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Thrombocytopenia following Percutaneous Coronary Intervention

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Background: *Thrombocytopenia following percutaneous coronary intervention (PCI) is an underappreciated condition that is often clinically challenging. There are no guidelines on the management of patients with this condition.*
Objective: *To review recent data in etiologies, risk factors, prevention, management, and prognostic implications of thrombocytopenia following PCI.*
Evidence Acquisition: *Search of MEDLINE, EMBASE, the Cochrane Database, and Google Scholar using the term thrombocytopenia + PCI and other relevant keywords to identify systematic reviews, clinical trials, cohort studies, case series, and case reports. The review was limited to English-language articles published between January 1980 and June 2009. Articles on patients with baseline thrombocytopenia prior to PCI were excluded.*
Evidence Synthesis: *Thrombocytopenia is not infrequent following PCI. The typical patient with post-PCI thrombocytopenia is on multiple therapies that can potentially cause a decrease in the platelet count. Identification of the cause is critical because management of the condition varies significantly based on the etiology. The severity of the thrombocytopenia also determines the clinical management of the patient. Several observational studies have demonstrated the adverse prognostic impact of the complication on clinical outcomes and have identified risk factors.*
Conclusions: *Judicious use of therapies that can cause thrombocytopenia, efficient detection of the cause of the decrease in platelet count, and appropriate management of the condition can potentially improve the quality of care and outcomes following PCI. Further research into risk factors that predispose post-PCI patients to developing thrombocytopenia is warranted.* (J Interven Cardiol 2011;24:15–26)

Introduction

Over 1.3 million percutaneous coronary interventions (PCIs) are performed annually in the United States.[1] Thrombocytopenia is not uncommon following PCI. In clinical trials up to 15% of patients undergoing PCI have postprocedure thrombocytopenia. In patients with acute coronary syndrome (ACS), PCI is an independent predictor of thrombocytopenia.[2] A growing body of data suggests a strong association between post-PCI thrombocytopenia and both short- and long-term adverse outcomes, including mortality, which is independent of baseline characteristics, despite variations in the definition of thrombocytopenia.[3–7]

The post-PCI patient is usually on multiple medications and therapies that could potentially cause thrombocytopenia. Antithrombotic agents, such as unfractionated heparin (UFH), low-molecular-weight heparins (LMWHs), direct thrombin inhibitors, and antiplatelet therapies, such as thienopyridines, and platelet glycoprotein IIb/IIIa inhibitors (GPIs), can all cause thrombocytopenia. Intraaortic balloon pump (IABP) is an important therapy that is commonly associated with the development of thrombocytopenia in this setting.

Identification of the correct cause of the thrombocytopenia is critical to prevent premature withdrawal of useful therapies. In this review, we will explore the various causes, risk factors, prevention, management, and prognostic implications of thrombocytopenia following PCI.

Evidence Acquisition

We searched MEDLINE, EMBASE, the Cochrane Database, and Google Scholar using the term

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thrombocytopenia + PCI and other relevant keywords or a combination (*thrombocytopenia, PCI, angioplasty, stenting, clinical studies, registry, prospective cohorts, cross-sectional cohorts, case-control, cohorts, case series, case reports, epidemiology, occurrence, incidence, causes, causation, diagnosis, management, prognosis, pseudothrombocytopenia, heparin-induced thrombocytopenia, abciximab, eptifibatide, tirofiban, IABP, thienopyridines, clopidogrel, ticlopidine, statins, angiotensin-converting enzyme inhibitors, lepirudin, argatroban, bivalirudin, fondaparinux, danaparoid)* to identify systematic reviews, clinical trials, cohort studies, case series, and case reports. The review was limited to English-language articles published between January 1980 and June 2009. Publications on patients with baseline thrombocytopenia prior to PCI were excluded.

Evidence Synthesis

Definition. The standard definition of thrombocytopenia—an absolute reduction in platelet count to $<150 \times 10^9$/L—also holds true for the post-PCI setting. In patients with thrombocytosis (clonal, or secondary/reactive from surgery, infection, cancer, acute, or chronic inflammation),[8] a relative decrease of 50% or more from the baseline count is a sensitive measure and a high pretest predictor of clinical events related to thrombocytopenia and therefore should also be considered significant even if the nadir count is not $<150 \times 10^9$/L.[9]

