Planning the Safety of Atrial Fibrillation Ablation Registry Initiative (SAFARI) as a Collaborative Pan-Stakeholder Critical Path Registry Model: A Cardiac Safety Research Consortium "Incubator" Think Tank

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Atrial fibrillation (AF) is a major public health problem in the United States that is associated with increased mortality and morbidity. Of the therapeutic modalities available to treat AF, the use of percutaneous catheter ablation of AF is expanding rapidly. Randomized clinical trials examining the efficacy and safety of AF ablation are currently underway; however, such trials can only partially determine the safety and durability of the effect of the procedure in routine clinical practice, in more complex patients, and over a broader range of techniques and operator experience. These limitations of randomized trials of AF ablation, particularly with regard to safety issues, could be addressed using a synergistically structured national registry, which is the intention of the SAFARI. To facilitate discussions about objectives, challenges, and steps for such a registry, the Cardiac Safety Research Consortium and the Duke Clinical Research Institute, Durham, NC, in collaboration with the US Food and Drug Administration, the American College of Cardiology, and the Heart Rhythm Society, organized a Think Tank meeting of experts in the field. Other participants included the National Heart, Lung and Blood Institute, the Centers for Medicare and Medicaid Services, the Agency for Healthcare Research and Quality, the Society of Thoracic Surgeons, the AdvaMed AF working group, and additional industry representatives. The meeting took place on April 27 to 28, 2009, at the US Food and Drug Administration headquarters in Silver Spring, MD. This article summarizes the issues and directions presented and discussed at the meeting. (Am Heart J 2010;159:17-24.e1.)

Atrial fibrillation (AF) is the most common arrhythmia seen in clinical practice.[1] Atrial fibrillation results in significant morbidity, mortality, and costs through hemodynamic impairment, disabling symptoms, and thromboembolic events. Although numerous medications have been developed for the treatment of AF, their efficacy is limited and concerns have been raised about their safety, especially in the elderly and in patients with structural heart disease.[1] Catheter ablation of AF using

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pulmonary vein (PV) isolation with various modifications was introduced more than a decade ago as a procedure to treat AF.[2-4] The American College of Cardiology (ACC)/American Heart Association/European Society of Cardiology 2006 guidelines for the management of AF and the Heart Rhythm Society (HRS), European Heart Rhythm Association, and European Cardiac Arrhythmia Society Expert Consensus Statement on Catheter and Surgical Ablation of AF indicate that catheter ablation is a reasonable therapeutic option to prevent symptomatic AF in patients refractory or intolerant to at least one antiarrhythmic medication.[1,5]

Although in several randomized clinical trials of catheter ablation of AF, freedom from AF was significantly higher with catheter ablation compared with antiarrhythmic medications, these were small trials performed by experienced operators on highly selected patients who had failed to respond to antiarrhythmic therapy. Some of these trials were single-center studies, and the follow-up period in most trials was limited to only 12 months. In addition, monitoring for AF during follow-up was highly variable across these trials.[6-13] The Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA) is a National Heart, Lung and Blood Institute (NHLBI)–funded multicenter study of catheter ablation versus pharmacologic therapy as treatment of symptomatic AF (NCT00911508).[14] This multicenter randomized study is intended to address many of the limitations of previous studies. Nonetheless, even CABANA will provide only limited insight into important aspects of this procedure such as the techniques, safety, and long-term effectiveness of AF ablation in routine clinical practice. With the emergence of catheters with US Food and Drug Administration (FDA) approval for AF ablation and growing numbers of AF ablation procedures nationwide that are performed by physicians with a variety of training and experience, there is a need to address the limitations of available data and other key concerns regarding the safety of AF ablation with the help of a national registry.[15] This is the intention of the Safety of Atrial Fibrillation Ablation Registry Initiative (SAFARI).

