CURRENT CONCEPTS REVIEW

The Perioperative Management of Antiplatelet and Anticoagulant Drugs in Hip Fractures: Do the Surgery as Early as Possible

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Abstract

Hip fractures are among the most common fractures operated by orthopedic surgeons. Many elderly patients, who account for a significant percentage of hip fractures, suffer from medical conditions requiring antiplatelet and anticoagulant administration. Meanwhile, considerable evidence recommends early surgery within 48b hours of admission. We aim to review the existing evidence regarding the perioperative management of antiplatelet and anticoagulant drugs in hip fractures. It was concluded that surgery for hip fractures in patients with antiplatelet drug consumption should not be delayed unless a clear contraindication exists. Active reversal strategies are indicated for patients with hip fractures and warfarin therapy. However, evidence for the safety of these agents in pregnancy, breastfeeding state, and adolescence has not yet been established. Little data exists about perioperative management of direct-acting oral anticoagulants in hip fractures. Early surgery after 12-24 hours of drug cessation has been suggested in studies; however, it should be employed cautiously. Despite extensive research, the importance of the issue necessitates additional higher-quality studies.

Level of evidence: V

Keywords: Anticoagulant, Antiplatelet agent, Hip fracture, Perioperative management, Vitamin K antagonists

Introduction

Hip fractures are among the most common fractures operated by orthopedic surgeons (1). With an increased average lifespan, the number of fragility hip fracture incidences is expected to increase, reaching 4.5 million individuals worldwide per year by 2050. There is considerable evidence to recommend early surgery within 48 hours of hip fracture admission to decrease mortality and morbidity rates. Delayed surgery increases the main sequelae of protracted bed rest, such as pressure ulceration, thromboembolism, pneumonia, and urinary tract infection (2-8). The National Institute for Health and Care Excellence (NICE) guideline for hip fracture also suggests surgery on the same day or the day after admission (9). One of the items of the UK Department of Health's best practice tariff for hip fractures is surgery within 36 hours (10). Many of these elderly patients suffer from medical conditions that necessitate chronic usage of antiplatelet and anticoagulant drugs: up to 50% of them use aspirin, and about 15% use warfarin (11). Perioperative management of these drugs is a growing challenge in hip fracture surgery that brings about specific questions that need to be answered: Which should be continued and which should be ceased? Is an active reversal technique indicated? If ceased or reversed, what are the medical consequences? Is it necessary to delay the surgery? Moreover, when is bridging therapy indicated?

The concerns with cessation or reversal of these medications are the increased risk of mortality and morbidity related to deep vein thrombosis, pulmonary thromboembolism, cardiovascular events, or

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cerebrovascular accidents (CVAs). On the other hand, excessive bleeding may occur during the surgery if the patients continue taking these medications. There are different strategies for managing these medications, including early surgery with continuing drugs, early surgery with discontinuing drugs or using reversals, or delaying the surgery until the effect of the drug vanishes. The present manuscript reviews the current evidence and guidelines regarding the perioperative management of antiplatelet and anticoagulant drugs in hip fractures. The sources of the current study were a personal collection of the relevant publications and searching Scopus, Web of Science, and PubMed databases using relevant keywords on the topic.

Antiplatelet therapy

Aspirin and clopidogrel are the most commonly used antiplatelet agents. Aspirin irreversibly inactivates the cyclooxygenase enzyme, which is responsible for thromboxane production for platelet activation and clot formation. Clopidogrel irreversibly binds to the receptor P2Y12 on platelets, facilitating platelet aggregating through the adenosine diphosphate (ADP) pathway (12).

