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Antithrombotic Use in the Year After Bioprosthetic Aortic Valve Replacement in the Veterans Health Administration System

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PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for 4 ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

Develop clinical policies informed by evidence;

Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and

Set the direction for future research to address gaps in clinical knowledge.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at Nicole.Floyd@va.gov.

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ABSTRACT

BACKGROUND

Recommendations about antithrombotic medication use after bioprosthetic aortic valve replacement (bAVR) vary, with ongoing controversy regarding the use of anticoagulation versus antiplatelet medication approaches. Our objective was to describe the antithrombotic medication practice across the Veterans Health Administration (VHA) in the year following bAVR. This report is a companion to the systematic review comparing antithrombotic strategies after bAVR produced in 2017 by the Evidence-based Synthesis Program Center in Portland, Oregon.[1]

METHODS

We used text mining of notes to identify patients who received a first bAVR during the fiscal year 2005-2015 period at any VHA facility. We used outpatient pharmacy data (both VHA and non-VHA pharmacy information) and text notes to identify antithrombotic medications in the first year post-bAVR, which were classified into 1 of 6 strategies: aspirin only, warfarin only, aspirin and warfarin, dual antiplatelet, other, and no antithrombotic medications. The outcomes, which were assessed over the first year post-bAVR, included: all-cause mortality, thromboembolism risk (*ie*, myocardial infarction/acute coronary syndrome, ischemic stroke, pulmonary embolism, peripheral arterial embolism), and bleeding events (*ie*, gastrointestinal, intracranial [hemorrhagic stroke and intracranial hemorrhage], genitourinary, retroperitoneal, and pulmonary bleeding events). Outcomes were identified using primary diagnosis codes from either Emergency Department (ED) visits or hospital admissions within 1 year of the bAVR procedure date. Analyses were descriptive; no multivariable modeling was conducted.

RESULTS

The study cohort included N=9766 unique Veterans who received bAVR at one of 47 facilities. The number of procedures per year has increased from 641 in fiscal year 2005 (FY2005) to 1282 in fiscal year 2015 (FY2015). Baseline characteristics of patients varied across the 6 antithrombotic medication strategies: patients with a prior major bleeding event were less likely to be prescribed aspirin or warfarin following bAVR, and patients with concomitant CABG were more likely to utilize dual antiplatelet therapy following surgery. The most commonly prescribed antithrombotic strategy was aspirin only (N=4758, 49%) followed by aspirin and warfarin (N=2992, 31%) and dual antiplatelet therapy (N=1562, 16%). Facility variation was observed in terms of the most common medication strategies that were prescribed. The proportion of patients receiving various antithrombotic medication strategies seemed relatively constant over time. Over the 1-year post-bAVR period, death was observed in 5% of patients and was most common among patients who did not receive any antithrombotic medications (12%). Overall, thromboembolic events were relatively uncommon (3.1%) within 1 year. Similarly, major bleeding events were also relatively uncommon (2.7%) over the first year post-bAVR. The highest observed bleeding rates were among patients receiving the combination of aspirin and warfarin (4.9%).

[1] Papak J, Chiovaro J, Noelck N, Healy L, Freeman M, Paynter R, Low A, Kondo K, McCarty O, Kansagara D. Comparing Antithrombotic Strategies after Bioprosthetic Aortic Valve Replacement: A Systematic Review. VA ESP Project #05-225; 2017.

CONCLUSIONS

These data demonstrate that bAVR procedures are increasingly being performed in VHA facilities and that aspirin alone continues to be the single most commonly used antithrombotic medication strategy post-bAVR. Future work should evaluate the risk-adjusted differences in outcomes according to alternative medication strategies.

BACKGROUND

Although bioprosthetic aortic valve replacement (bAVR) is generally well-tolerated, post-bAVR patients are at increased risk of thromboembolism, especially in the early post-procedural period.[1] However, recommendations about antithrombotic medication use after bAVR vary, with ongoing controversy regarding the need for and duration of anticoagulation versus antiplatelet medication approaches.[2-5] Following bAVR, patients may receive a variety of antithrombotic medications, including warfarin-based and antiplatelet-based strategies.

Several investigators have examined the association between alternative anticoagulation strategies and post-bAVR outcomes. For example, one large cohort study included 25,656 elderly patients receiving bAVR during the 2004-2006 period; the authors reported that the aspirin plus warfarin strategy, compared with aspirin alone, was associated with a reduced risk of death or embolic events but a higher risk of bleeding.[6]

The Veterans Health Administration (VHA) is the single largest healthcare system in the United States. Our objective was to describe the antithrombotic medication practice across the VHA system in the year following first bAVR during the FY2005-FY2015 period.

METHODS

DATA SOURCES

The VHA uses an electronic health record system known as the Veterans Information System Technology Architecture (VistA). VistA includes diagnoses, procedures, medications, laboratory values, physiologic measurements, and text notes and reports. Data are aggregated from VistA to the Corporate Data Warehouse (CDW), a national repository of clinical (and administrative) data that are stored in a relational database.[7] Data from multiple domains were used, including: inpatient and outpatient visits and associated diagnosis codes, surgery procedure codes and dates, laboratory data, orders (especially regarding medications), consults, allergies, health factors (including tobacco use and medication use), and pharmacy data. The Textual Information Utilities (TIU) documents store textual information from VistA, such as surgery notes, progress notes, and admission and discharge summaries, as well as notes that are sent to VHA providers from non-VHA providers. The VA Vital Status File (VSF) contains death dates for Veterans and was used to identify deaths after bAVR.[8,9] Linked VA Centers for Medicare and Medicaid Services (CMS) data were used to identify outcome events.

