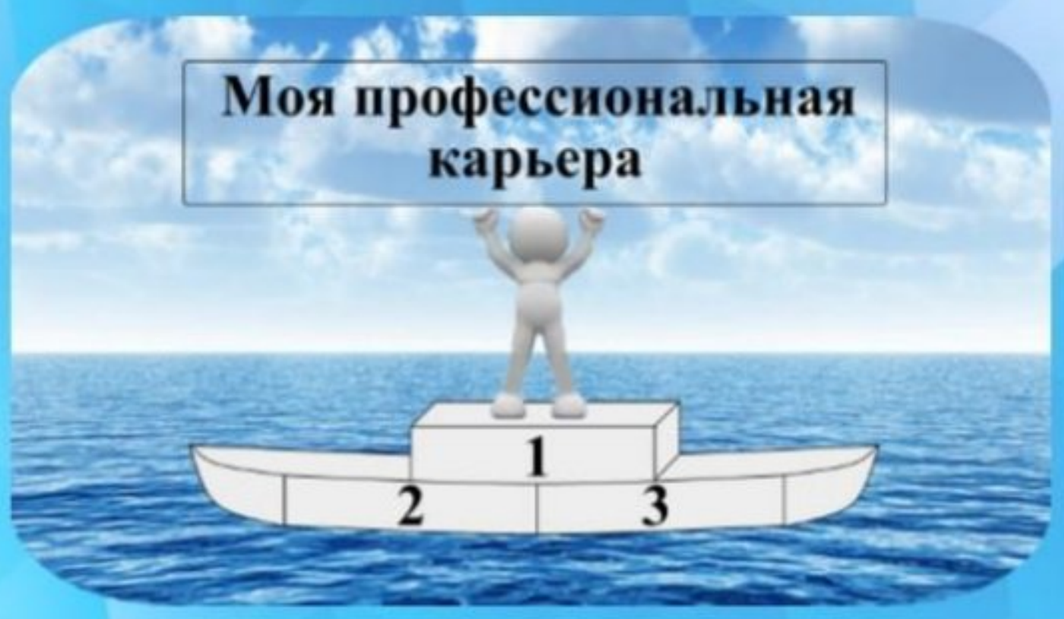

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KALIT SO'ZLAR: Mexanik yurak klapani, Antitrombotik terapiya, Trombotik asoratlar, Antikoagulyatsiya, Transezofagial exokardiyografiya, Geparinli ko'prig, Vitamin K antagonistlari,Ppast molekulyar og'irlikdagi Geparin (LMVH), Parchalanmagan geparin(UFH), Yangi oral antikoagulyantlar(NOAC).

КЛЮЧЕВЫЕ СЛОВА: Механический клапан сердца, Антитромботическая терапия, Тромботические осложнения, Антикоагуляция, Черезпищеводная эхокардиография, Гепариновый мостик, Антагонисты витамина К, Низкомолекулярный Гепарин (НМГ), Нефракционированный гепарин (НФГ), Новый пероральные антикоагулянты (NOAC).

KEY WORDS: Mechanical heart valve, Antithrombotic therapy, Thrombotic complications, Anticoagulation, Transesophagial echocardiography, Heparin bridging, Vitamin K antagonists, Low molecular weight Heparin (LMWH), Unfractionated Heparin(UFH), Noval oral anticoagulants(NOAC).

ANNOTATSIYA

Covid19 pandemiyasi butun dunyodagi hozirgi global muammo hisoblanadi. Jahon sog'liqni saqlash tashkiloti ma'lumotlariga ko'ra, 9 noyabr 2020 yilda pandemiya

tufayli 50 milliondan ortiq kasallanish xolati, koronavirus infeksiyasidan esa 1,3 milliondan ortiq o'lim qayd etilgan. Bugungi kunda koronavirus qurbonlari soni butun dunyoda o'sib bormoqda.
Qayd etilgan o'lim holatlari orasida yurak-qon tomir tizimi, nafas olish tizimi, onkologik kasalliklar patologiyasi bo'lgan aholi muhim o'rin tutadi. Maxsus xavf guruhiga koronar arteriya kasalligi, Diabetes mellitus, surunkali obstruktiv o'pka kasalliklari bo'lgan bemorlar kiradi.