Causes

Pseudothrombocytopenia. Pseudothrombocytopenia is an *ex vivo* artifact resulting from agglutination of platelets when the calcium content is decreased by blood collection in ethylenediamine tetraacetic (EDTA)-containing tubes.[10] As a result of platelet clumping, platelet counts reported by automated counters may be much lower than the actual normal circulating platelet count because these devices cannot differentiate platelet clumps from individual cells. If a low platelet count is obtained in EDTA-anticoagulated blood, a blood smear can be evaluated and a platelet count determined in blood collected into a sodium citrate or heparin tube, or ideally a smear of freshly obtained unanticoagulated blood, such as from a finger stick, can be examined. In patients undergoing PCI, pseudothrombocytopenia has been documented mainly in patients receiving abciximab. In four randomized trials of abciximab,[11] pseudothrombocytopenia occurred in 2.1% of abciximab-treated patients and in 0.6% of placebo-treated patients. Overall, pseudothrombocytopenia was the cause of 32.2% of all cases of thrombocytopenia in the overall study populations (placebo- and abciximab-treated) and 36.3% of all cases in the abciximab-treated group. Recognition of pseudothrombocytopenia is important because of the therapeutic implications.[12]

Unfractionated Heparin and Low-Molecular-Weight Heparin. The prevalence of heparin-induced thrombocytopenia (HIT) generally varies from 0.5 to 5% of patients, depending on the population studied, the type of heparin used, and the duration of heparin therapy.[13] Heparin, in either the unfractionated form (UFH) or the low-molecular-weight form (LMWH), is recommended as a standard of care anticoagulant therapy during PCI.[14] In the Complications After Thrombocytopenia Caused by Heparin (CATCH) registry,[15] 47% of patients admitted for ACS and 42% of patients admitted for myocardial infarction (MI) developed thrombocytopenia while receiving heparin therapy for 4 days or longer. The risk of HIT is lower with LMWH compared to UFH.[16–19]

HIT is caused by antibodies against complexes of platelet factor 4 (PF4) and heparin. These antibodies are present in nearly all patients who receive a clinical diagnosis of the disorder. In addition to thrombocytopenia and the presence of anti-PF4/heparin antibodies, venous or arterial thrombosis (most often, deep venous thrombosis [DVT], pulmonary embolism [PE], limb artery thrombosis, thrombotic stroke, myocardial infarction, and adrenal hemorrhagic necrosis [indicating adrenal vein thrombosis]) can occur.[20] Bleeding complications are rare.

There are three distinct temporal patterns of HIT: typical onset, rapid onset, and delayed onset.[21] Typical-onset HIT develops 5–14 days after initial exposure to UFH or LMWH. Rapid-onset HIT may occur within 24 h after either agent is initiated and results from residual anti-PF4/heparin antibodies that developed during a previous recent exposure (within the past 100 days, and especially the last 30 days). Delayed-onset HIT usually develops 7–40 days after UFH or LMWH is discontinued and usually after the patient has been discharged. Patients are found to have high titers of anti-PF4/heparin antibodies and are often readmitted with a new thrombosis. Thrombocytopenia may not

be observed initially, but develops soon after UFH or LMWH is given if this pattern is not recognized.

Platelet Glycoprotein IIb/IIIa Inhibitors (GPIs). Abciximab, eptifibatide, and tirofiban can all cause thrombocytopenia in a low but variable percentage of treated patients.[22,23] GPI-related thrombocytopenia is immune-mediated and often occurs rapidly within a few hours after the first administration of the drug due to the presence of naturally occurring drug-dependent antiplatelet antibodies.[24] Unlike HIT, GPI-associated thrombocytopenia can be profound, with platelet counts of $<20 \times 10^9$/L. With post-PCI patients treated with heparin and a GPI, an abrupt decrease in platelet count to $<20 \times 10^9$/L is almost always due to the GPI rather than to HIT.[25]

Rarely, GPI-associated thrombocytopenia can occur as long as 5–8 days after the first administration. While delayed thrombocytopenia is described to be mainly associated with abciximab,[26–33] cases have also been described in association with eptifibatide[34] and tirofiban.[35,36] The delayed onset of thrombocytopenia is explained by the persistence of platelet-bound drug for several days after treatment, rendering platelets susceptible to destruction by newly formed antibodies.[26,33]

Abciximab. About 1–2% of patients who receive abciximab develop thrombocytopenia.[3,37,38] After a second exposure to the drug, the rate for this complication rises to about 4%.[37] Although most patients with abciximab-associated thrombocytopenia recover uneventfully without major bleeding,[23] life-threatening bleeding can occur, including intracranial hemorrhage.[39,40]

Eptifibatide. The incidence of thrombocytopenia from eptifibatide is in the range of 0.2–1%.[41–43] While acute profound thrombocytopenia on second exposure has been described,[42,44–46] large studies involving eptifibatide have failed to document occurrence of this complication.[41,43]

The bleeding in eptifibatide-associated thrombocytopenia is usually minor bleeding, most commonly hematoma at the arterial access site, epistaxis, and petechiae.[42] A case of anaphylactic-type reaction with severe refractory hypotension,[47] and a case of deep venous thrombosis,[48] have been described in patients with eptifibatide-associated thrombocytopenia.

