



Review

Management of Intracranial Hemorrhage in the Setting of Mechanical Heart Valve Replacement Therapy

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Abstract: The management of an intracranial hemorrhage in patients receiving anticoagulant therapy presents a significant challenge for medical professionals. Anticoagulant treatment is intended to prevent blood clotting, but it can worsen active brain bleeds. Despite this risk, avoiding the prothrombotic state caused by mechanical heart valves remains crucial. Guidelines on managing this issue are currently lacking, prompting a review that delves into embryonic development and anatomical functions of heart valves, valve replacement therapy for diseased valves, and the need for anticoagulants. Ultimately, recent literature and cases inform discussion regarding how best to manage intracranial hemorrhages in patients with mechanical heart valves. The expectation is that this examination will offer valuable perspectives on the handling of intracranial bleeding among individuals with mechanical heart valves and stimulate additional investigations in this intricate domain, particularly through the lens of applied mechanics.

Keywords: intracranial; hemorrhage; mechanical; heart; valve; replacement; therapy



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1. Introduction

In the course of embryonic development, heart valves undergo a highly regulated process involving molecular signals, cellular divisions, and growth. Once matured, these valves maintain blood flow between the four chambers of the heart through rhythmic opening and closing during each heartbeat, which produces the familiar “lub dub” sound. Proper functioning of heart valves is crucial to systemic circulation; valve dysfunction may lead to life-threatening ischemia caused by inadequate blood supply to tissues. Heart valve impairment or damage can result from various factors such as congenital anomalies, infections, advancing age, or lifestyle choices such as diet and exercise patterns. It is imperative to comprehend the root causes of heart valve dysfunction and devise effective remedies for maintaining public health. Recent research endeavors have concentrated on creating novel techniques such as minimally invasive procedures and tissue-engineered valve replacements to repair or substitute damaged heart valves. These advanced approaches offer remarkable potential, with the capability to transform the field of cardiology entirely. By continuing our exploration into heart valve development and dysfunction, we can not only enhance our capacity for treating this disease but also gain valuable insights into wider cardiac mechanisms that could lead us towards innovative treatments for various cardiovascular conditions in future.

Heart valves can be limited or rendered dysfunctional by a variety of factors, ranging from developmental defects in utero to age-related wear and tear, infections, and diseases. Thanks to advancements in medical science, the surgical replacement of damaged heart valves with either mechanical or prosthetic ones has become an effective treatment option that enhances blood circulation and patient outcomes. However, both types of replacements carry potential advantages as well as risks: while mechanical heart valves are more durable than bioprosthetic ones, they may also induce a prothrombotic state during blood passage

through the valve. In other words, bioprosthetic valves have a shorter lifespan and may require redo surgeries over time but they do not cause blood clotting problems, which makes them a safer bet for patients who cannot tolerate long-term anticoagulant therapy. Thus, it is crucial to weigh the pros and cons of both replacement types carefully and for medical professionals to work with their patients in making an informed decision that aligns with their individual circumstances and health status.

Patients with mechanical heart valves are typically prescribed anticoagulant therapy to mitigate the risk of thrombotic events. However, this treatment approach also raises the likelihood of experiencing a thromboembolic event. These incidents involve blood clots that break free from the heart and travel to other parts of the body, such as the lungs, potentially causing blockages in arteries and leading to conditions such as pulmonary embolisms, which can be fatal. Due to these risks, individuals undergoing anticoagulation therapy require vigilant monitoring by physicians at all times. Regular medical checkups, diagnostic testing, and follow-up appointments are essential for patients with mechanical heart valves to prevent potential complications associated with anticoagulant therapy and to ensure the efficacy of their treatment plan. Moreover, an emphasis on healthy habits—such as regular physical activity, a balanced diet, and stress management techniques—can help further decrease the chance of complications and improve overall health outcomes for patients with heart valve replacements.

Valvular heart disease is one of the most common causes of cardiovascular morbidity in the United States, with about 2.5% of the U.S. population possessing some form of valvular heart dysfunction [1]. Many incidences of valvular heart disease require surgical replacement of the damaged valves. The use of artificial heart valves has been increasingly popular in the treatment of valvular heart disease. However, the use of artificial heart valves poses many potential risks and complications. Thrombosis is a serious complication of artificial valve replacement, most particularly mechanical heart valves, and requires patients to remain on anticoagulation therapy [2]. However, the use of anticoagulation therapy increases the risk of bleeding and may pose a conflict in patients presenting with intracranial hemorrhage. The illustration in Figure 1 depicts the benefit that reversing anticoagulation would provide to an active intracranial hemorrhage vs. the potential dangers of acute ischemic events in the setting of mechanical heart valves.

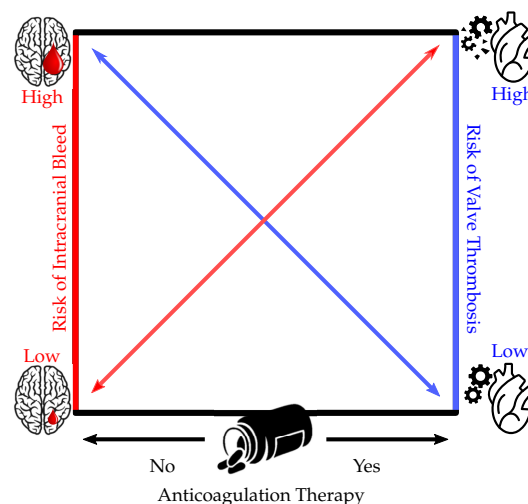


Figure 1. An illustration depicting the benefit that reversing anticoagulation would provide to an active intracranial hemorrhage vs. the potential dangers of acute ischemic events in the setting of mechanical heart valves.

This paper will discuss the management of intracranial hemorrhage (ICH) in the setting of mechanical heart valves. The paper will begin by discussing the normal functionality and structure of healthy heart valves, and then discuss various pathological states that require surgical replacement of the dysfunctional valve with a mechanical or bioprosthetic valve.

The differences, benefits, and risks of mechanical and bioprosthetic heart valves among different patient populations will then be analyzed. Next, the need for anticoagulation therapy and the various anticoagulant regimens will be discussed. Finally, this paper will discuss the management of intracranial hemorrhage in patients that are on anticoagulation therapy secondary to mechanical heart valve replacement. This paper will pay special attention to the appropriate use of bridging anticoagulation and the use of antifibrinolytic agents in patients with an intracranial bleed who are receiving anticoagulation therapy from a mechanical heart valve. In addition, the risks and benefits of various treatment strategies will be analyzed and discussed. The goal of this paper is to educate the reader regarding the clinical presentation and management of intracranial hemorrhage in the setting of a mechanically operated heart valve and to provide evidence-based recommendations for the optimal management of these patients [3].

