0.001.

controlling angina symptoms. Together, these current findings may influence future clinical practice guidelines from cardiology professional society on the management of angina.[15,19]

The results of this study are consistent with the existing literature on ranolazine versus other AAs as an add-on therapy for SIHD. In a meta-analysis of second-line, add-on agents for management of stable angina, ranolazine resulted in consistent improvement in angina control, as measured by the relative rate reduction (rate, 95% confidence interval) in angina frequency (0.2, 0.1 to 0.3) and long-acting nitrate use (0.3, 0.2 to 0.4), when used in combination with either a BB or a CCB.[20] In a retrospective study of 150 consecutive patients with refractory angina who were initiated on ranolazine as an add-on therapy, the number of patients requiring hospitalization and the frequency of those hospitalizations was lower in the year following ranolazine initiation than in the year prior (p = 0.002).[10] A retrospective analysis of 4,545 unmatched patients with chronic stable angina found that patients with add-on ranolazine were less likely to have a revascularization procedure in the 6 months following index prescription than those with add-on LANs (p <0.001) or those on a BB/CCB combination (p <0.001).[11] Similarly, a propensity-matched study of 8,008 patients found that patients on second line BBs or LANs had higher odds (odds ratio, 95% confidence interval) of percutaneous coronary intervention (BB 2.8, 2.2 to 3.5; LAN 2.1 1.7 to 2.6) and coronary artery bypass graft (BB 2.9, 2.0 to 4.1; LAN 2.3, 1.6 to 3.4) within 1 year of treatment initiation compared with those on ranolazine.[9] For those on CCBs, the odds of coronary artery bypass graft were comparable (1.3, 0.9 to 2.0) whereas the odds of percutaneous coronary intervention (1.5, 1.2 to 1.9) were significantly higher compared with those on ranolazine. Taken together, the use of ranolazine as add-on antianginal therapy in patients with SIHD may reduce downstream resource use in the inpatient setting.

The limitations of this study are similar to other retrospective studies using administrative claims data. First, there is the potential for misclassification of SIHD, covariates, or study outcomes when patients are identified through administrative claims data as opposed to medical records. However, this is likely to have affected cohorts similarly and is therefore unlikely to change the observed trends. Second, there may be residual confounding not accounted for by inverse probability of treatment weighting. Third, this study is limited to individuals with commercial health coverage or private Medicare supplemental coverage, and therefore may not be generalizable to the general population. A recent similar study by Bress et al reported variable results in veterans.[21]

Table 3
Revascularization rates during hospitalization during 12-month follow-up

Variable	Ranolazine (N = 19,574)	Beta blocker (N = 23,206)	p value*	Calcium channel blocker (N = 26,225)	p value*	Long-acting nitrates (N = 39,736)	p value*
Patients with revascularization procedure during hospitalization	1,077 (5.5%)	1,973 (8.5%)	<0.001	2,106 (5.3%)	0.305	1,810 (6.9%)	<0.001
Number of hospitalizations with revascularization (mean ± SD)	0.1 ± 0.3	0.1 ± 0.3	<0.001	0.1 ± 0.3	0.014	0.1 ± 0.3	<0.001
Hospital length of stay, days (mean ± SD)	0.3 ± 2.5	0.5 ± 2.1	<0.001	0.3 ± 2.2	0.878	0.4 ± 1.9	<0.001

Abbreviation: SD = standard deviation.
* p Value calculated versus ranolazine cohort.

In conclusion, second- or third-line ranolazine treatment in AA treated patients with SIHD was associated with fewer revascularization procedures and lower revascularization-associated follow-up healthcare costs compared with patients initiating BB or LAN, and comparable to patients initiating CCBs.

Disclosures

Ethics approval and informed consent

All study data were accessed with protocols compliant with US patient confidentiality requirements, including the Health Insurance Portability and Accountability Act of 1996 regulations. As all database used in the study are fully deidentified and compliant with the Health Insurance Portability and Accountability Act of 1996, this study was exempted from Institutional Review Board approval.

Conflict of interest

CH, LN, and BK are employed by Gilead Sciences Inc. NM and OT are employed by IBM Watson Health as consultants and received funding from Gilead Sciences Inc. to conduct this study. DSK received consulting fees from Gilead Sciences Inc for providing methodological and clinical expertise to this project. This research was presented in part at the 2018 AHA QCOR, conference in Arlington, VA.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.02.014.

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