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The Best Anticoagulation Therapy in Multiple-Trauma Patients with Mechanical Heart Valves: Evaluation of Latest Guidelines and Studies

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ABSTRACT

Background: It is common practice for patients with prosthetic cardiac devices, especially heart valve prosthesis, arterial stents, defibrillators, and pacemaker devices, to use anticoagulation treatment. When these patients suffer from multiple trauma after motor vehicle accidents, the best medical management for this challenging position is mandatory. This strategy should include a rapid diagnosis of all possible multiple organ injuries, with special attention to anticoagulation therapy so as to minimize the risk of thromboembolism complication in prosthetic devices. In this review, we describe the best medical management for patients with multiple trauma who use anticoagulants after heart valve replacement.

Methods: We searched electronic databases PubMed/Medline, Scopus, Embase, and Google Scholar using the following terms: anticoagulant, warfarin, heparin, and multiple trauma. Also, similar studies suggested by the databases were included. Non-English articles were excluded from the review.

Results: For patients who use anticoagulation therapy, teamwork between cardiac surgeons, general surgeons, anesthesiologists, and cardiologists is essential. For optimal medical management, multiple consults between members of this team is mandatory for rapid diagnosis of all possible damaged organs, with special attention to the central nervous system, chest, and abdominal traumas. With this strategy, it is important to take note of anticoagulation drugs to minimize the risk of thromboembolism complications in cardiac devices.

Conclusion: The best anticoagulant agents for emergency operations in patients with multiple trauma who are using an anticoagulant after heart valve replacement are fresh frozen plasma (FFP) and prothrombin complex concentrates (PCC).

INTRODUCTION

Recent breakthroughs in treatment of cardiovascular disease (eg, intra-arterial stent grafts, prosthetic valves, defibrillators, intra-cardiac pacemakers, heart transplant, and auxiliary ventricular devices) has led to mandatory use of anticoagulant agents such as warfarin, aspirin, clopidogrel, and ticlopidine [Nishimura 2015]. All patients undergoing cardiac surgery for reparation of valvular stenosis or insufficiency with biologic and homograft valves should take warfarin for 3 months [Nishimura 2015; Moeinipour 2015]. Lifetime warfarin should be administered in patients with mechanical valves. Temporary cessation in the drug intake may cause serious complications, including valvular thrombosis, coronary artery stenosis, thromboembolism, and death [Barwad 2012; Cannegieter 1994; Roudaut 2007]. Due to an increase in road accidents, these patients might possibly be referred to the traumatology wards with multiple traumas, and quick decision-making is of the utmost importance in these life-threatening situations. Therefore, it is preferred to transfer these patients to the intensive care unit (ICU) and keep them under careful monitoring. In addition, all measures in approaching a multiple traumatic patient, such as blood cross-match, reservation of blood, platelet, and fresh frozen plasma (FFP), and keeping injectable vitamin K available should be done with great pace and accuracy.

In this study, we aimed to evaluate and review the latest guidelines regarding patients with multiple trauma who use anticoagulants for their mechanical heart valve to determine the best therapeutic method in approaching these patients.

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MATERIALS AND METHODS

We performed a thorough literature search in Google Scholar, Scopus, and PubMed for articles published between 1966 and 2015 with the keywords "multiple trauma," "prosthetic heart valve," and "warfarin." The search results were studied and evaluated by a team comprising cardiac and general surgeons, and the appropriate results were included in the study. Studies published in any languages other than English were excluded from the review.

RESULTS

Vitamin K Oral Antagonists

Oral anticoagulants, which are kumarin derivatives (eg, warfarin), act as vitamin K antagonists by interfering with the effects of II, VII, IX, and X factors. Warfarin, fumarin, kumaklor, bromadiolone, and brodifacum are other drugs in this class [Nishimura 2015]. In addition, new anticoagulant drugs such as dabigatran is not recommended. [Chen 2012; Harper 2012; Steiner 2013; Lind 1997].

