# The Importance of Examining Blood Clotting Factors Pt and aPTT and Fibrinogen

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## Abstracts

Monitoring of blood clotting is done to manage hemostasis and bleeding in patients of trauma care unit and even going under surgical procedures. Then on the other hand, this monitoring also becomes important in cases of heart surgeries (CPB). The patients that are admitted in the hospital in a particular given scenario of perioperative setting, monitoring of blood clotting becomes very important. The components included are respective procedures, similar place of surgery, extent of injury, tissue loss and the level of hemostatic system. Surgical procedures that may cause bleeding because of the vascular nature of the tissue include tonsillectomy and vascular and cardiac surgery. This present study will present the importance of monitoring blood clotting factor Pt and aPTT and Fibrinogen. Study is based on secondary data and takes the reference from many of the previous studies. The reference is taken from 1995 to 2023.

Keywords: Blood Clotting, Pt, aPTT, Fibrinogen, Monitoring.

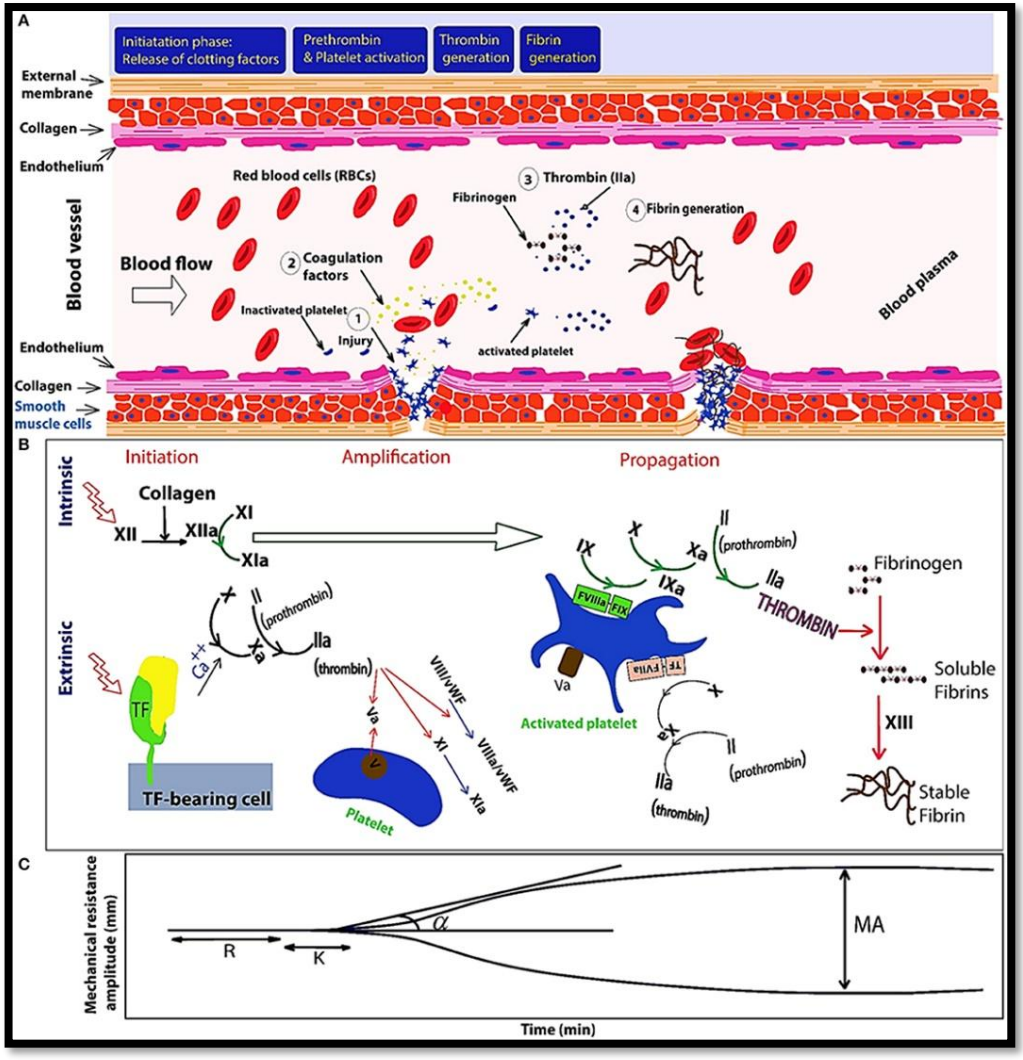
## 1. Introduction

Respective monitoring of blood clotting is done to manage hemostasis and bleeding in patients of trauma care unit and even going under surgical procedures. Then on the other hand, this monitoring also becomes important in cases of heart surgeries (CPB). The patients that are admitted in the hospital in a particular given scenario of perioperative setting, monitoring of blood clotting becomes very important. Blennerhassett et al (2019) The components included are respective procedures, similar place of surgery, extent of injury, tissue loss and the level of hemostatic system. Surgical procedures that may cause bleeding because of the vascular nature of the tissue include tonsillectomy and vascular and cardiac surgery. In other cases, the risk of bleeding is associated with the occurrence of adverse events, especially when bleeding occurs in the central nervous system or nearby sites (e.g., eye surgery). Patient-specific information, including the patient's medical history, previous surgeries for excessive bleeding, and family