Cohort Construction

We identified Veterans who received a bioprosthetic aortic valve (bAVR) procedure (with or without coronary artery bypass grafting [CABG]) in any Veterans Health Administration (VHA) facility during the period FY2005-2015. We first identified Veterans with a procedure code (CPT or ICD-9 procedure code) for AVR (ICD-9 procedure codes 35.05, 35.06, 35.21, 35.22; CPT 33361-33369, 33404-33406, 33410-33413). Although prior studies have identified bAVR based solely on CPT or ICD-9 procedure codes, our chart reviews indicated that these codes cannot reliably distinguish mechanical AVR from bioprosthetic AVR. Because our focus was on patients with bAVR, we needed to exclude patients with mechanical valve replacement

procedures. Therefore, we used text mining to differentiate between bioprosthetic AVR and mechanical AVR for patients with a procedure code for aortic valve replacement.

We used TIU notes in the CDW to identify patients who received bAVR. The Nurse Intraoperative Report (NIR) document was the primary source of valve information. The NIR contains information about: time in/out of operating room; type of operation; names of surgeon, anesthesiologist, nurses, and other operating room personnel; a list of all prostheses installed; medications provided; and other text notes. The NIR is organized in a similar way across most VHA facilities. The prosthesis list includes information on item name, vendor, model, lot/serial number, and size. We used this list to search for known bAVR models using a combination of vendor names and model numbers with wildcards to account for patterns within text (*eg*, Carpentier Edwards Perimount, model 2700/2700TFX). If the NIR was not available or could not be used to classify type of AVR, we used all other available text notes (*eg*, surgeon's operative report, anesthesiology report, inpatient progress notes) to identify AVR type. Our text mining approach was iterative, meaning that we used text mining strategies to search for bAVR and then conducted chart reviews (n=405) to refine and improve the text mining strategies. Patients classified as having mechanical AVR or those who could not be classified were excluded. We further excluded patients: with bAVR at a non-VHA hospital, who did not have any prescriptions dispensed from a VHA pharmacy in both the 1-year period before or after bAVR, who had a prior AVR procedure, with in-hospital death, who were still hospitalized 30 days following bAVR, who were discharged to hospice, who were transferred to a non-VHA hospital on the day of bAVR surgery, who left against medical advice, or who were admitted more than 30 days prior to the bAVR surgery (Figure 1).

Classification of Antithrombotic Medications

For each patient, we used a variety of data sources from the CDW to classify antithrombotic medication use in the year before bAVR and the year after bAVR. Specifically, we used outpatient pharmacy data for medications filled at VHA pharmacies (*ie*, medications prescribed by VHA providers and filled at a VHA pharmacy), order data from within the VHA that indicate whether a VHA-prescribed medication will be obtained at a non-VHA pharmacy (*ie*, medications prescribed by VHA providers that a patient intends to fill outside the VHA), non-VHA pharmacy files (*ie*, a Veteran reports a medication that he/she is taking that was prescribed by a non-VHA provider and was filled at a non-VHA pharmacy), and text notes. Similar to the cohort construction, we conducted iterative chart reviews to confirm the medication identification and classification strategies. The chart review-based iterative approach was especially helpful with identifying aspirin use because many Veterans obtain aspirin outside the VHA due to lower cost. The chart reviews were instrumental in identifying data domains which were available in the CDW (*eg*, health factors) that could be used to identify the "non-VHA" aspirin use. Antithrombic medications in the year following bAVR were classified into 1 of 6 strategies (Table1): aspirin only, warfarin only, aspirin and warfarin, dual antiplatelet, other, and no antithrombotic medications. Appendix A provides a summary of the chart review findings related to the classification of patients into medication strategies.

As a secondary analysis, we sought to examine the duration of warfarin and aspirin that was used for patients post-bAVR. In order to identify medication duration, we used days-supply information. In this way, we could identify the start of the medication (*eg*, the day the medication was filled) and with the days-supply information we could estimate the duration of time patients

received that medication. However, these analyses were limited because the non-VHA medication data did not include days-supply. Therefore, we could only use VHA-medication data for the examination of duration of antithrombotics.

Outcomes

The outcomes that described the potential benefits of antithrombotic medication use after bAVR included a reduction in all-cause mortality and thromboembolism risk (*ie*, myocardial infarction/acute coronary syndrome, ischemic stroke, pulmonary embolism, peripheral arterial embolism). The outcomes that describe the potential harms of antithrombotic medication use included gastrointestinal, intracranial [hemorrhagic stroke and intracranial hemorrhage], genitourinary, retroperitoneal, and pulmonary bleeding events. Outcomes were identified using primary diagnosis codes from either Emergency Department (ED) visits or hospital admissions within 1 year of the bAVR procedure date. Both VHA and Medicare data were used to identify outcome events within 30, 90, and 365 days of bAVR. A list of ICD-9 and ICD-10 diagnosis codes to identify outcome events is available upon request.

Analyses

Baseline characteristics included: age, gender, race, Charlson Comorbidity Score, history of tobacco smoking and other medical conditions (*eg*, history of atrial fibrillation), documented allergy to aspirin or warfarin, concomitant coronary artery bypass graft (CABG), prior history of a major bleeding event, and use of aspirin and warfarin in the 1-year prior to bAVR. Differences were examined in baseline characteristics across the six antithrombotic treatment strategies. These analyses were descriptive in nature, proportions were reported for binary characteristics, and outcomes and means with standard deviations (SD) were reported for continuous variables. No stochastic testing was conducted. No multivariable modeling was performed. Missing data were rare; no imputations were made. SAS Enterprise Guide 7.1 (Cary, NC) was used for data analysis. The study received institutional research approval and VHA Research and Development approval. Please contact the corresponding author for information about data sharing.

