NACB Laboratory Medicine Practice Guidelines

Evidence-Based Practice for Point-of-Care Testing

Coagulation

Marcia L. Zucker, Ph.D. (International Technidyne Corporation, Edison, NJ)

Vandita Johari, M.D. (Baystate Medical Center, Springfield, MA)

Valerie Bush, Ph.D. (Bassett Healthcare, Cooperstown, NY)

Srikantha Rao, M.D. (Penn State College of Medicine, Hershey, PA)

INTRODUCTION

Point-of-care coagulation testing has been termed the most rapidly growing point-of-care application in the hospital setting[1]. This rapid growth implies a widespread acceptance of the use of point-of-care coagulation assays, yet it is unclear if documentation exists showing a clinical advantage to these methodologies. The purpose of this guideline is to evaluate the available literature and identify those studies, if any, which objectively demonstrate the utility of point-of-care coagulation testing when compared to more traditional laboratory analyses.

The term “coagulation testing” is used to describe an ever growing selection of diagnostic tests. These range from the traditional global coagulation assays, *i.e*., the prothrombin time (PT) and activated partial thromboplastin time (aPTT), to assays specific to individual coagulation factors and their inhibition, *e.g.* factor VIII, fibrinogen, and anti-Factor Xa assays, to technologies designed to evaluate the process of clot formation and the influence of platelets and fibrinolysis on hemostasis, *i.e*., Sonoclot and thromboelastography (TEG).

This Laboratory Medicine Practice Guideline (LMPG) is targeted to address two basic questions:

1. Is there evidence of improved clinical outcome from the use of point-of-care coagulation testing?
2. What is the evidence that the current “standards of care” in point-of-care coagulation are appropriate?

Considering the wide range of clinical applications for these assays, a decision was made to evaluate only the global coagulation assays: the activated clotting time (ACT), the aPTT and the PT, including the calculation of the international normalized ratio (INR). It will be left to later updates to address the important issues of individualized heparin and protamine dosing for cardiac surgery, thrombin time based tests, heparin level measurement, heparin neutralization verification and TEG analyses, among others. Also left to later updates are the clinical utility of these assays for monitoring novel anticoagulants such as direct thrombin inhibitors and direct factor Xa inhibitors as well as the use of available electronic tools for management of anticoagulation therapy.

A critical assumption made in this document is that all point-of-care coagulation monitoring instruments are equally accurate and precise. There are insufficient data to allow recommendations based on specific instrumentation for these tests, and it must be the responsibility of the individual facility to evaluate available systems prior to implementation in a clinical setting. Although many of the studies described in this document were performed using point-of-care instruments that are no longer available in the marketplace, the value of the studies remains and should not be discounted.

Literature searches were conducted through online databases (PubMed, Medline, BioMedNet) and private libraries maintained by members of the LMPG team. Articles identified from author collections were only included if they are indexed on one of the three public search engines. All searches were performed using extremely broad search criteria. These searches were defined by the test name and any of the terms “bedside”, “point-of-care”, “near patient” or “whole blood”. The vast majority of the publications identified consisted of correlation analyses, either point-of-care to laboratory or between different point-of-care systems. Such studies were excluded from further consideration as they do not directly address the clinical utility of these systems. An overview of publications dealing with correlation analyses can be found in Zimmerman, 2000[2].

Summary of the Literature Survey

Activated Partial Thromboplastin Time (aPTT)

Is there evidence of improved clinical outcome using point-of-care aPTT testing?	
Abstracts	114
Systematic Review	35
Citations in final recommendation	16

Is there evidence of improved clinical outcome using point-of-care aPTT testing?

We recommend that the use of point-of-care aPTT be considered a safe and effective alternative to laboratory aPTT testing for anticoagulation and hemostasis monitoring.

(Class B, Level I at least one randomized controlled trial, Level II–1 small randomized controlled trials, non-randomized controlled trials, Level II-3 multiple time series without intervention).