Recognizing the potential value of a national AF ablation registry, the Cardiac Safety Research Consortium and the Duke Clinical Research Institute, Durham, NC, in collaboration with the ACC, the HRS, the Society of Thoracic Surgeons (STS), the NHLBI, the FDA, the Centers for Medicare and Medicaid Services (CMS), the Agency for Healthcare Research and Quality, the AdvaMed AF working group, and additional device and pharmaceutical industry representatives, organized an "Incubator" Think Tank meeting on April 27 to 28, 2009, at the FDA headquarters in Silver Spring, MD, to consider the development of SAFARI. The specific objectives of the meeting were to (1) introduce the public health context and rationale for an AF ablation registry; (2) discuss the strategic plan for the proposed registry effort; (3) identify potential registry participants and stakeholders; (4) develop a process to identify data elements to be collected in the registry; (5) identify key action items to facilitate implementation of the registry; and (6) form a registry planning committee to publish and implement the outcomes of the meeting. The names and affiliations of all participants in the meeting are listed in Appendix A.

Concept, challenges, uptake, and adoption of AF ablation

Although several randomized clinical trials have demonstrated that catheter ablation is more efficacious than antiarrhythmic medications at treating AF, these studies have several limitations. In addition to their inclusion and exclusion criteria that define selected populations compared with "real-world" clinical practice, these studies did not provide data on hard end points such as mortality and stroke. They used highly variable definitions of success (some included single and multiple ablation procedures and some allowed postprocedure antiarrhythmic drugs), and they had substantial differences in treatment modalities, follow-up, and monitoring for asymptomatic AF. In addition, each of these studies had a relatively small number of patients, making meaningful analyses of key subgroups difficult, and the heterogeneity mentioned above makes pooling data from these studies problematic.[6-13]

Because of these limitations, many uncertainties about AF ablation remain. Some of these uncertainties can be addressed by randomized clinical trials, as is the intent of the NHLBI-funded CABANA effort (NCT00911508).[14] Other important areas of public health interest and, in particular, the safety of AF ablation in clinical practice populations could be addressed through a prospectively designed national registry. With larger cohorts, fewer exclusions, and a wider range of sites and operator experience, a national registry could provide unique information on techniques and generalizability of outcomes, the long-term durability of the effect of the procedure, and the incidence and nature of late-manifesting and/or infrequent complications. As an ongoing effort, SAFARI could also provide longitudinal evaluation of these key procedural and safety metrics, even as the technical aspects of the procedure evolve over time.

National registries, federal paradigms, and lessons learned

Although the paradigm of national professional society or other pan-stakeholder collaborative registry efforts is fairly new, lessons learned from such efforts offer value to the initial phase of the SAFARI program. One endeavor to collect data on product performance that has been successful is the Interagency Registry for Mechanically

Assisted Circulatory Support (INTERMACS). INTERMACS is a national registry for patients who receive a mechanical circulatory support device for advanced heart failure. This registry was launched as a joint effort of the NHLBI, the CMS, the FDA, physicians, and industry representatives. Several lessons have been learned from this national registry, including the importance of collaboration and partnerships and how partnerships with registries augment both regulatory science and surveillance efforts.[16]

Likewise, several lessons have been learned from the National Implantable Cardioverter Defibrillator (ICD) Registry. This registry is a national quality improvement program that helps participating facilities measure and improve care for patients receiving ICDs. Although entering data into this registry is only mandatory for Medicare patients, most of the participating facilities enter data on all patients undergoing ICD implantation. One lesson learned from this registry is that it is important to specify the purpose of the registry early on. In the National ICD Registry, such information could potentially aid in improving physician/patient decision making, determining if patients in the registry are similar to those enrolled in the randomized clinical trials, generating hypotheses for future clinical trials, and determining the effectiveness of ICD therapy in subpopulations. Another lesson learned from the National ICD Registry is that it is important to define a priori how the registry will be used, who will analyze it, who will have access to it, and who will fund it.[17]

Lessons have also been learned from the STS Registry. This national registry collects data on patients undergoing cardiothoracic operations. Because of its many successes, the STS Registry has been used as a model for other national registries. Accomplishments of the STS Registry include tremendous growth in the number of participating sites and the number of surgical records available for analysis, the existence of internal and external audits, and the examination of risk-adjusted clinical outcomes. In addition, the STS Registry has been used as a national benchmark for performance and reporting of quality measures.[18] Many of these accomplishments can provide a model for a national AF ablation registry, in particular, the "roll-out" of the registry's infrastructure from pilot centers initially to a much wider base of centers over time and the emphasis on quality control metrics to ensure data quality. Nonetheless, challenges unique to the follow-up of AF ablation patients will need to be considered. The ICD, STS, and other national registries do not collect follow-up information beyond discharge from the hospital. Efforts have been successful in linking these registries with CMS data to obtain longitudinal information, but these are limited to what is available in the CMS database via International Classification of Diseases codes. For the AF registry, capturing some of the important long-term outcomes such as AF recurrences, especially when asymptomatic, is uniquely difficult. Another major challenge to longer-term follow-up is that many patients undergoing this procedure are exclusively followed by the referring physicians outside centers that perform the AF procedures.