RESULTS

The study cohort included N=9766 unique Veterans who received bAVR at one of 47 facilities, 41 of which performed at least 10 procedures during the study time frame (Figure 1). The number of procedures per year has increased from 641 in FY2005 to 1282 in FY2015 (Figure 2). The median number of patients per facility was 195 (range 1-697).

Baseline characteristics are shown in Table 1. Overall, patients with bAVR were male (99%), had a mean age of 70 years (SD, 8.9), were predominantly of White race (86%) and were hospitalized for 9 days (SD, 5) following bAVR. The majority of patients (70%) were using aspirin prior to bAVR. However, only 11% used warfarin prior to bAVR. Key differences in baseline characteristics were observed across the medication strategies (Table 2). As expected, patients with a prior major bleeding event were less likely to be prescribed aspirin or warfarin following bAVR. Patients with concomitant CABG were more likely to utilize dual antiplatelet therapy following surgery.

The most commonly prescribed antithrombotic strategy was aspirin only (N=4758, 49%) followed by aspirin and warfarin (N=2992, 31%) and dual antiplatelet therapy (N=1562, 16%; Figure 3). Most patients (N=9312, 95%) received aspirin at some point (alone or in combination with other medications) in the year following bAVR. One-third of patients (N=3175, 33%) received warfarin in the year following bAVR.

Facility variation was observed in terms of the most common medication strategies (Figure 4). This difference in medication strategies did not seem to be related to the prevalence of atrial fibrillation at each facility (Figure 4). The proportion of patients receiving various antithrombotic medication strategies seemed relatively constant over time (Figure 5).

Table 3 provides the outcome data (death, thromboembolic events, and major bleeding events) following bAVR. Death was observed in 5% of patients within 1 year and was most common among patients who did not receive any antithrombotic medications (12%). Overall, thromboembolic events were relatively uncommon (3.1%) within 1 year. Similarly, major bleeding events were also relatively uncommon (2.7%) over the first year post-bAVR. The highest observed bleeding rates were among patients receiving the combination of aspirin and warfarin (4.9%). Note: these differences are unadjusted for baseline characteristics.

A total of 1056 patients were on warfarin plus aspirin for the entire year post-bAVR. Among these patients, we sought to examine antithrombotic use in the pre-bAVR period, seeking any potential indications for long-term anticoagulation. Among these long-term warfarin plus aspirin patients: 525 (49.7%) had no antithrombotic pre-bAVR; 261 (24.7%) used aspirin alone pre-bAVR; 198 (18.8%) received warfarin pre-bAVR; and 72 (6.8%) were taking warfarin plus aspirin prior to their bAVR procedure.

The duration of medications could only be assessed among the sub-group of patients with VHA medication data (Table 4); given that many patients had both VHA and non-VHA sources of their antithrombotic medications, these results should be evaluated with caution. The data in Table 4 and Figure 6 suggests that among patients with both aspirin and warfarin in the post-bAVR period, the majority received a 90-day supply (70.7% for aspirin and 76.6% for warfarin).

DISCUSSION

These data provide the first national examination of antithrombotic medications for patients receiving bAVR in the VHA. The results demonstrate that although the number of bAVR procedures has doubled from 641 in FY2005 to 1282 in FY2015, practice patterns with regard to antithrombotic medication use have remained relatively stable over time. Specifically, nearly half of all bAVR patients are prescribed aspirin alone, a third receive the combination of aspirin and warfarin, and just a little over 10 percent receive dual antiplatelet agents.

The observed pattern of antithrombotic medications was similar to that reported by Brennan and colleagues regarding a US (non-Veteran) bAVR population in terms of aspirin alone use but differed for other antithrombotic medication strategies; they reported that 49% of patients were given aspirin, 23% aspirin plus warfarin, 12% warfarin alone, 8% dual antiplatelet therapy, and 7% no anticoagulation.[6] Therefore, the rates of warfarin alone (12% versus 2%) and no anticoagulation (7% versus 1%) were higher in the Brennan report than we observed in this VHA cohort. In contrast, the dual antiplatelet agent use was twice as high in the VHA (16%) as in the Brennan report. It may be that these observed differences could be explained by differences in baseline characteristics of the cohorts, although differences in reporting of comorbidities makes a direct comparison difficult.

The degree of variation in antithrombotic medications across facilities warrants further attention. Although differences in patient characteristics might explain this variation, it did not appear as if differences in atrial fibrillation accounted for the observed variation. Future research should include a detailed assessment of the risk-adjusted variation at the facility level.

Although the observed death and bleeding rates were lower than those reported by Brennan et al,[6] and the thromboembolism rates were higher, it is imperative that future work include multivariable modeling to account for the observation that patient characteristics varied across the medication strategies.

An innovation of this project was the use of text mining for cohort construction. This general approach to identifying populations of interest is gaining acceptance and popularity given the availability of notes (which contain text data) within the VHA Corporate Data Warehouse.[10] For example, Redman et al used natural language processes on CDW radiology reports to identify VHA patients with fatty liver disease.[11] In another example, Mowery et al used natural language processing on both radiology reports and TIU notes to identify patients with carotid stenosis.[12]

LIMITATIONS

Although these data provide a robust examination of bAVR procedures across the VHA system over time, several limitations should be noted. First, one facility was excluded because there were no TIU notes available for that facility, and therefore patients receiving a bAVR procedure could not be identified at that facility. Second, because we did not conduct full chart review nor interview clinicians, we cannot comment on the clinical reasoning for selecting certain antithrombotic medication strategies. Third, because the administrative data does not include a measure of patient preferences, we cannot examine the degree to which patients' preferences for or against a particular strategy contributes to practice. Fourth, we included VHA and non-VHA medication data but we appreciate that this will produce an underestimate of the rate of

medication (in particular, aspirin) use from non-VHA sources; the degree of underestimation is unknown. Finally, although we excluded patients with a prior history of AVR, distant prior AVRs (before our lookback period) might have been missed, and therefore some patients in this cohort may have had the bAVR as a second procedure.