We strongly recommend that therapeutic ranges, workflow patterns and cost analysis be evaluated, and where necessary altered, during the implementation of point-of-care aPTT testing to ensure optimization of patient treatment protocols.

(Class A, Level II-1 small randomized controlled trials, non-randomized controlled trials).

The literature regarding point-of-care aPTT, excluding straightforward analyses of correlation to the clinical laboratory aPTT, fall into three categories: Evaluations specifically designed to measure turn around time (TAT)[3, 4, 5]; evaluations of diagnostic accuracy using laboratory measurement of anti-Factor Xa activity as the gold standard[6-11]; and outcome studies[12-16]. Prospective studies of TAT have evaluated multiple patient populations, laboratory systems and point-of-care monitors, and all have shown that TAT, defined as time from sample draw to time of result availability, is significantly reduced with point-of-care testing ($p < 0.001 – p < 0.05$)[3, 4, 5].

These authors suggest that this significant reduction in TAT could lead to improved patient care, but do not directly address patient outcome questions.

The evaluations of diagnostic accuracy examined employ appraisals of clinical decision point agreement to determine if point-of-care aPTT monitors are as accurate as laboratory aPTT analyses for monitoring anticoagulation. All but one of these analyses use the chromogenic determination of anti-Factor Xa activity in the patient's blood as the standard for therapeutic decisions. The single investigation without anti-Factor-Xa values explored the efficacy of an aPTT assay as a pre-operative screening tool to predict which patients would exhibit severe bleeding following cardiac surgery. In this trial, Nuttal and colleagues[7] concluded that the Biotrack 512 point-of-care monitor had similar predictive value for bleeding tendency compared with standard laboratory tests (MLA Electra). Four articles reviewed evaluated point-of-care aPTT assays for monitoring heparin anticoagulation during continuous intra-venous heparin infusion. Therapeutic ranges in these studies were defined as 0.2 – 0.4[6]; 0.3 – 0.7[9, 11]; or 0.36 – 0.82[10] units/ml heparin as measured by chromogenic laboratory assays. In all reports, the point-of-care system (Biotrack 512[6], CoaguChek Plus[10], Hemochron 8000[9], Hemochron Jr Signature[11], TAS[10]) showed reasonable agreement with anti-Xa levels, at least equivalent to the levels of agreement seen for the laboratory aPTT. Several authors noted that the oft-quoted target range of 1.5 – 2.5 times normal was inappropriate for both the point-of-care and laboratory systems[9, 10]. Solomon and colleagues drew similar conclusions when the CoaguChek Plus and TAS systems were evaluated for determination of the appropriate time to remove the femoral access sheath following interventional cardiology procedures[8].

Three trials were identified evaluating the use of point-of-care coagulation assays to guide transfusions following cardiac surgery[12-14]. All three studies identified a sub-population of patients determined to have bleeding complications following heparin reversal with protamine. Two of the studies defined bleeding by visual inspection of the operative field at the end of procedure and implemented the point-of-care based transfusion algorithms using PT, aPTT and platelet count[12]

or function as measured by the bleeding time[13] in the operating room. Both groups found significant reductions in post-operative bleeding and blood product usage in the algorithm group compared to patients transfused by routine procedures (central laboratory test results[12] or clinician discretion[13]). The third trial conducted by Capraro and colleagues[14], did not introduce point-of-care testing for transfusion until after the patients left the operating suite. Bleeding in this trial was defined as chest tube drainage exceeding 1.5ml / kg / 15 minutes following initial draining of the mediastinal tubes. In contrast to the other studies, these investigators found no difference in bleeding or blood product usage between the two groups across the hospital stay. In fact, the algorithm controlled group received more platelets during the first hour than the control group. The authors suggest that this difference may be due to the use of the bleeding time to define the need for platelet transfusion. An explanation of the contradictory results between the Capraro study[14] and those by Despotis[12] and Nuttall[13] may lie in the time of algorithm initiation. Nuttall and coworkers noted that in both this and the Despotis studies, the lower number of coagulation product transfusions in the operating room in the algorithm group may have led to the significant reduction in bleeding observed in the intensive care unit. One explanation could be that the earlier directed transfusion therapy may have more efficiently corrected the hemostatic problems. If this is true, the lack of improved outcome in the Capraro evaluation may be due to the time of algorithm initiation. In any case, all these trials employed multiple point-of-care assays, so that the precise impact of the aPTT alone cannot be isolated from the other assays involved.