Although some studies showed that aspirin is associated with an increased risk of bleeding events (13), this has been questioned by recent clinical studies (14-17), and there is a clear trend toward early surgery in patients receiving aspirin. The guideline from the American College of Chest Physicians (ACCP), the Scottish Intercollegiate Guidelines Network (SIGN), The Association of Anesthetists of Great Britain and Ireland (AAGBI), and the British Society of Hematology (BSH) recommend that surgery should not be postponed because of aspirin. Aspirin can be discontinued for low-risk patients with acute coronary syndrome (ACS) according to the ACCP guideline and those without unstable angina or recent frequent transient ischemic attack according to the AAGBI guideline (9, 18-21).

Like aspirin, many studies have recommended that surgery be delayed due to clopidogrel consumption (15, 16, 22-41); however, some of these studies showed a significant increase in intraoperative bleeding and the need for transfusion (16, 22, 24, 27, 32, 36), but it was not associated with increased mortality and morbidity. In contrast, Collyer et al. (24) showed that withholding antiplatelet therapies during the perioperative period increases ACS risk. In their retrospective analysis of 114 patients receiving clopidogrel, clopidogrel was discontinued before surgery for 111 patients, and 23 (20.2%) of them experienced ACS. They also found that the length of clopidogrel withdrawal was significantly associated with an increased ACS incidence risk. They recommended continuing antiplatelet therapy and performing early surgery unless a clear contraindication existed. By reviewing nine articles, Mattesi et al., (42) concluded that normal protocols could manage patients on clopidogrel by performing early surgery and without withholding throughout the perioperative period regarding the increased risk of cardiovascular events after discontinuing clopidogrel. By evaluating 14 articles, Soo et al. (43) recommended early surgery without stopping clopidogrel. In 3 out of 14 studies, clopidogrel withholding was associated with increased pulmonary emboli risk, cardiovascular complications, and decubitus ulcers. They emphasized that it is unnecessary to delay surgery for patients on clopidogrel, and even delayed surgery may increase risks of serious complications. It should be noted that many of the studies in the literature are retrospective and non-randomized studies with low evidence levels, and prospective studies are rare. According to the SIGN and the AAGBI guidelines, surgery should not be delayed for patients with clopidogrel consumption. Because of the high risk of cardiovascular events in patients on clopidogrel, the AAGBI advised not to stop clopidogrel during the perioperative period (9, 19).

Dual antiplatelet therapy (DAPT) is indicated in high cardiovascular risk patients, such as patients with recent coronary intervention. A combination of aspirin and clopidogrel, prasugrel, ticagrelor, dipyridamole, or glycoprotein IIb/IIIa receptor inhibitors (e.g., abciximab, eptifibatide, and tirofiban) are mostly used as DAPT. The DAPT is associated with significantly more surgery-related bleeding (14.7%) than aspirin (4.1%) (44). Premature discontinuation of DAPT is the leading risk factor for stent thrombosis (45, 46). It is well known that surgical stress creates a prothrombotic state due to increased platelet activation and increased risk of thromboembolic events, making cessation of DAPT riskier in patients with hip fracture (47, 48). During the first 30 days of bare metal cardiac stents or the first six months of drug-eluting stents, the risk of stent thrombosis is high, necessitating DAPT. In patients on DAPT with a high risk of bleeding, the cessation of antiplatelet agents is not justified; the P2Y12 inhibitor can be replaced by enteral platelet glycoproteins IIb/IIIa receptor inhibitors, such as abciximab, eptifibatide, and tirofiban (12). These agents have a short half-life and can be rapidly discontinued and restarted postoperatively. According to the BSH, for patients on antiplatelet agents, intravenous tranexamic acid is recommended for urgent surgeries with a high risk of bleeding, and it is preferred over platelet infusion because of more predictable results. If there is an excessive perioperative or postoperative bleeding after tranexamic acid usage, or if the bleeding risk is perceived to be very high, infusion of two pools of donor platelets is also recommended. Platelet infusion is more effective if administered within 2 hours after the last dose of aspirin and 12–24 hours after the last dose of clopidogrel (21). Chechik et al. (16) assessed blood loss in 44 patients on antiplatelet therapy that 15 of them received both clopidogrel and aspirin. They reported increased blood loss in patients receiving both aspirin and clopidogrel compared to clopidogrel alone and aspirin alone. The high incidence of thromboembolic events (e.g., ACS and CVA) in patients with clopidogrel therapy was attributed to a higher prevalence of concomitant morbidities in these patients. They concluded that cessation of antiplatelet drugs would further increase the incidence of such

events, as Chassot et al. (49) had reported before.