The recommended dose of warfarin is based on reaching an appropriate international normalized ratio (INR), considering age, diet, weight, and genetic differences [Lind 1997; Crowther 2002].

In a meta-analysis on 13088 subjects, which was done in 1994, the risk of mechanical heart valve thrombosis was 1.7% and the risk of major events such as death, stroke, or major ischemia needing surgery in patients not taking anticoagulant drugs was 4% in each year [Cannegieter 1994].

The risk of these thrombotic events depends on the site of the valve and its type. For instance, the risk of thrombosis increases 5 times in mitral mechanical valves and the risk of major emboli increases 1.5 times in aortic mechanical valves [Cannegieter 1994; Jegaden 1994; Mérie 2012; Brown 2012; Berger 2015]. Ball and cage valves such as Star-Edwards are associated with a two-fold risk of embolism, compared to other valves such as carbomedics mitral valves [Cannegieter 1995]. Aspirin alone decreases the risk of thrombosis and major emboli to 1% and 2.2% in each year, respectively [Becattini 2012]. However, warfarin reduces the risk of these events to 0.2% and 1% in each year, respectively [Cannegieter 1995].

In another study, which was published in 1995, among 1608 patients who took anticoagulants, the total prevalence of thromboembolism in mechanical valves was 0.5% in a year [Cannegieter 1995].

Among severe complications of warfarin is bleeding, which is more likely to occur when the patient's INR is higher than 4-5 [Tonolini 2012]. This complication is more likely to happen following a trauma and lead to fatal consequences such as uncontrollable hepatic, intraperitoneal, retroperitoneal, intracranial, or intraarticular hemorrhage [Okamura 2012; Hering 2005].

The risk of major and severe bleeding for a patient with a mechanical valve who took warfarin was 0.34-1.32% each year [Hering 2005; Akhtar 2009]. One out of every 10 major bleed leads to death. The mortality rate of major bleeding in patients taking anticoagulant drugs such as warfarin was reported to be 9-11% in each [Cannegieter 1995; Becattini 2012; Tonolini 2012].

Major bleeding in a nonsurgical patient is defined as: 1) lethal hemorrhage; 2) symptomatic bleeding in a vital organ (intracranial, spinal, retroperitoneal, ocular, intraartricular, pericardial, or intramuscular such as iliopsoas hemorrhage and subsequent compartment syndrome); and 3) bleeding which leads to a 2.2 mg/dL drop in hemoglobin concentration or needs 2 or more units of whole blood transfusion [Cannegieter 1995; Becattini 2012; Tonolini 2012].

There are several risk factors that increase the risk of hemorrhage following anticoagulant agents such as warfarin, including INR >4 or 5, age >75 years, hypertension, history of stroke, simultaneous use of antiplatelet drugs such as Plavix and aspirin, and history of bleeding [Tonolini 2012; Marie 2012; Tran 2013].

Approximately 50% of all warfarin-induced bleeding is major. The most prevalent sites of anticoagulant-dependent bleeding are gastrointestinal tract (40-60%), urinary tract (15%), intracranial, and retroperitoneal [Pernod 2010].

A major concern in modern societies, severe traumas kill over 5 million people each year, and will reach an estimated mortality of 8 million in 2020. Hemorrhage is the major cause of mortality in these patients, but is a preventable cause. Therefore, appropriate management, including primary diagnosis, bleeding control, and maintenance of tissue perfusion and hemodynamic status is of cardinal importance [Spahn 2013].

About one-third of trauma patients with bleeding on admission have coagulopathy. Coagulopathy increases the risk of complications of trauma, such as multiple organ failure. The cause of coagulopathy is multifactorial. It occurs due to hemorrhagic shock (activation of anticoagulation factors and fibrinolysis pathway following the trauma), acidosis, blood dilution, and hypothermia [Floccard 2012; Mitra 2012]. In addition, patients with prosthetic valves are obliged to use anticoagulant agents, which indubitably aggravate their hemorrhagic complications.

