



The Concept of “Burden” in Atrial Fibrillation

Gregg F. Rosner, M.D., James A. Reiffel, M.D., and Kathleen Hickey, R.N., EdD, FNP.

From the Department of Medicine, Division of Cardiology, Columbia University Medical Center

Abstract

Over the last decade or so the term “burden” has become frequently encountered in manuscripts discussing atrial fibrillation (AF). AF “burden” is perhaps most commonly encountered in the electrophysiological context – the amount of time the patient is in AF out of the total monitored time (i.e., the percent of time one is in AF). However, “burden” in AF may also be used in other contexts, which we characterize below as “disease burden”, “clinical burden,” “economic burden.” Over the course of the disease progression and its therapy, such “burdens” may change, and may do so in parallel with each other or in opposite directions. This manuscript explores these various concepts of AF “burden” so as to emphasize to authors and readers that when using the term, its meaning must be made clear.

Introduction

Over the last decade or so the term “burden” has become frequently encountered in manuscripts discussing atrial fibrillation (AF).¹⁻³ Electrophysiologists have used it to generally mean the percentage of time that a patient is in AF – calculated from the total time in AF divided by the total monitored time.⁴ Conceptually, this burden may then be linked to some clinical outcome and/or therapeutic decision. For example, the TRENDS study examined whether there is a critical level of AT/AF burden that increases the risk of thromboembolic events independent of other known risk factors. The investigators found that the risk of thromboembolism doubled if AT/AF burden was ≥ 5.5 hours on any given day during the prior 30 days.⁵

Burden using the above electrophysiological definition can only be adequately assessed by some method of continuous monitoring for at least moderately prolonged periods of time (such as a month or more). Such assessments

have most often used continuously applied monitors, implanted monitors, or interrogation of implanted pacemakers or defibrillators.⁶ In contrast to the specific time-related definition of burden denoted above, to clinicians caring for the patient in the office, the term “burden” is more likely to mean the impact of AF upon the patient – the level to which AF symptoms have affected quality of life (QoL), the degree to which AF therapies have impacted QoL and cost, and/or the likelihood that AF will be frequent or long enough to necessitate chronic anticoagulation (all other factors being equal), and/or upon his/her family and/or caregivers. If you are a patient who is hospitalized and misses work, and/or has to spend money out of pocket on AF management, and/or has an embolic stroke and can no longer work or participate in activities, that is a burden – to the patient and their family– even if the AF has resolved. Patients with AF have been shown to have significantly poorer QoL compared with healthy controls, the general population, and patients with coronary artery disease.⁷ Furthermore, it has been demonstrated that AF has a similar perceived impact on

Corresponding Address : James A. Reiffel, M.D, 161 Fort Washington Ave, New York, NY 10032.

the QoL of spouses and patients.⁸ Hence, when we use the term “burden” in the setting of AF, we must be sure we define the term carefully (Table 1).

Importantly, the electrophysiological and the clinical concepts are only partly separate entities. For symptomatic patients, the more time they spend in AF, the more their QoL will be negatively impacted, the more they will pursue therapy, and the more the electrophysiological definition will approximate the clinical construct. To the extent that AF causes symptoms from the moment it begins to the moment it ends, but has no impact during sinus rhythm, the two definitions of burden would overlap entirely. What is less clear is the relationship between the percentage of time in AF and the need for (or lack thereof) chronic anticoagulation. Here, we remain uncertain as to whether and to what extent the precise or even approximate duration of an AF event has implications for thromboembolism.⁹ In this setting, whether AF is associated with symptoms (other than thromboembolic) or not is irrelevant. Consider paroxysmal AF (PAF) for example. AF lasting 2 minutes twice a year or lasting 18 hours every day would both be PAF, as would every duration in between. Their burdens defined by time could be precisely calculated. Calculating the clinical impact would be more difficult and less precise. Determining the burden threshold, if any, that would necessitate anticoagulation remains unknown.

Even less directly concordant is the burden due to a consequence of the AF (such as heart failure, hospitalization, embolism), in contrast to the actual time AF (which may be transient) that precipitated the event. Likewise, in patients who have periods of both symptomatic and asymptomatic AF, aside from the issue of anticoagulation, it may be only the symptomatic ones that pose a clinical burden. Moreover, to some extent, the burden imposed clinically on patients relates to potential side effects of the drugs used to treat their AF. If one uses a beta blocker to slow the ventricular rate, for example, and the patient has fatigue from the beta blocker, there is a clinical burden related to the therapy of the AF that is not mechanistically or temporally directly caused by the AF. Similar, in this respect, is the clinical burden imposed upon patients by the restrictions and concerns associated with anticoagulation. Anticoagulation is

a nuisance, carries a risk, interferes with lifestyle, may interfere with diet, requires monitoring, and carries a cost – none of which are desired by the patient, though most will accept it because it can prevent something worse (thromboembolism).