history. However, clinical studies are also frequently used for this assessment. The most commonly performed tests on patients during cardiac surgery include activated partial thromboplastin time (aPTT), prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (ACT). ACT is often used to monitor CPB anticoagulation. Mohammadi et al (2019)

Although laboratory tests using aPTT and PT are essential for monitoring anticoagulation and were developed shortly after the introduction of warfarin to detect abnormalities in hemostasis, the cost of these tests in predicting bleeding in surgical patients is extensive. Their use is further complicated by the likelihood of bleeding, test characteristics, and the potential for negative and false-negative results. For example, the aPTT may be prolonged in patients on lupus anticoagulants or type XII deficiency, but this length is not associated with bleeding risk. Dorgalaleh et al (2021)

Some of the previous researches published in 2000 to 2010 state that preoperative hemostatic testing before elective surgery was ineffective in patients without a history of abnormal bleeding and rarely resulted in changes to the patient's medical management. In addition, guidelines for pre-bleeding risk assessment state that hemostasis testing is a poor measure of blood flow and that routine testing is generally not recommended for patients without a history of bleeding. Despite these considerations, these coagulation tests are still widely used in clinical decision making in hospitalized patients. Feinbloom et al (2021) The aim of this review is to investigate the clinical use of aPTT and PT tests and their role in assessing perioperative bleeding risk for perioperative diagnosis. Furthermore, due to the widespread use of ACT in hospitals, its use in preventive maintenance of cardiopulmonary bypass will also be evaluated.




Source: Mohammadi et al (2019)

Figure 1: Primary And Secondary Phases of Hemostasis

Sourcing of aPTT

aPTT is considered as a specific coagulation monitoring test used for knowing the level of coagulation in a given patient and even for the patients who are suspected to have certain deficiencies related to components of coagulation. Such components may occur because of internal characteristics of the patients or the common process of coagulation. Toulon et al (2021)

This monitoring test of coagulation gets affected by a series of components i.e., VIII, IX, XI, XII, X, II, and even fibrinogen. The aPTT is widely used for monitoring anticoagulation therapy with low levels of heparin (from 0.1 IU/mL to approximately 1 IU/mL). Weitz et al (2017); Ignjatovic et al (2013)

The aPTT may vary among workers, and this individual variation is evident over a wider time period. The aPTT times used vary among laboratories using different equipment, as well as reagents with different sensitivities and lipid compositions. aPTT reagents are mixtures of phospholipids and activators such as kaolin, silica, or ellagic acid. Studies have shown that the response of various aPTT agents to mild to moderate coagulation disorders, particularly factors VIII and IX, varies greatly. In addition, aPTT is prolonged in 1.5% to 3% of the population with mild to severe type XII deficiency; however, this delay was not associated with an increased risk of bleeding. Barcellona et al (2017) The laboratory also determined that the time taken would be sufficient to cover 95% of healthy men and women, similar to those in the hospital. That is, 5% of normal people will exceed the time taken. Finally, there have been recent reports that increases in biological products such as C-reactive protein may be associated with active aPTT reagents and may lead to long-term complications with phospholipids commonly used in aPTT reagents, particularly phosphatidylcholine and phosphatidylethanolamine. Chornenki et al (2022)

Clinical Application of aPTT

As stated above this test is applied to check the unfractionated heparin and any other agent responsible for anticoagulant, this may also hold the inhibitors of direct thrombin. Halbmayer et al (1994) Limitations of this procedure include biological variability, insensitivity to some clinically important bleeding disorders (e.g., factor XIII deficiency, α2-antiplasmin deficiency), measurement and reagent variability, sensitivity to defects (low sensitivity of prothrombin to fibrin, prothrombinev), prolonged delay due to physical changes (e.g., pregnancy, physical stress, or injury), prolonged treatment interruption due to poor quality (e.g., type XII {the most common causes of an unexpected aPTT length of one}, prokallikrein, and high molecular weight kininogen deficiencies), and preanalytical errors such as inaccurate sample collection. Robert-Ebadi et al (2020); Sikes et al (2023)