In conclusion, these data demonstrate that bAVR procedures are increasingly being performed in VHA facilities. Aspirin alone continues to be the single most commonly used antithrombotic medication strategy post-bAVR. Future work should evaluate the risk-adjusted differences in outcomes according to alternative medication strategies.

Figure 1. Cohort Construction

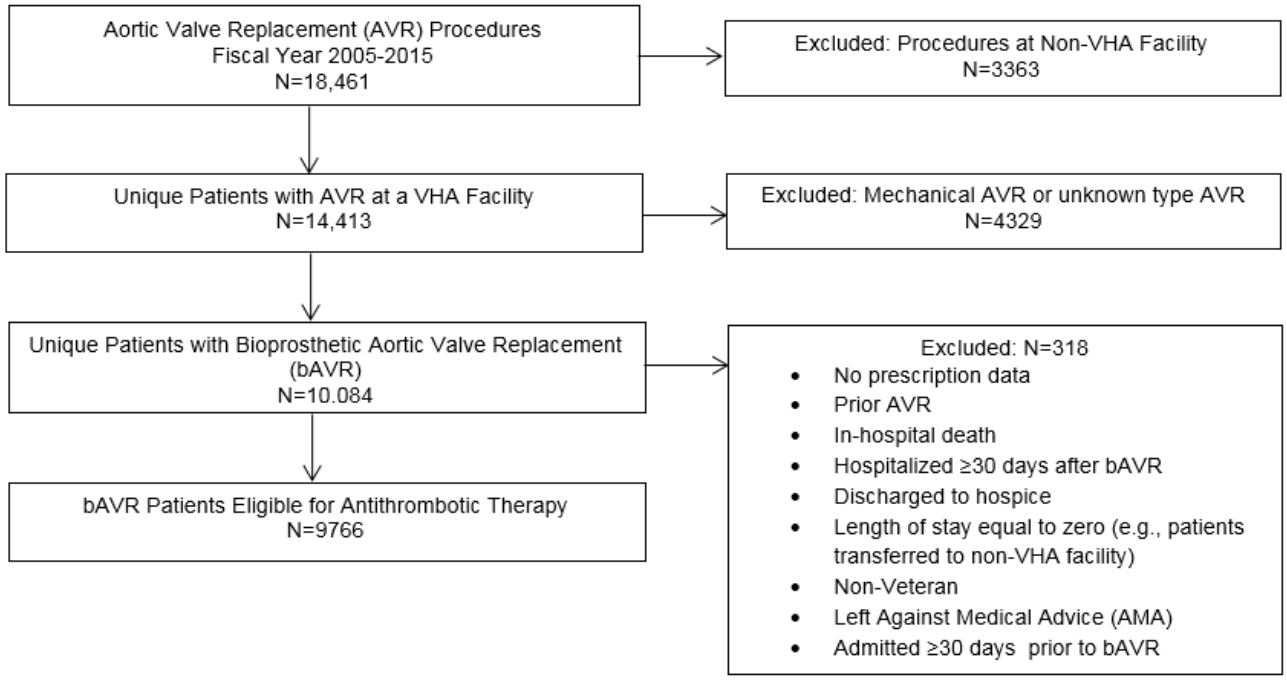


Figure 2. Number of Patients with Bioprosthetic Aortic Valve Replacements by Year

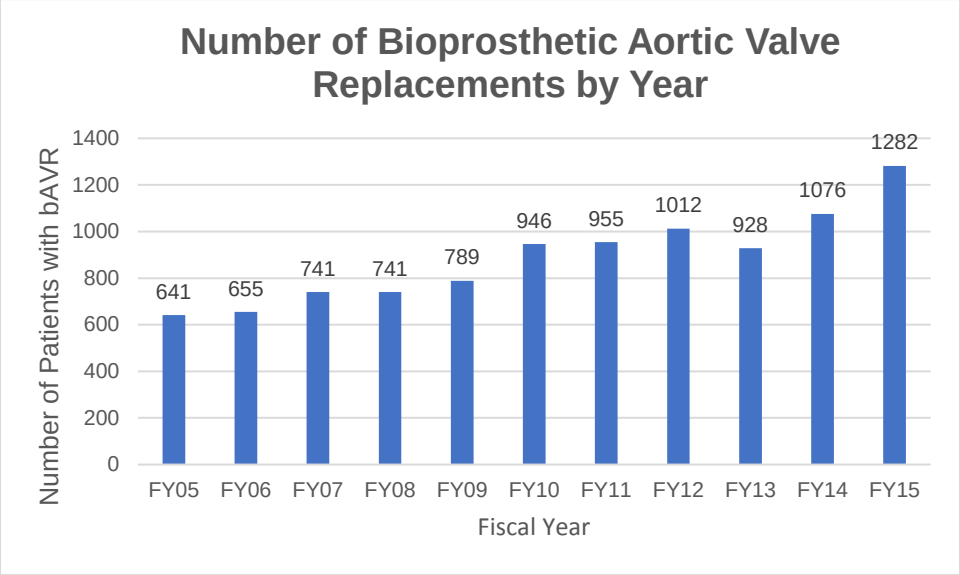


Figure 3. Antithrombotic Medication Use in Year after Bioprosthetic Aortic Valve (N=9766)