АННОТАЦИЯ

Пандемия Covid19 – текущая глобальная проблема стран всего мира. По данным ВОЗ по состоянию на 9 ноября 2020 года в ходе пандемии было зарегистрировано свыше 50млн случаев заболевания, более 1,3млн случаев смертности от коронавирусной инфекции. В настоящее время число жертв от коронавируса растет по всему миру. Среди зарегистрированных случаев смертности весомое место занимает население с сопутствующей патологией сердечнососудистой системы, дыхательной системы, онкозаболеваниями. В группу особого риска входят пациенты, у которых уже имеется ишемическая болезнь сердца, сахарный диабет, хронические обструктивные болезни легких.

ANNOTATION

The Covid19 pandemic is a current global problem of countries around the world. According to WHO, as of November 9, 2020, over 50 million cases of the disease were registered during the pandemic, more than 1.3 million deaths from coronavirus infection. Currently, the number of victims from coronavirus is growing worldwide. Among the registered cases of mortality, a significant place is occupied by the population with concomitant pathology of the cardiovascular system, respiratory system, oncological diseases. The group of special risk includes patients who already have coronary heart disease, diabetes mellitus, chronic obstructive pulmonary diseases.

INTRODUCTION

Surgical replacement of a diseased heart valve with a prosthetic valve aims to improve symptoms and prolong life but also exposes the patient to potential prosthesis-related complications. The frequency of serious complications depends on the valve type, position, and other clinical risk factors. Complications include embolic events, valve obstruction (due to thrombosis or pannus), bleeding complications of antithrombotic therapy, infective endocarditis, paravalvular and transvalvular regurgitation, hemolytic anemia, and patient-prosthesis mismatch.

The two major thrombotic complications of prosthetic valves are thromboembolism and prosthetic valve thrombosis (PVT). Thrombotic risk is higher with mechanical valves than with bioprosthetic valves [1,2].

Thromboembolic and anticoagulation-related problems are the most frequent complications of mechanical valves.

Thromboembolism — The term thromboembolism generally refers to clinical embolic events ascribed to thrombus. Thromboembolic risk varies with time after mechanical valve implantation (highest early on), valve position (higher for mitral than aortic valves), and valve type (highest for older generation valves, particularly ball-in-cage).

Early risk — Following mechanical valve replacement, the risk of thromboembolism is highest during the first three to six months (particularly the first 30 days), even with therapeutic-dose anticoagulation. While the relative risk of thromboembolism is high during the first three to six months after valve replacement, the period of highest risk is relatively short, which limits the absolute risk of thromboembolism in the early postoperative period. In an observational study, risk factors for early thromboembolism included temporary cessation of anticoagulation for pacemaker implantation and diabetes mellitus [3].

- Mitral valve – The risk of thromboembolism during the first 30 days after mechanical mitral valve implantation is high, even with therapeutic anticoagulation, as illustrated by the following studies:
  - In a prospective series of 149 patients who underwent mitral (or mitral plus aortic) mechanical valve replacement between December 2005 and May 2007 and were anticoagulated with a vitamin K antagonist (VKA; such as warfarin) with early bridging with intravenous (IV) unfractionated heparin (UFH), thromboembolic events during the first 30 days occurred in 22 patients (14.8 percent) [3].
  - In an earlier series of 112 patients who underwent mechanical mitral valve replacement between 1981 and 2004 and were anticoagulated with a VKA (with mean international normalized ratio [INR] of 3), the rate of thromboembolic events was 6 percent during the first 30 days (linearized rate of 68.6 percent per year) [4]. However, one-third of the patients had mitral ball-in-cage prostheses, which are associated with high rates of thromboembolism.
- Aortic valve – The early risk of thromboembolism following mechanical aortic valve implantation is lower than that following mechanical mitral valve implantation. In a series of 151 patients who underwent mechanical aortic replacement between December 2005 and May 2007 and received VKA with early IV UFH bridging, thromboembolic events occurred in 1.3 percent within 30 days after valve replacement [3].

