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Review

New Directions in Cardiac Arrhythmia Management: Present Challenges and Future Solutions

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ABSTRACT

Cardiac arrhythmias are a major contributor to population morbidity and mortality. Enormous advances in arrhythmia management have occurred over the 60 years since the founding of the Montreal Heart Institute, but important challenges remain. The purpose of this article is to identify the areas of cardiac arrhythmia therapy that need improvement and to discuss the evolving approaches that promise solutions. Challenges in diagnosis, detection, and risk-stratification include difficulties in separating benign from high-risk syncope and pinpointing the underlying causes, the detection of silent atrial fibrillation in patients at risk of stroke, and inadequate identification of sudden-death risk. Implantable devices are limited by the need for battery and device replacements, device complications like infection and dysfunction, and lead complications like fracture, infection, or displacement. Antiarrhythmic drug therapy, although widely used, is plagued by a very limited range of available agents, supply issues,

RÉSUMÉ

Les arythmies cardiaques contribuent grandement à la morbidité et à la mortalité de la population. Au cours des 60 années qui ont suivi la création de l'Institut de cardiologie de Montréal, des avancées énormes dans la prise en charge de l'arythmie ont été réalisées, mais d'importants défis demeurent. Le but de cet article est de déterminer les domaines de traitement de l'arythmie cardiaque où des améliorations s'imposent et de se pencher sur les approches évolutives qui s'avèrent prometteuses. Les défis liés au diagnostic, à la détection et à la stratification du risque comprennent les difficultés à distinguer la syncope bénigne de la syncope à haut risque et à préciser les causes sous-jacentes, la détection de la fibrillation auriculaire silencieuse chez les patients exposés à un risque d'accident vasculaire cérébral et la détermination inadéquate du risque de mort subite. Les dispositifs implantables sont limités par la nécessité de remplacer les piles et les dispositifs, les complications liées aux dispositifs comme

Cardiac arrhythmias are clearly an enormous clinical issue. For example, the American Heart Association estimates that bradyarrhythmias affect approximately 4% of the population, atrial fibrillation (AF) and flutter are present in 2.7-6.1 million Americans (expected to increase to approximately 5.6-12 million in 2050), and sudden cardiac death (SCD) occurs in $>$ 400,000 Americans annually.[1] The treatment of cardiac arrhythmias has advanced enormously in the 60 years since the founding of the Montreal Heart Institute in 1954. At that time, the only antiarrhythmic agents available were quinidine, procainamide, and digitalis, artificial pacemakers did not exist, external defibrillation had not yet been applied, continuous rhythm monitoring had not been invented, and the notion of intracardiac recording and stimulation was not even a dream. The subsequent development of a host of new technologies including intracardiac recording, stimulation and arrhythmia ablation, implantable devices, and remote rhythm monitoring, combined with breakthroughs in basic and clinical science, have created revolutions in arrhythmia management. Nevertheless, a large number of challenges remain. Fortunately, progress in all of these areas continues to be very rapid, promising to produce exciting solutions in the not so distant future. In this article, the outstanding challenges in cardiac arrhythmia management are reviewed, ongoing developments that will provide new options with which to handle these challenges are discussed, and aspects that are perhaps not being adequately addressed by present research programs are considered. We will cover a broad range of issues in antiarrhythmic therapy, with the exception of arrhythmia ablation because the subject of ablation is covered in depth in another article in this issue of the *Canadian Journal of Cardiology*.[2]

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Current Challenges in Arrhythmia Therapy

The management of cardiac arrhythmias has advanced enormously over the past 60 years. Nevertheless, a wide range of important challenges remain (Table 1).

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insufficient efficacy, and significant adverse effect risk. Health economic concerns include the high cost of new technologies, challenges in establishing cost effectiveness, and restrictive practices of government or third-party payers. Major improvements in arrhythmia management can be expected from new discoveries and technological developments in genetics, innovative diagnostic tools for arrhythmia monitoring, imaging and analysis, new approaches to antiarrhythmic drug development, biological therapies, and continuing improvement in implantable device technology like further miniaturization, leadless technology, and use of novel energy sources. As exciting as the developments in arrhythmia management have been in the past, we can look forward to exponential improvement in our ability to manage arrhythmia patients in the near future.