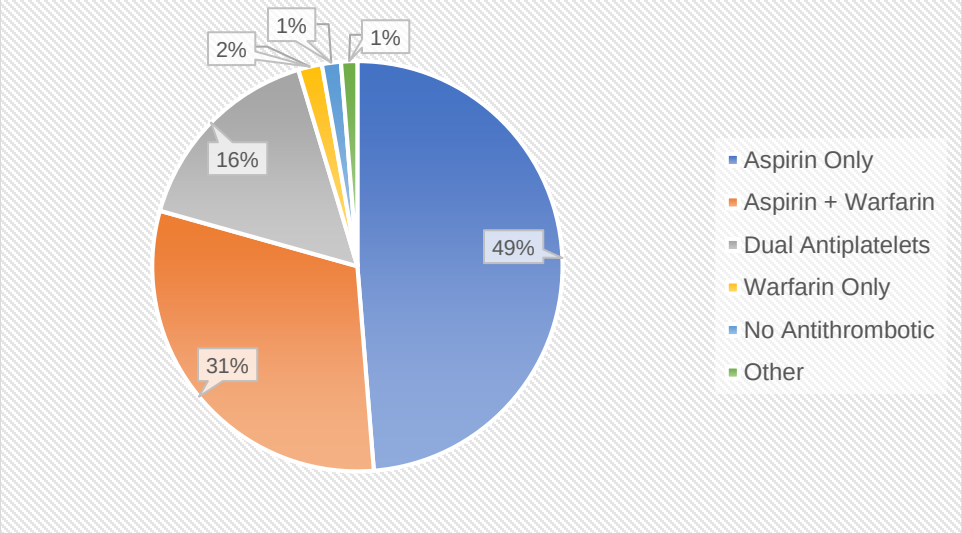
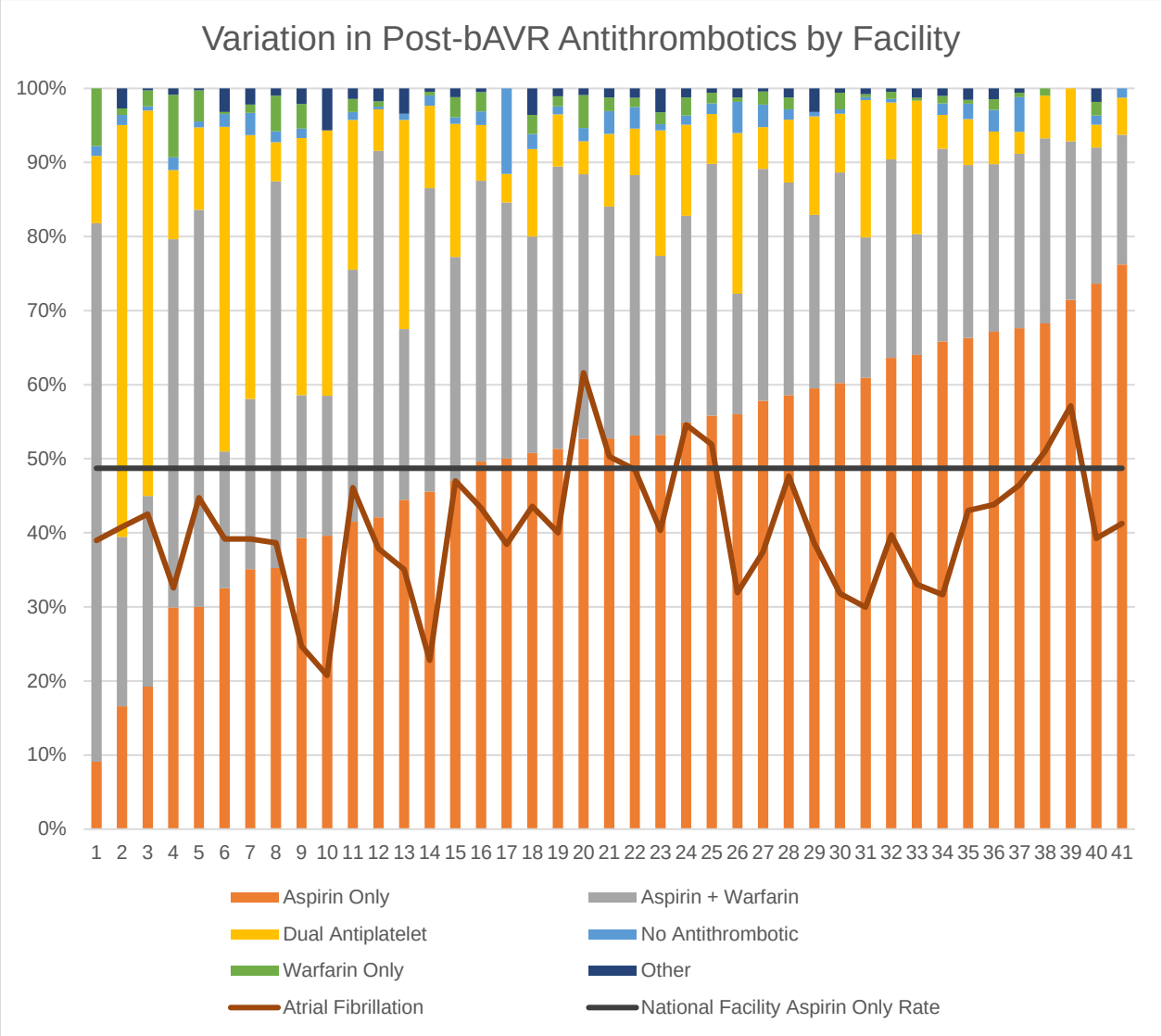


Figure 4. Variation in Post-bAVR Antithrombotic Medication Use by Facility



Legend: Facilities with fewer than ten bAVR patients were excluded from this figure. The facilities are ranked from left to right in terms of the proportion of patients who received aspirin only. The national mean facility aspirin only proportion is indicated by the black horizontal line. The facility proportion of patients with atrial fibrillation is indicated by the brown line.