2. Development of Normal Heart Valves

The four-chambered human heart has aortic and pulmonic valves governing blood flow to the aorta and pulmonary arteries, respectively. Those valves are hence termed the ventriculoatrial valves. The mitral and tricuspid valves separate the atria and ventricles and are hence named the AV valves. Valvulogenesis in the embryonic period begins with the formation of the endocardial cushion in the primitive heart. From the endocardial cushion, the individual leaflets and cusps are derived. The valve progenitor cells are highly proliferative in the endocardial cushion allowing for the formation of the leaflets and valve cusps [4]. The papillary muscles of the AV valves are derived from the developing ventricular walls [5]. The development of the valves is a complex process in which cells proliferate, differentiate, and undergo morphogenesis. Precise coordination of the development of the valves is coordinated through a vast number of biochemical and cellular processes. Of the many chemical mediators, NOTCH is one that has been extensively studied and has been shown to be crucial to the development of heart valves. NOTCH is an intracellular signaling pathway that allows for crosstalk crucial to cell fate in the formation of the valves [6]. A multitude of other biochemical mediators are essential for the formation of the heart valves and studies have indicated that congenital valve diseases are the consequence of dysfunctions in these signals [7,8]. The functions of heart valves depend largely upon the extracellular matrix [9]. In the prenatal stages, type III collagen is predominant in the extracellular matrix of heart valves. However, in postnatal stages, type I collagen becomes more predominant as this fiber type is better suited to support the mechanical function of the valves [10]. Although highly proliferative in the embryonic period, the heart valves cannot regenerate, and thus damage to an adult valve necessitates surgical repair [11]. Open-heart surgery has traditionally been the standard approach to the treatment of severely damaged or damaged heart valves. However, the risks associated with open-heart surgery increase with the increase in the age of patients and the number of co-morbidities that are present in older patients [12]. Additionally, improvements in technology such as less invasive surgical procedures have made alternative approaches to the treatment of damaged heart valves possible. Transcatheter aortic valve replacement (TAVR) has become a widely used procedure in the treatment of severe aortic stenosis in patients over the age of 80 years who are at high risk of developing complications from open-heart surgery [13]. Although the TAVR procedure is safe and the results from clinical trials have been encouraging, the long-term efficacy of the procedure has not been fully established [14]. Thus, further research is needed to elucidate the mechanisms underlying the endothelialization process in TAVR and identify patients who are likely to benefit from this procedure.

3. Dysfunction of the Heart Valves

When there is a disruption of normal heart valve development or function, many pathological states can arise. Valvular heart disease can be caused by congenital or acquired conditions. Diseased valves have also been noted to have a different structure than normal,

healthy valves. This includes cusp and leaflet thickening, disorganization of collagen fibers, and increased density of valvular interstitial cells. Furthermore, diseased heart valves often show calcification, which contributes to the dysfunctionality of the valve [15–19].

Common causes of valvular heart disease include endocarditis, myxomatous degeneration, infective endocarditis, connective tissue disease, trauma, systemic lupus erythematosus, and syphilis. There are several conditions that can affect the proper functioning of a patient's valve, which can result in significant morbidity and mortality for those who are affected. Diagnosis and treatment of these disorders is a major public health issue. In combination with efforts to curb the incidence of these diseases through early diagnosis and intervention programs, greater attention must also be given to research endeavors aimed at understanding the mechanisms behind the development of these diseases and their progression.

Congenital valvular heart conditions include bicuspid aortic valve, atrioventricular septal defects, tricuspid atresia, and Ebstein anomaly. These congenital heart defects are caused by a variety of factors, including genetics, maternal use of tobacco or certain medications, and environmental factors. These pathologies are often considered after the physician hears a murmur on a physical exam and refers the infant to a cardiologist for further workup. Different murmurs are associated with different valvular defects. If a soft I–II/VI murmur is heard at the upper sternal border and does not increase with the Valsalva maneuver or cause any cardiac symptoms, no further testing is required [20]. All other murmurs require further evaluation. The gold standard for the diagnosis and grading of congenital heart conditions is echocardiography. Infants that are born with such defects can be managed with medications such as beta-blockers, digoxin, and calcium blockers. Ultimately, patients often require surgical intervention as the ultimate treatment for their fatal condition. Surgical intervention involves valve repair or replacement. Complications of congenital valvular diseases include arrhythmias and heart failure, and often reoperation is required after surgery to prevent deterioration of valve function [21–23]. Complications of bicuspid aortic valves include increased risk for thoracic aortic aneurysms and dissections, as well as infective endocarditis and sudden cardiac arrest [24]. When a person suffers from congenital valvular disease, it is important to prevent complications from the disease as well as improve their quality of life as much as possible. Such interventions may involve the use of medications, surgical repair, or other types of treatment. New therapies based on gene therapy are currently being developed for the treatment of congenital heart disease. However, more research is needed before this therapy can be used in the treatment of patients with these disorders.

Acquired valvular heart conditions include aortic, pulmonic, mitral, and tricuspid dysfunction, the most common of which includes stenosis and regurgitation. The most common causes of acquired valvular heart disease include degenerative etiologies and infectious etiologies. Stenosis is a disorder caused by the thickening and stiffness of the mitral valve leaflets. This condition can lead to difficulty in breathing and reduced cardiac output. This can be caused by coronary artery disease or diabetes, both of which increase the formation of blood clots. It can also result in myocardial infarction and ischemia from an inability of blood to flow through the chambers. Various factors contribute to the dysfunction of heart valves. This includes chronic hypertension and hyperlipidemia, which can predispose to hypertrophy of the heart chambers and calcification of the valves [25–27]. Other causes of stenosis include rheumatic fever, viral infections, inflammation, and cancer. Treatment options include medication such as diuretics and anticoagulants, surgical procedures to repair the valve or replace the valve with an artificial one, or a combination of these methods. Treatment strategies for degenerative valvular heart disease vary based on the cause and severity of the condition. For mild cases of degenerative valve disease, conservative management is usually recommended. This involves the use of lifestyle modifications such as maintaining a healthy weight, quitting smoking, avoiding excessive alcohol use, and eating a nutritious diet. If symptoms do not improve with these lifestyle changes, then the doctor may recommend other treatment options such as medication or

surgery. In the case of severe degenerative valve disease, one may need to have surgery to replace the diseased valve with a prosthetic one. This can be performed either through a minimally invasive approach or using traditional open-heart surgery.

The most common infectious etiology of acquired valvular dysfunction is rheumatic heart disease, particularly due to the staphylococcus microorganism [26]. Rheumatic heart disease begins following a pharyngeal infection with group A beta-hemolytic streptococci. Infective endocarditis can result in valvular dysfunction and is one of the most common etiologies of mitral stenosis. Though the mitral valve is most likely to be impacted by infective endocarditis, the tricuspid valve is commonly affected by IV drug abusers. These patients require diagnostic imaging and monitoring with echocardiography. Treatment of infective endocarditis involves antimicrobial therapy and management of significant valvular dysfunction with medications that may include beta-blockers, calcium channel blockers, and digoxin. However, severe valvular dysfunction would require surgical intervention for definitive treatment. Infections are one of the most important causes of acquired valvular dysfunction. Bacterial endocarditis is associated with disruption of the glycocalyx coating of the valvular leaflets as a result of microbial adherence and subsequent damage resulting from bacterial toxins, leading to valve thickening and dysfunction. Bacterial endocarditis is typically treated with intravenous antibiotics and mycophenolate mofetil. Surgery may be required in severe cases when antibiotic therapy fails to improve clinical status or if the patient becomes septic and requires urgent intervention. Viral infections cause the majority of cases of myopericarditis, which is characterized by inflammation of the heart muscle and valves. There is no specific treatment for myopericarditis, which usually resolves without long-term sequelae. Myocarditis is more commonly caused by viral infections than bacterial infections and is usually associated with influenza. It most frequently affects the left ventricular myocardium and causes symptoms of heart failure. Valve dysfunction resulting from viral infection generally improves within several weeks without medical treatment. The incidence and prevalence of these diseases in the United States are low; however, these conditions can be serious and potentially life-threatening if left untreated.

