

The pacemaker and implantable cardioverter defibrillator recall issue – a Canadian perspective

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In 2005, an unprecedented number of recalls were issued on pacemakers and implantable cardioverter defibrillators. While recalls in the cardiac rhythm device industry are not new, the sheer magnitude of potentially affected patients in 2005 led to a great deal of concern, frustration, and even anger. Physicians have, in many instances, been uncertain when (or if) to recommend device replacement in an environment where the magnitude of the risk and the potential consequences of device failure have not been well defined in a timely way. Doctors and patients are now calling for reform of postmarket analysis and reporting mechanisms. The present article provides a uniquely Canadian perspective on this international issue. Potential solutions include the development of a set of realistic and common expectations, a restoration of confidence in postmarket analysis and reporting mechanisms, increased data transparency, and an increased role for patient and physician groups.

Key Words: *Implantable cardioverter defibrillator; Pacemaker; Postmarket analysis; Safety*

In Canada in 2006, there are more than 120,000 patients and 15,000 patients living with pacemakers and implantable cardioverter defibrillators (ICDs), respectively. Device patients are followed routinely to ensure the safe and effective operation of their devices. Most devices perform reliably throughout their expected service life (five to 10 years). Nevertheless, cardiac rhythm devices have a finite risk of failure.

In the past year, an unprecedented number of device advisories were issued, warning that some pacemakers and ICDs could suddenly fail (Table 1). The number of potentially affected patients has been overwhelming for some Canadian centres, leading to a great deal of concern, confusion, frustration, and even anger. Clinicians have, in many cases, been uncertain about what to do in an environment where the magnitude of the risk and the potential consequences of device failure are either uncertain or are dynamically evolving. There has been concern that inadequate guidance has been offered by regulatory agencies, industry and/or medical professional bodies in a timely fashion. Doctors and patients are now calling for

Le rappel de stimulateurs cardiaques et de défibrillateurs à synchronisation automatique internes – Une perspective canadienne

En 2005, les stimulateurs cardiaques et les défibrillateurs à synchronisation automatique internes ont fait l'objet d'un nombre de rappels sans précédent. Les rappels dans l'industrie des dispositifs du rythme cardiaque ne sont pas nouveaux, mais le nombre même de patients susceptibles d'être touchés en 2005 a suscité d'énormes inquiétudes, des frustrations et même de la colère. Dans bien des cas, les médecins n'étaient pas certains des indications pour recommander le remplacement du dispositif (ou de la nécessité de le faire), dans un contexte où l'importance du risque et les conséquences potentielles d'une défaillance du dispositif sont mal définies en temps utile. Les médecins et les patients demandent maintenant une réforme de l'analyse postcommercialisation et des mécanismes de déclaration. Le présent article fournit une perspective canadienne unique à l'égard de cette question d'intérêt international. Les solutions potentielles incluent la mise sur pied d'une série d'attentes réalistes et communes, le rétablissement de la confiance envers l'analyse postcommercialisation et les mécanismes de déclaration, une plus grande transparence des données et un rôle accru des groupes de patients et de médecins.

reform of postmarket analysis and reporting mechanisms to ensure adequate detection of device failures and delivery of appropriate, timely and clinically relevant communication to all stakeholders.

THE NATURE AND SCOPE OF THE PROBLEM

Although most implanted cardiac devices perform as designed, some may experience random component failure due to uncontrollable variations in manufacturing. At times, systematic failures that can be traced to a manufacturing or design issue and that affect a defined number of devices may be identified. This past year, an unprecedented number of these systematic failures were identified. An increase in the number of ICD recalls had been previously identified in the 1990s (1) and was attributed to the rising incidence of ICD implants, along with their increased complexity. So, in this sense, we are not dealing with a new problem. In fact, the North American Society of Pacing and Electrophysiology (now the Heart Rhythm Society) published a consensus conference document

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TABLE 1
Device recalls in 2005