Tirofiban. Tirofiban has been associated with a lower occurrence of thrombocytopenia and bleeding compared to abciximab.[3,38] Studies have shown the occurrence of tirofiban-associated thrombocytopenia to be in the range of 0.5–1.2%.[3,36,38,49,50]

Thienopyridines. Thienopyridines only rarely cause thrombocytopenia. However, thienopyridine-associated thrombocytopenia manifests usually as classic thrombotic thrombocytopenic purpura (TTP) with severe thrombocytopenia, microangiopathic hemolytic anemia, renal failure, and neurologic changes. The mechanism for TTP with the thienopyridines appears to be immune-mediated. The incidence of ticlopidine-associated TTP in the post-PCI population is about 0.02%.[51] The incidence of clopidogrel-associated TTP is too low to make any accurate estimates.[52] TTP associated with ticlopidine generally occurs between 2–12 weeks of initiation of therapy whereas in case of clopidogrel, it occurs earlier, within the first 2 weeks of use.[52,53]

Although thienopyridine-associated thrombocytopenia most often occurs in the setting of TTP, ticlopidine-associated thrombocytopenia can also occur as part of aplastic anemia[54] and clopidogrel-associated thrombocytopenia can also occur as isolated thrombocytopenia or idiopathic immune thrombocytopenia, and thrombotic thrombocytopenia purpura with the hemolytic uremic syndrome.[55,56]

In addition to the clinical manifestations of TTP, coronary artery thrombosis has been described with clopidogrel-associated TTP.[57,58]

Intraaortic Balloon Pumps. IABPs are a common cause of thrombocytopenia in the post-PCI population. The thrombocytopenia is felt to be due to mechanical destruction of circulating platelets by the repeated inflation and deflation of the IABP. In a study of 109 patients,[59] 47% of patients with IABPs developed thrombocytopenia compared to 12% of patients not on IABPs. In a contemporary retrospective cohort study of 107 patients who had an IABP,[60] the incidence of thrombocytopenia was 57.9%. In both studies, platelet counts fell steadily until the third or the fourth day of IABP use and then stabilized. The platelet count fell to <50% of baseline in 26% and 30.4% of patients with an IABP, respectively, in the two studies.

Heparin, either UFH or LMWH is considered to be standard therapy during use of IABP. In a study of 764 patients who had an IABP after cardiac surgery, there was an incidence of 4.5% for HIT.[61] HIT should be ruled out as the cause of thrombocytopenia in all patients with IABP.

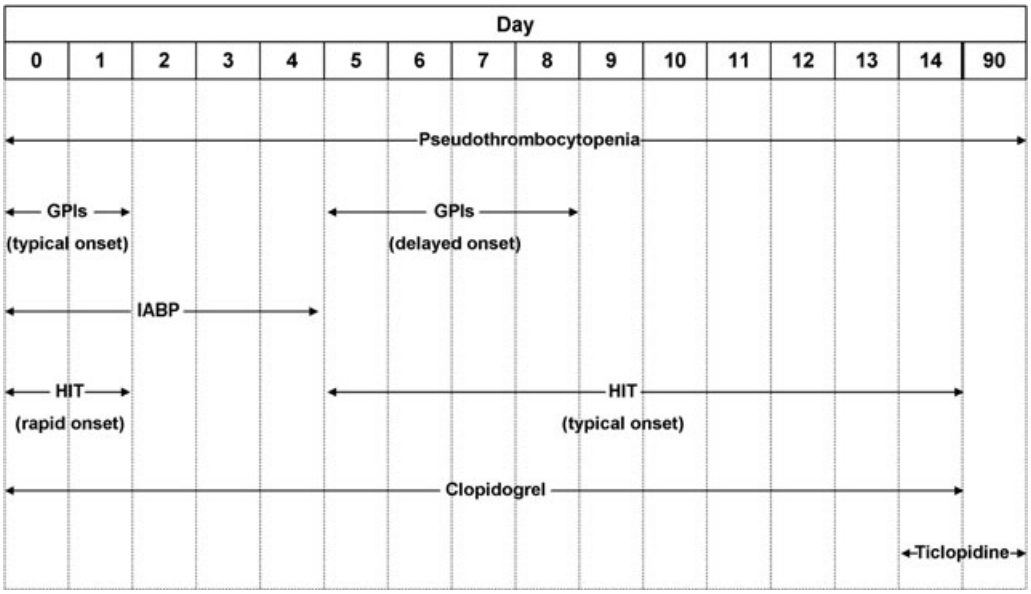

Figure 1. The common causes of post-PCI thrombocytopenia are listed according to their times of onset from the start of the therapy. Not included is delayed onset HIT, which occurs 7–40 days *after discontinuation* of heparin. GPI = glycoprotein IIb/IIIa inhibitor; HIT = heparin-induced thrombocytopenia; IABP = intraaortic balloon pump.

