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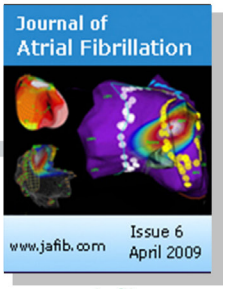

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Assessing Patient Management and Outcomes in Atrial Fibrillation: Does your Health Insurance Plan know more than your Doctor?

Sanjeev Saksena MD FHRS and April Slee, MS

a. Electrophysiology Research Foundation, Warren, New Jersey, and, b. Department of Medicine Robert Wood Johnson Medical School, New Brunswick, New Jersey,c. Axio Research Corporation, Seattle, Washington

Introduction

Assessing the landscape of any major public health challenge and the effectiveness of existing health care practices is a difficult proposition in any circumstance for health care planners and providers. To do so with relatively current health care data has not been a feasible reality. Too often health care planners have been relegated to use of venerable but dated clinical information. Equally often, clinical trial data collected for a purpose other than outcomes research have been extrapolated well beyond their original intent. The field of atrial fibrillation is no exception. The durable and well-reported Framingham study data have provided modern day framework for a natural history base of the disease over many decades.[1, 2] More recent analyses have shown worldwide similarity in patterns and increasing prevalence.[3, 4] The cascade of anticoagulant trials in the nineties with their meta-analyses and methodology also provided outcome endpoints that have been widely used as a benchmark.[5, 6] More recently, NIH clinical trials such as the AFFIRM trial have provided some outcomes analyses.[7] Yet these tools provide information that may have been captured some time ago and significantly lag current medical experiences and practice.

Background

With the establishment of the Medicare program has come the progressive development of its prospective reimbursement scheme over the last two-decade period. This program has increasingly matured, acquired serious complexity with a substantial underlying methodology. In a digital age, the Medicare database has become a substantial alternate resource for researchers seeking to examine modern health care in the United States of America. These data now provide source information for a vast range of medical subjects and specialties. Medicare data is often made available for analysis within a preceding three to five year period, and in some instances even within a two-year capture window. It has identified atrial fibrillation as one of the top diagnoses responsible for hospitalization in the USA [8]. As far aback as 1999, a total of 1,765,304 hospitalizations (137.1 per 1,000 Medicare enrollees) were reported among persons with AF in the Medicare population.[8]

Current literature

The incidence and prevalence of atrial fibrillation have been a staple subject for several large epidemiologic reports and widely analyzed.[3, 4] The risks of adverse cardiovascular outcomes including mortality, stroke and impaired quality of life have been well documented from these and clinical trial reports.[1-4, 7] These results have been used to justify a range of medical therapies from antiarrhythmic drugs, rate control drugs, anticoagulation and non

Corresponding Address : Sanjeev Saksena, MD, Medical Director, Electrophysiology Research Foundation, 161 Washington Valley Rd, Suite 201, Warren, New Jersey, 07059, USA.