AF ablation registry data elements

A working group for SAFARI was formed to develop AF ablation study draft metrics and a baseline data collection form. Members of this working group are listed in Appendix B. This working group generated a list of in-hospital outcome metrics and a list of postdischarge outcome metrics (Tables I and II), both of which were shared with other participants in the meeting. In addition, the group developed a draft data collection form that was circulated at the meeting for feedback. Participants largely agreed on the list of outcome metrics and their definitions but expressed concern over the procedural details to be collected. This discussion highlighted the need for SAFARI data collection forms to strike a balance between the desire for granular data and the cost and administrative burden of reliably collecting such data. One suggestion discussed would be to have all participating centers collect a core minimum data set and have selected centers collect more detailed data.

Short- and long-term safety and effectiveness outcomes for AF ablation: reaching consensus on definitions and data capture

Participants in the meeting discussed the potential for a national AF ablation registry to examine the following outcomes: (1) the durability of effect (≥5 years) of AF ablation; (2) symptomatic AF recurrence using symptom-driven event recordings; (3) asymptomatic AF recurrence and implications; (4) use of anticoagulation and antiarrhythmic medications in the periprocedural period and in follow-up; (5) the incidence of stroke and mortality; and (6) the safety and effectiveness of this procedure relative to procedural volume and experience. Participants emphasized the importance of such a registry in examining safety outcomes, especially because they relate to infrequent adverse events and the importance of including a broader mix of centers than is present in current industry-sponsored registries.

Participants in the meeting acknowledged that acute complications of AF ablation are easier to capture than chronic complications, because the latter depend on the development of an infrastructure including a database and a registry site network designed to collect such information with completeness and quality. In current practice, many patients are referred to specialty centers for ablation procedures but are followed long term by their local physicians. To capture long-term safety

Table I. Atrial fibrillation ablation study draft metrics before discharge*

1. Proportion of patients with absence of AF/flutter/tachycardia without antiarrhythmic drugs at discharge
2. Ablation—specific procedure performed:
   a. LSPV isolation
   b. LIPV isolation
   c. RSPV isolation
   d. RIPV isolation
   e. Ablation at fractionated electrogram sites in the left atrium
   f. Ablation at fractionated electrogram sites in right atrium
   g. Left atrial linear lesion—roof line
   h. Other left atrial linear lesion
   i. Ablation of autonomic ganglionated plexi
   j. Cavotricuspid linear lesion
   k. Other
3. EP end points:
   a. Achievement of bidirectional cavotricuspid isthmus block (if performed)
   b. Achievement of entrance and exit block (if performed):
      LSPV: Yes ____ No ____ Not performed ____
      LIPV: Yes ____ No ____ Not performed ____
      RSPV: Yes ____ No ____ Not performed ____
      RIPV: Yes ____ No ____ Not performed ____
   c. Verification of complete conduction block across linear left atrial lesions:
      Roof line: Yes ____ No ____ Not performed ____
      Other line: Yes ____ No ____ Not performed ____
   d. Ablation of fractionated sites slowed activation or terminated AF:
      Yes ____ No ____ Not performed ____
4. Proportion of patients with fluoroscopy dose >600 rad
5. Proportion of patients with at least one adverse event
6. Proportion of patients with at least one bleeding and/or vascular access complication
7. Proportion of patients with cardiac perforation with tamponade requiring pericardiocentesis or surgical intervention
8. Proportion of patients with a thromboembolic event
9. Proportion of patients with pneumothorax
10. Proportion of patients with phrenic nerve injury
11. In-hospital mortality—unadjusted and risk adjusted

Process metrics:
1. Anticoagulant prescribed at discharge
2. Membrane active antiarrhythmic drug prescribed at discharge:
   a. Prescribed as per procedure routine
   b. Prescribed because of a recurrence of AF/flutter/tachycardia postprocedure
3. Others: ACE inhibitors, statins, etc