Limited data for newer percutaneous ventricular assist devices such as the TandemHeart percutaneous ventricular assist device suggest the occurrence of mechanically induced thrombocytopenia with these devices as well.[62]

Other Rare Causes. A few case reports have described thrombocytopenia and TTP in association with angiotensin-converting enzyme inhibitors[63–65] and statins.[66–68] Three cases of disorders resembling HIT have been reported in association with fondaparinux.[69–71] The negligible frequency of thrombocytopenia from these agents makes them less likely culprits, and they should be considered only after all other potential causes have been excluded.

Finally, thrombocytopenia may be caused by medications, such as nonsteroidal anti-inflammatory agents, oral hypoglycemics, or certain antibiotics, and these noncardiac causes should not be overlooked in the post-PCI patient. The common causes of post-PCI thrombocytopenia are listed according to their times of onset from the start of therapy in Figure 1.

Risk Factors. Knowledge of risk factors for post-PCI thrombocytopenia allows for prevention of thrombocytopenia by judicious use of therapies, and targeted surveillance of patients at risk, for early detection of the condition. Other than the common causes of post-PCI thrombocytopenia—IABPs, heparin, and GPIs, other typical clinical risk factors for the complication mirror those for bleeding after PCI.

Age. Older age is an independent risk factor for thrombocytopenia after PCI in multivariate analyses.[5,7] Elderly patients are more likely to have comorbidities, such as peripheral vascular disease, renal dysfunction, cerebrovascular disease, and hypertension. They are also more likely to have complex lesions and multivessel disease.

Baseline Platelet Count. A lower baseline platelet count, usually $<200 \times 10^9$/L, independently predicts post-PCI thrombocytopenia.[4,5,7]

Weight. Similar to post-PCI bleeding risk, a lower weight is independently predictive of post-PCI thrombocytopenia.[4,5,7]

Renal Function. Again, similar to post-PCI bleeding risk, renal dysfunction is an independent risk factor for post-PCI thrombocytopenia.[3,6] Potential mechanisms for the complication in patients with renal dysfunction include intrinsic platelet dysfunction, reduced platelet aggregation, and abnormalities in platelet-endothelial interactions.[72]

Outcome of PCI. The outcome of PCI has been shown to be an independent risk factor for post-PCI thrombocytopenia.[6] Most failed PCI procedures are treated conservatively with medications and therapies that can potentially cause thrombocytopenia.[73] The

number and duration of these therapies are larger in patients with failed PCI, thus increasing the risk for thrombocytopenia. These therapies include heparin, GPIs, and IABP. The occurrence of HIT is dependent on the duration of heparin exposure.[20] More than 4 hours of pretreatment with heparin has been shown to be independently predictive of post-PCI thrombocytopenia.[3] Similarly, the occurrence and severity of IABP-related thrombocytopenia is dependent on the duration of IABP use.[60]

Prognostic Implications. Post-PCI thrombocytopenia has been demonstrated to carry both short-term and long-term prognostic implications (Table 1). The associations have been shown independent of multiple other associated variables in several studies.[3–7] While bleeding and transfusions are direct consequences of the thrombocytopenia, the pathophysiologic basis for the adverse nonhemorrhagic outcomes is unclear. The effect of thrombocytopenia on mortality and recurrent cardiovascular events may well be mediated by bleeding. Patients with heparin-induced thrombocytopenia and thrombocytopenia associated with TTP can have arterial thrombosis, including coronary thrombosis leading to ischemia, MI, or death. Another explanation could be the withdrawal or temporary withholding of standard antiplatelet therapy or other guideline-recommended therapies in patients with thrombocytopenia. Platelet and red cell transfusions in these patients can have prothrombotic consequences. Finally, it is possible that thrombocytopenia may simply be a marker of poor substrate or a sicker subset of patients, with unaccounted variables contributing to dissimilar outcomes between patients with and without the condition in the observational studies published thus far.

Platelet Count Monitoring for the Detection of Post-PCI Thrombocytopenia. The risk of post-PCI thrombocytopenia depends on the use of potentially thrombocytopenic therapies and the presence of risk factors for development of the complication. Thus, the need for, and the intensity of platelet count monitoring, should be decided based on the estimated risk for post-PCI thrombocytopenia in the individual patient. The intensity and timing of platelet count monitoring should also be based on the period of highest risk from the antiplatelet therapies used.