PT AND INR

PT measures the time required for clotting to occur after a tissue sample is added to recalcified citrated plasma in the laboratory and at the point of care (POC). PT is measured by adding thromboplastin (a mixture of tissue proteins, calcium, and phospholipids) to a patient's citrated plasma sample and forming blood. It can also be used to screen for deficiencies in one or more clotting factors (fibrinogen and factors II, V, VII, and X). The INR was introduced by the World Health Organization to overcome variations in PT results due to differences in thromboplastin reagents produced by different manufacturers. The INR is the ratio of the patient's PT value divided by the normal value (geometric mean PT value in non-anticoagulated patients) determined by the central local laboratory, increased to the International Sensitivity Index (ISI) value (usually between 1.0 and 2.0) for all reagents and assays used: INR 5 (PT patient/PT geomean) ISI. Munro et al (1997); Reeves et al (2003)

Table 1: Effects of genetic conditions on coagulation test results and bleeding risk

| Conditions in Which Abnormal Test Results Do Not Predict Bleeding Risk | Observations |
|---|---|
| Lupus anticoagulant/ — antiphospholipid antibodies | |
| Factor XII deficiency | Associated with prolonged aPTT but does not predispose to an increased risk in bleeding |
| Neurofibromatosis type I | Among 30 subjects with this condition, aPTT was prolonged in 11, factor XII levels were reduced in 3, vWF levels were reduced in 4, and PFA-100 closure times were elevated in 13. However, clinically perceived bleeding risk did not appear to be correlated with laboratory test results in most cases. |
| Noonan syndrome | May be associated with prolonged aPTT and low levels of clotting factors (particularly factors XI and XII), but coagulation test results did not correlate with bruising history and may not predict bleeding risk. |
| Conditions in Which Abnormal Test Results May Predict Bleeding Risk | Observations |
| Factor VII deficiency | The only congenital bleeding disorder characterized by isolated PT prolongation. It is clinically heterogeneous but life-threatening bleeding may occur[73] |
| Prothrombin (factor II) deficiency | Typically results in prolonged PT and aPTT, with increased risk of surgical-associated or trauma-associated bleeding |
| Factor XI deficiency | Associated with excessive bleeding following injury, surgery, or other invasive procedures, but may otherwise be asymptomatic. aPTT is prolonged by more than 2 SDs above the normal mean in patients with severe factor XI deficiency, but heterozygotes may have normal or only slightly prolonged aPTT values |
| Lupus-like anticoagulant | May cause prolonged PT and aPTT, although sensitivity varies; may sometimes be associated with impaired hemostasis |
| Sickle cell disease | May be associated with prolonged PT but trials are needed to clarify whether abnormal coagulation tests are associated with increased risk of perioperative bleeding |
| Rosenthal syndrome/factor XI deficiency | May be associated with prolonged PTT but PTT does not necessarily correlate with factor XI levels. Patients can be classified as low-risk or high-risk for elective surgery based on factor XI levels and prior surgical or family history |
| Type I Gaucher disease | Prolonged PT and variable clotting factor deficiencies plus potential for increased intraoperative and postoperative bleeding risk |
| Kasabach—Merritt syndrome | Associated with prolonged PT and aPTT, decreased hematocrit and fibrinogen levels, and severe risk of disseminated intravascular coagulation |
| Conditions in Which Normal/Mildly Abnormal Test Results Do Not Exclude Bleeding Risk | Observations |
| Hemophilia A (factor VIII deficiency) and Hemophilia B (factor IX deficiency) | PT is unaffected but aPTT should be prolonged |
| Passovoy factor deficiency | aPTT shows relatively mild prolongation but subjects bruise easily and have undue blood loss after procedures such as dental extraction and tonsillectomy |

## Application of aPTT and PT

Many of the previous researchers have given their view on the application of aPTT and PT as a monitoring procedure for coagulation and application & testing of the same. The most important conclusion of these reviews is that routine hemostasis testing using aPTT and PT is not useful in asymptomatic patients without known risk factors. In addition, the high probability of negative and false-negative results may lead to unnecessary alerts or false-positive results for aPTT and PT, respectively. Individual studies evaluating the value of preoperative aPTT and PT (as well as other tests) in predicting bleeding risk are given below. In general, aPTT and PT do not have the best value for subsequent bleeding risk. However, unlike the negative results of most of these studies, there is ample evidence to suggest that early testing is useful because it identifies individuals with blood disorders such as congenital factor X deficiency, mild hemophilia, and warfarin toxicity without a history of the condition. Chee et al (2008); Shetty et al (2003)

## Published Guidelines and Recommendations

As stated by Austin et al (2010), Preoperative testing can be helpful in assessing bleeding, but the results are often inconclusive. The authors state that a sufficient history of bleeding is the best way to screen patients before surgery. Due to the lack of data, pretesting guidelines published in 2003 by the National Institute for Clinical Excellence in the United Kingdom are based on expert opinion. In the United Kingdom guidelines, hemostatic tests (such as aPTT and PT/INR) are recommended (but not recommended) by the American Society of Anesthesiologists for patients with stage 3 heart disease undergoing major surgery. However, in general, this test is not recommended because of its low predictive value unless there is a history of abnormal bleeding.