Long-term risk — With anticoagulation, the long-term risk of symptomatic systemic thromboembolic complications in patients with mechanical valves is similar to that with bioprosthetic valves, which generally do not require long-term anticoagulation [5-9]. Some series have reported a higher risk of thromboembolism with mechanical valves than with bioprosthetic valves, even when the individuals with mechanical valves were receiving anticoagulation [10].

- Mitral valve – Patients with mechanical mitral valve prostheses have nearly twice the long-term thromboembolic risk of those with mechanical aortic valve prostheses (eg, 1.3 versus 0.8 percent per year) [11]. Rates of thromboembolism vary among

types of mechanical valves. As an example, in a series of 112 patients with mechanical mitral valve replacement who were anticoagulated (mean INR of 3), the long-term rate of thromboembolism was much higher for ball-in-cage valves, which are no longer implanted (eg, 8.5 percent per year), compared with tilting disk or bileaflet valves (3.1 percent per year) [4].

●Aortic valve – In patients with mechanical aortic valves who are treated with a VKA, the long-term incidence of thromboembolic events (predominantly cerebrovascular) is approximately 0.5 to 1.0 percent per year [1,11,12]. In comparison, a review of mechanical valve studies (with predominantly mechanical aortic valves) estimated the risk of major embolism as 1.3 percent per year with aspirin therapy alone and 4 percent per year with no antithrombotic therapy [11].

Prosthetic valve thrombosis — PVT can be symptomatic or subclinical, although the term PVT is sometimes used to denote symptomatic PVT. Risk factors for PVT include a mechanical (versus bioprosthetic) valve, mitral and tricuspid (versus aortic) valve positions, and, for mechanical valves, subtherapeutic anticoagulation.

●Symptomatic PVT occurs when thrombus on a valve causes symptomatic prosthetic valve dysfunction. PVT can cause prosthetic valve obstruction (stenosis) or, less commonly, prosthetic valve regurgitation. Symptomatic obstructive PVT is an infrequent complication of mechanical or bioprosthetic valves.

The reported incidence of symptomatic obstructive mechanical PVT ranges from 0.3 to 1.3 percent per year, with higher rates (6 percent) among patients treated with subtherapeutic anticoagulation [13-17]. In one report of mechanical PVT, 70 percent of patients with coagulation tests measured at the time of PVT indicated inadequate anticoagulation [15]. Though data are limited, mitral mechanical PVT is likely to be at least twice as frequent as aortic mechanical PVT (0.5 versus 0.1 percent annually) [11,18]. Tricuspid mechanical PVT has been estimated to be 20 times more frequent than left-sided mechanical PVT, although data are limited [18].

●Subclinical PVT occurs when PVT does not cause symptomatic valve dysfunction. Subclinical PVT (obstructive or nonobstructive) is probably more common than symptomatic PVT, but is of uncertain clinical significance. Limited data are available on the incidence of subclinical mechanical PVT, since surveillance transesophageal echocardiography (TEE) and four-dimensional computerized tomographic angiography (CTA) are generally not performed. In a study of 680 patients studied by TEE on day 9 after mechanical mitral valve replacement, abnormal findings consistent with valve thrombus were detected in 64 of 680 patients (9.4 percent) despite anticoagulation with IV heparin initiated six hours after valve implantation [19]. At intermediate-term (mean 34 months) follow-up, one or more complications (including transient ischemic attack, stroke, valve obstruction requiring surgery, and death) were observed in 3 of 29 patients with a <5 mm thrombus and in 11 of 35 patients with ≥5 mm thrombus. However, thrombus burden in mechanical valves is difficult to assess by any imaging modality due to prosthetic image artifact.

Patients with mechanical valves require anticoagulant therapy. This generally includes early bridging with heparin overlapping with long-term vitamin K antagonist (VKA) therapy.

Early heparin bridging — Following mechanical valve replacement, as soon as the risk of postoperative bleeding is considered acceptable, we suggest initiating early anticoagulation with heparin. Either intravenous (IV) unfractionated heparin (UFH) or subcutaneous low molecular weight heparin (LMWH) is used [2].

Postoperative anticoagulation requires careful management, as patients are susceptible to bleeding complications and to excessively high international normalized ratios (INRs) because of increased sensitivity to VKA therapy [20,21].