Patients who receive heparin (UFH or LMWH) with an unknown heparin exposure history or a history of heparin use within the previous 100 days should have a baseline platelet count prior to the PCI and a platelet count within 24 hours to identify patients with rapid-onset HIT.[20] All other post-PCI patients receiving UFH at therapeutic doses should have platelet counts tested at least every 2 days until day 14 of therapy or until UFH is stopped.[20] A platelet count should be measured immediately and compared with recent values in a patient who develops thrombosis during or soon after heparin therapy, or in a patient who develops an unusual clinical event in association with heparin therapy (e.g., heparin-induced skin lesions, acute systemic reactions—acute inflammatory, cardiorespiratory, neurological, or other unusual symptoms and signs within 30 minutes after a bolus of intravenous UFH).[20]

For patients receiving GPIs, testing platelet counts prior to treatment, 2–4 hours following the start of the therapy, and at 24 hours would detect most cases of typical-onset GPI-related thrombocytopenia.[74]

Similarly, daily platelet testing until day 4 of IABP therapy would detect most cases of post-PCI thrombocytopenia caused by the IABP.[59,60] Routine platelet monitoring is not appropriate for the detection of post-PCI thrombocytopenia from thienopyridines, given the low incidence of this condition.

Laboratory Testing to Determine the Cause of Post-PCI Thrombocytopenia. When thrombocytopenia is detected in the post-PCI patient, appropriate testing should be done to determine the cause of the decrease in platelet count (Fig. 2). Laboratory testing helps primarily in the diagnosis of pseudothrombocytopenia and HIT. In all patients with post-PCI thrombocytopenia, pseudothrombocytopenia should be excluded first, by repeating a platelet count using unanticoagulated blood or blood collected into sodium citrate or heparin.

When HIT is clinically suspected as a potential cause of post-PCI thrombocytopenia, platelet factor 4-dependent antigen assays should be performed.[20] Confirmatory testing using a sensitive washed platelet activation assay (platelet serotonin release assay or heparin-induced platelet activation [HIPA] test) may be appropriate if antigen assay results are weakly positive or indeterminate.[20] Although GPI- and thienopyridine-associated thrombocytopenia are immune-mediated, antibody testing is not routinely performed to make the diagnoses. Often, the exact cause of the post-PCI thrombocytopenia is only known retrospectively after the platelet count improves. For instance, a rapid increase in the platelet count following removal of IABP in a patient without HIT antibodies or clinical suspicion for GPI-associated thrombocytopenia

Table 1. Studies of the Prognostic Impact of Thrombocytopenia following Percutaneous Coronary Intervention

Study and Authors	Design	Setting of PCI	Sample Size	Definition(s) of Post-PCI Thrombocytopenia	Incidence of Post-PCI Thrombocytopenia	Adverse Outcomes Independently Associated with Post-PCI Thrombocytopenia
EPIC trial (Berkowitz et al.)[5]	Observational analysis of clinical trial data	High-risk PCI	2,099	Nadir platelet count of $<100 \times 10^9$/L	3.9%	Length of coronary care unit stay Length of hospital stay 30-day death 30-day MI 30-day CABG 30-day additional percutaneous revascularization 30-day IABP insertion
Kereiakes et al.[7]	Observational pooled analysis of EPIC, EPILOG, and EPISTENT clinical trial data	Stable and unstable CAD	7,290	Nadir platelet count of $<100 \times 10^9$/L	2.4%	In-hospital non-CABG major bleed In-hospital non-CABG minor bleed In-hospital non-CABG major/minor bleed In-hospital any transfusion In-hospital transfusion of whole blood/packed red blood cells or platelets 30-day death
TARGET study (Merlini et al.)[3]	Observational analysis of clinical trial data	Stable and unstable CAD	4,797	Nadir platelet count of $<100 \times 10^9$/L	2.1%	30-day death, MI, or TVR 30-day death 30-day TVR In-hospital major hemorrhagic complications
CADILLAC trial (Nikolsky et al.)[4]	Observational analysis of clinical trial data	Primary PCI for acute MI	1,975	Nadir platelet count of $\leq 100 \times 10^9$/L	2.5%	In-hospital any transfusion Length of hospital stay Cost of hospitalization 30-day death 1-year death
Guthrie PCI Registry (Shenoy et al.)[6]	Observational analysis of registry data from community practice	Stable and unstable CAD	1,302	Nadir platelet count of $<100 \times 10^9$/L or percent platelet count drop >50%	3.1%	In-hospital TIMI bleeding In-hospital transfusion of packed red blood cells Length of hospital stay 6-month MACE
CRUSADE Registry (Wang et al.)[2]	Observational analysis of registry data from community practice	Acute coronary syndrome*	36,182	Nadir platelet count of $<150 \times 10^9$/L Nadir platelet count of $<150 \times 10^9$/L or percent platelet count drop $\geq$50%	13% 13.6%	In-hospital death In-hospital nonfatal bleeding

*Only 65% of subjects in this study had a PCI.
CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; IABP = intraaortic balloon pump; MACE = major adverse cardiovascular events; MI = myocardial infarction; PCI = percutaneous coronary intervention; TIMI = thrombolysis in myocardial infarction; TVR = target vessel revascularization.