There is no particular guideline for newer ADP pathway blocking agents, such as ticagrelor and prasugrel. Ticagrelor is a more potent antiplatelet agent than the clopidogrel and may carry a higher risk of bleeding-related complications. Similar to clopidogrel, platelet infusion does not reverse the effect of ticagrelor (50, 51). Due to the increased administration, an antidote for ticagrelor is in development (52). Prasugrel is more potent and faster than clopidogrel, and platelet infusion is likely to be ineffective for correcting the bleeding diathesis if administered shortly after the last dose, like clopidogrel. Less potent antiplatelet agents, such as phosphodiesterase inhibitors (e.g., dipyridamole and cilostazol), are rarely mentioned in the literature. Based on the evidence cited and the guidelines, the surgery should not be delayed because of fewer antiplatelet activities (53, 54). Glycoprotein IIb/IIIa receptor inhibitors, such as abciximab, eptifibatide, and tirofiban, are combined with another antiplatelet agent in DAPT, and the recommendations above hold for this combination, too.

Due to the potentially increased risk of spinal hematoma after neuraxial anesthesia in patients receiving antiplatelets, guidelines have been developed to facilitate decision-making. According to the American Society of Regional Anesthesia and Pain Medicine (ASRA) guideline (55), neuraxial anesthesia is safe in patients with aspirin consumption, and no specific care is needed. Before the procedure, drug consumption should behold at different intervals based on the drug: 10 days for ticlopidine, 7-10 days for prasugrel, 5-7 days for clopidogrel and ticagrelor, 48 hours for cilostazol, and 24 hours for dipyridamole/ASA. For platelet GP IIb/IIIa inhibitors, the time to normal platelet aggregation is 24 to 48 hours for abciximab and 4 to 8 hours for eptifibatide and tirofiban. Clopidogrel can be restarted 24 hours postoperatively. The AAGBI guideline (56) recommended similarly: For aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), and dipyridamole, no additional care is needed before neuraxial anesthesia, clopidogrel and prasugrel should be discontinued 7 days before the surgery, and ticagrelor 5 days. According to the Stanford school of medicine (57), a 7-day interval is recommended for clopidogrel and prasugrel, and 14-day for ticlopidine [Table 1]. According to these guidelines, neuraxial anesthesia in antiplatelet consumption can be used after the cessation of drugs except aspirin and other NSAIDs. Restarting the drugs also has some limitations. Regarding these recommendations, general anesthesia seems a better choice in patients with hip fractures.

Table 1. The time needed after drug cessation for safe neuraxial anesthesia based on the American Society of Regional Anesthesia and Pain Medicine and the European Society of Regional Anaesthesia guidelines and information provided by drug manufacturers.

Drugs	Acceptable time after drug administration for block performance
Non-steroidal anti-inflammatory drugs	No additional precautions
Aspirin	No additional precautions
Clopidogrel	7 days
Prasugrel	7 days
Ticagrelor	5 days
Tirofiban	8 hours
Eptifibatide	8 hours
Abciximab	48 hours
Dipyridamole	No additional precautions
Warfarin	INR≤1.4
Rivaroxaban prophylaxis (CrCl > 30 mL/min)	18 hours
Rivaroxaban treatment (CrCl > 30 mL/min)	48 hours
Dabigatran prophylaxis or treatment	
(CrCl > 80 mL/min)	48 hours
(CrCl 50–80 mL/min)	72 hours
(CrCl 30–50 mL/min)	96 hours
Apixaban prophylaxis	24-48 hours