Point-of-care aPTT assays have also been an integral component of two large-scale, multicenter, randomized, controlled pharmaceutical trials. In a subset analysis of patients enrolled in GUSTO-I, Zabel and colleagues evaluated bleeding, transfusion requirements, recurrent ischemia and mortality at 30 days and one year for those patients monitored using point-of-care aPTT (CoaguChek Plus) compared to those monitored with local laboratory aPTTs[15]. The point-of-care group had a higher percentage of patients in therapeutic range at 12 and 24 hours, less severe or moderate bleeding and fewer transfusions that the laboratory group ($p<0.01$) although these

patients exhibited somewhat higher rates of recurrent ischemia (p=0.01). Mortality at 30 days and one year were equivalent in the two groups (p=0.27 & p=0.38, respectively).

As part of the PARAGON A clinical trial, investigators were required to employ point-of-care aPTT (Hemochron Jr) assays in order to maintain clinician blinding to therapeutic regimen[18]. A strong statistical trend (p=0.08) was observed between time to therapeutic aPTT and the 30-day death or myocardial infarction combined endpoint. The authors suggest that a change in clinical protocol to include more frequent testing (PARAGON A required testing at 6 – 12 hour intervals) might improve patient outcomes by increasing the likelihood of attaining therapeutic levels more quickly. Becker and colleagues[16] arrived at a similar conclusion following a randomized controlled trial evaluating weight-adjusted versus empirical heparin dosing as well as point-of-care (CoaguChek Plus) versus laboratory aPTT management of 113 patients with active venous or arterial thromboembolic disease requiring intravenous heparin therapy. While the time between sample draw and dose adjustment was significantly shorter for the point-of-care group (p=0.0001), no change in test frequency was made and no differences were observed in time to target range or time within range between the point-of-care and laboratory groups.

The need to change procedures in order to optimize the advantages of point-of-care testing was directly demonstrated by Nichols and coworkers[17] in their prospective, non-randomized analysis of the effect of point-of-care testing on patient wait times before and after elective invasive cardiology and radiology procedures. The authors conclude that point-of-care testing must be integrated into clinical management pathways if the benefits of the reduced turn around times are to have positive clinical impact.

Prothrombin (PT)/ International Normalized Ratio (INR)

Is there evidence of improved clinical outcome using point-of-care PT testing?	
Abstracts	132
Systematic Review	40
Citations in final recommendation	19

Is there evidence of improved clinical outcome using point-of-care PT testing?

In the hospital?

We recommend that the use of point-of-care PT be considered a safe and effective alternative to laboratory PT testing for hemostasis monitoring.

(Class B, Level I at least one randomized controlled trial, Level II–1 small randomized controlled trials, non-randomized controlled trials, Level II-3 multiple time series without intervention).

We strongly recommend that critical ranges, workflow patterns and cost analysis be evaluated, and where necessary altered, during the implementation of point-of-care PT testing to ensure optimization of patient treatment protocols.

(Class A, Level II-1 small randomized controlled trials, non-randomized controlled trials).

As seen for the aPTT, the vast majority of literature identified in this search consisted of clinical correlation analyses between point-of-care PT/INR monitors and hospital based laboratory systems. Fewer articles specifically addressed TAT for the PT test, but again, unsurprisingly, all these studies showed statistically significant improvement in TAT with point-of-care[4, 5, 19]. The studies by Despotis[12], Nuttall[13], Capraro[14] and Nichols[17] included PT testing in their evaluations. These trials showed improved patient outcomes[12, 13] or no effect on outcome[14] following cardiac surgery and reduced wait times surrounding interventional cardiology and radiology procedures[17].