Figure 5. Variation in Antithrombotic Medication Use by Fiscal Year

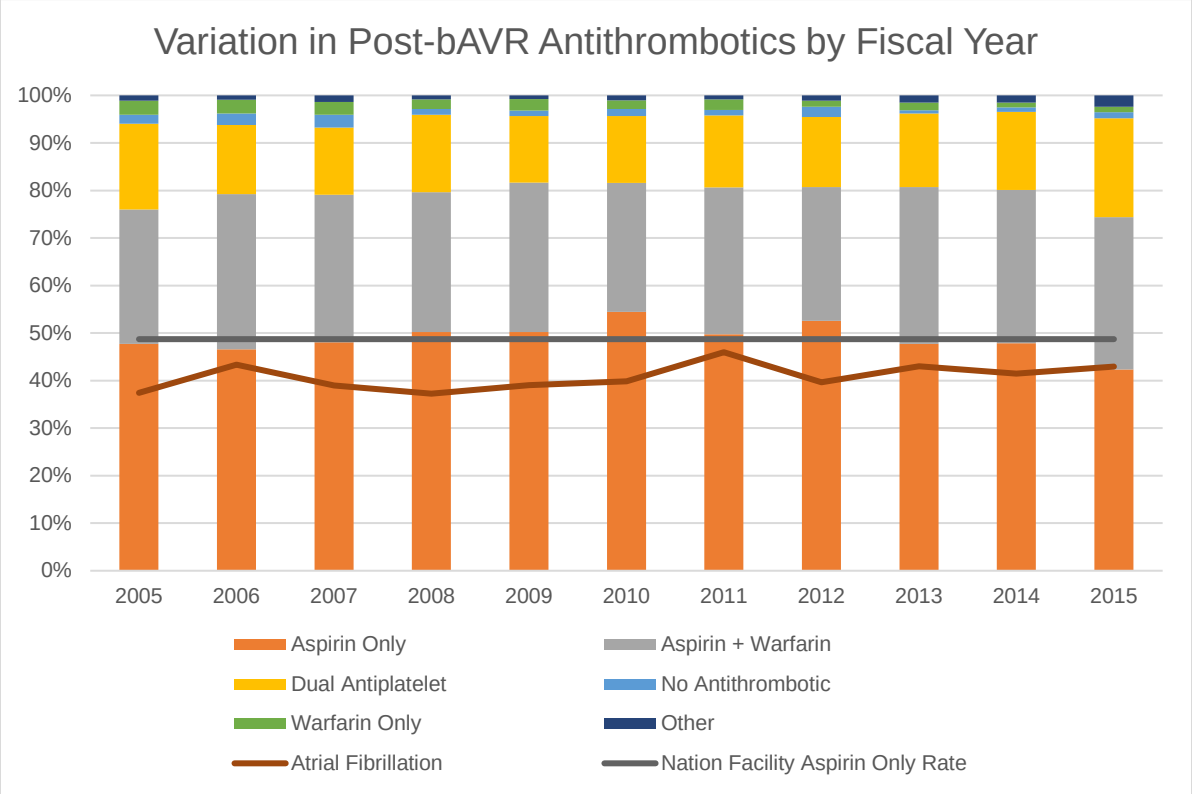


Figure 6. Medication Use Among Patients with Warfarin Plus Aspirin Among Patients with VHA Prescriptions (N=2241)