Vitamin K antagonists

Warfarin and other vitamin K antagonists (VKAs) inhibit the synthesis of vitamin K-dependent procoagulant factors, including II, VII, IX, and X factors, and proteins C and S. Anticoagulant action is monitored using the International Normalized Ratio (INR). Indications to use VKAs include the presence of atrial fibrillation, prosthetic heart valves, acute venous thromboembolism, and transient ischemic episodes (58). Recent studies have shown that the INR>1.5 does not increase the risk of bleeding and transfusion rate (59). It is generally accepted that for major surgeries like hip surgery, the INR should be lower than 1.5 (60-62). The INR level below two is also mentioned in the literature to be safe (63).

Warfarin's half-life is 36 hours; it should be stopped five days before elective surgery to achieve normal hemostasis, which is unfavorable for hip fracture patients. The required interval before the surgery may be further increased in old patients. Furthermore, Bansal et al. (64) showed that the INR trend was very unpredictable in patients with hip fractures. Surprisingly, they indicated that the INR increased the following day after stopping the warfarin in 12 out of the 25 patients. Stopping warfarin and waiting until the INR drops or the "watch and wait" strategy leads to significant surgical delay in patients on warfarin consumption. Multiple studies have shown that different active reversal strategies reduce the time to surgery without increasing the risk of bleeding-related complications or thromboembolic events (10, 11,

64-78).

No specific guideline is available for an active warfarin reversal strategy. Four main products used in reversal strategies include oral and intravenous vitamin K, fresh frozen plasma (FFP), and prothrombin complex concentrates (PCCs). Vitamin k administration is studied in most studies and is considered a safe approach without increasing thrombotic complications (10, 11, 64-78). Both the oral and intravenous routes are considered equally effective for vitamin K administration, but the oral administration has a slower effect than intravenous (IV) infusion (63, 79). Anaphylaxis has been reported after intravenous injection; however, it is infrequent, with a prevalence of 1:13000 (80). Severe reactions and even deaths are reported; therefore, slow infusion of low doses with close monitoring is recommended (81, 82). Later resistance to warfarin and a longer warfarin administration period are other concerns that have been questioned by some studies (83). Although different doses of vitamin K from 1mg (65) to 10mg (72), are used in various studies, there is a clear trend toward higher IV vitamin K doses in the literature.

The FFP can reverse anticoagulation immediately without causing any resistance to warfarin or heparin. However, its effect dissipates within 8–12 hours, and it is optimally administered within 4 hours of the procedure with vitamin K to increase the duration of action. Anaphylactoid reactions, alloimmunization, excessive intravascular volume, and transmission of infections may occur due to FFP administration (84). Ranhoff et al. (67) and Vitale et al. (68) used FFP in addition to vitamin K and reported faster surgery without increased complications. The PCCs contain high concentrations of the coagulation factors, including II, VII, IX, and X factors, inactivated by warfarin, which could be administered rapidly. The advantages of PCCs in comparison to FFP include having smaller volumes, being faster (five times faster than FFP), and having no risk for transfusion-related acute lung injury (85, 86). The main concern with PCCs is their association with thrombogenic events, such as stroke, myocardial infarction, pulmonary embolism, disseminated intravascular coagulation, and deep vein thrombosis (87). Buecking et al. (72), Combettes et al. (88), and Mattison et al. (78) reported the use of PCCs in selected hip fractured patients with good results and without complications.

On the other hand, Richard Ng et al. (89) reported a significant increase in rates of cardiac events and 30-day mortality among patients who received Octaplex (a prothrombin complex concentrate). They recommended caution against administering both FFP and PCCs in patients for warfarin reversal. The majority of patients with hip fractures do not require immediate surgery. It seems that the risks of administering PCCs to reverse anticoagulation generally outweigh the benefits; therefore, FFP and PCCs are considered the second-line options in reversal protocols. However, FFP and PCCs are options for faster reversal, and they might be helpful in particular circumstances.