As with the aPTT discussion, the impact of the PT test itself cannot be isolated from other point-of-care tests employed or the procedural changes implemented for these study populations.

Two pharmaceutical treatment evaluations utilizing point-of-care (CoaguChek[20], ProTime[21]) PT monitoring were identified. While there were no INR specific endpoints described in these controlled trials, investigators participating in both studies noted that the warfarin anticoagulation arm of the study showed good therapeutic management.

Is there evidence of improved clinical outcome using point-of-care PT testing?

In the anticoagulation clinic?

We recommend that the use of point-of-care PT be considered a safe and effective alternative to laboratory PT testing for oral anticoagulation monitoring and management.

(Class B, Level II-1 –controlled trials without randomization, Level II-2 - Cohort or case-control analytic studies, Level III – opinions of respected authorities).

The use of point-of-care PT/INR devices has been shown to be safe and effective in several studies in oral anticoagulation clinic populations[22 - 25]. In addition to evaluating the correlation of the point-of-care system (CoaguChek[22, 24], ProTime[23]), patient and clinician satisfaction was assessed by questionnaire. Satisfaction was the only endpoint evaluated in the study by Choudry and colleagues[26]. In these studies both the patients and the clinicians preferred using fingerstick samples on the point-of-care system to venous sampling for laboratory testing. This is a rapidly growing management strategy for patients on long-term vitamin K antagonist anticoagulation in which a highly experienced, dedicated staff can help to provide optimal management to this patient population[25].

Is there evidence of improved clinical outcome using point-of-care PT testing?

For Patient Self-testing / Self-Management?

We recommend the use of point-of-care PT as a safe and effective method for oral anticoagulation monitoring for appropriately trained and capable individuals.

(Class B, Level I at least one randomized controlled trial, Level II–1 - small randomized controlled trials, non-randomized controlled trials, Level III - opinions of respected authorities).

Another growing management strategy for oral anticoagulation monitoring is patient self-testing (PST) and its extension, patient self-management (PSM). In either scenario, the patient, or their caregiver, monitors the patient's INR at home with a point-of-care monitor. PST patients then report the result to the clinic or doctor responsible for their care who determines any required warfarin dose adjustments. PSM patients generally use an algorithm provided by a medical professional to adjust their own dose based on the INR reading. There have been a large number of studies evaluating the efficacy of PST and/or PSM compared to routine medical care (testing and dose adjustment by primary care physician) and to oral anticoagulation clinic care. Endpoints include time in therapeutic range as well as, in some trials, incidence of hemorrhage or thromboembolism. Several recent reviews of these studies have been published[27-30]. In each study, PST or PSM has been shown to be superior to routine medical care and at least equivalent to oral anticoagulation clinic management. One confounding factor in these studies is the frequency of PT/INR testing. The inverse correlation of time between tests and time in therapeutic range has been clearly demonstrated[31] and PST/PSM patients routinely monitor their PT/INR at higher frequencies than patients monitored by laboratory based strategies.

Activated Clotting Time (ACT)

Is there evidence of improved clinical outcome using ACT testing? Is there evidence for optimal target times to be used with ACT monitoring?	
Abstracts	370
Systematic Review	57
Citations in final recommendation	46

Is there evidence of improved clinical outcome using ACT testing?

Is there evidence for optimal target times to be used with ACT monitoring?

In cardiovascular surgery?

We strongly recommend ACT monitoring of heparin anticoagulation and neutralization in the cardiac surgery arena. .

(Class A, Level I at least one randomized controlled trial, Level II–1 - small randomized controlled trials, non-randomized controlled trials).

There is insufficient evidence to recommend specific target times for use in ACT managed heparin dosing during cardiovascular surgery.

(Class I – conflicting evidence across clinical trials).