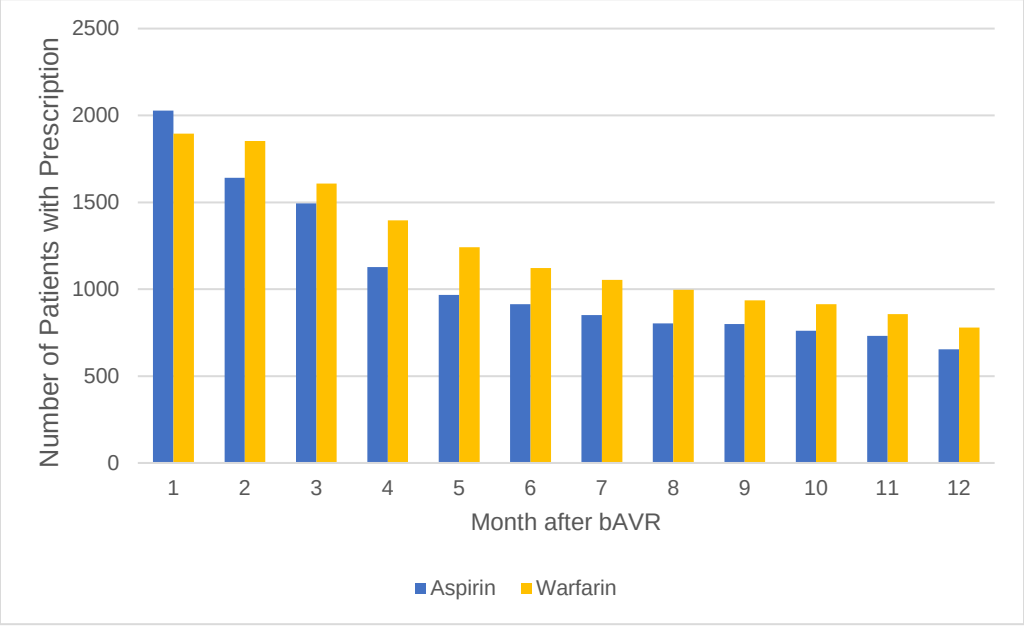


Table 1. Antithrombotic Medication Classification

CATEGORY	MEDICATIONS	COMMENT
Warfarin	Warfarin	Warfarin was included in both the warfarin-only group and in the warfarin plus aspirin group.
Aspirin	Aspirin	Aspirin was included in the aspirin-only, aspirin plus warfarin, and dual-antiplatelet groups.
	Aspirin/Dipyridamole	
	Dipyridamole	
Non-aspirin Antiplatelets	Clopidogrel	These agents were classified in the dual anti-platelet and "other" groups.
	Ticlopidine	
	Prasugrel	
Direct oral anticoagulants	Dabigatran	These agents were included in the "other" antithrombotic category.
	Apixaban	
	Rivaroxaban	
	Edoxaban	
	Betrixaban	
	Eribaxaban	
Full-Dose Low Molecular Weight Heparins	Ardeparin	These agents were not included in the final antithrombotic classification system because they were used either in the inpatient period for thromboembolism prevention or in the outpatient period as bridging to warfarin.
	Bemiparin	
	Certoparin	
	Dalteparin	
	Enoxaparin	
	Nadroparin	
	Parnaparin	
	Reviparin	
	Tinzaparin	
Other	Danaparoid	These agents were only considered if they were used for chronic antithrombotics (as opposed to isolated inpatient purposes); they were rarely observed except for fondaparinux which was not used for chronic antithrombotic purposes.
	Lepirudin	
	Bivalirudin	
	Argatroban	
	Eptifibatide	
	Fondaparinux	
	Idraparinux	
	Tirofiban	
	Bciximab	

Table 2. Baseline Characteristics of Patients with bAVR by Anticoagulation Strategy

Characteristic	Cohort (N=9766)		Aspirin + Warfarin (N=2992, 30.6%)		Aspirin Only (N=4758, 48.7%)		Dual Antiplatelets (N=1562, 16.0%)		No Antithrombotic (N=146, 1.5%)		Other (N=125, 1.3%)		Warfarin Only (N=183, 1.9%)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Male	9633	98.6	2956	98.8	4693	98.6	1547	99.0	139	95.2	118	94.4	180	98.4
Age: mean ± SD	69.7±8.9		70.4±8.7		69.1±9.1		70.1±8.8		69.0±9.9		70.5±8.5		7.16±9.3	
Charlson Comorbidity Index: mean ±SD	2.5±2.1		2.7±2.1		2.3±2.0		3.0±2.3		2.1±1.9		2.6±2.2		2.8±2.1	
Race														
White	8346	85.5	2578	86.2	4043	85.0	1341	85.9	121	82.9	107	85.6	156	85.3
Black	851	8.7	232	7.8	449	9.4	130	8.3	17	11.6	8	6.4	15	8.2
Other	131	1.3	48	1.6	52	1.1	23	1.5	0	0.0	4	3.2	4	2.2
Unknown	438	4.5	134	4.5	214	4.5	68	4.4	8	5.5	6	4.8	8	4.4
Tobacco Smoking	2723	27.9	781	26.1	1364	28.7	453	29.0	41	28.1	41	32.8	43	23.5
Past Medical History														
Myocardial Infarction	1036	10.6	334	11.2	400	8.4	270	17.3	8	5.5	15	12.0	9	4.9
Congestive Heart Failure	2853	29.2	1074	35.9	1142	24.0	483	30.9	33	22.6	38	30.4	83	45.4
Diabetes Mellitus	3836	39.3	1195	39.9	1768	37.2	717	45.9	39	26.7	59	47.2	58	31.7
Atrial Fibrillation	4919	41.1	1967	65.7	1379	29.0	422	27.0	48	32.9	60	48.0	134	73.2
Ischemic Stroke	563	5.8	207	6.9	199	4.2	125	8.0	7	4.8	12	9.6	13	7.1
Prior Bleeding Event*	235	2.4	79	2.6	113	2.4	32	2.1	7	4.8	2	1.6	2	1.1
bAVR + CABG Procedure	4600	47.1	1469	49.1	2033	42.7	943	60.4	36	24.7	57	45.6	62	33.9
Allergy to Aspirin	282	2.9	63	2.1	98	2.1	51	3.3	10	6.9	42	33.6	18	9.8
Allergy to Warfarin	31	0.3	10	0.3	14	0.3	5	0.3	0	0.0	2	1.6	0	0.0
Medication Use in Year Prior to bAVR														
Aspirin	6852	70.2	2057	68.8	3428	72.1	1233	78.9	40	27.4	55	44.0	39	21.3
Warfarin	1105	11.3	869	29.0	92	1.9	34	2.2	5	3.4	17	13.6	88	48.1
Length of Stay, Admission to Discharge (Days): Mean ± SD	11.5±7.1		12.8±7.3		10.9±6.8		10.7±6.6		13.1±8.9		12.0±7.7		15.1±8.3	
Length of Stay, bAVR to Discharge (Days): Mean ± SD	9.3±5.1		10.4±5.4		8.8±4.9		8.6±4.8		10.4±6.5		9.6±5.6		12.0±5.8	

*Prior bleeding events includes only those with an Emergency Department visit or inpatient stay.