Risk stratification is necessary to plan a reversal strategy and whether bridging therapy is needed or not. Two systematic reviews showed that routine bridging therapy did not decrease thrombotic events and was associated with bleeding-related complications (90, 91). The clinical indication of warfarin, time of anticoagulation, and patient's comorbidities are considered during the risk assessment. According to the BSH guideline (21), patients with venous thromboembolism, atrial fibrillation, and mechanical heart valve are at high-risk for thrombosis, and bridging therapy with low molecular weight heparin or heparin should be considered for them (not absolutely indicated). For high-risk patients, a multidisciplinary approach with the cooperation of anesthesiologists, cardiologists, and haematologists is necessary to manage the condition. In low-risk patients, bridging therapy is not indicated, and routine reversal strategies could be used.

Ahmed et al. (71) proposed an evidence-based protocol for active warfarin reversal. After implementing the protocol, the median time from admission to surgery decreased from 73 hours to 37.7 hours. Moreover, all of their patients used 1 mg vitamin K and bridging therapy. Warfarin can be started 24 hours after surgery for uncomplicated patients with proper hemostasis. Individualized planning with senior surgeons and internists should be employed for complicated cases. In another study, Diament et al. (10) suggested a new algorithm to save more time and money. They suggested stopping warfarin and administering 2 mg vitamin K IV before knowing the INR level in low-risk patients in the emergency department. If the INR does not drop under 1.5, it is recommended to administrate 3 mg vitamin K IV. In case of being unsuccessful again, PCCs are recommended to correct the INR. This recommendation is based on the fact that they called it "Early Trigger". They hypothesized that waiting for the INR result leads to a significant delay in surgery, and they reduced the time to surgery from 53.71 hours to 37.61 hours by omitting this time.

The SIGN (9) recommended active reversal strategies with low dose vitamin K (1-2.5 mg) administered either IV or orally. The FFP should not be used where there is no contraindication to the use of vitamin K. According to the BSH guideline (21), 5 mg vitamin K IV could be used to reverse anticoagulation if patients can wait for 6-8 hours, which is possible in patients with hip fracture. If there is adequate hemostasis, warfarin can be resumed on the evening of surgery (or the next day) at the usual maintenance dose (19) or two initial days of the double maintenance dose (92).

According to the ASRA guideline (55), in patients with long-time warfarin therapy, anticoagulant therapy must be stopped (ideally five days before the planned procedure), and the INR should be normalized before initiation of a neuraxial block. This recommendation is because in the first 1 to 3 days after discontinuation of warfarin therapy, despite a decrease in the INR, the coagulation status (reflected primarily by factors II and X levels) may not be adequate for hemostasis [Table 1]. This is different from the AAGBI guideline (56), where the AAGBI suggests the INR≤1.4 is acceptable for a neuraxial block.

Table 2. When to consider bridging with the treatment dose of heparin in patients who stop warfarin if the thrombotic risk is incredibly high

Consider bridging with treatment dose heparin in	
VTE	Patients with a VTE within the previous 3 months Very high-risk patients, such as patients with a previous VTE while on therapeutic anticoagulation who now have a target INR of 3.5
AF	Patients with a previous stroke/TIA in the last 3 months Patients with a previous stroke/TIA with three or more of the following risk factors: • Congestive cardiac failure • Hypertension (>140/90 mmHg or on medication) • Age > 75 years • Diabetes mellitus
MHV	MHV patients other than those with a bicuspid aortic valve and no other risk factors

VTE, venous thromboembolism; INR, international normalized ratio; AF, atrial fibrillation; TIA, transient ischemic attack; MHV, mechanical heart valve

Direct-acting oral anticoagulants (DOACs)