Choice of heparin for bridging — The choice of heparin for early anticoagulation is based upon the following considerations

●UFH – IV UFH is generally chosen if the patient has an elevated bleeding risk or may require another invasive procedure, since reversal of anticoagulation is faster upon discontinuation. In the early postoperative period, IV UFH can be readily administered because the patient is already hospitalized. However, initial underdosing may occur as the dose is titrated, and there may be increased bleeding compared with LMWH at therapeutic or supratherapeutic levels of UFH.

●LMWH – Subcutaneous LMWH is more convenient to use and may result in a more predictable degree of anticoagulation [21-23]. However, LMWH is not as easily reversed as IV UFH should bleeding develop.

How to bridge

●Heparin – For early therapeutic heparin bridging, one of the following agents is started 12 to 24 hours after valve surgery [2], unless there is a contraindication such as active bleeding.

•IV UFH (eg, a starting dose of 18 units/kg/hour; no bolus) adjusted to achieve an activated partial thromboplastin time (aPTT) 2 times control

•Subcutaneous therapeutic weight-adjusted, twice daily LMWH (eg, enoxaparin 1.0 mg/kg every 12 hours). If monitored, the target anti-factor Xa level is generally 0.5 to 1.0 IU/mL four to six hours after injection.

If a patient is ready for discharge when the INR is not yet therapeutic, the patient may be switched from UFH to LMWH to facilitate outpatient management.

●Overlap with VKA – The VKA is generally started 12 to 24 hours after the procedure unless there is a contraindication. Intravenous UFH or subcutaneous LMWH should be discontinued once the INR has been in the therapeutic range for two consecutive days. The VKA should be started as soon as is prudent in consultation with the surgeon, since indirect evidence on pregnant patients with mechanical valves suggests that heparin therapy may be inferior to VKA therapy in preventing thrombotic complications

The following issues are discussed separately:

●Reversal of the anticoagulant effects of UFH and LMWH.

●Use of LMWH or UFH during pregnancy in patients with mechanical valves.

Efficacy and safety — Evidence is limited to guide heparin bridging in the early postoperative period. The rationale for early bridging is that it may reduce the

substantial risk of thromboembolism immediately after valve replacement, and at least five days of VKA therapy is usually required to achieve a therapeutic INR.

A meta-analysis included 23 observational studies of a total of 9534 patients who underwent mechanical valve replacement with outcomes assessed during the hospitalization period or the first 30 days [24]. A lower thromboembolic rate was observed in the group of patients receiving bridging therapy (VKA plus UFH or LMWH) than in patients receiving VKA with no bridging therapy (1.1 versus 2.1 percent). A higher rate of bleeding was observed with patients receiving VKA plus LMWH (5.5 percent) than in patients treated with VKA plus UFH (2.2 percent) or VKA alone (1.8 percent). The effect of anticoagulation monitoring was not assessed. An additional limitation is that most of the included studies had only one treatment arm, so the comparisons are largely between studies, not within studies.

A later meta-analysis included three studies with a total of 553 patients studied early after mechanical valve replacement and three studies with a total of 813 patients with mechanical valves studied after noncardiac surgery [25]. All studies were observational, each study included two treatment groups (LMWH or UFH), and follow-up duration ranged from 30 days to six months. The risk of thromboembolism was lower in the pooled LMWH group than in the UFH group, but the confidence interval was wide (0.6 versus 1.9 percent; risk ratio [RR] 0.34, 95% CI 0.12-0.95). The risk of major bleeding was similar in the two groups (9.2 versus 10.1 percent; RR 0.94, 95% CI 0.68-1.30).

The largest study to assess the safety and efficacy of LMWH was performed in 1063 patients followed for six weeks after undergoing mechanical heart valve replacement (79 percent aortic) [26]. A single 40 mg dose of enoxaparin was administered on the first postoperative day, followed by a reduced, weight-adjusted dose of LMWH (approximately 0.8 mg per kg with a maximum dose of 80 mg) every 12 hours, started on the second postoperative day. A VKA was started on the first or second postoperative day. The rate of thromboembolism was 1 percent, and the rate of major bleeding was 4.1 percent. The dose of LMWH used in this study was lower than the standard therapeutic dosage.