Table 3. Outcome Events Among Patients with bAVR by Anticoagulation Strategy

Outcome	Cohort (N=9766)		Aspirin + Warfarin (N=2992)		Aspirin Only (N=4758)		Dual Antiplatelet (N=1562)		No Antithrombotic (N=146)		Other (N=125)		Warfarin Only (N=183)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Death														
30 Days	51	0.5	15	0.5	23	0.5	9	0.6	1	0.7	3	2.4	0	0.0
90 Days	146	1.5	49	1.6	59	1.2	18	1.2	10	6.9	6	4.8	4	2.2
365 Days	454	4.7	170	5.7	184	3.9	63	4.0	17	11.6	9	7.2	11	6.0
Myocardial Infarction														
30 Days	31	0.3	9	0.3	15	0.3	7	0.5	0	0.0	0	0.0	0	0.0
90 Days	55	0.6	17	0.6	24	0.5	14	0.9	0	0.0	0	0.0	0	0.0
365 Days	136	1.4	47	1.6	46	1.0	43	2.8	0	0.0	0	0.0	0	0.0
Ischemic Stroke														
30 Days	29	0.3	18	0.6	5	0.1	5	0.1	0	0.0	0	0.0	0	0.0
90 Days	50	0.5	23	0.8	11	0.2	14	0.9	0	0.0	0	0.0	0	0.0
365 Days	89	0.9	36	1.2	20	0.4	28	1.8	0	0.0	2	1.6	3	1.6
Embolism														
30 Days	29	0.3	21	0.7	4	0.1	3	0.2	0	0.0	1	0.8	0	0.0
90 Days	51	0.5	38	1.3	6	0.1	5	0.3	0	0.0	1	0.8	1	0.6
365 Days	88	0.9	68	2.3	7	0.2	9	0.6	0	0.0	2	1.6	2	1.1
Any Thromboembolic Event														
30 Days	87	0.9	46	1.5	24	0.5	15	1.0	0	0.0	1	0.8	1	0.6
90 Days	153	1.6	75	2.5	41	0.9	33	2.1	0	0.0	1	0.8	3	1.6
365 Days	306	3.1	146	4.9	73	1.5	78	5.0	0	0.0	4	3.2	5	2.7
Major Bleeding Event														
30 Days	70	0.7	36	1.2	20	0.4	13	0.8	1	0.7	0	0.0	0	0.0
90 Days	128	1.3	66	2.2	36	0.8	23	1.5	1	0.7	1	0.8	1	0.6
365 Days	260	2.7	147	4.9	69	1.5	34	2.2	2	1.4	3	2.4	5	2.7

Table 4. Patterns of Aspirin Plus Warfarin Use after bAVR based on VHA Prescriptions*

Medication Use	Aspirin + Warfarin* (N=2241)	
Aspirin: Days-Supply		
Mean (SD), Median (Range)	168 (119), 124 (1-365)	
Days-Supply, n (%)		
≥30	2142	(95.6)
≥90	1585	(70.7)
≥180	980	(43.7)
≥365	219	(9.8)
Aspirin Use by Month		
Month 1	28028	(90.5)
Month 2	1641	(73.2)
Month 3	1493	(66.6)
Month 4	1127	(50.3)
Month 5	968	(43.2)
Month 6	913	(40.7)
Month 7	851	(38.0)
Month 8	804	(35.9)
Month 9	800	(35.7)
Month 10	761	(34.0)
Month 11	732	(32.7)
Month 12	654	(29.2)
Warfarin: Days-Supply		
Mean (SD), Median (Range)	192 (119), 180 (1-365)	
Days-Supply, n (%)		
≥30	2149	(95.6)
≥90	1717	(76.6)
≥180	1137	(50.7)
≥365	263	(11.7)
Warfarin Use by Month		
Month 1	1896	(84.6)
Month 2	1853	(82.7)
Month 3	1608	(71.8)
Month 4	1397	(62.3)
Month 5	1241	(55.4)
Month 6	1121	(50.0)
Month 7	1053	(47.0)
Month 8	997	(44.5)
Month 9	935	(41.7)
Month 10	913	(40.7)
Month 11	856	(38.2)
Month 12	779	(34.8)

*Aspirin and warfarin use data were obtained from several sources. However, only VHA prescription files include the days-supply. Among the N=2992 patients with aspirin and warfarin use within 1 year of discharge from bAVR, N=2241 had VHA prescriptions for both aspirin and warfarin. Most of these patients had data stating that in addition to the VHA aspirin they also had non-VHA aspirin use (even among patients with 365 days-supply of VHA aspirin).

APPENDIX A: CHART REVIEW SUMMARY

Chart reviewer examined the electronic medical record data for any information about medications including: anticoagulation clinic notes, provider progress notes, pharmacy notes, discharge summaries, CAPRI medication tab information, and VistaWeb pharmacy VHA & non-VHA information.

WARFARIN ONLY

We examine notes from 79 warfarin-alone patients seeking to identify any missed aspirin use; we found that 77 had a documented aspirin allergy, 1 patient had a note that indicated that the patient was receiving aspirin in the non-VA setting and this was recorded as non-VA "ASA" and was therefore not identified in the NLP algorithm that searched for the term "aspirin," and 1 patient had a plan to use warfarin for only 3 months and then start aspirin but no follow-up records were present and therefore it appeared as if the patient only received warfarin. To summarize, the warfarin-only classification appeared to have been correct in 78/79 charts (98.7%).

NO ANTITHROMBOTIC MEDICATION

We completed a total of 33 chart reviews for patients who were classified in the "no antithrombotics" group. The most commonly cited reasons why patients were prescribed no antithrombotic medications included the following:

- No medications were named or described in the notes or orders, therefore it appears from the chart review as if there was no specific antithrombotic medication plan (n=11)
- The patient began care at a new facility very soon after surgery, and the new provider did not follow up on a plan from the first facility or did not develop an anticoagulation plan (n=7)
- High risk of bleeding (n=4)
- Allergic to aspirin, never prescribed another medication (n=5)

LOW MOLECULAR WEIGHT HEPARIN

We reviewed a total of 24 charts of patients receiving low molecular weight heparin (LMWH): 15 were for bridging to warfarin therapy and 9 were for deep vein thrombosis (DVT) prophylaxis. Within each medication classification, the use of LMWH was for 1 of these 2 reasons.

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