Device*	Worldwide failure rate at time of first disclosure (failures/total devices implanted [%])†	Nature of defect
Medtronic Marquis ICD (Medtronic Inc, USA)	9/90,000 (0.01)	Rapid battery depletion due to a specific internal battery short mechanism
Guidant Ventak PRIZM 2 DR ICD (Guidant Corporation, USA)	28/26,000 (0.1)	Deterioration in a wire insulator within the lead connector block, resulting in a short circuit
St Jude Photon DR Photon Micro VR/DR and Atlas VR/DR ICDs (St Jude Medical Inc, USA)	60/36,000 (0.167)	A vendor-supplied memory chip can be affected by background levels of atmospheric ionizing cosmic radiation, triggering a temporary loss of pacing and a permanent loss of defibrillation support
Guidant Contak Renewal 3 and 4, Renewal 3 and 4 AVT, and Renewal RF ICDs (Guidant Corporation, USA)	4/46,000 (0.009)	Magnetic switch may stick in the closed position, inhibiting the ability to deliver tachyarrhythmia therapies
Guidant Ventak Prizm AVT, Vitality AVT and Contak Renewal AVT ICDs (Guidant Corp, USA)	2/20,950 (0.0095)	Random memory error causes functional 'latching' that limits available therapy
Guidant Pulsar Max, Pulsar, Discovery, Meridian, Pulsar Max II, Discovery II, Virtus Plus II, Intelis II and Contak TR pacemakers (Guidant Corporation, USA)	69/78,000 (0.09)	A hermetic sealing component may experience degradation, resulting in higher than normal moisture content within the case, potentially resulting in premature battery depletion and/or inappropriate accelerometer function
Guidant Insignia and Nexus pacemakers (Guidant Corporation, USA)	36/49,500 (0.073) (first failure mode) 16/341,000 (0.0047) (second failure mode)	Foreign material within a crystal timing component may lead to loss of pacing, loss of telemetry or reversion to VVI mode
Medtronic Sigma pacemakers (Medtronic Inc, USA)	19/40,000 (0.0475)	Separation of redundant interconnect wires on hybrid terminal blocks
ELA Alto ICDs (ELA Medical, Italy)	11/430 (2.6) (manufactured between April 2003 and July 2003) 2/1856 (0.11) (manufactured between August 2003 and August 2004)	Metal migration resulting in loss of pacing and defibrillation capabilities

*In many cases, only a selected subpopulation of the listed devices was affected by the recall; †Some groups of recalled devices experienced failure in clusters early in device life, while others experienced clusters of failures later in device life; therefore, some of these observed failure rates change more over time than others. Data from references 10 to 12. ICD Implantable cardioverter defibrillator

on device recalls in 1996 (2) following a meeting in Toronto, Ontario, that called for the establishment of a national pacemaker registry and the creation of a recall task force (neither of which has occurred in either Canada or the United States). The Canadian Working Group on Cardiac Pacing guidelines (3) for pacemaker follow-up in Canada in 2000 referred specifically to recalls and proposed a framework for dealing with them; they then recommended that all device follow-up centres develop a specific plan.

What changed in 2005 was the enhanced diagnostic features in devices that provided more detailed information about device performance and reliability. This information, coupled with the more rapid transmission of and widespread access to information, has led to the public becoming aware of reliability issues at the same time as physicians. One of the early advisories, regarding Guidant's PRIZM 2 DR ICD (Guidant Corporation, USA), was issued by Guidant and the United States Food and Drug Administration (FDA) only after *The New York Times* broke a story about a young, American patient with hypertrophic cardiomyopathy who died when his ICD failed to rescue him from sudden cardiac death (4,5). It was determined that the device had failed, and furthermore, that the defect was a problem that was occurring systematically, although only in a very small percentage of all manufactured devices. It subsequently became clear that the problem had first been detected three years earlier (in 2002), and while Guidant Corporation apparently fulfilled all of their legal

obligations to notify the regulatory agencies, they elected not to notify patients or doctors directly about this until *The New York Times* article was going to press. The reason for not notifying the medical community until the media became aware of the problem was because the failure rate was estimated to be 0.1%, which the company felt was in the range of random component failure and not sufficient to warrant enhanced surveillance or other medical intervention.

What was also new in 2005 was the reaction of the electrophysiology community in North America to the first ICD advisory – the Medtronic Marquis ICD (Medtronic Inc, USA) recall. Many physicians elected to replace, on an urgent basis, a large number of devices subject to this recall, despite the fact that the estimated failure rate at the time of notification was 0.01% and ICD battery failure could be detected by a simple daily assessment performed by the patient at home. A daily magnet check was estimated to minimize the risk of a severe adverse event, such as failure to detect and treat a life-threatening ventricular arrhythmia or failure to pace over the long term, to less than 0.005%. It has been estimated that more than 11,000 ICDs were replaced as a consequence of this recall, although no patient deaths or injury have yet been reported due to premature battery failure (6). Furthermore, it has been estimated that more than 200 infections alone would be expected to be associated with these replacements.

