Patient Self-Testing and Patient Self-Management of Oral Anticoagulation: Is It Too Late?

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The coumarin-type vitamin K antagonists have been the principal oral anticoagulant agents for a variety of thrombotic diseases since the early 1940s. Their use has grown considerably in the last decade as randomized controlled trials substantiate new indications for therapy such as atrial fibrillation [1]. However, there are many difficulties associated with the use of oral anticoagulants, resulting in a high rate of serious adverse events and a high risk-to-benefit profile [2]. Oral coagulants have a narrow therapeutic window of efficacy and safety. Many factors influence the pharmacodynamic response such as diet, drugs, co-morbid conditions, and age predisposing to therapeutic instability; and maintaining patients within the therapeutic window requires considerable effort and expertise on the part of healthcare providers. To complicate matters, the assay used to assess anticoagulant response, the prothrombin time, is plagued with its own problems of standardization. Use of the international normalized ratio to standardize reporting of results has improved therapy, but discrepancies in test results still exist [3]. Accordingly, maintaining patients within the therapeutic range is difficult and requires expert dose adjustment and a coordinated approach to care, as is practiced in specialized programs known as anticoagulation clinics. Unfortunately, most "usual care" is provided by individual physicians within the context of their practice without coordinated processes in place to follow and track patient results and without high quality dose management. Such care results in a remarkably high incidence of major hemorrhage and thrombosis that approximates 15% per year [2]. Most events occur when the INR is out of therapeutic range. This rate can be significantly reduced to 3–5% by providing care through an anticoagulation clinic [2]. Anticoagulation clinics achieve these better outcomes by maintaining patients in therapeutic range for a greater percentage of time than in usual care.

In the mid-1980s, point-of-care prothrombin time technology was introduced using portable instruments that are able to measure an INR from a fingerstick sample of capillary whole blood [4]. Given their size, portability and ease of use, these devices allow patients to measure their own PT at home (patient self-testing) and, with proper education, manage their own anticoagulation dosing (patient self-management). Since the initial Biotrack instrument was introduced, several devices have been developed, all of which employ tissue thromboplastin to initiate the process of coagulation, but they use different means to detect clot formation [Table 1]. Exhaustive correlation studies have been done to assess the accuracy and precision of POC instruments compared with plasma-based PT using international standards. These have consistently confirmed the adequacy of the POC method to monitor oral anticoagulation, especially with INR results in or near the therapeutic range [5].

There was great hope that developing PST or PSM models of care would vastly improve the outcomes of therapy. With this in mind, a number of clinical trials demonstrated improved outcomes as measured by time in therapeutic range or, in some instances, reduced major hemorrhage or thrombosis when compared to a usual-care model [Table 2] [6–15]. However, the hoped-for widespread application of such testing never developed in the United States, or in many other countries outside of Germany, where, in contrast to other regions, a number of factors coalesced to promote such therapy. Currently, more than 70,000 individuals in Germany with mechanical heart valves or atrial fibrillation are monitoring and managing their own therapy at home.

The major barrier to greater use in the USA and elsewhere has been reimbursement limitations by the major insurers (Medicare in the U.S.). Only recently has the U.S. government issued a reimbursement guideline for home monitoring in patients with mechanical heart valves [16]. Another barrier to implementation has been the lack of large-scale, well-designed, randomized controlled trials, especially using the gold standard or anticoagulation clinic model of care as the comparator group. Only now are such studies emerging, showing that the benefits of PST or PSM are less impressive than when such therapy is compared to a usual-care model of management [Table 2]. Larger studies will be needed to demonstrate meaningful benefit given the very low number of adverse events.

In a stable therapeutic environment such studies would eventually be completed, but the therapeutic modality of anticoagulant therapy is anything but stable. New agents are entering the field and additional agents are on the horizon that may ultimately make the vitamin K antagonists obsolete [17]. Of particular interest are agents that can be given orally, have a

INR = international normalized ratio
PT = prothrombin time

POC = point-of-care
PST = patient self-testing
PSM = patient self-management

Table 1. Capillary whole blood (point-of-care) PT instruments

Instrument sample	Clot detection methodology	Home use approval	Type sample
Protime Monitor 1000 Coumatrak* Ciba Corning 512 coagulation Monitor* CoaguChek Plus* CoaguChek Pro* CoaguChek Pro/DM*	Clot initiation: thromboplastin Clot detection: cessation of blood flow through capillary channel		Capillary WB Venous WB
CoaguChek TAS Analyzer *Rapidpoint* Coag	Clot initiation: thromboplastin Clot detection: cessation of movement of iron particles	CoaguChek	Capillary WB Venous WB Plasma
ProTIME Monitor Hemochron Jr# GEM *PCL*#	Clot initiation: thromboplastin Clot detection: cessation of blood flow through capillary channel	ProTIME Monitor	Capillary WB Venous WB
Harmony	Clot initiation: thromboplastin Clot detection: cessation of blood flow through capillary channel	Yes	Capillary WB
AvoSure Pro + AvoSure Pro AvoSure PT	Clot initiation: thromboplastin Clot detection: thrombin generation detected by fluorescent thrombin probe	Avosure PT	Capillary WB Venous WB Plasma
INRatio	Clot initiation: thromboplastin Clot detection: change in electrical impedance		Capillary WB

* All instruments in this category are based on the original Biotrack model (ProTime Monitor 1000) and licensed under different names. The latest version available is the CoaguChek Pro and Pro/DM (as models evolved they acquired added capabilities). Earlier models are no longer available.

\# Hemochron Jr and GEM PCL are simplified versions of the ProTIME Monitor.

Table 2. Studies of patient self-testing and patient self-management of oral anticoagulation stratified by whether the comparator group is a usual-care or anticoagulation clinic model of care

Study [ref]	Study groups	Time in range	Adverse events
Beyth [6] 2000 (RCT)	PST* vs. UC	56 vs. 32%	14 vs. 25%
Horstkotte [7] 1996 (RCT)	PSM vs. UC	92 vs. 59%	5.4 vs. 14.5%
Hasenkam [8] 1997 (cohort)	PSM vs. UC	77 vs. 59%	No AE
Sawicki [9] 1999 (RCT)	PSM vs. UC	57 vs. 34%	3 vs. 1
Koertke [10] 2001 (RCT)	PSM vs. UC	78 vs. 61%	2.9 vs. 4.7%
White [11] 1989 (RCT)	PST* vs. ACC	87 vs. 68%	No AE
Kaatz [12] 2001 (RCT)	PST* vs. ACC	63 vs. 65%	NA
Ansell [13] 1995 (cohort)	PSM vs. ACC	88 vs. 66%	No AE
Watzke [14] 2000 (RCT)	PSM vs. ACC	86 vs. 80%	2 vs. 0
Cromheecke [15] 2000 (crossover)	PSM vs. ACC	55 vs. 49%	No AE

* Dose management for PST group performed by an anticoagulation clinic.
RCT = randomized control trial, PST = patient self-testing, PSM = patient self-management, UC = usual care, ACC = anticoagulation clinic, AE = adverse events, NA = not available.

predictable therapeutic effect and thus do not require anticoagulation monitoring, and have little or no interaction with food or other medications. Although it may be several years before such agents are proven suitable for thromboembolic prophylaxis in patients with mechanical heart valves, it may be a relatively short time before they are approved for use in patients with atrial fibrillation, venous thromboembolism and similar problems. With the possible decline of the vitamin K antagonists, POC monitoring for oral anticoagulant therapy may be a technology whose time has come, but may soon be gone.

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