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Anticoagulation Failure: Deep Vein Thrombosis Despite Severe Coagulopathy in a Patient with Mechanical Heart Valves

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A B S T R A C T

The management of patients with mechanical heart valves on chronic warfarin therapy is a delicate balance between preventing thromboembolism and avoiding hemorrhage. The emergence of an acute thrombotic event despite a critically elevated International Normalized Ratio (INR) represents a profound clinical paradox and a significant management dilemma. This report details such a case, offering a deep exploration of the underlying pathophysiology. A 34-year-old female with dual mechanical heart valves for severe rheumatic heart disease, maintained on a variable-dose warfarin regimen, presented with acute deep vein thrombosis (DVT) of the right lower limb. Her INR was critically elevated at 7.78. A detailed history revealed recent poor oral intake followed by inconsistent dietary changes, contributing to extreme INR lability. Diagnostic investigations confirmed a non-occlusive, distal DVT. The management strategy involved immediate cessation of warfarin without the administration of reversal agents, prioritizing the prevention of mechanical valve thrombosis. The INR was allowed to normalize gradually over 72 hours, with concurrent clinical improvement. Warfarin was cautiously re-initiated, and a long-term management plan focusing on intensive education and monitoring was established. In conclusion, this case demonstrates that a supratherapeutic INR does not confer absolute protection against venous thrombosis in patients with potent, underlying prothrombotic risk factors. The principles of Virchow's triad—particularly venous stasis from chronic heart failure and a persistent hypercoagulable state from prosthetic valves and systemic inflammation—can override the systemic anticoagulant effect measured by the INR. Management of this paradox requires a highly individualized, pathophysiology-driven strategy that carefully weighs the competing risks of hemorrhage, thrombus extension, and catastrophic valve thrombosis.

1. Introduction

The advent of prosthetic valve replacement surgery has fundamentally altered the natural history for patients with severe valvular heart disease, offering a dramatic improvement in prognosis at the cost of a lifetime of complex medical management.[1] For individuals with mechanical heart valves, lifelong anticoagulation with a vitamin K antagonist (VKA), most commonly warfarin, is the undisputed cornerstone of therapy. This strategy is essential to mitigate the risk of devastating thromboembolic events, including valve thrombosis and systemic embolism, which arise from the inherent thrombogenicity of the prosthetic material.[2]

However, warfarin is a notoriously difficult medication to manage. It possesses a narrow therapeutic window, and its dose-response relationship is subject to significant inter-individual and intra-individual variability, influenced by genetic polymorphisms (CYP2C9, VKORC1), concomitant medications, and dietary intake of vitamin K.[3] The therapeutic goal is to maintain the International

Normalized Ratio (INR) within a specific target range—typically 2.5 to 3.5 for patients with mechanical mitral and aortic valves—a perpetual balancing act for both patient and clinician. An INR below this range elevates the risk of life-threatening thrombosis, while an INR above this range exponentially increases the danger of major, and potentially fatal, hemorrhage.[4,5]

Separate from arterial thromboembolism, venous thromboembolism (VTE), which encompasses deep vein thrombosis (DVT) and its feared complication, pulmonary embolism (PE), constitutes a major global health burden. The pathogenesis of VTE is classically understood through the lens of Virchow's triad: venous stasis, endothelial injury, and a hypercoagulable state.[6,7] Patients with significant underlying cardiac pathology, such as chronic heart failure and atrial fibrillation, frequently seen in long-standing rheumatic heart disease, harbor multiple potent risk factors for VTE. Reduced cardiac output and systemic venous congestion promote profound stasis in the lower extremities, while the associated systemic inflammation and neurohormonal activation contribute to a chronic, low-grade hypercoagulable state.

The clinical scenario becomes exceptionally complex and precarious when a patient on chronic, seemingly effective anticoagulation develops an acute VTE. It evolves into a true therapeutic paradox when this new thrombotic event occurs in the context of a supratherapeutic INR, a state indicating excessive anticoagulation and a high intrinsic bleeding risk. This situation confronts clinicians with a formidable dilemma: how does one manage an acute thrombus, which itself requires anticoagulation, in a patient who is simultaneously at high risk of bleeding from the very class of medication needed? Standard treatment algorithms for DVT are not designed for such a paradoxical presentation, necessitating a nuanced, individualized approach grounded in a deep understanding of coagulation pathophysiology and risk stratification.[8-10]

The novelty of this case report lies in its detailed exploration of this clinical paradox, dissecting the intricate pathophysiological mechanisms that can permit localized thrombus formation despite a state of profound systemic coagulopathy. The aim of this report is to detail the diagnostic and therapeutic challenges encountered in managing acute DVT in a patient with dual mechanical prosthetic heart valves and severe warfarin-induced coagulopathy, and to provide a comprehensive, pathophysiology-driven framework for clinical reasoning in this high-stakes scenario. By presenting a comprehensive account of the case and an in-depth analysis of the underlying principles, we seek to provide valuable insights for clinicians navigating this ultimate "anticoagulation tightrope."