Kamal et al (2007) Recommendations for the interpretation and follow-up of prolonged PT, aPTT, and bleeding time in the elderly have been published. The authors state that correlation of these tests with the patient's clinical and hemostatic history is important. In 2008, the British Safety Committee published guidelines stating that a presumptive diagnosis of hemostasis is a poor predictor of bleeding risk after surgery or related procedures. In 2010, a group of experts in the United States published a "consensus" on hemostasis, in which they said that currently available routine hemostasis tests, including PT/INR and aPTT, are not relevant to the difficulty of hemostasis and may deceive physicians. Other tests, such as thromboelastography, are considered time-consuming and difficult. They also emphasize the need for management, research studies, and extensive lists and research articles to answer important questions about clinical hemostasis, as well as the development of tests that can predict bleeding and complications and guide treatment when necessary. In 2011, the European Society of Anaesthesiology published guidelines for the preoperative evaluation of adults who are not undergoing surgery. Similar to previous guidelines and recommendations, the authors state that “the routine use of coagulation tests is not recommended unless there are special circumstances in the medical history.”

## Testing Variability

For PT and aPTT, clinicians define the “margin of error” by which POC results are compared to results from standard laboratory tests. In general, limiting false-positive results refers to the

difference between two results obtained by various methods that could harm or pose a risk to patient safety. However, most laboratory tests have at least 5 to 10 percent variability, depending on the test alone.

PT

The clinical area for PT is defined as "normal" and is approximately 1.5 times higher than normal. For a PT reagent with an ISI of 1.0, a PT time of 1.5 times will always be equal to 1.5 INR. When using the POC PT test, the amount of biological variation (inter- and intra-individual variation) that is considered equivalent also varies between 5% and 10%. Therefore, for an INR of 1.5, the "grey area" would be 1.4 to 1.6, leading to the same clinical decision for the POC PT test as for the laboratory test – in general, the cut-off point for adjusting the INR from 1.4 is the same up to 1.6. It is important to define the limits of false positives, as this will also change the course of treatment. For example, for PT, it should be noted that for PT, fresh ice, thawed or liquid plasma cannot be administered compared to the PT POC test for plasma. In order to clearly prescribe anticoagulants to patients, doctors more often use the chromogenic factor warfarin because there is a difference in the increase in INR compared with anticoagulants. The results of these tests can be used to guide intervention or other medical decisions.

aPTT

For the aPTT, the limit of erroneous results for comparison of the aPTT POC test to an aPTT laboratory test depends on whether the test is being used for diagnostic or therapeutic purposes. The baseline aPTT value is a critical factor for monitoring anticoagulants, because anticoagulant therapy is usually directed at increasing the aPTT over a wide range, from 1.5 to 2.5 times control values. For the 5% to 10% variability, this usually has minimal impact over a 5% to 10% coefficient of variation. Also, for therapy for bleeding, the goal is to reduce the aPTT to less than 35 s, which is considered normal. Although guidelines still suggest plasma as a therapy for a prolonged aPTT, there are few data to support that practice. No randomized controlled trials have evaluated whether fresh frozen plasma administration corrects abnormal aPTT results or indeed elevated PT values and is effective in stopping bleeding. 85–88 Moreover, several uncontrolled trials have found that fresh frozen plasma does not effectively correct an abnormal PT or aPTT.

## 2. Conclusion

The clinical context, medical history, and associated factors must be considered when interpreting the results of coagulation abnormalities. For example, patients receiving anticoagulant therapy may intentionally prolong PT and INR values. Similarly, patients with liver disease may have abnormal PT and PTT due to adverse effects of coagulation factors. Addressing uncertainty is multidisciplinary. Hematologists can work with other medical specialists to determine the cause and develop appropriate therapy. This may include checking blood clotting factors, treating anticoagulant medications, or addressing certain conditions that cause abnormal blood flow. Coagulation studies provide important information about a person's clotting system, helping doctors assess the risk of bleeding or thrombosis. Knowing normal and abnormal values for PT, PTT, INR, and D-dimer is important for proper interpretation and

management of coagulopathy. Regular monitoring and collaboration between doctors is important to ensure good patient care and to prevent complications related to abnormalities. Coagulation testing using aPTT and PT tests are not reliable predictors of excessive perioperative bleeding risk in patients without other known risk factors. Although routine preoperative use of these tests is common, the data do not support their utility for screening. However, they are used extensively for anticoagulation monitoring with many different anticoagulation agents. A thorough patient and family history, together with physical examination, is vital to identify patients at increased bleeding risk; in such cases, follow-up hemostatic testing may be appropriate.

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