Healthcare Costs of Direct Oral Anticoagulants Among Medicare Patients with Nonvalvular Atrial Fibrillation and Multimorbidity

Poster
EE411

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Introduction

- Atrial fibrillation (AF), the most common heart dysrhythmia diagnosed in the United States, is associated with a significant increase in the risk of stroke/systemic embolism (SE).[1]
- Nonvalvular AF (NVAF) generally coexists with numerous comorbid conditions (hypertension, heart failure etc.) and these patients are categorized as multimorbidity patients (at least 2 or more comorbid conditions).[2]
- Though NVAF patients with multimorbidity likely have increased cost, particularly for stroke/SE (S/SE) and major bleeding (MB), there is limited literature on cost these patients incur within the context of newer direct oral anticoagulants (DOACs) compared to warfarin and when comparing DOAC to DOAC.

Objective

- The goal of this study was to evaluate cost differences between S/SE and MB among NVAF patients with multimorbidity prescribed DOACs or warfarin by comparing DOAC to warfarin and DOAC to DOAC.

Methods

Study Design / Data Source

- This was an observational retrospective cohort analysis using data from US Centers for Medicare and Medicaid Services (CMS).

Patient Population

- NVAF patients age ≥65 with an OAC (apixaban, rivaroxaban, dabigatran or warfarin) prescription from January 1, 2013 – December 31, 2017, were included in the study. The first OAC prescription date was designated as the index date.
- Patients had 12 months of continuous health plan enrollment including medical and pharmacy benefits prior to the index date (baseline period).
- Patients had a high ARISTOTLE multimorbidity level (≥6 comorbidities)[3]
- Additional inclusion and exclusion criteria are shown in Figure 1.
- The follow-up period ranged from 1-day post-index date until the earliest of the following: 30 days post-discontinuation, switch, death, end of the study period, or end of continuous medical or pharmacy enrollment.

Cohorts

Patients were assigned to the following cohorts based on index treatment:

- Apixaban
- Rivaroxaban
- Dabigatran
- Warfarin

Cohorts were matched via propensity scores to yield the following study groups:

- Apixaban-rivaroxaban
- Apixaban-dabigatran
- Apixaban-warfarin
- Dabigatran-rivaroxaban
- Rivaroxaban-warfarin
- Dabigatran-warfarin

Study Outcomes:

- Health care costs were evaluated during the follow-up period and included all-cause healthcare costs and medical costs related to S/SE and MB in the following settings: inpatient, ER, office, other outpatient, and other (durable medical equipment, home health agency, hospice, skilled nursing facility). Health care costs were calculated per patient per month (PPPM) and adjusted to 2017 US dollars.

Statistical Analysis

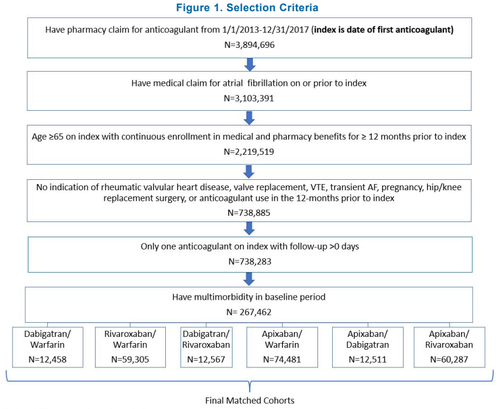
- All study variables were analyzed descriptively.
- Cost was reported as per patient per month (PPPM).
- Groups were compared using the chi-square test/ Fisher's exact test for categorical variables and student's t-test/Wilcoxan rank sum test for continuous variables. Fisher's exact and Wilcoxan rank sum were used for non-normal distributions. P-values <0.05 indicated statistically significant differences.
- Adjusted all-cause cost was estimated using generalized linear models.
- Adjusted costs due to S/SE and MB were estimated using two-part models with bootstrapping.

Results

Baseline Results

- Of the 3,894,696 patients who used an anticoagulant, 738,283 met all initial inclusion criteria and 267,462 were considered to have multimorbidity (Figure 1).

Figure 1. Selection Criteria



AF: atrial fibrillation; VTE: venous thromboembolism

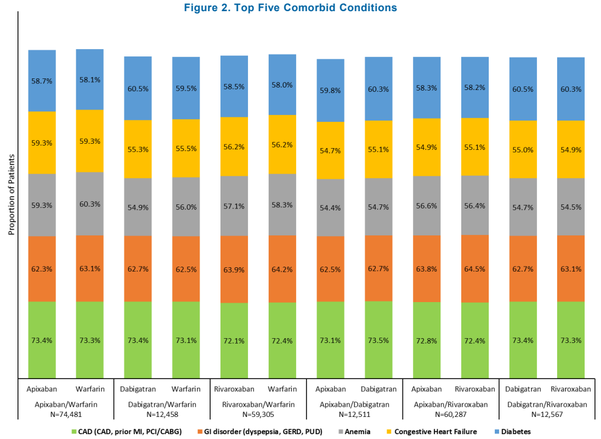
- Patients were ~78 years of age at index and female (≥ 50%) across all treatment pairs (Table 1).
- Patients averaged between 7 and 8 comorbidities and an average Deyo-Charlson Comorbidity Index (D-CCI) score between 5 and 6 across all treatment pairs (Table 1).
- Prevalence of comorbidities part of and not part of the multimorbidity definition was consistent across all treatment groups (Figure 2).
- Concomitant medication use, the HAS-BLED score and CHA_2DS_2-VASc score were consistent across all treatment groups (Table 1).