By far the largest number of outcome related publications for point of care coagulation testing is represented by studies performed in cardiac surgery or percutaneous coronary intervention applications with the Activate Clotting Time (ACT). First described by Hattersley in 1966[32], the use of the ACT to predict heparin requirements ad the cardiopulmonary bypass surgery target recommendation was described by Bull and colleagues in 1975[33, 34]. In general, these publications fall into one of two categories, those evaluating the use of the ACT to optimize heparin and protamine dosing and those studies that specifically examine patient outcome.

In the cardiovascular surgery studies, accurate dosing was defined as predicting the dose required to obtain an ACT above a predefined clotting time (range 400 – 600 seconds)[35 - 39]. Employing the Hemochron ACT test, these investigators clearly showed the differing heparin requirements between patients as well as between populations[36-38], most notably pediatric versus adult patients[35]. Two studies evaluated the correlation of the ACT to heparin level determined either through laboratory assays[37] or using the Hepcon (now Medtronics HMS) system[40] to measure heparin level. Both studies support the use of the ACT showing good correlation to heparin level for ACTs below 600 seconds[37] and a strong correlation between post-operative bleeding and elevated ACTs following heparin reversal[40].

Cardiac surgery outcomes are defined as post-operative blood loss as measured by chest tube drainage over 12 or 24 hours, blood product usage and total heparin and/or protamine given. In all studies reviewed, if statistical analyses were employed, there was a statistically significant decrease in each of these parameters when ACT managed heparin dosing was compared to empirical dosing. The earliest studies[41 – 43] indicated reductions of near 50% in blood loss in the initial post-operative 12 hour period for patients monitored by ACT to optimize anticoagulation versus those patients dosed empirically with 2 – 4 mg/kg heparin and additional heparin administered on a time post bolus basis.

Later studies, employing combinations of the Hemochron, HemoTec (now Medtronics ACTII) or HMS systems confirmed these findings[44- 46] adding additional observations on reduced blood product usage[47, 48]. Interestingly, one study[49] noted no reduction in post-operative blood loss but significant reductions in intra-operative blood loss as well as heparin and protamine doses given for ACT monitored patients compared to the empirically dosed group ($p<0.001$). Changes in dosing with ACT varied by trial with reports of increased[46] and decreased[41, 44, 49] heparin in the ACT group. All studies agreed that ACT monitoring reduced the total protamine dose[38, 44-46, 49] given, in one case, this reduction correlated closely with reduced 24 hour blood loss ($p=0.02$)[45]. The target times employed for the ACT monitored groups varied widely with each author

recommending differing minimal ACTs for safe extracorporeal circulation. These recommendations range from 350 seconds[45] to targeting values in excess of 500 seconds[47] to achieve optimal patient outcomes.

Questions surrounding optimal target times are further confounded by evaluations comparing heparin coated tubing or heparin bonded tubing versus standard tubing use in the extracorporeal circuit. These studies suggest comparable or improved outcomes using target times as low as 180 seconds with fully heparin bonded circuits when compared to either routine or heparin coated circuits with ACT targets of >450 seconds[50-52].

Is there evidence of improved clinical outcome using ACT testing?

Is there evidence for optimal target times to be used with ACT monitoring?

In interventional cardiology?

We strongly recommend ACT monitoring of heparin anticoagulation and neutralization in the cardiac surgery arena.

(Class A, Level II–1 - small randomized controlled trials, non-randomized controlled trials, Level II-2 – Case controlled analytic studies from more than one center or research group).

We recommend the use of target times specific to ACT system used that differ if specific platelet inhibitors are used concurrently with heparin.

Without intravenous platelet inhibitors, the evidence suggests that target of >250 seconds using the Medtronics ACTII or >300 seconds using the HEMOCHRON FTCA510 tube assay are appropriate.

(Class B – Level II–1 - small randomized controlled trials, non-randomized controlled trials, Level II-2 – Case controlled analytic studies from more than one center or research group).