Process comparisons:
1. Use of transesophageal echocardiogram before procedure
2. Use of heparin therapy during procedure
3. Use of warfarin therapy during procedure
4. Use of general anesthetic during procedure
5. Use of intracardiac echocardiogram during procedure
6. Use of low molecular weight heparin therapy postprocedure

Data quality metrics:
1. Proportion of patients with PV isolation performed as part of the AF ablation procedure

Utilization metrics:
1. Median postprocedure length of stay (patients admitted for this procedure)
2. Median procedure duration (catheter placement to removal)

LSPV, Left superior PV; *LIPV*, left inferior PV; *RSPV*, right superior PV; *RIPV*, right inferior PV; *EP*, electrophysiology; *ACE*, angiotensin-converting enzyme.
*The data collection form is preliminary and will be further modified, shortened, and tested before adoption.

Table II. Atrial fibrillation ablation study draft metrics after discharge*

1. Proportion of patients with minimal or no symptoms of AF
2. Freedom from documented AF/flutter/tachycardia (minimum duration >30-s episode) on a 48-h Holter or any other electrocardiographic recording (event recorders, etc):
   a. All patients
   b. Patients without membrane active antiarrhythmic drug
   c. Patients with membrane active antiarrhythmic drug
3. Readmission (all-cause):
   a. AF, atrial flutter, or atrial tachycardia
   b. Other cardiovascular event
   c. Complication of the procedure
   d. Repeat ablation procedure for recurrent AF/flutter/tachycardia
   e. Surgical procedure for recurrent AF/flutter/tachycardia
   f. Other
4. Proportion of patients with cerebrovascular accident
5. Proportion of patients with permanent pacemaker implanted
6. Proportion of patients with esophageal perforation or fistula with demonstrable ulceration
7. Proportion of patients with phrenic nerve injury
8. Proportion of patients with PV stenosis ≥75% requiring intervention
9. Proportion of patients with vascular injury—AV fistula
10. Proportion of patients with vascular injury—pseudoaneurysm
11. Mortality

Data quality metrics:
1. Proportion of patients who receive follow-up 3 m after the procedure
2. Proportion of patients who receive follow-up 1 y after the procedure

AV, Arteriovenous.
*The data collection form is preliminary and will be further modified, shortened, and tested before adoption.

problems will require the ability to accommodate the care patterns of AF ablation patients. There was also consensus among participants that capturing the details of the index procedure is important to understanding the heterogeneous practices. These procedural details include (1) the type of procedure performed; (2) whether additional triggers were targeted; (3) the sites of extra-PV foci; (4) areas of fractionated electrograms; (5) areas of autonomic ganglionated plexi that were targeted; and (6) locations of any linear lesions. There was agreement that for acute success, isolation of the PV needs to be demonstrated at the completion of the procedure. The group acknowledged that although atrial arrhythmias occurring in the first 2 to 3 months after AF ablation do not preclude longer-term success, these early arrhythmias likely have an impact on patients, and identifying ablation strategies that can reduce the risk of these arrhythmias may be clinically important. Thus, collecting data on these early recurrences was thought to be desirable. There was consensus that electrocardiographic monitoring during follow-up is needed for optimal assessment of effectiveness; however, the intensity and timing of monitoring have not been resolved. Participants in the meeting acknowledged this as one of the most challenging aspects of a national AF ablation registry. In order for effectiveness outcomes to be meaningful, some consistency in follow-up and monitoring and in the definition of outcomes is needed; however, the balance between an

observational registry designed to capture practice outcomes and a prescriptive monitored regimen driven by protocol or by guidelines needs to be carefully considered.

A consensus was achieved that the initial focus of SAFARI will be on safety outcomes with the intent to try to extend the focus to effectiveness outcomes in the future. Participants in the meeting agreed that to be meaningful, assessment of these safety outcomes will have to be stratified by the techniques used and adjusted for patient comorbidities.