In recent years, DOAC drugs have emerged as an alternative to warfarin and are used more frequently in patients with high-risk thromboembolic events. Clinical trials have shown no inferiority of these drugs compared to warfarin in preventing thromboembolic events. DOACs are now endorsed as the first-line treatment for some conditions, such as preventing stroke and systemic embolism in nonvalvular atrial fibrillation and treatment of venous thromboembolism. Not requiring routine drug monitoring and very predictable pharmacokinetic profiles are the main advantage of DOACs (66, 93-95). These drugs are direct thrombin inhibitors (e.g., dabigatran) or direct factor Xa inhibitors (e.g., rivaroxaban, apixaban, edoxaban, and betrixaban) (96). In contrast to antiplatelet and VKAs, little data exists about the perioperative management of DOACs in hip fractures. Guideline recommendations are based on elective surgeries and are somewhat conservative.

The BSH recommends a delay of 48 hours before elective surgery with a significant risk of bleeding and a normal kidney function. The drug should be stopped 48 hours before elective surgery in normal patients consuming rivaroxaban, apixaban, and edoxaban, and 72 hours in patients with renal impairment. Dabigatran should be stopped 48 hours before elective surgery. For those with creatinine clearance (CrCl) less than 50 ml/hour, 96 hours interval is recommended. The DOACs could be restarted 48 hours after surgeries with a high risk of bleeding (21). In addition, the drug manufacturers recommend at least 24 hours interval before surgery for rivaroxaban and edoxaban. Dabigatran should be stopped for at least 12 hours from the last dose before surgery. Four days before high-risk elective surgery is recommended in those with a CrCl less than 50 ml/hour. In contrast to the BSH guideline, DOACs could be restarted as soon as possible after surgery, and the 48 hours interval has not been mentioned in manufacturers' recommendations (97-99). The SIGN has not mentioned DOACs in the guideline.

Patients on DOACs have to wait longer for surgery than the patients on VKAs and patients not anticoagulated (18, 100-103). Some recent studies have shown that patients on DOACs are not at the risk of increased bleeding and mortality, and delay of the surgery may not be needed. After evaluating 89 patients with hip fracture and DOACs consumption, Schermann et al. (100), concluded that using DOACs was not associated with an increased perioperative blood loss or mortality compared to the controls. They also indicated that DOACs administered patients had to wait longer for surgery and that delayed surgery was found to be an independent predictor of mortality. By comparing 63 patients on DOACs to 63 matched controls, Mullins et al., (102) found no relationship between the time of admission to operation interval and the probability of transfusion. They recommended definitive surgical treatment at the earliest opportunity. Franklin et al. (103) reported no adverse outcome with early surgical fixation (before 48 hours) in 19 patients on DOACs. Lai et al. (104) recommended delaying the surgery at least 12 hours and ideally 24 hours after the last dose in emergencies.

Experts' opinions suggest using oral activated charcoal in the setting of recent ingestion (within 2 hours). However, it might not be applicable for hip fracture surgery. A hemodialysis is an option in patients on dabigatran with impaired renal function who will require more time for drug clearance. Rivaroxaban and apixaban are highly protein binding, and dialysis is unlikely to be helpful for these drugs' clearance. Prophylactic administration of PCCs or FFP is not routinely indicated unless there is a severe bleeding risk associated to the DOACs usage (105).

Idarucizumab is a reversal agent for dabigatran, and andexanet is a reversal drug for rivaroxaban, apixaban, and edoxaban. According to the BSH, a reversal agent should reverse DOACs before emergency invasive procedures and surgeries where the bleeding risk is considered significant. No study about reversal agents in hip fracture exists. The BSH recommends using tranexamic acid to mitigate the bleeding effect of DOACs.