With the intravenous platelet inhibitors abciximab or eptifibatide, a target of 200-300 seconds is recommended, with tirofiban and somewhat tighter range of 250 – 300 seconds is recommended.

(Class B – Level I- at least one randomized controlled trial).

Published references in the cardiac catheterization laboratory consist primarily of studies of patients undergoing percutaneous transluminal coronary angioplasty (PTCA) rather than other interventional procedures. Only one publication was identified which specifically examined patient outcomes comparing anticoagulation management with ACT to empirical, unmonitored heparin dosing[53]. In this retrospective study, records were examined for 1200 sequential PTCA procedures. The group managed by ACT showed increased risk of abrupt or late vessel closure based on pre-procedure demographic analyses, yet showed a statistically significant reduced incidence of closure than the historic controls ($p<0.05$). In studies of this population comparing the clinical utility of ACT monitoring versus fibrinopeptide A formation, ACTs exceeding 200 seconds were shown to be indicative of significant reduction of thrombin formation[54]. The ACT was also shown to be superior to the laboratory aPTT for monitoring anticoagulation in this population as judged by heparin dose response[55] and cost[56] when clinical outcomes were similar for the ACT and aPTT groups.

Other studies reviewed looked to establish optimal target times for patients undergoing PTCA to minimize both bleeding and ischemic complications. Ogilby and colleagues[57] reported no bleeding or ischemic complications in 108 patients treated with target Hemochron ACTs of >300 seconds, while Kaluski and coworkers[58] advocate lower levels of heparinization targeting ACTs (unspecified system) of 160 – 240 seconds. In this group of 341 patients, there were 6 occlusive events and one myocardial infarction within 14 days of procedure, but no bleeding complications.

Retrospective analyses of more than 1200 patients each were employed to identify patients who experienced abrupt vessel closure and case match them with at least twice their number of

patients without ischemic complications[59, 60]. Ferguson and coworkers[59] were able to identify a target value of 250 seconds on the HemoTec system as significantly reducing ischemic complications ($p<0.001$). These investigators further determined, that a change in ACT on this system of less than 150 seconds in response to a 10,000 unit heparin bolus was also indication of increased thrombotic events. While Narins and colleagues[60] were unable to identify an ideal target time for the Hemochron system, their data also showed a significant increase in ischemic events in patients with lower ACTs ($p=0.004$). This study showed no relationship of elevated ACTs with increased bleeding complications. In contrast, Hillegass and colleagues[61] found a significant correlation ($p<0.001$) between elevated ACT times and bleeding in his prospective evaluation of 429 patients. Reviews of the existing literature by Ferguson[62] and Klein and Agarwal[63] in 1995 and 1996, respectively, both recommended that target times be ACT system specific and that optimal targets for PTCA are >250 – 275 seconds for HemoTec and >300 – 350 seconds for Hemochron ACTs. These values are lower than those arrived at by Chew and coworkers[64] in 2001 after their metaanalysis of data from 6 interventional trials, 5 including platelet inhibitors and one comparing heparin and bivalirudin anticoagulation. In these studies, 95% of the ACT results were obtained with Hemochron or Hemochron Jr ACTs, the remainder with the HemoTec. Chew's group concluded that the lowest composite ischemic event rate in patients receiving only heparin was seen in the ACT range of 350-375 seconds, with significant bleeding observed if the ACT exceeded 400 seconds.

Target time recommendations for patients receiving heparin with concurrent intravenous antiplatelet therapy are best obtained from the clinical trials of these antiplatelet agents[65-67]. Both the EPILOG[65] and ESPIRIT[66] studies showed an optimal outcome (minimizing both ischemic and bleeding events) when ACTs were maintained between 200 and 300 seconds in the presence of abciximab or eptifibatide, respectively. The EPILOG study employed Hemochron ACTs, while the type of ACT system in use was not reported for the ESPIRIT. In the TACTICS trial[67], there was a clear relationship between ACT values below 250 seconds and ischemic

complications (p=0.043) and a trend toward increased bleeding for clotting times in excess of 300 seconds (p=0.08).