2. Case Presentation

A 34-year-old Indonesian female presented to the emergency department of Mangusada Regional Hospital with a chief complaint of progressive right leg swelling, discomfort, and extensive bruising that had developed spontaneously over the preceding week. The patient described the swelling as initially subtle but progressing to involve the entire leg from the ankle to the knee. It was accompanied by a constant, dull, aching pain and a sensation of profound heaviness, which was exacerbated by standing and partially relieved by leg elevation. She denied any history of preceding trauma, surgery, prolonged immobilization, or recent long-distance travel. When questioned about systemic symptoms, she explicitly denied experiencing chest pain, shortness of breath, palpitations, or hemoptysis. While she reported no active, overt bleeding from sites such as the nose or gums, or in the gastrointestinal tract (hematuria, melena), she did note an increased propensity for bruising on her limbs over the past several weeks (Table 1).

The patient's medical history was significant and complex, rooted in a childhood diagnosis of severe rheumatic heart disease (RHD). This chronic inflammatory condition led to progressive, multi-valvular dysfunction, culminating in a definitive cardiac surgical procedure two years prior (in 2023). She underwent a dual mechanical valve replacement

(St. Jude Medical Masters Series, 25mm in the mitral position and 19mm in the aortic position), a tricuspid valve annuloplasty repair (Edwards Lifesciences MC3 Annuloplasty Ring, 28mm), and a concomitant left atrial appendage exclusion.

Table 1. Clinical findings on admission

A Comprehensive Summary of the Patient's Initial Presentation

Patient Profile

Age & Sex	Primary Diagnosis	Key Complicating Factor
34-year-old Female	Acute Deep Vein Thrombosis	Severe Warfarin Coagulopathy

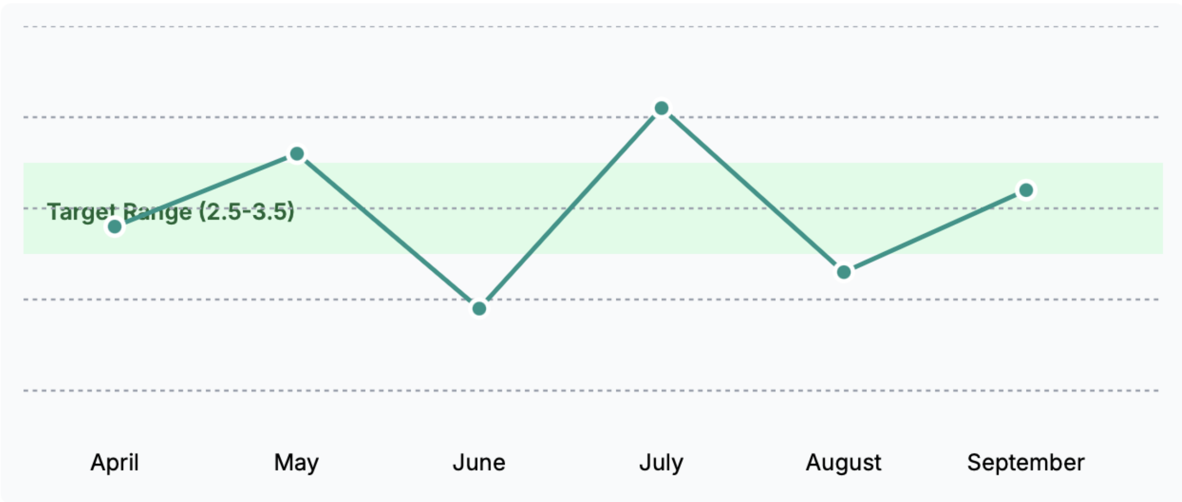
PARAMETER	RESULT	REFERENCE RANGE	INTERPRETATION
Coagulation Profile			
International Normalized Ratio (INR)	7.78	2.5 – 3.5 (Therapeutic)	Critically High
Prothrombin Time (PT)	81.5 sec	11.0 – 13.5 sec	Critically High
Activated PTT (aPTT)	45.2 sec	25.0 – 35.0 sec	High
D-dimer	1840 ng/mL	< 500 ng/mL	Markedly Elevated
Complete Blood Count			
Hemoglobin	11.8 g/dL	12.0 – 16.0 g/dL	Slightly Low
Platelet Count	210,000/µL	150,000 – 450,000/µL	Normal
Metabolic & Cardiac Biomarkers			
Creatinine	0.9 mg/dL	0.6 – 1.2 mg/dL	Normal
NT-proBNP	1250 pg/mL	< 300 pg/mL	Very High