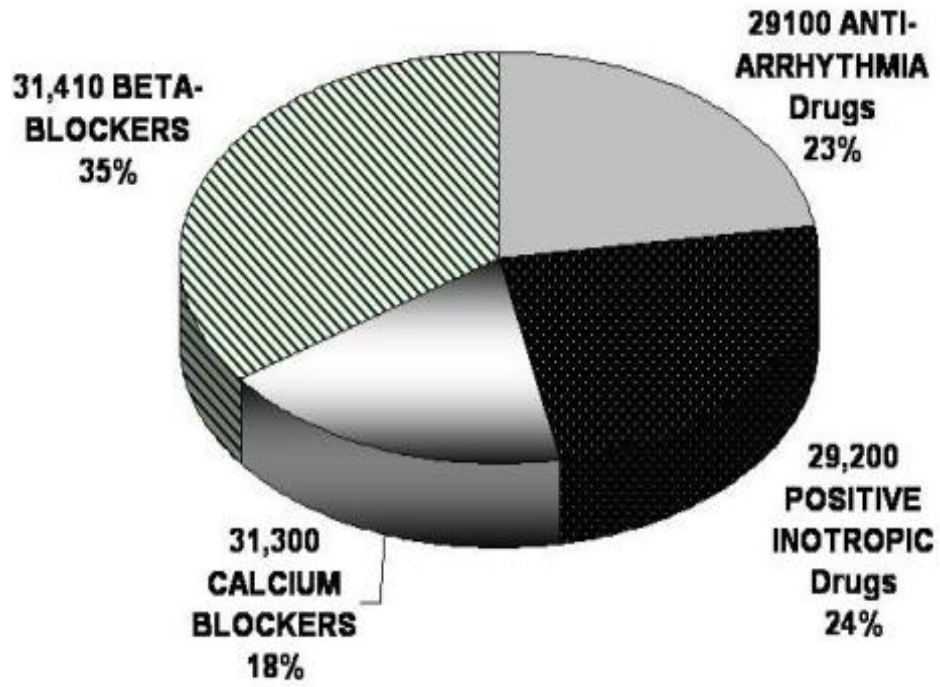
pharmacologic approaches such as ablation and device therapy. Clinical reports using both observational and clinical trial data have emerged with increasing swiftness. Clinical practice guidelines have evolved from both sources of information and enshrine best medical practice with currently available information.[9] These guidelines have been promulgated to influence physician management of atrial fibrillation along best medical practice. The impact of these guidelines has not been systematically assessed and real world physician behaviour is still poorly defined. A smattering of market research reports, often based on physician prescribing practices, provide limited insight. Figure 1 shows prescription practices of antiarrhythmic drugs from such data and suggests that rate control is the dominant practice strategy in atrial fibrillation. Rate control mandates antithrombotic therapy in the vast majority of patients. However, obtaining widely applicable data from a large health care segment of the population that is current and broadly applicable or reliably analyzable in its component groups remains a major health care information challenge.

The Need for Better Data in Atrial Fibrillation

One inevitable limitation of the Medicare data is the age segment. While many chronic diseases extend into the population of patients older than 65 years, the earlier stages of disease, where intervention may be most effective, may not be captured. Atrial fibrillation is dubbed as a "disease of the elderly", but may often develop in patients who are in their 50s or 60s – as many as 15 years before patients become Medicare eligible. Early management of AF can influence later outcomes, but data from this period of the disease are remarkably sparse. In recent years, private health insurance coverage provided by employers or by the self-employed has become fairly standard, despite increasing concerns of absent coverage for many Americans in their working years. These plans now collect and review many aspects of health care provided to their clients including demographic profiles, disease patterns, health care resource utilization, pharmacotherapy, compliance and provider behaviour. Mining this database can provide researchers with another look at health care in a different segment of society.

In a recent report, Walker and Bennett undertake an ambitious analysis of epidemiologic outcome aspects of atrial fibrillation in the United States using a proprietary health insurance plan database.[10] Patient records were selected using ICD 9 diagnosis codes and pharmacy claim data. Remarkably,

Figure 1: Prescriptions of antiarrhythmic drugs in atrial fibrillation patients. Note that rate control therapy dominates the market as defined by this parameter. Source: December 2007 Verispan PDDA.Drug Use by USC



available data was very broad based; available information included physician provider claims and hospitalizations in covered patients. Outpatient laboratory service provider care was analyzed in 30% of the population using plan-contracted laboratories. Patients included a broad range of demographics including Medicare age groups. Unusual strengths of this database included drug use data even when the drug was priced below the copay amount. Limitations of the database include veterans' benefits supplementing health care usage in this segment, and inpatient laboratory data. Interestingly, the database analysis was exempt from institutional review board requirements as study data were anonymized according the Health Insurance Portability and Accountability Act standards.