Essential Principles of Management of a Multiple Trauma Patient with Prosthetic Valve

1) Minimizing the interval between the traumas and required emergent surgery. Prompt use of tourniquet in order to control the bleeding of limbs, even until 2 h for amputated or severely damaged limbs [Cothren 2007].

2) Using norm ventilation, since higher mortality rates have been reported with hyperventilation in trauma patients [Spahn 2013].

3) Diagnosis and monitoring of bleeding with a quick assessment of trauma mechanism, primary response and primary survey, using the available algorithms in the ICU such as trauma associated severe hemorrhage (TASH), and advanced trauma life support (ATLS) [Spahn 2013].

4) Immediate surgical operation for patients with hemorrhagic shock and a known source of bleeding. Pelvic fractures are most common after road accidents. About 60% of pelvic fractures happen following motorcycle accidents and 23% occur due to falling [Ziran 2014; Mauffrey 2014]. Pelvic fractures are strongly accompanied by intra-abdominal bleeding, head traumas, and other injuries in up to 70% of cases, which indicates high-energy trauma [Mauffrey 2014; Gualdo 2013]. Unstable pelvic fractures which are associated with severe bleeding are the main cause of death in these patients [Matityahu 2013; Vaidya 2012].

5) In patients with hemorrhagic shock whose source of bleeding is unknown, an immediate search for the source is essential (using chest X-ray, pelvic radiograph, abdominal ultrasonography [US] or diagnostic lavage, and CT scans in advanced centers) [Bouglé 2013; O'Neal 2012]. In case any abdominal fluid is detected by US or CT, or the patient's hemodynamic status is unstable, surgical intervention is a must.

6) At the time of admission, platelet count, PT-APTT, and fibrinogen level should be evaluated (using Viscoelastic method) to assess coagulopathies. Thromboelastometry and portable coagulometry are also used in emergent cases.

7) In patients with shock, crystalloid serums are preferable. If no response is seen, vasopressors such as norepinephrine can be used. Coagulopathy-induced hypothermia should also be corrected in these patients [Bouglé 2013; O'Neal 2012].

8) In multiple trauma patients who use warfarin, immediate CT scan and neurosurgery consultation is recommended if GCS (Glasgow coma skill) is below 14.

DISCUSSION

Although patients who take warfarin are at an increased risk of mortality and complications in case of severe trauma, this risk is preventable by measures such as immediate reversion of warfarin effects. There are some measures recommended for eliminating the effects of warfarin, including vitamin K, plasma, cryoprecipitate, recombinant VIIa factor, and factor concentrates [Brunicardi 2015].

In case of severe warfarin-induced bleeding in trauma patients with mechanical heart valves, the best therapeutic method is fresh frozen plasma (FFP). Safe use of prothrombin complex, vitamin K, recombinant VIIa factor, and concentrates are controversial [Brunicardi 2015; Panduranga 2012]. In older patients and patients with a risk of cerebral hemorrhage, factor concentrates such as cryoprecipitate and fibrinogen are preferable. In hemorrhage-induced hypovolemic state the choice is FFP. In patients with INR below 1.5, surgical operations can be performed with no need for blood products. In patients with INR of 1.5-1.9, FFP should be used [Brunicardi 2015].

The use of vitamin K (fitonadion) is not generally recommended in patients with prosthetic valves, unless in rare cases, in which 1 mg IV or PO is used. Its effect appears 6-12 h later and it is not recommended in patients who require immediate reversion of warfarin effects [Nishimura 2015; Tran 2013; Tran 2014; Badami 2014].

According to the American Heart Association (AHA), FFP is the best product in case immediate reversion of warfarin effects is needed. However, the Australian Hematology Association suggests prothrombin complex concentrates (PCC), which consists of factors II, VII, IX, and X as the first choice in these cases, and mentions FFP as the second choice [Nishimura 2015].

