Beyond Indications
Postmarket Surveillance and the Importance of Expanded and Off-label Use of Transcatheter Devices in Structural and Congenital Interventions

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In September of this year, the US Food and Drug Administration (FDA) Center for Devices and Radiological Health published a document entitled, “Strengthening Our National System for Medical Device Postmarket Surveillance.” In addition to summarizing the current process and mechanisms for monitoring medical devices after commercial approval, the document proposed the following specific actions to improve the efficiency and quality of postmarket surveillance of medical devices in the United States:

1. Establish a unique device identification system and promote its incorporation into electronic health information;
2. Promote the development of national and international device registries for selected products;
3. Modernize adverse event reporting and analysis; and,
4. Develop and use new methods for evidence generation, synthesis, and appraisal. [1, p. 4]

The intended focus of this initiative is laudable and much needed, as the current system, discussed in this journal earlier this year, is widely believed to be overly time consuming and expensive, and to place the United States at a competitive and technological disadvantage to many other countries. As with many of the investigational mechanisms used to assess new medical technologies, these initiatives are likely to lend themselves most easily to devices that are used widely and in relatively consistent applications. With the introduction and evolution of this forward thinking upgrade of the postmarket medical device surveillance system, let us hope that low-volume, off-label, and other marginal device use remains within its purview so that we can collectively move toward a better understanding and oversight of such device applications, as well as those with broader market applications.

It is no secret that the majority of transcatheter interventions for congenital heart disease in the United States are performed with devices that are not approved for the use in question. As the field of structural interventional cardiology has come into its own, it too has become populated with frequent off-label device usage. To most congenital interventionalists, this fact hardly bears remarking, as it is a pervasive and unavoidable condition of the field, with few devices developed specifically for the relatively small pediatric/congenital market. With the imminent tightening of healthcare reimbursement, it is unclear how this fundamental practice will be regarded by payers. Unlike many of the costly devices that have assumed a prominent place in adult cardiovascular medicine recently, such as implantable cardioverter defibrillators and transcatheter aortic valves, most congenital procedures are not directly subject to criteria set by the Centers for Medicare and Medicaid Services. Strict adherence to utilization guidelines has not necessarily driven reimbursement patterns for most of the devices used in congenital interventional cardiology, although National Coverage Determinations will clearly limit the off-label use of potentially high-impact devices such as transcatheter aortic valve prostheses. It is quite possible, however, that the trend among other payers to tier reimbursement according to standardized measures of quality will cut a wide swath such that procedures that incorporate off-label device use will become natural targets for marginalization.

In addition to the aforementioned initiative regarding postmarket surveillance, the FDA has indicated a commitment to support and facilitate mechanisms by which approved medical devices that are often used but not labeled for pediatric or congenital conditions can obtain a legitimate indication. Although this commitment has yet to be translated into significant commercial achievement, it is evidenced by the recent collaborative Pediatric Device Consortium Grant Program, as well as multiple FDA conferences and workshops devoted to pediatric devices. The agency has also demonstrated a proactive stance toward working with professional societies and industry to get a larger segment of current off-label pediatric device use squarely on the books. These trends signify an awareness of the exigencies of device approval for relatively rare conditions (ie, most congenital applications), which will hopefully extend to more creative and expedient processes for approving new devices as well.

An obvious case in point is the class of devices designed for transcatheter occlusion of holes, vessels, and other communications. Transcatheter atrial septal defect closure was first reported in 1976. The following year, Rashkind et al pioneered the use of a double disk occlusion device for closure of patent ductus arteriosus. The possible application of that device to other purposes was quickly realized, and in many ways it represents the prototype for subsequent double disk catheter-delivered closure devices. In the years since, and particularly
with the proliferation of devices of different shapes, sizes, and mechanical characteristics, transcatheter occlusion devices have become the most versatile gadgets in the toolkits of structural and congenital interventional cardiologists. The list of intracardiac, vascular, and extra-cardiovascular holes, communications, vessels, and spaces that have been reportedly closed or occluded with septal, ductal, and similar occlusion devices is long and impressive. And the creative implementations, adaptations, and modifications that interventionalists have applied in this ever-expanding compendium are equally remarkable. Not quite as voluminous, but equally or even more important, is the list of complications that have been reported for these devices, whether in typical or more esoteric applications.

The extent to which occlusion devices, particularly those designed for specific intracardiac or vascular interventions, have been enlisted in the management of unusual anomalies and lesions is a matter of fact that should elicit no surprise. It goes without saying that one of the compelling aspects of practicing structural or congenital interventional cardiology is the rarity and variety of the conditions that are encountered and the importance of creativity and adaptability, with many potential needs not served by targeted, approved devices. To this end, published case reports can serve as useful catalysts to expand the conceptual and technical horizon for how devices and other tools may be used and, to an even more important end, drawing attention to the various pitfalls that can be encountered with such devices, whether used for indicated or off-label uses. Filling that niche in the base of knowledge is likely a major reason that this and many other journals continue to publish case reports. But case reports along these lines also highlight the fact that our collective understanding of how such devices are used in the real world is sorely lacking. The limitations in our knowledge are not specific to off-label and one-off circumstances, but often pertain equally to the approved, labeled indication(s) for the device. Thus the enthusiasm for and recent emphasis by the FDA on improved and expanded mechanisms of postmarket surveillance to bolster the US system for regulation of medical devices.

The conundrums that can arise from a lack of robust data about both common and unique practice are highlighted when problems or perceived problems with a device surface. The recent FDA conference devoted to septal occlusion devices and erosions is an obvious example of this phenomenon,9 as was the withdrawal of humanitarian device exemption approval for 2 patent foramen ovale closure devices in 2006,10 which ultimately led to calls for randomized controlled trials of patent foramen ovale closure for stroke prevention.11 Similarly, when prospective studies are equivocal or limited to patient cohorts that may not reflect the broader target clinical population, we can find ourselves in a no man’s land of sorts, as seems to be the case presently with patent foramen ovale closure, despite extensive ongoing investment in this area on multiple fronts.12,13

With the promise of more and increasingly sophisticated transcatheter devices for valve replacement and repair, heart failure, and, yes, occlusion of various deleterious communications, it is only reasonable to expect that insight into use and longer-term outcomes will become ever more critical for sorting out the inevitable complexity of how the devices are used and their impact beyond the procedural and short-term horizon. The interventional community should applaud the FDA’s new initiative and actively partner with the agency and industry to ensure that formation, support, and participation in registries are prioritized, for example, and to advance the efficiency of our process for determining the efficacy and safety of cardiac devices. This effort should include the less common forms of utilization that most of us in congenital and structural interventional cardiology believe have served our patients and us so well over the years. If the dynamic matrix in which development, regulation, and use of medical devices occur truly functions as an ecosystem, as has been proposed, it is important to understand that even peripheral elements of that ecosystem are essential to its flourishing and, therefore, must be tended.

Disclosures
None.

References

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