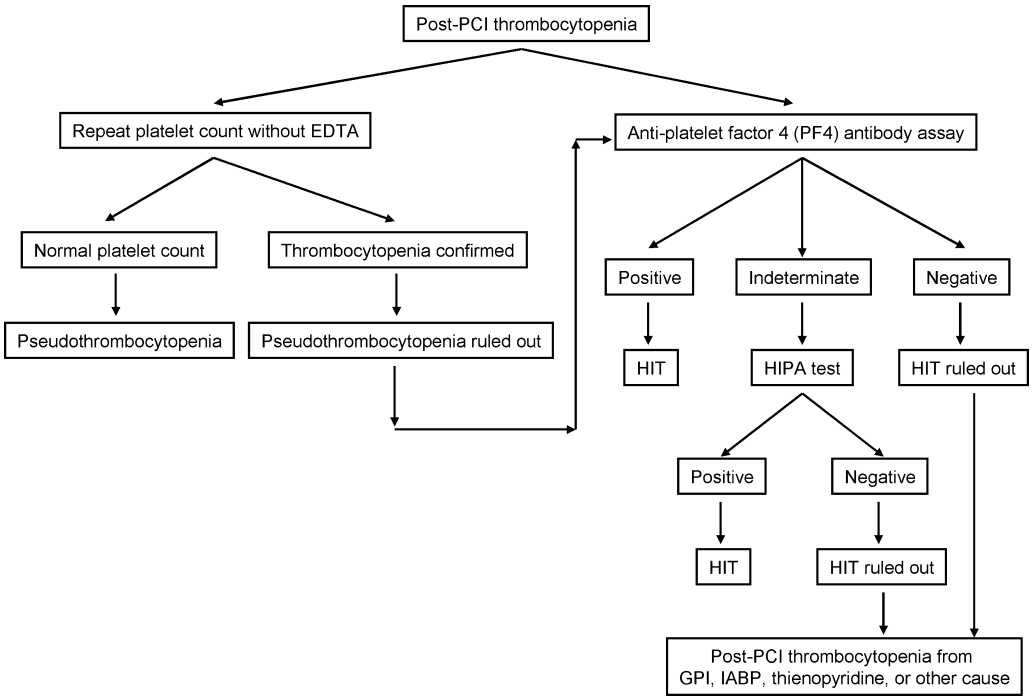

Figure 2. Laboratory testing to determine the cause of post-PCI thrombocytopenia. EDTA = ethylenediaminetetraacetic acid; GPI = glycoprotein IIb/IIIa inhibitor; HIPA = heparin-induced platelet activation; HIT = heparin-induced thrombocytopenia; IABP = intraaortic balloon pump; PCI = percutaneous coronary intervention.

confirms the IABP as the cause of the post-PCI thrombocytopenia.

Treatment of Post-PCI Thrombocytopenia. Treatment of post-PCI thrombocytopenia should be directed toward the cause and the severity of the complication (Fig. 3). Pseudothrombocytopenia does not warrant any treatment. When HIT is strongly suspected or confirmed as the cause, all forms of heparin should be discontinued and further heparin avoided, including incidental heparin exposure from intravascular catheter "flushes." A nonheparin alternative anticoagulant must be used, such as lepirudin, argatroban, bivalirudin, fondaparinux, or danaparoid. Table 2 lists the mechanisms of action and recommended dosing of these alternative anticoagulants in the setting of post-PCI HIT.[20] Since warfarin predisposes to microvascular thrombosis in patients with acute HIT, it should not be started until substantial resolution of thrombocytopenia has occurred (preferably, platelet count $>150 \times 10^9$/L). Reversal of warfarin anticoagulation with vitamin K is recommended when HIT is diagnosed after warfarin has already been started. Deep venous thrombosis of the lower extremities should be ruled out and prophylactic platelet transfusions should be avoided since they rarely raise platelet counts and can theoretically precipitate thrombosis.[75]