Long-term anticoagulation — A VKA is the recommended long-term anticoagulant for mechanical valves. Dabigatran is contraindicated due to inferior efficacy and safety relative to a VKA, and the other direct oral anticoagulants (DOACs) have not been adequately studied.

Initiation of VKA — The initiation of a VKA such as warfarin early after valve replacement requires close attention to control of the INR. After valve surgery, patients are at risk for thromboembolic complications as well as bleeding complications (eg, hemopericardium) and may have transiently increased sensitivity to warfarin [20,21,27,28]. Possible mechanisms for increased sensitivity include hypoalbuminemia and the use of antibiotics after surgery. Patients often require measurement of the INR two to three times per week as therapy is initiated.

Target INR and monitoring

General approach — The dosage of VKA (eg, warfarin) is adjusted as needed to achieve the target INR [1,2]. The target INR varies based upon:

●The risk of thromboembolism and thrombosis for the specific type of valve (eg, high risk with a ball-in-cage valve). Thus, it is helpful for each patient to carry a card with information about any implanted valve prosthesis and for clinicians to maintain this information as a key entry in the problem list of the medical record.
●Valve position (eg, higher risk of thrombosis with a mitral valve compared with an aortic valve).
●Presence of risk factors for valve thrombosis: prior thromboembolism, atrial fibrillation, rheumatic mitral stenosis (any degree), and left ventricular ejection fraction <35 percent.

The approach described here follows the convention in the 2020 American College of Cardiology/American Heart Association (ACC/AHA) and 2021 European Society of Cardiology (ESC) valve guidelines, which specify INR targets rather than ranges [1,2]. The acceptable range extends to 0.5 INR units on each side of the target. The use of targets was deemed preferable to ranges because it is more likely to reduce the time the INRs are closer to the upper or lower limit of the range.

When a patient has more than one mechanical valve, the highest applicable target INR is used.

VKA therapy requires ongoing monitoring of the INR. Frequent monitoring is required when establishing the VKA maintenance dose, when there is an intercurrent illness or a potentially interacting exposure (such as change in medication or diet), and when the INR is outside the target range.

When a patient is on a stable maintenance VKA dose with established therapeutic INR level, frequency of INR monitoring can be extended, but the INR should, at a minimum, be checked at least monthly in patients with mechanical valves (and at least twice per month in patients with an On-X aortic valve treated with a target INR of 1.5 to 2.0 plus low-dose aspirin).

A number of options are available for the outpatient management of VKA anticoagulation. These include supervision by a hospital anticoagulation service, community-based practice, anticoagulation clinic, or self-monitoring and self-management programs. Vigilance is required in all settings, as all patients receiving a VKA are at risk for having an INR outside of the target range.

Efficacy and safety — Since anticoagulation with a VKA has been the accepted antithrombotic therapy for mechanical valves for decades, contemporary data are limited.

In the PROACT randomized trial, 201 adults without thromboembolic risk factors who underwent implantation with an On-X mechanical aortic valve were randomly assigned to dual antiplatelet therapy (DAPT; aspirin plus clopidogrel) versus a VKA (INR 2 to 3) plus low-dose aspirin [29]. The trial was terminated for excess thromboembolic events in the DAPT group at up to 8.8 years of follow-up (4.86 versus 0.29 percent per patient-year; RR 16.69, 95% CI 2.20-127). Major bleeding rates were similar in both arms (2.08 versus 2.62 percent per patient-year; RR 0.79, 95% CI 0.28-2.23), and mortality was not statistically different (1.74 versus 1.16 percent per patient-year; RR 1.49, 95% CI 0.40-5.55).

An earlier meta-analysis compared VKA and aspirin therapy from observational studies and randomized controlled trials involving 13,088 patients with mechanical valves followed for a mean of 4.4 years [11]:

- The risk of major systemic embolism causing death, residual neurologic deficit, or peripheral ischemia without antithrombotic therapy was 4 percent per year. The risk was lower in patients treated with aspirin(1.4 percent per year) or a VKA (1 percent per year [similar to other estimates of risk for such patients] [12,30]).
- The risk of valve thrombosis limiting valve function and diagnosed at surgery or autopsy without antithrombotic therapy was 1.8 percent per year. The risk was similar in patients treated with aspirin (1 percent per year) and was significantly lower with a VKA (0.2 percent per year). However, this analysis likely substantially underestimated the risk of valve thrombosis given the restrictive definition used for valve thrombosis.
- The total thromboembolism risk (including minor thromboembolism, transient cerebral or peripheral ischemia, major systemic thromboembolism, and valve thrombosis) without antithrombotic therapy was 8.6 percent per year without antithrombotic therapy, 7.5 percent per year with aspirin and 1.8 percent per year with a VKA.
- Among patients treated with a VKA, the risk of thrombotic complications was higher with mitral valve prostheses than aortic valve prostheses. For major systemic embolism, the risks were 1.3 percent per year (mitral valve) and 0.8 percent per year (aortic valve); for valve thrombosis, risks were 0.5 percent per year (mitral) and 0.1 percent per year (aortic); and for total thromboembolism, 2.7 percent per year (mitral) and 1.1 percent per year (aortic).
- The risk of bleeding (including cerebral, major, and minor bleeding) was 4.6 percent per year in patients receiving antiplatelet therapy plus a VKA, 1.9 percent per year in patients receiving a VKA alone, and 0.5 percent per year in patients receiving antiplatelet therapy alone.

Limitations of the above meta-analysis include low number of events, likely inadequate reporting of events (with major embolic events most reliably reported), inclusion of observational studies along with randomized trials, and inclusion of older studies (published from the 1970s to 1992) with limited brain imaging and echocardiography data [11]. Since most patients in studies published after 1985 received VKA therapy, the meta-analysis included older studies to evaluate the risk of lack of anticoagulation. A majority of patient years in the study involved older valves that have higher thrombogenicity (such as Bjork-Shiley, Starr-Edwards, Lillehei-Kaster, and Omniscience) [31].

Lower INR target for On-X aortic valve — The PROACT trial results support use of a lower INR target (1.5 to 2.0) in combination with low-dose aspirin in selected patients with On-X aortic valves [29]. The trial enrolled 375 patients with risk factors for thromboembolism who underwent surgical aortic valve replacement with the On-X mechanical bileaflet valve with at least twice monthly home monitoring of the INR [29,32]. All patients received routine warfarin with a target INR of 2 to 3 for the first three months after valve implantation and aspirin 81 mg

indefinitely. Participants were randomly assigned to lower-dose warfarin (target INR 1.5 to 2) or standard warfarin (target INR 2 to 3) beginning three months after valve replacement. At a median of 5.1 years of follow-up, the lower-dose warfarin group experienced significantly lower rates of major bleeding (1.59 versus 3.94 percent per patient-year), while rates of neurologic events were similar in the two groups (2.01 versus 1.65 percent per patient-year) [29]. These results led to approval of an expanded labeling claim for the On-X valve, including an INR target of 1.5 to 2 beginning three months after valve replacement, by the US Food and Drug Administration (FDA) and the Conformitè Europëenne (CE) mark in the European Union.

A limitation of the PROACT trial is that the comparator was standard warfarin (with target INR 2 to 3) plus low-dose aspirin, which differs from the 2020 ACC/AHA and 2021 ESC guideline recommendations for mechanical valves, which do not recommend routine aspirin therapy [1,2]. Another limitation is that patients with atrial fibrillation at high risk for thromboembolism were not included in the trial (patients with atrial fibrillation had a CHA_2DS_2-VASc score ≤ 1) .

DOACs are not used — DOACs should **not** be used in patients with mechanical prosthetic heart valves. All patients with mechanical prosthetic valves require lifelong anticoagulation with a VKA (eg, warfarin).

DOACs include the oral direct thrombin inhibitor dabigatran and the direct factor Xa inhibitors rivaroxaban, apixaban, and edoxaban. These anticoagulants are **not** approved for use in patients with mechanical prosthetic heart valves. Randomized trials of rivaroxaban, apixaban, or edoxaban have not been completed in patients with mechanical valves, and dabigatran was demonstrated to be inferior to a VKA for mechanical valve thromboprophylaxis.

Dabigatran is contraindicated — Dabigatran is contraindicated in patients with mechanical heart valves. An FDA drug safety communication cited the results of the RE-ALIGN randomized trial, which demonstrated that dabigatran was associated with a higher risk of thromboembolic events and bleeding than warfarin in patients who had undergone mechanical valve replacement (aortic or mitral valve replacement within the past seven days or mitral valve replacement at least three months earlier) [33,34].