Another way of looking at burden in patients with AF might be to view “disease burden” as recurrences of AF, and their frequency, duration, and severity, while one might view the “clinical burden” as what happens as a result of that recurrence – a physician visit, a hospital visit, a chronic complication, the addition of another therapy, and so forth. If we were to put a cost on this burden, it is the “clinical burden” rather than the “disease burden” that becomes the important cost driver.

Substantial overlap between the different definitions will at times exist. For example, arrhythmia burden may at times and in some patients be a subset of clinical burden. However, they may be separate. For example, if rare AF episodes occur in a patient with high-risk embolic markers, the burden is that of chronic anticoagulation, even though the arrhythmic burden itself is minimal.

Superimposed on the above is the additional concept of “total societal burden” or “economic burden” of AF that the American College of Cardiology/American Heart Association/European Society of Cardiology describe as “huge.”¹⁰ AF currently affects 1-1.5% of the population in the developed world and the prevalence of AF is expected to triple by 2050.¹¹ In recent years we have been spending over 6.6 billion dollars/year in the United States on AF care – much related to in-hospital costs. If we were to include indirect costs this figure would exceed well over 8 billion dollars per year.¹² Data from the Euro Heart Survey on AF revealed that the total annual costs of AF amounted to €272 million in Greece, €3286 million in Italy, €526 million in Poland, €1545 million in Spain, and €554 million in the Netherlands.¹³ Therefore, we all pay for it, not just the patients. Hence, to the extent we can reduce these components and complications we can reduce the societal burden of AF.

Additionally, there is also the burden placed by AF upon the family and caregivers. A considerable amount of time is spent by advanced practice nurses, for example, educating individuals and

Table 1

Landmark Trials in Atrial Fibrillation and Left Ventricular Dysfunction

Arrhythmia Burden	Total time in AF divided by the total time in sinus rhythm.
Disease Burden	Recurrences of AF, and the frequency, duration, and severity of episodes.
Clinical Burden	The level to which AF symptoms, treatment and/or a consequence of AF (e.g. stroke, heart failure) affects quality of life and cost.
Economic Burden	Total cost (both direct and indirect) associated with AF symptoms, consequences, treatments and/or resultant complications.

families about AF. Topics necessary to explain in order to provide good care and maximum patient and family follow up with therapies employed include the underlying pathophysiology of AF, existing AHA/ACC guidelines, the interplay of cardiovascular risk factors, medication adherence, treatment options/potential risks and benefits, among others. Several challenges exist both for the practitioner and families related to education such as time constraints that exist in the fast paced clinical environment, language barriers, etc. Additional practical issues exist for family members related to AF such as the cost burden associated with medications, the burden of getting anticoagulants monitored, and getting to appointments (i.e. due to fragility, limited mobility, resources, caring for a spouse other family member with co-existing conditions, employment/childcare responsibilities).

Educating the family and creating a sense of empowerment and involvement in the clinical management can have profound impact. For example, the wife of one of our patients who prepares all the meals for the family was shocked to learn by limiting the sodium intake of her husband she impacted on improving his CHF, HTN and decreasing the frequency of his PAF.

Family members can be encouraged to learn how to check a pulse and actively watch, record and report certain signs and symptoms of AF such as palpitations, shortness of breath vs. ignoring/not seeking further evaluation or assuming such symptoms are normal or age related. This would certainly avert some clinical situations such as unidentified tachycardia induced cardiomyopathy, CHF exacerbation, inappropriate ICD shocks and their associated costs and impact on QoL.

Numerous topics will need to be addressed in the

future on how best to educate individuals and families regarding AF. This may include a national AF prevention program with active involvement from individuals in the community who are trained in AF education. How this may alter the cost burden on society remains to be determined.