4. Mechanical and Bioprosthetic Heart Valves

In cases of valvular heart disease, replacement of the damaged valve is often the indicated treatment to relieve symptoms and complications. The two major methods of heart valve replacement include mechanical heart valves and bioprosthetic heart valves. Currently, there is no perfect valve substitute available to replace the natural valve. There has been much controversy about the optimal choice of the prosthetic valve since the inception of the technique itself [28]. Mechanical heart valves are made of carbon and metal, while bioprosthetic heart valves are usually made from animal or host tissue [29]. Bioprosthetic valves are treated in order to make sure they are not rejected by the autoimmune system of the human body. A topic of common debate revolves around which method of valve replacement is favorable with better outcomes. There are many risks and benefits to the use of mechanical and bioprosthetic valves, which have been extensively studied and have shown either similar outcomes in patients or greater favorability for mechanical heart valves [28]. Given the nature of a cardiac surgical procedure, patients undergoing valve replacement are at risk for complications such as bleeding, infection, and clotting. There are different types of anticoagulant drugs used to prevent blood clots in patients with prosthetic valves; however, they can also increase the risk of bleeding in some cases [30]. Management of anticoagulation therapy can be difficult when patients are receiving multiple medications for other health conditions, including heart failure. Anticoagulants have a narrow therapeutic window and should be monitored closely by physicians to minimize the risk of bleeding and other side effects [31]. It is critical for patients to receive proper education about the management of these medications and the risks associated with anticoagulation therapy. In order to improve the outcomes of patients who suffer from valvular heart disease, researchers continue to explore new treatment options. With the development of less invasive surgical techniques and improved medical therapies,

the number of patients who undergo valvular heart surgery is increasing each year. The use of new technologies has significantly decreased postoperative recovery time and decreased complication rates in patients undergoing valvular heart surgery. In addition to having better clinical outcomes, these new technologies are also expected to reduce the cost of care [32]. Cardiac surgeons now have the ability to perform more complex procedures using minimally invasive approaches, enabling faster recovery times and limited damage to the heart. Newer treatments may also enable long-term survival for patients with advanced heart disease who would not otherwise be eligible for surgery [33].

Bioprosthetic heart valves have many benefits and drawbacks. Bioprosthetic valves are less thrombogenic than mechanical heart valves, which decreases the risk of clot formation and thromboembolism. They also decrease the need for lifelong anticoagulation, which mechanical heart valves require. This is especially beneficial to younger patients, most particularly women of childbearing age and pregnant patients. However, the use of bioprosthetic heart valves poses the risk of structural deterioration [34]. Structural valve degeneration can manifest as pannus growth, calcification of the leaflet, connective tissue delamination, or ruptures and perforation of the valve [35]. There are many mechanisms behind this process. One proposed mechanism includes macrophage infiltration of the bioprosthetic valve and calcium deposition. Structural valve degeneration can also occur secondary to extracellular matrix disintegration from mechanical stress as well as chronic inflammation. This weakening of the valve allows for penetration and destruction of red blood cells, which can result in oxidation of the extracellular matrix, and ultimately, deterioration of the valve. Furthermore, bioprosthetic heart valves may have a decreased risk for thrombosis; however, they also possess a decrease in durability that requires a need for reoperation [36]. The presence of particulate matter and debris is also a potential concern with bioprosthetic valves because of the likelihood of increased valvular stenosis over time [37]. Finally, tissue harvesting for surgical implantation of bioprosthetic valves may be associated with an increased risk of infection as well as bleeding complications [38]. Despite these potential complications, the decreased risk of thromboembolism associated with the use of bioprosthetic valves may outweigh their potential risks. The decision to use a bioprosthetic valve over a mechanical valve should be discussed between the surgeon and the patient. Patients who are at greater risk for thromboembolism may require treatment with anticoagulation to decrease this risk, regardless of the treatment option used. Ultimately, the decision to use either a bioprosthetic or mechanical valve should be made based on the individual patient's clinical status and preferences.

Mechanical heart valve replacement is another common method of treating valvular heart disease. Mechanical heart valves are beneficial in that they have increased durability and a decreased need for reoperation [39,40]. However, mechanical heart valves pose a greater risk for thrombosis, and therefore require lifelong anticoagulation. This can increase the risk of bleeding and can be problematic in hemorrhagic patients [41]. Despite this drawback, mechanical heart valves have statistically been shown to have a better prognosis in multiple studies. This is likely due to the strength of mechanical valves, which increases their longevity and prevents the need for further invasive procedures. Patients that comply with anticoagulation therapy are able to avoid the thrombotic potential of the valve, and the functionality of the valve remains intact [42]. Advances in medical technology continue to improve the safety and efficacy of mechanical heart valves. Surgical techniques for minimally invasive implantation allow shorter recovery times and better outcomes for patients. Cardiologists have been performing surgical valve replacement for decades, but the procedure has been refined over the years to reduce the risk of complications. In the early days, open-heart surgery was the standard treatment for mitral regurgitation and aortic stenosis. A median sternotomy was used to open the chest cavity of the patient so that the diseased valve could be removed and a prosthetic valve could be installed in its place. The procedure was generally associated with significant postoperative morbidity and mortality. Over time, new techniques have been developed to reduce the risks associated with open-heart surgery. It is possible to use these techniques by making smaller incisions

and using less invasive techniques such as transcatheter aortic valve replacement (TAVR) or transcatheter mitral valve replacement (TMVR) in place of more invasive ones. TAVR and TMVR are minimally invasive alternatives to conventional open-heart surgery for the treatment of aortic stenosis and mitral regurgitation. In both procedures, the device is inserted through a small incision in the groin and positioned in the heart without requiring direct access to the heart or blood vessels. The devices eliminate the need for major cardiothoracic surgery and are associated with less postoperative morbidity and mortality than open-heart surgery. Both TAVR and TMVR involve the use of a catheter-based system to replace the native valve with an artificial one. TAVR involves the use of a balloon-tipped catheter to gently expand the existing aortic valve and implant a prosthetic valve in its place. In TMVR, a mechanical stent is implanted using a series of catheters to bypass the obstruction that is preventing proper blood flow through the mitral valve. In some cases, TAVR and TMVR can be performed as outpatient procedures eliminating the need for hospitalization. TAVR and TMVR offer several advantages over traditional open-heart surgery including faster recovery times and reduced risk of complications. Patients who undergo TAVR or TMVR experience less pain, nausea, and shortness of breath after surgery than those with open-heart surgery. They also tend to recover faster and return to their regular activities sooner than patients who undergo open-heart surgery. However, there are potential risks associated with both TAVR and TMVR. These risks include device migration and infection as well as the potential for blood clot formation at the insertion site of the catheter. TAVR has been performed on more than 200,000 patients worldwide since its introduction in 2011 and TMVR has been used in more than 3500 patients in the U.S. and Europe since it was approved in 2015. Because TAVR and TMVR represent new and emerging technology, there is limited information about their long-term efficacy and safety. Further research is necessary to determine whether these procedures are safe and effective for use in broader patient populations.