Table 1. Patient Characteristics

Patient Characteristics	DOAC	Warfarin (Reference)	P-value	STD*	DOAC	DOAC (Reference)	P-value	STD*
	Apixaban N=74,481	Warfarin N=74,481			Apixaban N=12,511	Dabigatran N=12,511		
Age	79.6 (7.7)	79.1 (7.7)	<.0001	7.1	78.2 (7.4)	78.2 (7.4)	0.5346	0.8
Gender								
Male	34,094 (45.8%)	34,805 (46.7%)	0.0002	1.9	5,947 (47.5%)	6,011 (48.0%)	0.4180	1.0
Female	40,387 (54.2%)	39,676 (53.3%)	0.0002	1.9	6,564 (52.5%)	6,500 (52.0%)	0.4180	1.0
Mean # of Comorbidities	7.8 (1.7)	7.8 (1.7)	0.4963	0.4	7.6 (1.7)	7.6 (1.7)	0.7493	0.4
Baseline Comorbidity								
Deyo-Charlson Comorbidity Index	5.6 (2.8)	5.3 (2.7)	<.0001	9.8	5.2 (2.7)	5.0 (2.6)	<.0001	9.2
$CHADS_2$ Score	3.7 (1.3)	3.7 (1.3)	<.0001	3.2	3.6 (1.3)	3.6 (1.3)	0.4140	1.0
CHA_2DS_2-VASc Score	5.9 (1.5)	5.8 (1.5)	<.0001	2.5	5.7 (1.5)	5.7 (1.5)	1.0000	0.0
HAS-BLED Score	4.3 (1.1)	4.2 (1.1)	0.1312	0.8	4.1 (1.1)	4.1 (1.1)	0.1513	1.8
	Dabigatran N=12,458	Warfarin N=12,458			Apixaban N=60,287	Rivaroxaban N=60,287		
Age	78.2 (7.4)	77.7 (7.4)	<.0001	7.3	78.7 (7.5)	78.8 (7.5)	0.0604	1.1
Gender								
Male	5,979 (48.0%)	6,160 (49.4%)	0.0218	2.9	28,060 (46.5%)	27,645 (45.9%)	0.0165	1.4
Female	6,479 (52.0%)	6,298 (50.6%)	0.0218	2.9	32,227 (53.5%)	32,642 (54.1%)	0.0165	1.4
Mean # of Comorbidities	7.6 (1.7)	7.7 (1.7)	0.0283	2.8	7.6 (1.7)	7.7 (1.7)	0.1956	0.7
Baseline Comorbidity								
Deyo-Charlson Comorbidity Index	5.0 (2.6)	5.1 (2.7)	0.0021	3.9	5.3 (2.7)	5.1 (2.7)	<.0001	9.1
$CHADS_2$ Score	3.6 (1.3)	3.6 (1.3)	0.0298	2.8	3.6 (1.3)	3.6 (1.3)	0.5359	0.4
CHA_2DS_2-VASc Score	5.7 (1.5)	5.7 (1.5)	0.1721	1.7	5.7 (1.5)	5.7 (1.5)	0.8509	0.1
HAS-BLED Score	4.1 (1.1)	4.2 (1.1)	0.0013	4.1	4.2 (1.1)	4.1 (1.1)	<.0001	2.3
	Rivaroxaban N=59,305	Warfarin N=59,305			Dabigatran N=12,567	Rivaroxaban N=12,567		
Age	78.8 (7.5)	78.3 (7.5)	<.0001	7.3	78.1 (7.3)	78.1 (7.4)	0.5466	0.8
Gender								
Male	27,420 (46.2%)	28,090 (47.4%)	<.0001	2.3	6,053 (48.2%)	6,055 (48.2%)	0.9799	0.0
Female	31,885 (53.8%)	31,215 (52.6%)	<.0001	2.3	6,514 (51.8%)	6,512 (51.8%)	0.9799	0.0
Mean # of Comorbidities	7.7 (1.7)	7.7 (1.7)	0.8163	0.1	7.6 (1.7)	7.6 (1.7)	0.3636	1.1
Baseline Comorbidity								
Deyo-Charlson Comorbidity Index	5.1 (2.7)	5.1 (2.7)	0.1256	0.9	5.0 (2.6)	5.0 (2.6)	0.1307	1.9
$CHADS_2$ Score	3.6 (1.3)	3.6 (1.3)	<.0001	2.5	3.6 (1.3)	3.6 (1.3)	0.3084	1.3
CHA_2DS_2-VASc Score	5.7 (1.5)	5.7 (1.5)	0.0011	1.9	5.7 (1.5)	5.7 (1.5)	0.5841	0.7
HAS-BLED Score	4.2 (1.1)	4.2 (1.1)	0.0002	2.2	4.1 (1.1)	4.1 (1.1)	0.7315	0.4