Quality control and postmarket data collection

For an AF ablation registry to be useful, the quality of data collection must be carefully monitored. Several strategies, many from prior registry efforts, were highlighted in support of this objective, including (1) use of standardized data elements and definitions developed and agreed upon by national experts in the field; (2) formal site-based training on data collection and entry with easy access to clearly communicated data field definitions; (3) development of a secure, user-friendly, Web-based system of data entry for participating sites; (4) rigorous electronic quality checks on entered data; and (5) a national on-site audit program applied to a random sample of sites. Data need to be collected on consecutive patients and by personnel familiar with the procedure but independent from the team performing the procedure. In addition, data collection needs to be confidential and Health Insurance Portability and Accountability Act compliant. This can be accomplished by (1) ensuring that appropriate safeguards are in place to protect health information and to maintain the confidentiality of patient data; (2) obtaining appropriate internal approval in accordance with each institution's own policies; and (3) complying with all applicable laws and regulations.

Adjunctive therapy

Antiarrhythmic medications and anticoagulants are important for AF management before and after AF ablation. Whether the traditional risk markers for thromboembolism are adequate or appropriate after AF ablation is uncertain. Laboratory parameters that might be followed to indicate risk are unknown because of the absence of adequate mechanistic studies regarding AF recurrence. In addition, there are no data on whether a history of bleeding is a contraindication to ablation and whether and when warfarin can be stopped after a successful ablation if the clinical characteristics would call for chronic anticoagulation. These uncertainties have made the development of a standardized algorithm for anticoagulation before and after AF ablation very challenging. The registry may help inform the development of such an algorithm. In addition, the registry may provide data on how much AF should trigger an intervention for initiation or reinitiation of rate control, an antiarrhythmic drug, and reablation; whether ablation alters the response to previously tried antiarrhythmics; and whether any specific antiarrhythmic drug(s) is particularly effective for postablation recurrences.

New paradigms of collaborative infrastructure: impact of the fabric supporting safety registry efforts

For a registry to be successful, all stakeholders need to be involved early on, a solid infrastructure based on transparent public-private partnerships needs to be developed, quality of data collection needs to be ensured, and an incentive for participation needs to be established. Three approaches to encourage participation were discussed: (1) pay sites money for participation and send benchmarking reports regarding quality improvement and quality assessment; (2) link mandatory participation to reimbursement; or (3) offer additional reimbursement incentives for the procedure if the operator/center participates in the registry. The latter 2 approaches were deemed by some to be advantageous because they ensure participation of most providers and most patients; however, many of the meeting participants did not support this approach due in part to the multiple payers other than Medicare covering the largely younger than 65-year-old patients currently undergoing AF ablation. For these latter 2 approaches to work, CMS and third-party payers would need to make an independent determination regarding reimbursement decisions. In addition, many participants felt that the registry needs to have a defined beginning and end and needs to be linkable to other registries and databases while ensuring patient approval and maintaining patient confidentiality. In any event, the success of the registry will depend heavily on the ability to secure funding for well-performed data collection and on the ability to get long-term data, especially on patients not followed by the electrophysiologist who performed the ablation procedure. Potential sources of funding were considered, but no consensus on this issue was reached.

Prospective registry objectives and publications/information dissemination: governance processes, regulatory, and statistical considerations

One of the critical first steps in developing a national AF ablation registry is to prospectively specify the hypotheses and the primary questions to be addressed. It is essential that analysis and interpretation of the registry's data be performed in an objective and scientific manner. It

was clearly recognized that retrospective ad hoc analyses of registry data are far less informative than prospective analysis plans that statistically accommodate a nonrandomized registry setting.

Reporting and publications based on registry data are imperative to the use of the registry as a means of disseminating safety and other related information. Such reports should use clearly defined objective criteria for data analysis, strive to eliminate bias, and reflect the purposes for which the registry was established. In particular, the meeting participants agreed that data from the registry that may constitute a potential safety signal must be disseminated in an objective unbiased fashion. They also agreed that an annual report on the registry and its results would be very helpful and that publications must identify the registry as the source of data.

In developing data collection forms and in choosing variables, participants in the meeting agreed that the following issues should be considered: (1) questions that the registry will address; (2) how the data will be analyzed; (3) the need for a data coordinating center to measure and monitor data quality, manage information, provide timely reports, and coordinate data analyses, data management, and statistics; (4) length and extent of data collection in follow-up; (5) a sufficiently large number of patients to permit estimation of event rates with a high degree of precision; (6) ensuring that participating physicians/centers enroll all patients undergoing an AF ablation procedure including those whose procedure was terminated before any ablation was performed; and (7) how the data will be used.