The Valve Academic Research Consortium (VARC)-3 criteria provide a clinical classification for bioprosthetic valve dysfunction (BVD) as assessed through echocardiographic imaging. Bioprosthetic valves have limited durability due to structural deterioration. BVD categories are divided into two types: structural and non-structural. Structural BVD refers to intrinsic changes in the prosthetic valve, such as wear and tear, leaflet disruption or obstruction, flail leaflet, calcification, stent fracture, or deformation. These changes are categorized into three stages determined by echocardiography. In Stage 1, there is evidence of structural deterioration without hemodynamic compromise. In Stage 2, there is evidence of both structural and moderate hemodynamic valve deterioration. Moderate hemodynamic valve deterioration is defined as an increase in the mean transvalvular gradient greater than 10 mmHg resulting in a mean gradient greater than 20 mm Hg with concomitant decreases in AVA (greater than or equal to) 0.3 cm^2 or greater than 25% and/or decrease in DVI (greater than or equal to) 0.1 or (greater than or equal to) 20% compared to echocardiography assessment performed one to three months postprocedure. Alternatively, it can be defined as a new occurrence/increase in grade-1-or-greater intraprosthetic AR leading to severe/moderate AR. Stage 3 signifies evidence of structural damage coupled with severe hemodynamic valve deterioration. Severe hemodynamic valve deterioration is characterized by an increase in the mean transvalvular gradient greater than 20 mmHg, which leads to a mean gradient greater than 30 mmHg. This condition also involves a concomitant decrease in AVA of more significant than or equal to 0.6 cm^2 or greater than 50%, and/or DVI reduction that is equal to or exceeding 0.2 cm^2 or up to 40% compared with echocardiography assessment carried out one to three months postprocedure. Alternatively, severe hemodynamic valve deterioration can be defined as the occurrence of grade two intraprosthetic AR resulting from moderate-to-severe AR progression. Nonstructural BVD describes any anomaly not intrinsic to the prosthetic valve but still causing valve dysfunction. This includes paravalvular regurgitation, subvalvular pannus overgrowth, and inappropriate positioning or sizing. The clinical consequence of BVD is bioprosthetic valve failure (BVF). It is defined as any significant bioprosthetic valve dysfunction with clin-

ically expressive criteria or Stage 3 hemodynamic valve deterioration related to permanent changes in the prosthetic valve confirmed by imaging of morphologic leaflet/stent abnormalities and/or invasive assessment of valve hemodynamic dysfunction. Alternatively, valve reintervention due to hemodynamic/symptomatic indication for a new intervention or death caused by faulty valves can constitute BVF [43].

A few points outlining the basic differences between mechanical and bioprosthetic heart valve replacements are summarized in Table 1. Many studies have been conducted to compare the outcomes and mortality risks of mechanical and bioprosthetic heart valves. In their study, Head et al. concluded that the risk-to-benefit ratio of mechanical and bioprosthetic valves favored the use of mechanical heart valves in patients younger than 60 years of age [44]. This is supported due to the decreased need for reoperation, which would ultimately increase mortality due to the invasive nature of valve replacement procedures. Another study conducted by Azari et al. concluded that the 10–20-year death rates for biological valves were significantly higher in comparison to mechanical prostheses [45]. Biological heart valves also demonstrated a higher incremental cost-effectiveness ratio and lower long-term success rates, making mechanical heart valves the favorable option. However, it was also concluded that bioprosthetic valves would be a more reasonable option for patients over the age of 70 years. This is due to the overall shorter survival of patients falling in this age range, and the decreased likelihood of reoperation after initial treatment. Furthermore, Diaz et al. performed a meta-analysis comparing the long-term outcomes of mechanical and bioprosthetic heart valves in patients between 50 and 70 years of age and reported a statistically significant survival advantage with mechanical heart valves [46]. Tao et al. similarly concluded that mechanical heart valves have a significantly better prognosis in patients with infective endocarditis [47]. Yu and Wang reported findings suggesting that mechanical mitral valve replacement may be a more reasonable alternative in patients aged 50–70 years with rheumatic heart disease [48]. However, in a retrospective cohort study conducted by Lameijer and his peers, it was concluded that mechanical heart valves posed greater complications in pregnant women than bioprosthetic valves due to the increased risk of thrombosis and bleeding complications [49]. In a similar study by Kyto and his colleagues that compared outcomes after mechanical and biological aortic valve replacement in infective endocarditis patients, mechanical heart valves were associated with lower mortality in patients less than 70 years of age [50]. In terms of the tricuspid valve, Palacios and his peers concluded that the mortalities of biological and mechanical valves were similar [51]. Lubiszewska and his peers conducted a study to analyze the long-term results of mechanical heart valves in congenital heart disease among 44 patients ranging from 1.3 to 15 years of age. It was concluded that mechanical heart valves were effective in the atrioventricular position and the aortic orifice, providing a seven-year survival rate of 93.4%. However, mechanical valve replacements in the tricuspid position were more prone to thrombosis and occlusion [52]. Another study compared the quality of life and anxiety of younger patients that were treated with mechanical and prosthetic heart valves. It was concluded that mechanical heart valves were associated with increased anxiety in patients due to the sound of the valve and the need for anticoagulation [53]. Pragt et al. concluded that although mechanical heart valves were associated with an increased risk for thrombosis, this risk factor can be overcome with anticoagulation, and furthermore, bioprosthetic valves have an unavoidable risk for deterioration and worse outcomes than mechanical valves [54]. In conclusion, both mechanical and biological valves have advantages and disadvantages in their use for the treatment of infective endocarditis. It is important to keep in mind that no single type of valve is ideal for all patients. Rather, an individualized approach should be taken for each patient to determine the optimal treatment for their condition. This may require the use of multiple types of valves or alternative treatments such as conservative management or surgical replacement of the diseased heart valve. Further research is required to investigate the comparative outcomes of different types of valves in different patient populations in an effort to determine the ideal type of valve for each patient. Utilizing a combination of experimental and computational methodologies

can offer an in-depth comprehension of the intricate phenomena linked with heart valve function and disease [55].

Table 1. Mechanical vs. Bioprosthetic Valves.