When GPIs are suspected to be the cause of the post-PCI thrombocytopenia, treatment should be based on the severity of the thrombocytopenia. In patients with bleeding complications or platelet count of $<50 \times 10^9$/L, the GPI should be discontinued. For platelet counts between 50×10^9/L and 100×10^9/L, the count should be repeated in 2-hour intervals. The GPIs should be stopped only if the platelet count continues to fall or bleeding complications occur. Platelet transfusions are not recommended except when bleeding is associated with the thrombocytopenia.[22] Platelet transfusions are more effective in raising the platelet count when the thrombocytopenia is from abciximab as opposed to eptifibatide or tirofiban because of differences in drug stoichiometry. Abciximab is a large molecule that is predominantly bound to glycoprotein IIb/IIIa receptors with few drug molecules available in the plasma to bind to new glycoprotein IIb/IIIa receptors on transfused platelets. Eptifibatide and tirofiban, on the other hand, are small molecules that are more freely available in

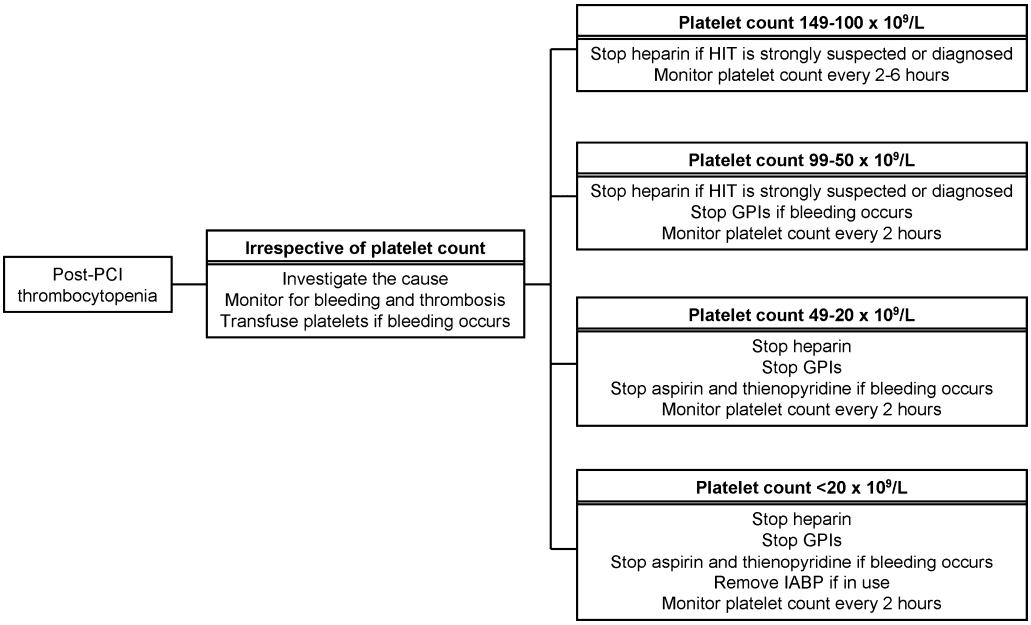

Figure 3. Management of post-PCI thrombocytopenia based on nadir platelet count. GPI = glycoprotein IIb/IIIa inhibitor; HIT = heparin-induced thrombocytopenia; IABP = intraaortic balloon pump; PCI = percutaneous coronary intervention.

the plasma to bind to the new glycoprotein IIb/IIIa receptors on transfused platelets.[76]

There are no data on the issue of aspirin or thienopyridine use in the setting of severe asymptomatic thrombocytopenia. It is our opinion that aspirin and thienopyridines should not be discontinued unless the patient has significant bleeding associated with post-PCI thrombocytopenia.

Prevention of Post-PCI Thrombocytopenia. The incidence of HIT is dependent on the type and duration of heparin use. LMWH should be preferred over UFH, if clinically feasible, due to the relatively lower risk of HIT. Routine use of heparin following PCI is not recommended.[77–84] When there is an indication for heparin following PCI, such as residual coronary thrombus, significant residual dissection, left ventricular thrombus, atrial fibrillation, or suboptimal PCI result, LMWH should be used.

Longer duration of counterpulsation with IABPs can result in lower platelet counts.[60] Thus, IABPs should be expediently removed as soon as the clinical status of the patient permits.

Although heparin may prevent IABP-related thrombotic events, no data exist to support this belief. One study that randomly assigned 153 patients to receive heparin or no heparin while on IABP found no difference in the incidence of limb ischemia.[85] Another study of 252 patients in the coronary care unit randomly assigned patients to either a universal heparin strategy (all patients given heparin) or a selective heparin strategy (heparin only for clinical indications) found that the selective heparin strategy was superior to the strategy of universal heparin use.[86] Thus, selective use of heparin, preferably LMWH, only for clinical indications, could reduce the risk of HIT in this population.