Walker and Bennett analyzed a population of plan members aged 40 years or older who had coverage for both medical and pharmacy services over a six year period from 1999-2005. Both non-valvular atrial flutter and atrial fibrillation were analyzed and a diagnosis of mitral valve disease was an exclusion criterion. The base analysis was a descriptive analysis of medical practice in the broad population of 116,969 patients making this one of the largest data sets analyzed. A nested subgroup analysis of laboratory and patient data was performed in patients using contracted laboratory services. Principal diagnoses were used for endpoints of stroke, cerebral hemorrhage and thromboembolism, which may have underestimated event rates relegated to secondary diagnosis status. The descriptive demographic data is unique in capturing incidence and prevalence data in the 40-59 year age group of over 30,000 insured AF patients. Approximately, 36% of patients were in the > 75 year age group. These two extreme demographic age groups provided very large patient numbers for analysis. Cardiac dysrhythmia was the most common diagnosis for management in the overall group and prevalent cases, suggesting that coding and clinical presentation were well matched. This finding is not always seen in cardiac arrhythmias, for example in patients with ventricular tachycardia or ventricular fibrillation where it may remain a secondary diagnosis. Better coding procedures at the provider level may be responsible for this improvement. While confirming hypertension as the major disease diagnosis in new incident cases in this large swath of age groups, respiratory disease and dyslipidemia emerged as next in line, in stark contrast to clinical trial data such as AFFIRM. Reasons for this difference may include a change in a point of engagement of the health care system, perhaps at an earlier high risk population stage.

Few other clinical data are reported that describe cardiovascular status in particular. Risk factors and prevalence data for stroke risk were more detailed with expected factors of advanced age and hypertension having prevalence rates of >30%. Coronary disease, diabetes and heart failure followed with substantial prevalence rates of 14 to 21%. Most patients had one risk factor, while 34% had more than one risk factor. Risk factors for bleeding were quite uncommon with only 3% having renal failure, giving a truly different perspective from anticoagulant trials in the elderly.[7] Stroke rates exceeded bleeding complications by a factor of 10. Stroke incidence in the population was 1.3 per 100 pt years and gastrointestinal bleeding incidence was 0.8% with intracranial bleed averaging 0.3%. Thromboembolic events including pulmonary embolism had incidence ranging from 0.18 to 0.2%. There was an average of one AF hospitalization in the follow-up period.

The major focus of the report rotates on anticoagulant drug use patterns and their correlation with INR values in the nested analysis. Actual rates of prescription of warfarin and antiplatelet agents were lower than expected (45% and 6%, respectively). Of particular interest beyond the rates of prescription were the duration and variables involved in their use. The average time to discontinuation was about 4 months for both agents. The AFFIRM trial published at the turn of the millennium, has promoted anticoagulation as a lifelong strategy when feasible. It would have been interesting for the authors to have performed a time-dependent analysis on this aspect. Importantly, women were less likely to receive anticoagulation and common risk factors such as hypertension, diabetes and coronary disease were only weak predictors (odds ratio 1.11 to 1.18) of its use. Poor management of warfarin was seen in one-third of patients who spent >80% of their time outside the therapeutic INR range and only 19% remained in the recommended range virtually all of the time, underscoring the difficulties in warfarin management and effective implementation. In current reports, warfarin usage has plateaued between 50 – 60%.[6]

Therapeutic INR rates improved from 40-45% early on to around 60%. As expected, inability to comply with warfarin follow-up or high risk bleeding situations often precluded warfarin use, but surprisingly a history of a fall or intracranial vascular malformation did notpreclude use. Not surprisingly, the data confirmed prior studies showing a doubled risk of stroke and five fold risk of embolism with sub therapeutic INR values and a doubled risk of bleeding with supratherapeutic values.[7]