	Mechanical	Bioprosthetic
Percentage of use [56–59]	≈20%	≈80%
Durability [60]	up to 30 years	up to 15 years
Need for Replacement/Repair [61,62]	Lower Risk	Higher Risk
Morbidity/Mortality with Reoperation [63]	Higher Risk	Lower Risk
Thromboembolism [2,64]	Higher Risk	Lower Risk
Anticoagulation [65,66]	Lifelong	3+ months

5. Complications of Artificial Heart Valves

There are many complications that can arise from artificial heart valves. These complications include infection, hemolysis, and thromboembolism. Thromboembolism, as mentioned previously, is managed with anticoagulation therapy and will be discussed further in this paper. Some potential hemostatic and hemodynamic factors involved in the development of prosthetic valve thrombosis are summarized in Figure 2 by anatomical location. Infective endocarditis is a very common complication following valve replacement. The most common organism to infect prosthetic valves is *Staphylococcus aureus* [67–69]. Methicillin-resistant *Staphylococcus aureus* has been associated with an increase in the mortality rate for patients following prosthetic valve replacement. Management of this complication includes antibiotic therapy with vancomycin and rifampin. The use of aminoglycosides can also promote sustained susceptibility to rifampin [70–72]. Another complication of prosthetic heart valve replacement is hemolysis, which is usually secondary to structural deterioration of the valve, mechanical trauma to red blood cells, and leakage of fluid [73]. Patients with this complication may present with fatigue, jaundice, and dark urine. Treatment involves iron and folate supplementation and transfusions if necessary. Beta-blockers have also been seen to decrease the extent of hemolysis [74]. Patients presenting with paravalvular regurgitation would most likely require surgical intervention to treat the anemia [73]. Mitral stenosis causes a decrease in effective ventricular filling and systolic dysfunction of the left ventricle, eventually leading to heart failure and death. Artificial mitral valve replacement is considered for patients with symptomatic severe mitral stenosis who either cannot tolerate percutaneous balloon valvuloplasty or have undergone unsuccessful therapy [75]. Similar to aortic stenosis, patients with chronic mitral stenosis tend to be older and have a higher incidence of concomitant diseases such as coronary artery disease and diabetes [76,77]. Patients undergoing mitral valve replacement are typically placed on dual antiplatelet therapy to prevent thromboembolic events [78]. The most common complications associated with this surgery are thromboembolism and acute kidney injury [79]. Other complications include hemodynamic instability after discharge from the hospital, recurrent mitral stenosis, infection at the surgical site, abnormal heart rhythm, paravalvular leak, death, stroke, and heart attack. Treatment of these complications varies depending on the cause and may include antibiotics, blood products, anticoagulation therapy, and diuretics. Prognosis varies based on the underlying cause of the disease and the severity of symptoms prior to surgery.

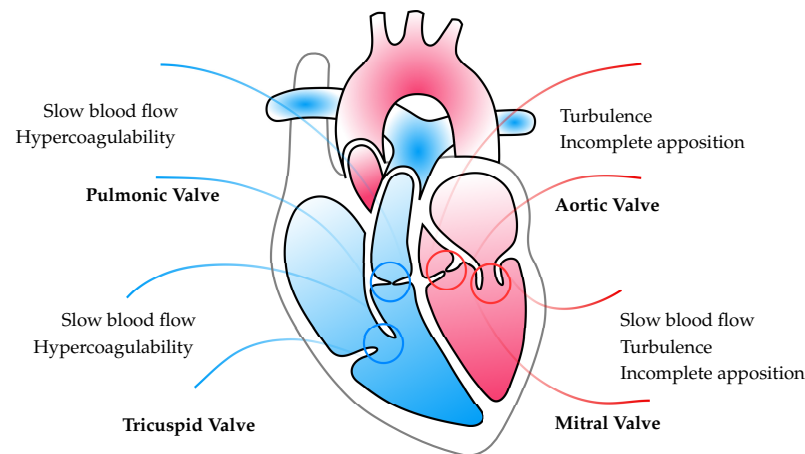


Figure 2. Hemostatic and hemodynamic factors involved in the development of prosthetic valve thromboses. Additional information regarding Slow blood flow [80,81], Hypercoagulability [82,83], Turbulence [84,85], and Incomplete apposition [86,87] can be found through the cited sources. See [2] for a more detailed list of factors involved in prosthetic valve thrombosis.

6. Mechanical Heart Valves Background

Since the first heart valve replacement in 1952, mechanical heart valves have developed over fifty designs differing primarily in valve geometry and material. Mechanical heart valves have three main designs: caged ball valves, tilting disk valves, and bileaflet heart valves [88]. The caged ball design makes use of a metal cage to house a silicone ball. When the heart contracts and causes increased pressure, the ball rises to the top of the cage to prevent forward blood flow. When the pressure decreases and the heart relaxes, the ball falls to the bottom of the cage and allows for blood to flow. This design has a high tendency to cause blood clots and is no longer used. Tilting disk valves are made of metal rings that are covered by fabric upon which the valve is placed. When the chamber pressure drops, the valve opens to allow the flow of blood, and it closes to prevent backflow. The bileaflet valves consist of two semicircular leaflets. This design is considered the least thrombogenic of the mechanical heart valves [89]. Further advancements in mechanical heart valves are being studied for uses such as total artificial hearts, a solution in research to address the dilemma of the limited number of heart transplant options [90,91].

The pros of mechanical heart valves include durability and simplicity of use. These devices are more durable than biological valves and can be used in patients with severe heart disease who are unable to undergo valve replacement with bioprosthetic valves. The simplicity of use also makes them preferred in patients with limited life expectancy. However, one of the major drawbacks is the increased risk of thromboembolism due to the mechanical action of the valves [92] and the tendency for calcification over time [93]. For this reason, mechanical valves are not used in patients with compromised cardiac function and are usually replaced by prosthetic bioprosthetic valves after several years. As a result, many patients who have had a mechanical valve placed face the prospect of having a second valve replacement surgery later in life. The cons of mechanical heart valves include high cost and lack of long-term effectiveness [45]. Mechanical valves require periodic replacement because of wear and deterioration over time. This makes these valves expensive over the long term when compared to biological valves which require only occasional replacement. In addition, mechanical valves need to be replaced more often because they are less effective at preventing blood clots and are less tolerant of blood thinning medication. For these reasons, patients taking anticoagulants have a higher chance of developing a blood clot that could lead to stroke or death if they undergo a surgical procedure to replace their mechanical valve with a biological one.

7. Thromboembolism and the Need for Anticoagulation

The majority consensus among researchers concludes that patients with mechanical heart valves have favorable outcomes with lesser need for reoperation [94]. As mentioned

earlier, mechanical heart valves carry a greater risk of thromboembolism [95]. The mechanism behind the thrombogenic nature of mechanical heart valves can best be explained by Virchow's triad. Virchow's triad explains the factors that contribute to thrombus formation, which include venous stasis, endothelial injury, and hypercoagulable state [96]. Endothelial injury can occur from a lack of prosthetic biocompatibility between the prosthetic valve and the suture zone. In addition, turbulent flow can lead to stasis and ultimately result in thrombus formation [97]. Furthermore, the use of mechanical heart valves poses a significant risk for thrombosis and necessitates lifelong anticoagulation. Optimally managing anticoagulation therapy is vital in the postoperative period. Over-anticoagulation can pose a hemorrhagic risk while under-anticoagulation can pose a risk for thrombosis. Addressing the risk of thrombosis must be customized to the patient based on their individual presentation and medical risk factors [98].