Thus, AF burden is a complex construct with various meanings which are interrelated but do not necessarily move in parallel. Take for instance, the clinical situation where a rhythm-management strategy is undertaken while treating a patient with PAF or recurrent persistent AF. Treatment with an antiarrhythmic medication may result in several different outcomes. If we leave the financial cost associated with antiarrhythmic therapy out of the equation for the moment, one possible outcome would be sustained maintenance of sinus rhythm without any adverse side effects from the medications. This would result in a decrease in both disease burden and clinical burden. However, if we reduce disease burden with an antiarrhythmic regimen, but it causes side effects, it might increase the clinical burden, or alter its components. For example, if we were to convert persistent AF to PAF with the use of antiarrhythmic therapy, it is possible that we could decrease disease burden while actually increasing clinical burden. In the AFFECTS Registry, more patients with PAF were symptomatic than were patients with persistent AF.¹⁴ Interestingly, persistent AF was more likely to be associated with dyspnea, fatigue, and exercise tolerance than was PAF, while PAF was more likely to be associated with palpitations and/or chest discomfort.¹⁴ The impact on QoL and possibly consequences and costs of these different presentations would unlikely be the same. In both the AFFECTS Registry¹⁴ and the RECORD AF Registry¹⁵, patients with PAF were more likely to be treated with a chronic

antiarrhythmic regimen than were patients with persistent AF – and thus exposed to their consequences and costs. Notably, if the antiarrhythmic regimen has no effect on the maintenance of sinus rhythm but results in substantial side effects, disease burden would be unaltered while the clinical burden to the patient would increase.

Given the rising incidence and prevalence of AF worldwide, the high cost associated with the disorder at both the individual and societal levels, and greater interest in AF as a disorder requiring therapy, we anticipate readers will encounter the term “burden” in the setting of AF with ever increasing frequency. Importantly, given its various meanings, authors must be sure to define the term carefully when it is employed and readers must be sure they understand it.

References

1. Heemstra, H.E., et al., The burden of atrial fibrillation in the Netherlands. *Neth Heart J*, 2011.
2. Berkowitsch, A., et al., Evaluation of atrial fibrillation burden before catheter ablation predicts outcome after pulmonary vein isolation. *Indian Pacing Electrophysiol J*, 2009. 9(3): p. 138-50.
3. Santini, M. and R.P. Ricci, The worldwide social burden of atrial fibrillation: what should be done and where do we go? *J Interv Card Electrophysiol*, 2006. 17(3): p. 183-8.
4. Euler, D.E. and P.A. Friedman, Atrial arrhythmia burden as an endpoint in clinical trials: is it the best surrogate? Lessons from a multicenter defibrillator trial. *Card Electrophysiol Rev*, 2003. 7(4): p. 355-8.
5. Glotzer, T.V., et al., The relationship between daily atrial tachyarrhythmia burden from implantable device diagnostics and stroke risk: the TRENDS study. *Circ Arrhythm Electrophysiol*, 2009. 2(5): p. 474-80.
6. Seet, R.C., P.A. Friedman, and A.A. Rabinstein, Prolonged rhythm monitoring for the detection of occult paroxysmal atrial fibrillation in ischemic stroke of unknown cause. *Circulation*, 2011. 124(4): p. 477-86.
7. Thrall, G., et al., Quality of life in patients with atrial fibrillation: a systematic review. *Am J Med*, 2006. 119(5): p. 448 e1-19.
8. Bohnen, M., et al., Quality of life with atrial fibrillation: do the spouses suffer as much as the patients? *Pacing Clin Electrophysiol*, 2011. 34(7): p. 804-9.
9. Khoo, C.W., et al., Atrial fibrillation, arrhythmia burden and thrombogenesis. *Int J Cardiol*, 2011.
10. Fuster, V., et al., 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 Guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in partnership with the European Society of Cardiology and in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *J Am Coll Cardiol*, 2011. 57(11): p. e101-98.
11. Savelieva, I. and J. Camm, Update on Atrial Fibrillation: Part I. *Clinical Cardiology*, 2008. 31(2): p. 55-62.
12. Wolowacz, S.E., et al., The cost of illness of atrial fibrillation: a systematic review of the recent literature. *Europace*, 2011.
13. Ringborg, A., et al., Costs of atrial fibrillation in five European countries: results from the Euro Heart Survey on atrial fibrillation. *Europace*, 2008. 10(4): p. 403-11.
14. Reiffel, J.A., et al., Practice patterns among United States cardiologists for managing adults with atrial fibrillation (from the AF-FECTS Registry). *Am J Cardiol*, 2010. 105(8): p. 1122-9.
15. Camm, A.J., Breithardt, G., Crijns, H. et al. Real-life observations of clinical outcomes with rhythm- and rate-control therapies for atrial fibrillation. RECORDAF (registry on cardiac rhythm disorders assessing the control of atrial fibrillation). *J Am Coll Cardiol* 2011; 58:493-501.