Conclusions

Thrombocytopenia is not infrequent following PCI. It is an underappreciated condition that can be clinically challenging. Several observational studies have demonstrated the adverse prognostic impact of the complication on clinical outcomes and have identified risk factors. The typical patient with post-PCI thrombocytopenia is on multiple therapies that can potentially cause a decrease in the platelet count. Identification of the cause is critical since management of the condition varies significantly based on the etiology. The severity of the thrombocytopenia also determines the clinical management of the patient.

Table 2. Anticoagulants for Use in Patients with Heparin-Induced Thrombocytopenia following Percutaneous Coronary Intervention

Anticoagulant	Pharmacology
Lepirudin	Mechanism of action: Direct thrombin inhibitor.
	Dose: Optional bolus (*) at 0.20–0.40 mg/kg IV followed by continuous infusion at an initial rate of 0.05–0.10 mg/kg per hour IV (target aPTT 1.5–2.0 times patient's baseline or mean of laboratory normal range).[20]
	Adjustments: Dose should be adjusted in patients with renal dysfunction; serum creatinine 1.0–1.6 mg/dL (90–140 microM/L)—starting dose of 0.05 mg/kg per hour, serum creatinine 1.6–4.5 mg/dL (140–400 microM/L) – starting dose 0.01 mg/kg per hour, serum creatinine >4.5 mg/dL (>400 microM/L)—starting dose 0.005 mg/kg per hour.[20]
Argatroban	Mechanism of action: Direct thrombin inhibitor.
	Dose: Continuous infusion at initial rate of 2 μg/kg/min IV (no initial bolus).
	Adjustments: Dose should be adjusted in patients with moderate to severe hepatic dysfunction. In patients with total serum bilirubin >1.5 mg/dL (>25.5 micromol/L), a lower dose of 0.5–1.2 μg/kg/min is recommended. A similar dose is recommended in those with combined hepatic/renal dysfunction, heart failure, severe anasarca, or who are postcardiac surgery.[87]
Bivalirudin	Mechanism of action: Direct thrombin inhibitor.
	Dose: Approved only for use during PCI; use for treatment of HIT is "off label." Continuous infusion at initial rate of 0.15–0.20 mg/kg per hour IV (target aPTT 1.5 – 2.5 times patient's baseline or mean of laboratory normal range. No bolus is necessary.
	Adjustments: The dose should be lowered to 0.14 mg/kg per hour in patients with renal dysfunction, 0.03–0.05 mg/kg per hour in those with renal or combined hepatic and renal dysfunction, and 0.03–0.04 mg/kg per hour in patients receiving continuous renal replacement therapy.[88]
Fondaparinux	Mechanism of action: Factor Xa inhibitor.
	Dose: Approved for treatment and prophylaxis of DVT and PE; efficacy in HIT is unclear and appropriate dosing for this setting is uncertain. A dose of 2.5–7.5 mg/day can be considered depending on the clinical scenario.
	Adjustments: Clearance of this drug is reduced in subjects with reduced creatinine clearance; fondaparinux was not given to patients in phase II or III studies who had serum creatinine levels >1.8 mg/dL. Thus, fondaparinux should not be used in patients with creatinine clearance <30 mL/min.
Danaparoid	Mechanism of action: Factor Xa inhibitor.
	Dose: Not available in the US. Bolus adjusted to body weight as 1,500 units IV for <60 kg, 2,250 units IV for 60–75 kg, 3,000 units IV for 75–90 kg or 3,750 units IV for >90 kg, followed by a maintenance dose of 400 units/h IV x 4 h, then 300 units/h IV x 4 h, then 200 units/h IV, subsequently adjusted by anti-Xa levels (target, 0.5–0.8 anti-Xa units/mL).[20]
	Adjustments: Adjustment may be necessary in patients with severe renal impairment. Patients with serum creatinine levels >2.0 mg/dL should be carefully monitored.

*The initial IV bolus can be omitted except in case of life- or limb-threatening thrombosis, the recommended dosing differs from the FDA-approved dose on the package insert, and the recommended target therapeutic aPTT range (1.5–2.0 times baseline) differs from the package insert (1.5–2.5 times baseline).
aPTT = activated partial thromboplastin time; DVT = deep venous thrombosis; HIT = heparin-induced thrombocytopenia; IV = intravenous; PCI = percutaneous coronary intervention; PE = pulmonary embolism.

Judicious use of therapies that can cause thrombocytopenia, efficient detection of the cause of the decrease in platelet count, and appropriate management of the condition can potentially improve the quality of care and outcomes following PCI. Further research into risk factors that predispose post-PCI patients to developing thrombocytopenia is warranted.

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