l'infection et le dysfonctionnement, et des complications liées à la sonde comme la fracture, l'infection ou le déplacement. Bien que le traitement antiarythmique soit largement utilisé, le nombre très limité d'agents disponibles, les problèmes d'approvisionnement, l'efficacité insuffisante et le risque important d'effets indésirables entravent son utilisation. Les préoccupations économiques liées à la santé portent sur le coût élevé des nouvelles technologies, les difficultés à établir le rapport coût-efficacité et les pratiques restrictives du gouvernement ou des tiers payeurs. On peut s'attendre à ce que les nouvelles découvertes et les développements technologiques de la génétique, les outils diagnostiques innovateurs pour la surveillance de l'arythmie, l'imagerie et l'analyse, les nouvelles approches pour le développement des antiarythmisants, les traitements biologiques et l'amélioration continue de la technologie des dispositifs implantables comme davantage de miniaturisation, de technologie sans sonde et d'utilisation de nouvelles sources d'énergie puissent apporter de nettes améliorations à la prise en charge de l'arythmie. Aussi passionnant que ce que les développements dans la prise en charge de l'arythmie ont pu être dans le passé, on peut s'attendre dans un avenir rapproché à une amélioration exponentielle de notre capacité à prendre à charge les patients souffrant d'arythmie.

Challenges in diagnosis, detection, and risk stratification

Syncope can result from serious cardiac arrhythmias, and from a host of other conditions ranging from very benign to life-threatening. The diagnosis of syncope remains difficult and consequently the management is problematic. The hospital costs in patients with a primary discharge diagnosis of syncope are of the order of $940 million per year in the United States.[3] Present approaches to diagnosis incorporate a range of clinical tools from simple history and physical examination to sophisticated monitoring. Nevertheless, the diagnosis is in many cases presumptive, often leaving patient management to a "best guess" approach, particularly for the very common benign syncopal syndromes.[3]

AF is a very important cause of stroke, and in too many cases stroke is the first recognized manifestation of AF.[4] Strokes due to silent AF constitute a public health problem in some ways analogous to the complications of hypertension before hypertension detection and management programs became widespread and efficient.

The prevention of SCD due to ventricular tachycardia (VT) or ventricular fibrillation was revolutionized by the recognition of the limitations of antiarrhythmic drug therapy and the introduction of implantable cardioverter defibrillators (ICDs).[5] However, optimal use of these potentially life-saving devices remains challenging. In particular, the current risk stratification tools focus on the identification of subjects at relatively high risk for later major events. Unfortunately, the identifiable "high-risk" groups comprise only a small proportion of the total number of annual events (Fig. 1), with most sudden deaths occurring in apparently low-risk subgroups with few known risk factors.[6] As such, although the current narrow definition of risk identifies individuals most likely to benefit from the intervention, the effect for society as a whole is limited. A better appreciation of the underlying factors precipitating sudden death in wider contexts might allow for a broader application of more specific prophylactic therapy. Additional challenges inherent in SCD risk stratification include the fact that risk factors can be dynamic (eg, varying autonomic tone, left ventricular function, etc), exhibit temporal variations (eg, time since myocardial infarction), and exist on a continuum, whereas clinical decisions are binary (eg, ICD implantation). Moreover, patients might have competing risks for nonsudden death, such as mortality from heart failure, which must be factored into risk stratification considerations.

Table 1. Current challenges in arrhythmia therapy*

1. Challenges in diagnosis, detection, and risk stratification
   a. Difficulty separating benign from higher-risk syncope
   b. Detection of clinically silent AF and increased stroke risk
   c. Inadequate risk stratification for sudden death (most cases cannot be predicted)
2. Limitations of implantable devices
   a. Need for battery and device replacements
   b. Device complications (infection, dysfunction)
   c. Lead complications (fracture, infection, displacement)
3. Issues with antiarrhythmic drugs
   a. Limited range of available choices
   b. Availability problems
   c. Insufficient efficacy
   d. Adverse effects
4. Health economics concerns
   a. Cost issues with new technologies, medications
   b. Difficulty establishing cost effectiveness
   c. Restrictive practices of third-party or government payers

AF, atrial fibrillation.

*Issues with ablation are not presented here because they are discussed in detail in the article by Andrade et al[2] in this supplement to the *Canadian Journal of Cardiology*.

Limitations of implantable devices

The development of highly sophisticated cardiac implantable electronic devices (CIEDs) has produced breathtaking advances in the care available to patients with bradyarrhythmias, ventricular tachyarrhythmias, and congestive heart failure. As a result of changing population