Additionally, anticoagulant management must be monitored on a regular basis to ensure optimal results [99,100]. It is important to note that no clinical trials have demonstrated the superiority of one surgical technique over another in terms of the long-term durability of the prosthesis or clinical outcomes. It is therefore up to the surgeon to select the technique that best meets the patient's specific needs. Mechanical heart valves are superior to bioprosthetic valves in terms of durability; however, patients experience an increased risk of developing stroke, and long-term anticoagulant therapy is required [40]. With regard to mitral stenosis, older-generation mechanical valves have higher regurgitant volumes compared to newer-generation valves [101]. Thus, for patients with significant regurgitation secondary to mitral valve disease, a bileaflet mechanical valve is the preferred treatment option. However, patients with mild-to-moderate regurgitation should opt for a bileaflet mechanical valve to minimize the risk of future valve failure [102]. Therefore, it is imperative to carefully assess each patient's condition before deciding which type of valve to use. With regard to mitral valve repair techniques, the most commonly used procedure is annuloplasty ring implantation. An annuloplasty ring can be used to reduce the size of the annulus by reshaping the valve leaflets back into their normal anatomic position. This procedure can be performed either endoscopically or via an open approach. Various different techniques have been developed for annuloplasty ring implantation. These include traditional anterior leaflet relocation techniques as well as novel septal-based approaches that involve the use of flexible cables and anchor devices [103]. Mitral valve repair is often performed in patients with low ejection fraction due to the presence of comorbidities that preclude the placement of a mechanical valve. Furthermore, mitral valve repair may be preferable in patients who do not have sufficient coaptation between the anterior and posterior leaflets of the valve after native valve replacement [104]. Although the treatment of mitral valve regurgitation is largely successful, mortality remains high in the absence of medical therapy in these patients [105].

8. Anticoagulants and Their Reversal Agents

Anticoagulants are medications that act upon the body's coagulation cascade, a system responsible for the clotting of blood. Through acting on different enzymes and mediators of the cascade, anticoagulants are designed for prophylaxis and prevention of clots. The reversal of anticoagulants is essential in the case of an adverse reaction, such as an inappropriate hemorrhage. As such, different reversal strategies are available for many of the anticoagulants that are used [106]. Some may be administered systemically while others require IV administration. The reversal of anticoagulants can be a challenging process in clinical practice and can typically be safely accomplished. There are three main types of anticoagulants that are clinically used today—vitamin K antagonists (warfarin), direct thrombin inhibitors, and direct factor Xa inhibitors. Of these three types, warfarin is the only one that can be reversed using an antidote.

Warfarin is an anticoagulant agent that inhibits the Vitamin K gamma-carboxylation of coagulation factors II, VII, IX, and X, thus preventing these factors from effectively being able to coagulate blood. Its reversal involves the administration of Vitamin K, either

orally or intravenously, which will allow for the de novo synthesis of coagulation factors. The INR, a measure of the extrinsic pathway of coagulation that involves the cofactors inhibited by warfarin, is increased with its administration. The administration of Vitamin K intravenously begins to reduce INR in 1–2 h and its effects peak in 4–6 h. Fresh frozen plasma (FFP) is derived from donor blood, and it contains coagulation factors. It can be administered to replete the coagulation factors to reverse the effects of warfarin. However, it must first undergo ABO testing. FFP has an onset of action of 13–48 h after administration. Prothrombin complex concentrates (PCC) contain nonactivated coagulation factors and are available in three and four-factor concentrates. PCC has an onset of reversal within 10–30 min of administration [107–109]. Activated prothrombin complex concentrate (aPCC) contains both factor Ia and Factor Va, and has an immediate effect on anticoagulation [110].

Heparin is an anticoagulant that binds to antithrombin. This complex then irreversibly binds to coagulation factor II and inhibits the coagulation pathway through effects on factors II, Xa, IXa, XIa, and XIIa. Low molecular weight Heparins (LMWH) are a class of anticoagulants that are depolymerized heparins, thus having a smaller molecular weight. This class indirectly inhibits coagulation factor Xa by activating antithrombin III. Fondaparinux is a synthetic molecule that selectively inhibits factor Xa. It varies from heparin and LMWH by having no effect on factor II. The reversal agent for heparin is protamine sulfate [111]. Protamine sulfate, a positively charged molecule, is capable of reversing the inhibition of antithrombin III. While effective with heparin, protamine sulfate is only 60% effective at reversing LMWH. Fondaparinux is not reversed by protamine. Andexanet alfa, a recombinant factor Xa, is effective at reversing factor Xa inhibitors such as fondaparinux [112]. Aripazine, a synthetic molecule with factor Xa activity, has shown effectiveness against factor Xa inhibitors. In a trial with 40 human volunteers, it was shown to completely reverse the effects of LMWH [113]. In addition to Aripazine, PPC, and FFP, Dabigatran, a direct thrombin inhibitor, has been shown to be reversed by Idarucizumab, a monoclonal antibody [114–119]. Anti-Xa agents may be more effective than anti-IIa agents in patients with acute coronary syndrome (ACS) who are receiving dual antiplatelet therapy. Clinical trials suggest that the use of direct thrombin inhibitors as alternatives to oral anticoagulation may increase the risk of bleeding in patients with ACS undergoing percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) [120]. However, in clinical practice, some investigators have observed that outcomes of patients with ACS using dabigatran or rivaroxaban did not appear to be compromised when its use was compared to conventional therapies (heparin and warfarin) [121]. Future studies are needed to evaluate the efficacy of direct thrombin inhibitors in these patients.

Platelets play a significant role in creating clots. Agents such as aspirin, which inhibits the enzymes COX-1 and COX-2, as well as P2Y₁₂ receptor inhibitor agents such as clopidogrel, ticlopidine, and prasugrel are used to prevent platelet aggregation. Desmopressin, which increases the concentration of Factor VIII, has been shown to be a useful agent in reversing antiplatelet agents [115]. Antibiotics have been shown to reduce the risk of endocarditis in patients with prosthetic valves [122], but the evidence is lacking for routine use in all patients with prosthetic valves. Non-steroidal anti-inflammatory drugs should be avoided if possible because prolonged use has been associated with accelerated degeneration of prosthetic valve leaflets [123]. Cardiac surgery is a high-risk procedure that involves the use of multiple medications including anesthetic agents, anticoagulants, antibiotics, antiarrhythmics, diuretics, analgesics, muscle relaxants, and antiemetics. These medications can increase the risk of bleeding.

A newer anticoagulation agent, Factor XI inhibitors, has been introduced as a potentially favorable alternative to the current options available. Factor XI inhibitors work on the intrinsic pathway of the coagulation cascade and are activated by Factor XIIa. The promising aspect of using Factor XI inhibitors is that, due to their impact on the intrinsic pathway, they can achieve the goal of avoiding thrombosis while reducing bleeding risk. Furthermore, although factor XI plays a significant role in thrombus formation, its presence has little impact on homeostasis [124]. This new method of selectively targeting the intrinsic

pathway paves the way for promising innovations in anticoagulation therapy and has potential use in critical patient collectives such as those discussed in this paper. Although it is a relatively new agent that has been brought forth for discussion, several trials have been conducted on the use of Factor XI inhibitors, such as Osocimab, in preventing venous thromboembolism. One study by Weitz and his team found that preoperatively using a Factor XI inhibitor to prevent VTE in patients undergoing total knee replacement surgery had similar or greater success rates compared to enoxaparin with lower bleeding rates [125]. Such studies present an optimistic outlook on the future of anticoagulation therapy and the utilization of Factor XI inhibitors.