For the registry to be useful, the group emphasized the importance of broad representation of patients and sites. This would allow comparisons among patient subgroups, types of sites, and levels of experience; examination of different ablation strategies and techniques; and assessment of factors that are predictive of various adverse outcomes. Because SAFARI is intended to complement large randomized clinical trials of AF ablation such as CABANA, the group agreed that the registry and the CABANA trial should be consistent in the data collected and definitions of variables (NCT00911508).[14]

There was consensus on the importance of first doing a pilot registry with a limited number of sites then expanding it to a larger number of sites. The possibility of taking advantage of the registry's data collection framework to embed randomized clinical trials within the registry framework was also discussed.

To design the registry, an executive operations committee has been formed and a steering committee representing the different stakeholders will be formed. The mandate to these committees will be to define objectives; to decide on data to be collected, analyses to be performed, and articles to be published; and to oversee implementation, access to data, and data integrity including data security and Health Insurance Portability and Accountability Act compliance. For this effort to be successful, funding needs to be secured from different sources. One of the stated intents of this postmarket registry is to capture real-world experience with AF ablation procedures performed using legally marketed ablation catheters. However, industry participants expressed a concern that their participation in the registry may imply industry's promotion of off-label use of catheters included in the registry but not FDA approved for the treatment of AF. FDA recognizes this concern and will evaluate options to address this issue. Patient consent and/or institutional review board approval issues will also need to be addressed before registry implementation.

Putting it all together: priorities and objectives for an AF ablation safety registry

Participants in the meeting agreed that a national AF ablation registry effort such as SAFARI offers potential opportunities. First, this registry could provide data on AF ablation in routine clinical practice because it relates to the number of procedures performed, techniques used, characteristics of operators, procedural settings, and target populations. Second, the registry could help answer questions that are not possible to answer with randomized clinical trials including which catheters and ablation devices are being used, how patients undergoing this procedure in routine clinical practice differ from those enrolled in clinical trials of AF ablation, how the outcomes of this procedure differ between routine clinical practice and clinical trials, whether the procedure is being done in compliance with practice guidelines, and the effect of the procedure on outcomes of subgroups of patients not enrolled or not well represented in clinical trials. Third, this registry could provide information on patterns of drug use for patients who undergo this procedure, including rate and rhythm control and anticoagulation before and after AF ablation. Fourth, the registry could provide data on the durability of outcomes over several years, the incidence of infrequent and/or late-manifesting complications, and the ability to generalize outcomes to less experienced centers (complications, symptom control, long-term AF sequelae—stroke, heart failure, death). Fifth, the registry could allow the assessment of health care use pre- and post-AF ablation, especially in Medicare patients. Sixth, the registry could offer ongoing quality assurance at both the operator and center levels and could facilitate focused quality improvement through benchmarking and quality measures. Finally, the registry could result in the generation of hypotheses and the estimation of event rates to help inform sample size calculations for future randomized clinical trials.

An ongoing postmarket national AF ablation registry could also facilitate postmarket regulatory evaluation of devices, as well as drugs, related to the safety of AF ablation. Randomized premarket investigational device exemption studies have some limitations, including the relatively modest number of enrolled patients, the selection process intrinsic to randomized trials requiring informed consent, the limited number of participating sites that are typically well-experienced and "high-volume" centers, and the relatively brief follow-up period. A broad-based registry could help overcome many of these limitations. With common data definitions and forms, such a registry could provide a core data set that may reduce variability in collection and analysis of data and may enhance the efficiency of the regulatory review process and concomitantly reduce research and development costs and time delays for manufacturers. The registry can serve to fill data and knowledge gaps, with particular relevance to rare and longer-term safety end points in the postmarket period. Whether an effort such as SAFARI could also impact the burden of premarket studies of new devices or device iterations for AF ablation remains to be demonstrated; however, the formation of a framework for a core minimum data set for safety outcomes could help guide both pre- and postmarket studies.