Post-operatively, her course was complicated by the development of persistent atrial fibrillation and symptomatic heart failure with a mildly reduced ejection fraction (HFmrEF). Her medication regimen was extensive, including lifelong anticoagulation with warfarin. Due to a documented history of significant INR lability, her warfarin dose was on a complex, variable schedule: 4 mg daily on Sunday, Monday, Wednesday, Thursday, and Friday, and 3 mg on Tuesdays and Saturdays. To objectively characterize her INR control, a review of her records from the preceding six months was conducted, as detailed in Table 2.

Table 2. Patient INR History

A 6-Month Retrospective Analysis Prior to Admission

INR Fluctuation Over Time



DATE OF TEST	INR VALUE	STATUS	CLINICAL NOTE
April 15, 2025	2.8	Therapeutic	Value within target range.
May 12, 2025	3.6	Supratherapeutic	Slightly above range; dose adjusted.
June 18, 2025	1.9	Subtherapeutic	Below target; dose increased.
July 21, 2025	4.1	Supratherapeutic	Significantly high; held one dose.
August 19, 2025	2.3	Therapeutic	Returned to subtherapeutic range.
September 22, 2025	3.2	Therapeutic	Value within target range.

Her other maintenance medications included bisoprolol 2.5 mg once daily, candesartan 4 mg once daily, spironolactone 25 mg once daily, and furosemide 40 mg once daily. She had a remote history of an ischemic stroke in 2019 with minor residual neurological deficits. When initially questioned about recent lifestyle changes, the patient reported good medication adherence but admitted to recent inconsistencies in her diet, including an increased consumption of green leafy vegetables. This history was initially perplexing, as increased vitamin K intake would be expected to lower, not raise, the INR. Upon careful and empathetic re-questioning, a more nuanced sequence of events emerged. The patient clarified that approximately ten days prior to presentation, she had suffered from a minor viral illness with associated malaise and significantly reduced appetite, during which her oral intake was poor for about a week. Following this period, feeling weak, she attempted to "catch up" on her nutrition by consuming large portions of vegetable-rich meals in the three days immediately preceding her hospital visit. This revised history provided a more plausible explanation for the extreme INR elevation: an initial sharp rise due to poor intake and VKA potentiation, followed by a failed, patient-led attempt at dietary correction.

On arrival, the patient was alert, oriented, and in mild distress from her leg pain. Her vital signs were: blood pressure 88/60 mmHg (noted to be at the lower end of her baseline), heart rate 97 beats per minute (irregularly irregular), respiratory rate 18 breaths per minute, temperature 37.1°C, and oxygen saturation 98% on room air. The cardiovascular examination was notable for the distinct, sharp, high-pitched metallic S1 and S2 clicks, characteristic of her prosthetic valves. The rhythm was tachycardic and irregularly irregular, consistent with atrial fibrillation. A grade II/VI holosystolic murmur was audible at the lower left sternal border, unchanged from her baseline and consistent with known mild tricuspid regurgitation. There was no new murmur, gallop, or pericardial rub to suggest acute valve dysfunction or pericarditis. Her jugular venous pressure was estimated at 8 cm H_2O, indicating mild central venous pressure elevation.

Examination of the lower extremities revealed marked asymmetry. The right lower limb was visibly swollen from the ankle to the tibial tuberosity. Calf circumference measurement was 38 cm on the right compared to 33 cm on the left. There was 2+ pitting edema extending to the mid-shin. Large, non-tender ecchymoses in various stages of evolution (ranging in color from deep purple to greenish-yellow) were present over the anterior and medial aspects of the right calf. The limb was warm to the touch, and there was exquisite tenderness to deep palpation of the calf muscles (a positive Moses' sign). Homans' sign was negative. The dorsalis pedis and posterior tibial pulses were palpable and symmetric bilaterally. The remainder of the physical examination was unremarkable.