As DOACs have become more popular, laboratory tests are emerging to monitor drug levels, especially in life-

threatening bleedings and emergency surgeries. Little data exist about the role of laboratory tests to monitor blood levels of DOACs and whether it helps in decision-making about the operation time in hip fractures or not. Byron et al. (106) used an ecarin chromogenic assay (ECA) dabigatran concentration of <50 ng/mL as a threshold for safe surgery in an 86-years-old man with dabigatran consumption. It should be noted that this laboratory monitoring led to a 5-day delayed surgery. Some newer studies suggest that a DOACs-calibrated anti-Xa assay is the best method for screening and quantifying DOACs activity. Because this is not available in many medical centers, other routine tests can be used: normal thrombin time (TT) and general anti-Xa assay can effectively rule out the presence of physiologically significant levels of dabigatran and FXa inhibitors, respectively. There is no role for PT/aPTT for these purposes. Because of little experience in this field, results should be interpreted with caution (107, 108). More studies are needed to evaluate the efficacy of these laboratory tests in patients with hip fractures.

According to the ASRA guideline (55), rivaroxaban, apixaban, edoxaban, and betrixaban should be discontinued 72 hours before a neuraxial block. Dabigatran should be discontinued 72 hours before a neuraxial block in patients with a CrCl of 80 mL/min, 96 hours in patients with a CrCl of 50 to 79 mL/min, and 120 hours in patients with a CrCl of 30 to 49 mL/min. Neuraxial blocks in patients with a CrCl of less than 30 mL/min are not suggested. For performing a neuraxial block before the suggested interval, rivaroxaban or anti-factor Xa activity level should be checked. An acceptable level of residual DOACs activity to proceed with a neuraxial block remains undetermined. The AAGBI guideline (56) recommends an 18-hour interval before a neuraxial block in patients with a prophylactic dose of rivaroxaban and 48 hours if a treatment dose is used. For dabigatran, CrCl is important: if CrCl 80 mL/min, a 48-hour, if CrCl 50–80 mL/min, a 72-hour, and if CrCl 30–50 mL/min, a 96-hour interval is suggested. For apixaban prophylaxis, a 24-48 hours interval is recommended.

In summary, surgery for hip fractures in patients with antiplatelet drug consumption should not be delayed unless a clear contraindication exists. Although there is a risk of excessive bleeding, mortality and morbidity related to delayed surgery and thromboembolic events after drug cessation would be greater than the risk of bleeding-related complications. For DAPT, it is recommended to use tranexamic acid as the first-line choice and platelet infusion as the second line. Except for aspirin, neuraxial anesthesia can be used only after antiplatelet cessation; therefore, general anesthesia is preferred. Despite these shreds of evidence, Pean et al. (109), in a survey of 67 orthopedic surgeons in the US, reported that great controversy exists over whether a delay in surgery is necessary for patients on antiplatelet therapy or not. Over a quarter of surgeons continue to opt for surgical delay in patients with hip fractures. These findings are in agreement with previous surveys (110, 111).

Active reversal strategies are indicated for patients with hip fracture and warfarin therapy. In high-risk patients, a multidisciplinary approach with anesthesiologists, cardiologists, and haematologists should be employed. Intravenous vitamin K is the safest method to decrease the INR for early surgeries. The PCCs or FFP should not be used as the first-line reversal agent. Since the ASRA guideline questions the safety of a neuraxial block in the early phase after the INR normalization, general anesthesia may be a safer approach.

Little data exists on the perioperative management of DOACs in hip fractures, and most guidelines recommendations are based on drug half-life, which is applicable for elective surgeries. Although recent studies on hip fractures suggest early surgery after 12-24 hours of drug cessation, caution must be exercised because of the limitations of these studies. For neuraxial anesthesia, time from DOACs cessation, type of drug, and CrCl should be considered.

Reversal agents will be used when rapid reversal of anticoagulant effects is required, such as when emergency surgery is needed and when uncontrollable and life-threatening bleeding occurs. However, to the best of our knowledge, there is no conclusive evidence for the effects of idarucizumab in pregnant women, breastfeeding states, and adolescents.

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