AF: atrial fibrillation; VTE: venous thromboembolism

Figure 2. Top Five Comorbid Conditions

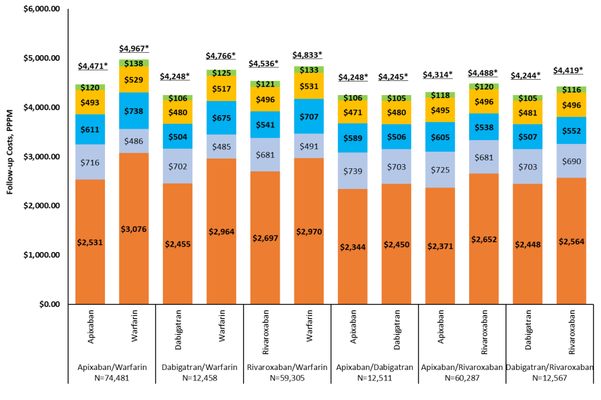


CABG: coronary artery bypass graft; CAD: coronary artery disease; GERD: gastroesophageal reflux disease; GI: gastrointestinal; MI: myocardial infarction; PCI: percutaneous coronary intervention; PUD: peptic ulcer disease

Outcomes

- All-cause costs during follow-up varied between $4,244 PPPM and $4,967 PPPM (Figure 3).
- Inpatient and pharmacy costs were the primary contributors to total all-cause costs (Figure 3).

Figure 3. PSM Costs During Follow-up PPPM



ER: emergency room
*Total cost: includes cost for durable medical equipment, skilled nursing, home health agency, and hospice

Table 2. GLM-adjusted Costs

	Marginal Effect		Difference	95% CI		P-value
	Drug 1	Drug 2		Lower	Upper	
Apixaban (drug 1) vs Warfarin (drug 2)						
Total all-cause medical cost	$3,754	$4,481	$720	$626	$814	<0.001
MB related medical cost	$213	$358	$147	$111	$183	<0.001
Stroke/SE related medical cost	$71	$106	$34	$6	$62	0.018
Dabigatran (drug 1) vs Warfarin (drug 2)						
Total all-cause medical cost	$3,545	$4,281	$738	$486	$989	<0.001
MB related medical cost	$235	$330	$92	$32	$153	0.003
Stroke/SE related medical cost	$64	$104	$42	$2	$81	0.038
Rivaroxaban (drug 1) vs Warfarin (drug 2)						
Total all-cause medical cost	$3,855	$4,342	$480	$354	$607	<0.001
MB related medical cost	$307	$341	$36	$5	$67	0.024
Stroke/SE related medical cost	$70	$103	$33	$13	$53	0.001
Apixaban (drug 1) vs Dabigatran (drug 2)						
Total all-cause medical cost	$3,509	$3,542	$36	-$152	$223	0.711
MB related medical cost	$192	$241	$48	-$16	$113	0.141
Stroke/SE related medical cost	$55	$64	$8	-$18	$33	0.562
Apixaban (drug 1) vs Rivaroxaban (drug 2)						
Total all-cause medical cost	$3,589	$3,806	$218	$114	$321	<0.001
MB related medical cost	$209	$306	$96	$55	$137	<0.001
Stroke/SE related medical cost	$70	$69	-$1	-$37	$35	0.940
Dabigatran (drug 1) vs Rivaroxaban (drug 2)						
Total all-cause medical cost	$3,541	$3,729	$187	-$40	$414	0.107
MB related medical cost	$240	$294	$56	$1	$110	0.045
Stroke/SE related medical cost	$64	$74	$11	-$19	$42	0.469

CI: confidence interval; GLM: generalized linear model; MB: major bleeding; SE: systemic embolism

- Compared to warfarin, DOACs (apixaban, rivaroxaban, dabigatran) had significantly less cost for any reason (all-cause), medical costs related to stroke/SE and medical cost related to MB (Table 2).
- When comparing DOAC vs DOAC, cost was generally similar; though apixaban use showed significantly lower all-cause and MB-related costs when compared to rivaroxaban (Table 2).

Limitations

- As with all claims data, laboratory results such as international normalized ratios were unavailable, diagnoses were identified using International Classification of Diseases, 9th/10th Revision, Clinical Modification (ICD-9/10-CM) codes, and drug prescriptions were identified through prescription claims. Missing values, coding errors, and lack of clinical accuracy may have introduced bias into the study.
- Observed outcomes are short-term, and may not reflect long-term outcomes for these patients.
- The study design is observational and not a cost-benefit study, as such any cost-benefit conclusions are limited and interpreted accordingly.

Conclusions

- NVAF patients with multimorbidity incurred varying all-cause, S/SE and MB costs when comparing DOACs to warfarin and DOACs to DOACs.
- Patients with DOAC use continually incurred lower cost than warfarin.
- Patients with apixaban use incurred lower all-cause and MB related medical cost than those with rivaroxaban use.

References

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Disclosures

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