The most unique aspects of this data set are its size and its existence outside the framework of a clinical trial. The size in relationship to other studies has been described previously. A randomized clinical trial of this size with this level of detail would not currently be feasible. Unlike other large retrospective studies, this analysis was performed on very recent data, so inference is not affected by new therapeutic agents and treatment strategies. Since these data emerge from a non-clinical trial setting, the treatment patterns are regulated by clinical judgment and patient adherence rather than a protocol. The absence of inclusion criteria implies that this analysis contains a broader spectrum of patients with AF that a clinical trial would contain – the sickest patients are often underrepresented or absent from clinical trial data. These data could offer an accurate reflection of real-world treatment patterns, and as in prior reports, we note a marked divergence from clinical guidelines.[9, 11, 12] While lifelong use of warfarin is recommended, the reality in this data set is that treatment is intermittent rather than continuous, and the median time to discontinuation was just over 4 months. In the NABOR study and other analyses, only persistent/permanent atrial fibrillation and age > 80 years influenced warfarin usage rather than risk factors for stroke.[13] For the subset of patients with INRs, only 19% spent most of their time within the therapeutic range. In a recent review, clinical trials show rates of 60 – 65%, raising a potential dichotomy with practice guidelines and trial data.

Despite the authors' efforts to identify a robust population for health care resource use analysis using exclusively private insurance, there is no guarantee that all resource use, and especially prescription drug use, were reported. This concern is a major limitation of this analysis. The authors do not show enough information about the age distribution to determine what percent of the cohort was eligible for Medicare. It would be interesting to know how Medicare-eligible patients were using their private insurance plans.[14] For patients enrolled in Medicare, private insurance would have been the secondary payor on prescription drugs. The claims may or may not have been received by the private insurance company. Government employees who are veterans may have accessed care through the VA system, and is not possible to know what percent of claims were filled by payors other than private insurance. Walker et al found that 48% of patients who should have been anticoagulated had no claims for warfarin, but this could be an overestimate of untreated patients due to claims filed to other payors. As the authors note, diagnosis information is difficult to obtain. It is inevitable that some patients had conditions for which warfarin was contraindicated. It would be interesting to know if any patients without warfarin claims did have claims for other drugs contraindicated with warfarin.

The lab data presented is also probably not a random selection of data from participants in the health plan, and systematic differences between patients who did and did not have INR data could bias the results. Only labs qualified to be in the network reported data, and facilities serving certain demographic groups or employment status may have been more likely to use a network lab than other sites. The authors were aware of this problem and examined differences in patients who did and did not have INRs in the database. Since INRs could have been conducted at a non-network lab, the absence of INR data does not necessarily imply that INR estimations were not performed.

The authors correctly point out many of the strengths, weaknesses and appropriate interpretations of their data. While retrospective, the data do modify our understanding of patient presentation in engagement of outpatient health care systems and move us away for randomized clinical trial settings that often start in the hospital. The large sample size exceeded by only one other report, along with real world pharmacy usage data is a useful addition to our information base.[3] As the authors note, these data originated outside of a randomized clinical trial, and may more accurately describe standard practice. As expected, the limitations of outpatient diagnosis coding, which

is less likely to be as robust as hospital coding, and the index INR values as reflective of the whole experience in some patients, drug compliance and out of system drug purchases remain issues in the data set. Yet overall, the data do confirm the difficulties in implementing a warfarin based anticoagulant strategy in the community with lack of penetration of practice guidelines being impeded, most probably not by physician or patient education, but by real-life single drug related limitations and interactions and compliance with follow-up testing procedures.

Future Directions

All in all, this report is a relevant and current look at a very broad AF population from an epidemiologic and health care delivery viewpoint. Findings should stimulate health care planners to focus to a greater extent on the point of engagement of the health care delivery system, i.e. the outpatient entry point, and seek better techniques to improve risk recognition by patients and warfarin usage. The recent availability of home monitoring kits for warfarin, anticoagulation clinics and dietary instruction, along with potential genetic typing for metabolic enzyme status offer new options for improving best medical practice with existing therapy.[15] It is increasingly likely that more insurance plans will provide this type of preventative and proactive intervention to reduce health care expenditures due to preventable complications. For pharmaceutical drug development, this report co-authored by an epidemiologist from this industry, clearly sets the stage for the need for new therapeutic agents such as factor 10a inhibitors that are in the pipeline. However, the uptake of new therapeutic paradigms is often beset with new challenges in acceptance and implementation at the provider, patient and health care delivery system levels. In the immediate future, adjustment to warfarin management is likely to yield more immediate results for health care planners, physicians and patients.

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