EDITORIAL

The checklist manifesto for mechanical circulatory support: Targeting anti-coagulation efficiency

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In his book, The Checklist Manifesto: How to Get Things Right, Atul Gawande describes the origins of the checklist that involved the airline industry beginnings of the B-17 airplane. The test plane’s flight ended in a deadly crash deemed due to pilot error. The B-17 was felt to be too much plane for one pilot and was abandoned as the next generation long-range bomber for the U.S. military. A persistent group of pilots developed a checklist of tasks to be performed for each phase of flight take-off, inflight, and landing. The B-17 went on to play a successful role in the U.S. military and, as a result, the checklist became a critical instrument for aviation to execute repeatedly during each flight segment.

A checklist protects against failures, ensures safety, and decreases variations in actions. It serves to discipline a complex environment and reduces complacency for simple tasks that induce boredom but may influence critical success. Several examples of successful checklists exist in health care. The use of central line insertion checklists was associated with a significant reduction in infections. After studying the use of the checklist in several other professions, Dr. Gawande proceeded to examine its use and success in surgical situations and has continued to publish studies on the profound effect of such a simple tool on patients’ morbidity and mortality.

In this issue of the Journal, the MAGENTUM-1 study investigators evaluate the safety and clinical outcomes of low-intensity target anti-coagulation with an international normalized ratio (INR) of 1.5 to 1.9 in a pilot cohort of 15 patients implanted with the newer HeartMate 3 left ventricular assist system. The hypothesis that led to their study included the observation of an absence of de novo pump thrombosis in this device that had been engineered to facilitate hemocompatibility. The authors utilize another form of an “interventional” checklist using specific but uniform anti-coagulation strategies and pump thrombosis monitoring protocols. The results of their study demonstrate that the strategy is safe, with only 1 patient developing a gastrointestinal bleed. The other 14 patients reached the desired clinical outcome of survival free of pump thrombosis, disabling stroke (Modified Rankin Scale >3), or major bleeding (excluding peri-operative bleeding) at a minimum post-implant follow-up of 6 months.

Perhaps one of the most relevant findings of the study is the high INR efficiency achieved, with the center time in the therapeutic range (TTR) of 75.3%. The basis of this high-efficiency TTR is multifactorial and can be explained by the anti-coagulation protocols used, training of dedicated personnel expert in the management of anti-coagulation, and close collaboration across continents to ensure proper monitoring of patients. It is important to point out that the benefit of dedicated, trained personnel following specific protocols leads to a reduction in practice variation (“smoothing effect”) by decreasing outcome variation and establishing adherence to a consistent framework for decisionmakers. Interestingly, anti-coagulation protocols developed in Boston were implemented in Prague with continued cross-continent collaboration that allowed for a further secondary safety net. These practices and findings led to a very important question: Does warfarin efficiency at lower targets “outperform” lower efficiency at higher targets?

Published data from warfarin-treated patients have shown that both TTR and variability in INR range are linked to risks of adverse events such as thrombosis and bleeding. Razouki et al evaluated the effect of variability in INR as well as the overall TTR achieved in over 40,000 patients on
warfarin for atrial fibrillation. They assessed 3 categories of TTR (high > 70%, moderate 50% to 70%, low < 50%) and divided log INR variability into 2 categories, stable or unstable. The results demonstrate that, regardless of TTR category, unstable control or higher log INR variability performed better for predicting ischemic stroke and major bleeding in their model. It is likely, however, that, in practice, providers have become too indifferent to the effect of INR instability and have not placed enough emphasis on ensuring that patients remain within the TTR without allowing for fluctuations in INR from high to low. In the field of mechanical circulatory support, the MAGENTUM-1 study has demonstrated that a detailed anti-coagulation protocol, trained personnel, and focused attention that limits practice variation may be labor-intensive and costly, but the end result is exactly what we should strive to achieve for our patients.

The MAGENTUM-1 findings are important in view of the recent publication of the 2-year outcomes of the MOMENTUM 3 trial. In the trial, implantation of the magnetically levitated centrifugal-flow HeartMate 3 pump was found to be associated with a superior clinical outcome of survival free of disabling stroke or reoperation or need to replace or remove a malfunctioning device, compared with the HeartMate II axial-flow pump. MOMENTUM 3 also showed a reduction in stroke rates, both ischemic and hemorrhagic. However, the rate of first occurrence of gastrointestinal bleeding in the HeartMate 3 pump was no different, although a trend toward reduction in recurrent bleeding was noted. It remains unknown at this time whether this was due to changes in anti-coagulation management in the trial due to clinical perceptions of enhanced hemocompatibility.

Intriguingly, MAGENTUM-1 has demonstrated that low-intensity anti-coagulation was safe even in patients with atrial fibrillation, as long as the left atrial appendage was occluded at the time of implant, but it was closely coupled with a structured pump thrombosis surveillance algorithm, another important checklist. Other possible hypotheses raised by the MAGENTUM-1 findings include: patients with the HeartMate 3 pump should utilize a narrow focus INR, and therefore the emphasis should be on TTR efficiency; and, perhaps importantly, in situations of sub-therapeutic INR, intensive bridging with heparin may not be required. MAGENTUM-1 is a precursor to a large, randomized trial to define effectiveness in clinical outcomes between low-intensity and normal-intensity anti-coagulation.

Dr. Gawande noted that, “under conditions of complexity, not only are checklists a help, they are required for success.” There are few areas more complex than the clinical playing field of mechanical circulatory support.

**Disclosure statement**

H.O.V. is a consultant for Abbott. P.A.U. has no disclosures.

**References**