In cases with a low to moderate risk of bleeding, 2 units of FFP are used, while 4 units are used in cases with severe risk. The patient's INR should be checked after an hour. PCC commences for patients with INR >2 and cerebral hemorrhage [Nishimura 2015; Tran 2013; Tran 2014; Badami 2014].

The time of post-operation warfarin resumption is 7-14 days in severe cerebral bleeding and 2-3 days in non-cerebral bleeding [Panduranga 2012].

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REFERENCES

Akhtar RP, Abid AR, Zafar H, Khan JS. 2009. Aniticoagulation in patients following prosthetic heart valve replacement. Ann Thorac Cardiovasc Surg 15:10-7.

Badami KG. 2014. An update of consensus guidelines for warfarin reversal. Med J Australia 200:80.

Barwad P, Raheja A, Venkat R, Kothari SS, Bahl V, Karthikeyan G. 2012. High prevalence of silent brain infarction in patients presenting with mechanical heart valve thrombosis. Am J Cardiovasc Drugs 12:345-8.

Becattini C, Agnelli G, Schenone A, et al. 2012. Aspirin for preventing the recurrence of venous thromboembolism. New England J Med 366:1959-67.

Berger PB, Vedamurthy D, Casale A, et al. 2015. The risk of thromboembolic complications without anticoagulation after surgical aortic valve replacement with a bioprosthesis. J Am Coll Cardiol 65(10_S).

Bouglé A, Harrois A, Duranteau J. 2013. Resuscitative strategies in traumatic hemorrhagic shock. Ann Intensive Care 3:1.

Brown ML, Park SJ, Sundt TM, Schaff HV. 2012. Early thrombosis risk in patients with biologic valves in the aortic position. The Journal of thoracic and cardiovascular surgery. 144:108-11.

Brunicardi F, Andersen D, Billiar T, et al. 2015. Anticoagulation and bleeding. Schwartz's Principles of Surgery,10th ed.

Cannegieter SC, Rosendaal FR, Briët E. 1994. Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. Circulation 89:635-41.

Cannegieter SC, Rosendaal FR, Wintzen AR, van der Meer FJ, Vandenbroucke JP, Briet E. 1995. Optimal oral anticoagulant therapy in patients with mechanical heart valves. New England J Med 333:11-7.

Chen BC, Viny AD, Garlich FM, et al. 2012. Hemorrhagic complications associated with dabigatran use. Clin Toxicol 50:854-7.

Cothren CC, Moore EE, Hedegaard HB, Meng K. 2007. Epidemiology of urban trauma deaths: a comprehensive reassessment 10 years later. World J Surg 31:1507-11.

Crowther MA, Douketis JD, Schnurr T, et al. 2002. Oral vitamin K lowers the international normalized ratio more rapidly than subcutaneous vitamin K in the treatment of warfarin-associated coagulopathy: a randomized, controlled trial. Ann Int Med 137:251-4.

Floccard B, Rugeri L, Faure A, et al. 2012. Early coagulopathy in trauma patients: an on-scene and hospital admission study. Injury 43:26-32.

Gualdo JC, Fernandez DB, Serra JT, Hernández JT, Vicente DP, Alemany RM. 2013. Pelvic fractures in polytrauma: which classification system better predicts hemodynamic instability? Eur Orthopaed Trauma 4:35-9.

Harper P, Young L, Merriman E. 2012. Bleeding risk with dabigatran in the frail elderly. New England J Med 366:864-6.

Hering D, Piper C, Bergemann R, et al. 2005. Thromboembolic and bleeding complications following St. Jude Medical valve replacement: results of the German experience with low-intensity anticoagulation study. Chest 127:53-9.

Jegaden O, Eker A, Delahaye F, et al. 1994. Thromboembolic risk and late survival after mitral valve replacement with the St. Jude Medical valve. Ann Thorac Surg 58:1721-7.

Lind S, Callas P, Golden E, Joyner Jr K, Ortel T. 1997. Plasma levels of factors II, VII and X and their relationship to the international normalized ratio during chronic warfarin therapy. Blood Coagulation & Fibrinolysis 8:48-53.