In Canada, the response to the Medtronic Marquis Advisory varied considerably by centre. More than 500 ICDs

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were replaced. Some centres elected to replace less than 10% of devices subject to this recall (only those who were truly pacemaker dependent or those with very frequent ventricular arrhythmias), whereas other centres elected to replace over 50% of devices subject to this recall. In retrospect, physicians likely overreacted to this recall but were concerned by the potential magnitude of the risk to their patients. Certainly, lessons were learned from this initial ICD recall because far fewer ICDs were replaced with the subsequent ICD recalls issued by both Guidant Corporation and St Jude Medical Inc.

Unpublished reports from the Canadian Heart Rhythm Society (CHRS) Working Group on Device Advisories have confirmed significant infection rates in the population that underwent device replacement, and deaths from infection have occurred. These sobering data have served to highlight the need for a very careful risk-to-benefit analysis when considering replacement for advisory patients.

Industry-physician-patient communication

Many physicians felt frustrated that they were not involved in the discussion of patient management related to these recalls in a timely fashion. The rapid dissemination of information to the public created a sense of urgency and need to react. Part of the problem is that Health Canada does not always differentiate advisories by category or severity. Any notification by a manufacturer to the medical community is classified as a recall. This encompasses the trivial notification of a typographical error on a product label to a potentially life-threatening device malfunction. In an effort to provide some guidance to the medical community, the CHRS developed specific guidelines for physicians related to the Medtronic Marquis recall, and these were disseminated to the medical community within 10 days of this recall. The CHRS also developed a template letter that follow-up clinics could use for patient notification.

Thus, the recall issue has become every bit as much about communication, process and optics as it is about an objective assessment of real risk. Device companies report all device failures to the regulatory agencies. However, there are no regulatory standards as to when they should share this information with doctors and patients. Each company may have a different threshold for notifying the medical community of a potential device malfunction. The absolute magnitude of the 'risk of failure' as well as potential clinical consequences of the defect need to be considered when notifying physicians and patients about a potential device malfunction. If, in the interests of transparency and openness, we set the 'reporting bar' very low, we run the risk of inundating doctors and patients with so much information that it just becomes 'white noise' and perhaps even serves to undermine efforts to communicate really serious issues when they arise. Until national or international standards are set related to disclosure of device performance, we can expect the industry to report problems with increasing frequency.

It will be important for physicians and health professionals involved in patient follow-up to remember, as they help patients understand the implications for them, that the number of recalled devices is usually orders of magnitude greater than the number of actual device failures. The perception of the scope of the problem, therefore, differs considerably depending on whether one considers this to be a recall problem, a device failure problem or a problem of adverse events attributable to device failure. It is also important to remember lessons from previous device recalls. For example, far more patients were harmed

by the extraction of normally functioning Teletronics Atrial J leads (Teletronics Pacing Systems, USA) than were harmed by the fracture of the retention wire (the reason for the recall).

What is a 'recall'?

The use of the term 'recall' to describe the communications issued by both industry and regulatory bodies (Health Canada and the FDA) has led to confusion among patients and physicians. Some perceive that the term implies that the device must be explanted or at least removed from the shelf. In fact, neither of these scenarios is necessarily the case.

Health Canada assigns a numerical designation (ie, type I, II or III) to a particular product to indicate the relative degree of health hazard presented by the product. A type I recall is issued in a situation in which there is a reasonable probability that the use of, or exposure to, a product will cause serious adverse health consequences or death. A type II recall is issued in a situation when the probability of serious adverse health consequences is remote. Finally, a type III recall is issued if there is a concern, but the product is not likely to cause any adverse health consequences (7).

The FDA has virtually identical definitions for device recalls (8). However, they also use additional classifications:

- A market withdrawal occurs when a product has a minor violation that would not be subject to FDA legal action. The firm removes the product from the market or corrects the violation. For example, a product removed from the market due to tampering, without evidence of manufacturing or distribution problems would be a market withdrawal.
- A medical device safety alert is issued in situations in which a medical device may present an unreasonable risk of substantial harm. In some cases, these situations also are considered recalls.

The nature of risk and risk assessment

How are risks assessed? How are risks described? How are risks perceived? How are risks managed? The device manufacturer's assessment of risk is highly focused on the 'monthly failure rate' of a given device as a result of a particular defect – a highly technical view of risk. Device manufacturers aim to quantify risk, consider the clinical implications of the risk and then make a decision based on whether that number has reached a certain threshold. Clinical decision-making, however, takes this technical view of risk assessment and decision-making as the mere starting point. Once the magnitude of risk is established, many other variables must then be considered. These variables include the potential consequences of device failure, how to best communicate this information to patients and how individual patients may react to this information. For example, some patients may be more comfortable with taking a 1% to 2% 'upfront' risk of a complication from device replacement rather than live with an 'ongoing' incremental risk of, say, 0.1% of device failure posed by the potential defect. The decision to replace the device may therefore be reasonable for such a patient. For others, however, it would be exactly the wrong thing to do.