The initial dabigatran dose (150, 220, or 300 mg twice daily) was based on baseline kidney function, and doses were adjusted to obtain a trough plasma level of ≥ 50 ng/mL. Warfarin dosing was adjusted to a target INR of 2 to 3 or 2.5 to 3.5, depending upon thromboembolic risk factors.

The trial was stopped early after 252 patients had been enrolled because of excess of thromboembolic and bleeding events in the dabigatran group.

- Stroke occurred in nine patients (5 percent) in the dabigatran group (all in the early treatment cohort) and in no patients in the warfarin group. Valve thrombosis without clinical symptoms was detected in five patients, all in the dabigatran group (3 percent).
- Bleeding events were significantly more frequent in the dabigatran group (27 versus 12 percent in the warfarin group). Major bleeding (all pericardial and in the

early treatment cohort) occurred in seven patients (4 percent) in the dabigatran group and in two patients (2 percent) in the warfarin group.

Selective use of aspirin — A VKA alone is sufficient antithrombotic therapy for most patients with a mechanical valve. Addition of aspirin to the VKA is not required unless there is a concurrent indication for aspirin (except for patients with an aortic On-X valve). When added to anticoagulation, antiplatelet agents decrease thromboembolic risk but increase the risk of major bleeding [35]. Selective use of aspirin as an adjunct to VKA for patients with mechanical valves is based on the recognition that most trials supporting routine addition of aspirin were conducted decades ago in patients with older-generation prosthetic valves and high rates of additional vascular risk factors [1,2,17,35]. The quality of the included studies was generally low, likely reflecting less advanced trial methods when the trials were performed.

For patients with a mechanical valve who have a concurrent indication for aspirin and/or other antiplatelet therapy, a decision on whether to add an antiplatelet agent is based on the estimated benefits (reducing risk of coronary stent thrombosis) and bleeding risks, as discussed separately.

SUMMARY AND RECOMMENDATIONS

- Risks of mechanical valves – Thromboembolic and anticoagulation-related problems are the most frequent complications of mechanical valves. The two major thrombotic complications are thromboembolism and prosthetic valve thrombosis (PVT).
- Thromboembolism – Thromboembolic risk varies with time after mechanical valve implantation (highest in the immediate postoperative period), valve position (higher for mitral and tricuspid than aortic valves), and valve type (highest for older generation valves, particularly ball-in-cage). Patients with mechanical mitral valve prostheses have nearly twice the long-term thromboembolic risk of those with mechanical aortic valve prostheses (1.3 versus 0.8 percent per year).
- Prosthetic valve thrombosis – The incidence of symptomatic obstructive mechanical PVT ranges from 0.3 to 1.3 percent per year, with rates up to 6 percent per year among patients receiving subtherapeutic anticoagulation.
- Anticoagulation – Patients with mechanical prosthetic valves require anticoagulation. This generally involves early bridging with heparin and long-term therapy with a vitamin K antagonist (VKA) such as warfarin.
- Early heparin bridging – We suggest early heparin bridging with rather than no bridging (Grade 2C). Either intravenous unfractionated heparin (UFH) or subcutaneous low molecular weight heparin (LMWH) is used. Heparin bridging is continued until the international normalized ratio (INR) is therapeutic for two consecutive days.
- Long-term anticoagulation – For patients with mechanical valves, recommended a VKA rather than a direct oral anticoagulant (DOAC) (Grade 1B). The target INR varies with valve position, valve type, and thromboembolic risk factors.

DOACs are not approved for use for mechanical valves. Dabigatran confers a higher risk of thrombosis and bleeding than VKAs, and the safety and efficacy of other DOACs are unknown.

●Aspirin – For most patients with a mechanical valve, a VKA is sufficient for thromboprophylaxis, and routine aspirin therapy is not required (except for patients with an aortic On-X valve treated with a low INR target). For patients who have a concurrent indication for aspirin and/or other antiplatelet therapy, a decision on whether to add an antiplatelet agent balances the estimated benefits (reducing risk of coronary stent thrombosis) and bleeding risks.

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