9. Efficacy of Different Anticoagulant Regimens with Mechanical Heart Valves

Mechanical heart valves create a prothrombotic state that necessitates the use of anticoagulants. Warfarin is the preferred anticoagulant treatment for patients who have mechanical heart valves [126–128]. A trial by Eikelboom et al. that compared Dabigatran with Warfarin in patients with mechanical heart valves found that Dabigatran was associated with a significantly increased risk of adverse bleeding events. They concluded that Dabigatran showed no benefit while demonstrating increased risk in their patients who had undergone either mitral or aortic valve replacement [129]. Sun et al. concluded that it would be reasonable to begin Warfarin therapy soon after the heart valve replacement procedure once hemostasis is secure, within 6–24 h after surgery [130]. In a randomized control trial, Kovac et al. similarly found that bridging therapy, using another anticoagulant to serve as a “bridge” until the slower-acting warfarin is administered, was not found to have any benefits in patients immediately after mechanical heart valve replacement. They studied bridging with dalteparin [131]. Puskas et al. concluded that patients with mechanical heart valves who were maintained on the dual antiplatelet therapy of aspirin and clopidogrel experienced higher rates of thromboembolism and valve thrombosis as compared to controls on warfarin [132]. However, aspirin can be used as an effective adjunct to warfarin. Pengo et al. concluded that low-dose warfarin with aspirin therapy was as effective as mid-high-intensity warfarin during the first six months after mechanical heart valve replacement [133]. A controlled trial by Turpie et al. showed that aspirin in addition to warfarin reduced mortality and embolism in patients with mechanical and bioprosthetic heart valves [134]. Similarly, Larson et al. demonstrate in a meta-analysis of over 4000 patients from controlled trials, that adding low-dose aspirin to warfarin reduces mortality and reduces the risk of strokes [135]. Analyses of data from other studies suggest that the bleeding risk from dual antiplatelet therapy is less than that of warfarin or aspirin alone and appears to be similar to warfarin plus clopidogrel [136]. Schaefer et al. suggest that concurrent use of warfarin and aspirin therapy in patients without a heart valve replacement or recent acute coronary syndromes is associated with an increased risk of bleeding and related hospitalization [137]. The authors concluded that the addition of aspirin to warfarin did not increase bleeding, but patients should be instructed to seek medical advice if bleeding develops.

Patients maintained on warfarin therapy need continuous monitoring of the INR to ensure that the anticoagulation is within the therapeutic range. Dauphin et al. and Thompson et al. compared laboratory-monitored INR as opposed to patients monitoring the INR themselves in what is termed self-monitored INR. They both concluded that patients with mechanical heart valves with self-INR monitoring led to better stability of the INR in the therapeutic range [138,139]. Zhu et al. similarly studied an internet-based INR monitoring system in which patients can use telehealth to track INR and compared it to a control group using conventional INR monitoring through laboratories. They similarly found that internet-based INR monitoring had a significantly higher percentage of patients within the therapeutic range [140]. Henegan et al. conducted a meta-analysis with data from 6417 patients and concluded that self-monitoring of INR is a safe option for patients of all ages [141]. Mair et al. also concluded that self-management of anticoagulation after heart valve replacement is superior to conventional methods [142]. Matchar et al. conclude

that self-testing at home did not have any significant advantages in preventing thrombotic events in comparison to clinical testing and therefore cannot state an advantage for at-home INR testing [143]. Zhang et al. also proposed that measuring D-dimer, a protein level that elevates in the setting of blood clots, can help guide the intensity of anticoagulation treatment. In their prospective controlled clinical study, 748 patients with mechanical heart valves were followed and the group concluded that D-dimer-based adjustments in anticoagulation intensity led to a lower incidence of thrombotic events [144].

Pregnant women with mechanical heart valves are at an increased risk for thrombosis because pregnancy itself is associated with hypercoagulation. This risk is further complicated as warfarin, the drug of choice for anticoagulation in mechanical heart valves, is considered to be teratogenic to the fetus [145,146]. In a prospective trial, Quin et al. found that an adjusted dose of LMWH was a therapeutic option in women with mechanical heart valves as 11 out of 12 pregnancies resulted in live births. However, the dose of LMWH needs to be closely monitored as there was a thrombotic event associated with sub-therapeutic anticoagulant levels [147]. Saeed et al. similarly conducted a prospective trial analyzing LMWH therapy during pregnancy in patients with mechanical heart valves. None of the women developed valvular thrombosis, and the study found that LMWH should be dosed such that anti-Xa levels remain at 1.0–1.2 U/mL [148]. Lee et al. retrospectively compared pregnant women with mechanical heart valves receiving LMWH therapy as opposed to warfarin therapy. The patients on LMWH had a significantly higher percentage of live births and healthy babies as opposed to the warfarin group [149]. Dos Santos et al. compared two medical centers, one of which maintained women with mechanical heart valves on LMWH throughout the pregnancy, and another that began the pregnancy with LMWH and switched to warfarin after the first trimester. They concluded that warfarin remains the most effective option for preventing valve thrombosis while LMWH offers the greatest chance of live birth without significant malformation of the fetus [150]. In a systematic review covering 120 clinical trials and case reports, Seshadri et al. concluded that LMWH can be used as a safe anticoagulant in pregnant females with mechanical heart valves [151]. Furthermore, in a case report by Yan et al., a patient with gallbladder cancer and hepatic metastases who could not remain on warfarin therapy was successfully maintained on LMWH therapy, providing the potential for therapy other than warfarin even in non-pregnant patients [152].

10. Risk for Intracranial Hemorrhage with Anticoagulants and Its Management

Intracranial hemorrhage in the setting of mechanical heart valves is a situation complicated by the opposing natures of the problems. An ICH is a situation in which bleeding in the brain would benefit from coagulation and clotting of the bleeding [153]. Mechanical heart valves are the opposite; they create a prothrombotic state, and therapy is geared toward preventing valve thrombosis so that an embolism does not occur elsewhere in the body. The lack of evidence and guidelines further complicate the issue [154]. In a cross-sectional study administered to neurologists and neurosurgeons, Alkherayf et al. concluded that a wide variation existed in the approaches of patients with mechanical heart valves with ICH, likely influenced by patient and valve-related factors [155]. Romualdi et al. concluded that stopping anticoagulant therapy for as much as fourteen days is safe in the setting of ICH with a mechanical heart valve [156]. In a review of thirty-nine patients' cases of ICH with mechanical heart valves, Wijdsicks et al. similarly concluded that temporary interruption of anticoagulants for up to two weeks is safe in patients without prior history of embolic events [157]. In a case report, Shah et al. withheld warfarin in a patient with ICH and mechanical heart valves while the patient underwent a decompressive craniotomy. The medical team resumed anticoagulation five days postoperatively and the patient remained well on discharge and suffered no acute events in 12 weeks of monitoring [158]. In a review, Flaherty et al. conclude that compared to other patients with ICH, those on anticoagulation are at greater risk of hematoma expansion and thus should have their anticoagulation reversed [159]. In a retrospective cohort study, Kuramatsu et al. found

that the reversal of anticoagulation within 4 h of ICH was associated with lower rates of hematoma expansion [160]. In a retrospective series, Bashline et al. analyzed 63 patients with ICH and mechanical heart valves and concluded that withholding anticoagulation for at least ten days was not associated with any thrombotic events due to valve thrombosis [161]. Colantino et al. also cite hematoma expansion as the greatest risk to continuing anticoagulants with an ICH and recommend that anticoagulants not be considered for the first twenty-four hours after an ICH [162].