Clinicians who are involved in patient care decisions with device recall patients must take care to fully inform themselves of the technical information on risk that is available

and actively engage the patient in the development of the management plan – offering both data and comfort. The physician's role should be to help clarify, quantify and objectify, but also to work to reduce the fear and misconceptions that inevitably arise whenever the term 'recall' is used. Placing the issue in the appropriate context provides perspective, establishes trust and lays the groundwork for rational decision-making.

Moving forward

The lessons learned from device recalls in 2005 suggest the need for improvement in postmarket surveillance and communication of device performance.

Disclosure of information

One major issue arising from these recalls is the nature of disclosure to the clinical and patient communities. Professional medical societies and patient advocacy groups are calling for earlier and more comprehensive information sharing with respect to postmarket device performance. However, if patients and physicians were actively notified every time a new entry was made into the FDA database, they would be awash in a mass of unfiltered information that would be very difficult to interpret and to act on. In addition, if we demand that companies notify us every time a design change is made to improve a theoretically inferior component (that has not yet caused any harm), they would quickly lose their motivation to make continuous improvements. On the other hand, as one patient advocate has said, "If DaimlerChrysler can send me a recall notice when there is a bolt loose in my car, then my (ICD) manufacturer must, too" (9). Clearly, there must be a balance between the noble objective of transparency and free exchange of information and the reality that completely raw and unfiltered information delivered in great quantity would likely undermine the communication objective.

Policy conference on pacemaker and ICD performance

On September 16, 2005, the Heart Rhythm Society and the FDA sponsored a policy conference to discuss these issues in Washington, DC, USA (9). The conference was attended by clinicians, patients, scientists, industry representatives and the FDA. A series of presentations were made, each followed by an expert panel discussion and audience participation. Topics covered included technology, performance and surveillance, postmarket analysis and reporting, the role of external databases in postmarket surveillance, risk-benefit communications and what patients need and want to know from their physicians.

Potential solutions

Pacemakers and ICDs are generally very reliable. However, there will always be failures. Some will be random component failures and others will be systematic failures. Some failures will have dire clinical consequences; others will have minimal or no clinical consequences. Some failures will lead to recalls and other advisory actions while others will not. A standard prospective surveillance program is absolutely essential. This system must have appropriate scientific and regulatory governance to restore public confidence.

The solution, in our view, must incorporate the following elements:

1. **The development of a set of realistic and common expectations among patients, caregivers, industry and regulatory bodies regarding device performance.** Everyone needs to accept and believe that 'less than perfect' is okay. (There is, after all, no other choice in the matter.) However, international standards on reporting device performance that are acceptable to all stakeholders need to be defined.
2. **Restoration of confidence in postmarket analysis and reporting mechanisms.** Whether concerns are real, perceived or both, the result of erosion in confidence in device therapy can be substantial, leading to significant psychological distress, consumption of resources, 'knee jerk' reactions to recalls that may well do more harm than good, and even underutilization of appropriate device therapy in newly presenting patients. Active surveillance methods tracking device performance should be undertaken by all manufacturers, because this can lead to early detection of device failures.
3. **Data transparency.** Although device companies have done a good job of reporting problems with devices to Health Canada and the FDA, the companies still have discretion as to when to notify regulatory agencies, clinicians and patients. International standards and independent audits of data must become part of the reporting process. More legitimacy will come if clinicians and patients play a more active role in the monitoring of device performance. However, automatic transfer of raw data without analysis or context would be overwhelming to the clinical and patient communities.
4. **Physicians and patients must do their part.** Canadian federal law requires that physicians report device concerns to Health Canada in the event of patient injury. Device malfunction may not always cause patient injury. A robust method for physicians to report any incidence of device malfunction to both Health Canada and industry would strengthen early detection of systematic failures. In addition, devices that have been explanted due to malfunction or unexplained sudden death must be returned to the manufacturer for careful analysis and reporting to regulatory bodies and the physician. Because most devices are explanted as they approach elective replacement indicators, it is not practical or economically feasible to analyze every explanted device.

CONCLUSIONS

Pacemakers and ICDs are a mainstay of cardiac rhythm management in 2006. An increase in device recalls recently, however, has focused attention on the legitimacy of current postmarket analysis and reporting mechanisms. We are currently in the midst of a major 'culture shift', both in terms of our expectations of device performance and in terms of our demand for more physician and patient involvement in postmarket monitoring of device safety and reliability. Standardized, inclusive and independent assessments of device performance will help to restore confidence and improve the reliability of device therapy.

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