Participants in the meeting acknowledged several areas of uncertainty that need to be addressed regarding how the registry should be implemented, including many questions about infrastructure both centrally and at individual centers. For the necessary infrastructure and services, a range of costs and expenses will need to be covered; however, the management of such costs is currently undefined. Prior registries have been either voluntary (STS and the CathPCI Registry) or linked to reimbursement (ICD Registry and CARE Registry on carotid artery stenting procedures). Determining the best funding mechanism for this registry early on was identified as one of the most critical first steps to the success of this registry. Second, important decisions need to be made about the magnitude of data collection because there is a trade-off between granularity and quality of data as well as between data comprehensiveness and clinician burden/cost. Third, a strategy could be developed to incorporate data from other health care agencies into this registry or to link SAFARI with other databases. Fourth, a tiered approach for this registry may be most reasonable because a small amount of data is mandated from all centers on consecutive patients undergoing AF ablation, and more extensive data are gathered by selected centers. Fifth, investment in a national registry will certainly require substantial resources. Such investments must be balanced with other important safety and clinical effectiveness studies such as CABANA and premarket trials of new technology (NCT00911508).[14] Finally, technology for AF catheter ablation is still evolving; whether the registry could enhance that evolution for the benefit of patients and health care providers remains to be seen.

Next steps and milestones

Most participants in the meeting agreed on the usefulness of the SAFARI effort. They also agreed that for the registry to work, several steps need to be taken. First, enough resources need to be secured and a solid infrastructure needs to be established. Second, electrophysiologists performing AF ablation and their professional organizations (HRS, ACC) need to buy into the SAFARI endeavor and potentially even help develop a system for obtaining long-term data on patients followed exclusively by the referring physicians. Third, questions, hypotheses, data elements, and end points need to be specified and defined a priori, ideally in close collaboration with the CABANA trial. Fourth, the data collection tools need to be pilot tested to determine what works and what does not work. Finally, the data collection process needs to be easy, modifiable, and applicable to clinical practice. The group emphasized the importance of continued collaboration among all the stakeholders. It is expected that a follow-up Think Tank meeting will be held in early 2010 to review progress made in building a national AF ablation registry and to determine what data on pre- and post-AF ablation anticoagulants, antiarrhythmic medications, and rate controlling medications can also be captured by this registry. Understanding how preablation medications affect the short- and long-term outcomes of the procedure and how the procedure impacts the effectiveness and safety of these medications postablation will be of importance.

Conclusions

There was consensus among most participants in the meeting that a national AF ablation safety registry would be useful. This registry could not only provide important information on AF ablation in routine clinical practice and patterns of drug use before and after AF ablation, but it could also provide data on the appropriateness, safety, and effectiveness of the procedure and the durability of its effect. The registry can aid in quality improvement, benchmarking, quality measures, and postmarket product surveillance of devices used in this procedure. Not only does the registry have the potential to help answer clinically important questions regarding whether the benefit of AF ablation in the registry is of comparable magnitude with that observed in clinical trials, but it can also help generate hypotheses and inform sample size calculations for future randomized clinical trials. If successfully executed, the SAFARI effort could potentially reduce the costs and time delays of selected new device safety evaluations while providing higher quality information

on the safety of AF ablation overall. If carefully planned and executed, the AF ablation registry has great potential to contribute significantly to the management of AF.

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Views expressed in this article reflect the opinions of the authors only and not the official policy of the Food and Drug Administration, the Agency for Healthcare Research and Quality, the Department of Human Services, or the remaining authors' affiliated organizations.

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Participants from the FDA: Felipe Aguel, PhD, Randall Brockman, MD; Daniel Canos, PhD; Danica Marinac-Dabic, MD, PhD; Jun Dong, MD, PhD; Benjamin Eloff, PhD; Thomas Gross, MD, MPH; Elias Mallis; Ellen Pinnow, MS; Wendy Sanhai, PhD; Daniel Schultz, MD; Art Sedrakyan, MD, PhD; Norman Stockbridge, MD; Douglas Throckmorton, MD; Bram Zuckermanm, MD

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Participants from the ACC: Janet Wright, MD

Participants from the Industry: Brenda Aker; Burke Barrett; Julie Broderick, MSc; Ruey Dempsey; David Feigal, MD, MPH; John Finkle, MD; Mark Gordon; Mark Grant, MD, MPH; Andrew Koren, MD; Jay Millerhagen, MBA; Philip Sager, MD; Dan Schaber, PharmD; Lynette Voshage-Stahl; Melissa Walker, MS, RAC; Marcia Yaross, PhD

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Appendix B. SAFARI Working Group

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