Is there evidence of improved clinical outcome using ACT testing?

Is there evidence for optimal target times to be used with ACT monitoring?

In extracorporeal membrane oxygenation?

We strongly recommend ACT monitoring to control heparin anticoagulation during extracorporeal membrane oxygenation (ECMO). (Class A – Level III – opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees).

We recommend that ACT target times for ECMO be determined based on the ACT system in use. (Class B – Level III – opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees).

Since 1990 the results of three large surveys of ECMO practices have been published[68-70]. ACT monitoring was employed by all survey respondents in each year although the mix of systems changed from 1990 to 1996 (the 2002 survey did not list specific ACT instrumentation). Target ranges reported in 1990 for "typical" patients ranged from 180 – 240 to 220 – 260 with lower ranges for "bleeding" patients[68]. The average target range reported in 2002 was 180 – 220[70]. Colby and colleagues[71] emphasized the need to set target ranges based on the ACT system in use. Without changing target ranges, changing the ACT system from the Hemochron 400 to the Hemochron Jr ACT-LR let to reduce circuit life and increased circuit clotting (p=0.035). Changing the target range from 200 – 220 to 220-240 for the Hemochron Jr system led to improved circuit longevity and reduced circuit clots (p=0.049). There were no differences in bleeding complications across the three treatment groups.

Is there evidence of improved clinical outcome using ACT testing?

Is there evidence for optimal target times to be used with ACT monitoring?

In other applications (e.g. vascular surgery, intravenous heparin therapy, dialysis, neuroradiology, etc.)?

There is insufficient evidence to recommend for or against ACT monitoring in applications other than cardiovascular surgery, interventional cardiology or extracorporeal oxygenation. (Class I).

While several publications refer to the use of the ACT for a wide variety of other clinical applications, few focus on the ACT itself or its effect on patient outcome. Mabry and colleagues[72, 73] have described the clinical utility of the ACT (manual or Hemochron) in monitoring patients in peripheral vascular surgery recommending targets of 180 – 200 seconds. Ouseph and coworkers[74] showed the efficacy of defined Hemochron ACT based algorithms for increasing dialyzer reuse in patients requiring chronic hemodialysis. Simko and coworkers[75] found the ACT to be as useful as the aPTT for monitoring intravenous heparin therapy, while Smythe and colleagues[76] found the aPTT to be a more accurate monitor. Many studies state that ACTs are used for example, in neuroradiology, femoral sheath removal following cardiac catheterization procedures and electrophysiology, but these studies simply reference a target time without indication as to the clinical benefit of these procedures.

SUMMARY AND FUTURE DIRECTIONS

Overall, point-of-care coagulation testing is appropriate in a wide range of clinical applications. Implementation of point-of-care aPTT and PT testing in the in-patient setting may require evaluation and adjustment of institution established therapeutic targets, clinical decision points and general work flow in the area(s) affected by this testing. Whether or not implementation of point-of-care aPTT and PT testing in this environment can truly improve patient outcome is not yet clear and requires additional investigation, though there is a clear impact on turn around time and the availability of laboratory results.

Point-of-care PT/INR testing is required in the patient self-testing and patient self-management paradigms for oral anticoagulation therapy management. While it is still unclear whether the

outcome improvements observed compared to routine care are due to the use of point-of-care or to the increased frequency of testing, the benefits of these management modalities are clear. There is a clear association of the frequency of INR testing and maintenance of therapeutic range.

The use of ACT testing in cardiac surgery and cardiac catheterization laboratories shows the strongest impact on improving patient outcome. Despite this clear evidence, the target times employed in these clinical arenas stem from historical clinician comfort rather than clear evidence, yet another area requiring future trials. Furthermore, the ACT is used in a large number of other clinical applications with some indication, but insufficient conclusive evidence, to determine optimal patient treatment. It is critical that trials be designed and conducted to determine the optimal use of this assay, and optimal target times for use of the ACT in all clinical arenas.

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