Marie I, Leprince P, Menard J-F, Tharasse C, Levesque H. 2012. Risk factors of vitamin K antagonist overcoagulation. QJM 105:53-62.

Matityahu A, Marmor M, Elson JK, et al. 2013. Acute complications of patients with pelvic fractures after pelvic angiographic embolization. Clin Orthopaed Rel Res 471:2906-11.

Mauffrey C, Cuellar III D, Pieracci F, et al. 2014. Strategies for the management of haemorrhage following pelvic fractures and associated trauma-induced coagulopathy. Bone & Joint. 96:1143-54.

Mérie C, Køber L, Olsen PS, et al. 2012. Association of warfarin therapy duration after bioprosthetic aortic valve replacement with risk of mortality, thromboembolic complications, and bleeding. JAMA 308:2118-25.

Mitra B, Cameron PA, Mori A, Fitzgerald M. 2012. Acute coagulopathy and early deaths post major trauma. Injury 43:22-5.

Moeinipour AA, Shamlou AS, Lotfalizadeh M, Esfahanizadeh J, Mottahedi B, Hoseinikhah H. 2015. Evaluation of last guidelines and studies about the best treatment with anticoagulant during pregnancy in woman with mechanical heart valves. Iranian J Obstetrics Gynecology Infertility 18:15-9.

Nishimura RA, Warnes CA. 2015. Anticoagulation during pregnancy in women with prosthetic valves: evidence, guidelines and unanswered questions. Heart heartjnl-2014-306500.

Okamura H, Yamaguchi A, Nagano H, et al. 2012. Mid-term outcomes after aortic valve replacement with the 17-mm St. Jude Medical Regent valve. Circulation 76:365-71.

O'Neal P, Moore Jr F, Gawande A, Cho N, Moalem J, Ruan D. 2012. Hemorrhagic shock as the initial manifestation of pheochromocytoma: report of a sequential management strategy. Endocrine Practice 18:e81-e4.

Panduranga P, Al-Mukhaini M, Al-Muslahi M, Haque MA, Shehab A. 2012. Management dilemmas in patients with mechanical heart valves and warfarin-induced major bleeding. World J Cardiol 4:54.

Pernod G, Godier A, Gozalo C, Tremey B, Sie P. 2010. French clinical practice guidelines on the management of patients on vitamin K antagonists in at-risk situations (overdose, risk of bleeding, and active bleeding). Thrombosis Research 126:e167-74.

Roudaut R, Serri K, Lafitte S. 2007. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. Heart 93:137-42.

Spahn DR, Bouillon B, Cerny V, et al. 2013. Management of bleeding and coagulopathy following major trauma: an updated European guideline. Crit Care 17:R76.

Steiner T, Böhm M, Dichgans M, et al. 2013. Recommendations for the emergency management of complications associated with the new direct oral anticoagulants (DOACs), apixaban, dabigatran and rivaroxaban. Clin Res Cardiol 102:399-412.

Tonolini M, Ippolito S, Patella F, Petullà M, Bianco R. 2012. Hemorrhagic complications of anticoagulant therapy: role of multidetector computed tomography and spectrum of imaging findings from head to toe. Current problems in diagnostic radiology 41:233-47.

Tran HA, Chunilal SD, Harper PL, Tran H, Wood EM, Gallus AS. 2013. An update of consensus guidelines for warfarin reversal. Med J Aust 198:198-9.

Tran HA, Chunilal SD, Tran H. 2014. An update of consensus guidelines for warfarin reversal. Medical J Australia 200:82.

Vaidya R, Kubiak EN, Bergin PF, et al. 2012. Complications of anterior subcutaneous internal fixation for unstable pelvis fractures: a multicenter study. Clin Orthopaed Rel Res 470:2124-31.

Ziran NM, Smith WR. 2014. Pelvic fractures. Management of musculoskeletal injuries in the trauma patient: Springer; p.143-63.