The extent of anticoagulation also plays a role in the complications of ICH. In a retrospective analysis, Flaherty et al. found that warfarin was associated with larger ICH volume, but only when the INR was observed to be greater than 3 [163]. In a prospective study, Flibotte et al. found warfarin to be the sole predictor of hematoma expansion [164]. During pregnancy, a woman is in a hypercoagulable state. This complicates the management of an ICH with mechanical heart valves. In a case report, Oguz et al. treated a pregnant woman with ICH and mechanical heart valves by reversing anticoagulation while her hematoma was surgically evacuated. Based on their approach, Oguz et al. recommend the complete reversal of anticoagulants in a pregnant patient with mechanical heart valves who presents with ICH [165]. It is not always the case for the reversal of anticoagulation to be the approach to an ICH in the setting of mechanical heart valves. In a patient with mechanical heart valves and an ICH, Maingi et al. considered the risks and benefits of withholding anticoagulation and adjusted the anticoagulants to achieve an INR of 1.5 to minimize the risks of thromboembolic events [166]. In considering the reversal of anticoagulants, Eikelboom et al. propose 4-factor PCC as the standard of care in patients with warfarin-associated ICH [167]. In a multicenter prospective trial, Steiner et al. concluded that 4-factor PCC was superior to FFP in normalizing the INR and with faster INR normalization [168]. The evaluation of an appropriate time window in which to restart anticoagulation after pausing the regimen has been the subject of numerous trials and investigations. Kuramatsu et al. studied the outcomes of anticoagulation resumption amongst mechanical heart valve patients who experienced hemorrhage in a multi-center cohort study. The investigation concluded that restarting anticoagulation less than two weeks after ICH was associated with increased hemorrhagic complications [154]. Alkherayf et al. conclude in their meta-analysis that an optimal timeframe in which to resume anticoagulation following ICH in a patient with mechanical heart valves is inconclusive; however, they do similarly state that delayed restart is protective against the recurrence of hemorrhage [169]. In a case series, Wan et al. noted that the time to reinstitute therapy did not correlate with outcomes and associated thromboembolic risk [170]. Despite these risks, resuming anticoagulation should be considered in all patients [171]. Further research and clinical trials can assist with the development of standards and protocols for reinitiating anticoagulant therapy following ICH in patients with mechanical heart valves.

11. Discussion

Mechanical heart valves have increasingly become the preferred treatment for patients with valvular heart disease because they eliminate the associated complications associated with the use of natural valves such as the re-operation rate, thromboembolic events, and infective endocarditis. The use of mechanical valves has led to a significant decrease in the mortality of patients with valvular heart disease. However, they are also associated with a risk of systemic thromboembolism including pulmonary embolism and deep vein thrombosis. Although the risk of stroke is low, there is a risk of neurologic events such as transient ischemic attacks in patients with mechanical heart valves. In addition, there is an increased risk of bleeding with the use of mechanical valves compared to those with natural valves. The increased risk is due to the design of the device, which allows blood to flow around the disc in only one direction. This causes some red blood cells to collide with the device and damage them. This increases the risk of the formation of blood clots in the bloodstream. These clots can block arteries or veins and cause serious problems if they travel to the lungs or heart. As a result, patients receiving mechanical heart valves

must be carefully monitored for signs and symptoms of bleeding and thrombus formation. They require frequent blood tests to monitor their coagulation profile to ensure that they are not developing a blood clot in their bloodstream. They may also receive anticoagulant medications to help prevent the formation of a blood clot and prevent damage to their internal organs. Anticoagulants are given to prevent the formation of blood clots in the bloodstream. They can also reduce the risk of a stroke in patients with a prosthetic heart valve. However, these medications may also increase the risk of bleeding in some patients. Patients receiving a mechanical heart valve need to be closely monitored by their doctor to detect early signs of potential complications such as thromboembolism or hemorrhage. This will allow them to receive early treatment and avoid the potential for serious complications. Patients also need to be closely monitored for changes in their vital signs, especially during a hospital stay. Any signs of illness or deterioration in their health should be reported to the physician to ensure they are receiving the appropriate treatment. Finally, it is important to keep in mind that living with a heart valve replacement is a long-term commitment. It is essential to continue taking all of the medications as prescribed to avoid developing another complication. Doing this will help patients maintain healthy lives and avoid developing new conditions. With proper treatment, most patients with a mechanical valve will be able to lead healthy and active lives with minimal complications for the remainder of their lives. In some cases, however, a patient's health may decline over time due to factors such as poor nutrition or lack of exercise. In these cases, a patient may need a redo valve or even a heart transplant to avoid the onset of more severe complications.

In the situation that a patient for whom anticoagulants are necessitated due to mechanical heart valves is found to have an ICH, the evidence reviewed in this article points to the direction of withholding anticoagulation until the hemorrhage is resolved. Brain hemorrhages pose many life-threatening and altering complications such as midline shift. Addressing this immediate emergency comes with a decision to withhold anticoagulation and risk the ischemic complications of valve thrombosis. Further studies and meta-analyses are warranted to create guidelines for clinicians to follow in a situation where the management of these two serious complications contradicts one another. This will further our understanding of how these choices affect patient morbidity and mortality outcomes and determine what is an acceptable risk level when faced with such situations. Furthermore, the ability to predict with greater certainty the impact of anticoagulation therapy on the risk of thromboembolic events and bleeding should be identified so that the need for this therapy can be more accurately determined in the appropriate clinical setting. Further research is needed to identify the optimal duration and level of anticoagulation required to minimize the risk of both bleeding and thromboembolic complications in patients with mechanical heart valves.

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Abbreviations

The following abbreviations are used in this manuscript:

US	United States
ICH	Intracranial Hemorrhage
AV	Atrioventricular
TAVR	Transcatheter Aortic Valve Replacement
IV	Intravenous
TMVR	Transcatheter Mitral Valve Replacement
FFP	Fresh Frozen Plasma
PCC	Prothrombin Complex Concentrates
LMWH	Low Molecular Weight Heparins
ACS	Acute Coronary Syndrome
PCI	Percutaneous Coronary Intervention
CABG	Coronary Artery Bypass Graft
INR	International Normalized Ratio
VARC	Valve Academic Research Consortium
BVD	Bioprosthetic Valve Dysfunction
BVF	Bioprosthetic Valve Failure
AVA	Aortic Valve Area
DVI	Doppler Velocity Index
AR	Aortic Regurgitation
VTE	Venous Thromboembolism

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