Urgent laboratory investigations were performed. The coagulation profile was strikingly abnormal, revealing a critically elevated INR of 7.78 (therapeutic target: 2.5-3.5) and a prothrombin time (PT) of 81.5 seconds. The D-dimer level was significantly elevated at 1840 ng/mL (reference <500 ng/mL), suggesting active fibrin formation and degradation consistent with acute thrombosis. Her complete blood count showed a mild normocytic anemia, but her platelet count was normal. Renal and liver function tests were within normal limits, making cardiac hepatopathy or renal failure unlikely contributors to the coagulopathy. Her NT-proBNP was significantly elevated, confirming a state of chronic myocardial stress and volume overload consistent with her heart failure diagnosis (Table 1).

An urgent Doppler ultrasound of the right lower extremity was performed to confirm the clinical suspicion of DVT. The examination revealed a lack of complete compressibility of the right anterior tibial and peroneal veins upon transducer pressure. Within these distal segments, intraluminal echogenic material was visualized, consistent with acute deep vein thrombosis. The thrombus was characterized as non-occlusive, with some residual color flow demonstrated around the material. Importantly, the common femoral, femoral, and popliteal veins were patent, compressible, and showed normal flow augmentation with calf compression. A transthoracic echocardiography (TTE) was performed to urgently assess cardiac function and, critically, the status of the prosthetic valves, given the anticoagulation derangement. The mechanical aortic and mitral valves were well-seated with normal-appearing, non-restricted disc motion. Doppler interrogation revealed mean gradients across the aortic valve of 12 mmHg and across the mitral valve of 5 mmHg, both well within the normal range for these prostheses, effectively ruling out obstructive valve thrombosis.

There was no evidence of paravalvular leak. The left ventricular ejection fraction was calculated at 43.7% (confirming HFmrEF). The left atrium was severely enlarged. The previously repaired tricuspid valve showed mild residual regurgitation, and the estimated pulmonary artery systolic pressure was 35 mmHg. The patient was diagnosed with acute right lower extremity distal DVT in the setting of severe warfarin-induced coagulopathy. This diagnosis presented a significant therapeutic challenge, requiring an immediate, carefully balanced intervention. She was admitted to the cardiac care unit for continuous hemodynamic monitoring.

The primary management steps were as follows; (1) Anticoagulation Management: Warfarin was immediately discontinued. The central clinical decision was whether to administer an active reversal agent. Given that the patient was hemodynamically stable and exhibited no signs of major or life-threatening bleeding (such as intracranial or gastrointestinal hemorrhage), the decision was made to pursue a conservative strategy. This involved withholding warfarin and allowing the INR to decline naturally without administering Vitamin K or prothrombin complex concentrate (PCC). This approach was chosen to avoid a precipitous drop in INR, which could create a rebound hypercoagulable state and place her mechanical valves at an unacceptably high risk of catastrophic thrombosis; (2) Monitoring and Supportive Care: The patient's INR was monitored every 12 hours to track its decline. Her maintenance heart failure medications were continued. She was placed on bed rest with the affected leg elevated above the level of the heart to promote venous return and reduce edema.

Over the next 72 hours, the patient's clinical condition and laboratory parameters improved steadily. The leg swelling and tenderness gradually subsided. She developed no new signs of bleeding or thrombosis. The serial INR measurements showed a predictable, progressive decline: 5.20 at 24 hours, 2.80 at 48 hours, and 1.51 at 72 hours. Once the INR fell to 1.51 (below the therapeutic range), the risk of prosthetic valve thrombosis became the predominant clinical concern, outweighing the risk from the stable, distal DVT. After careful deliberation, warfarin was cautiously re-initiated at a lower, modified daily dose of 3 mg. The patient remained hospitalized for two additional days for close INR monitoring. She received intensive, repeated counseling from a clinical pharmacist regarding warfarin therapy, the critical importance of a consistent diet, the signs of both bleeding and thrombosis, and the absolute necessity of adhering to her scheduled INR checks. She was discharged on day five with a stable INR of 2.3. The patient was followed closely in the outpatient anticoagulation clinic. Her follow-up course is summarized in Table 2. Her leg swelling completely resolved within two weeks. At her six-month follow-up, she remained free of any recurrent thrombotic or bleeding complications, with her INR control notably improved.

3. Discussion

This case presents a compelling clinical paradox that strikes at the very heart of our understanding of hemostasis and its therapeutic manipulation: the de novo development of an acute deep vein thrombosis (DVT) in a patient with a profound, iatrogenic systemic coagulopathy, evidenced by a critically elevated International Normalized Ratio (INR) of 7.78. Such an event fundamentally challenges the simplistic, albeit common, clinical assumption that a high INR provides absolute and uniform protection against all thrombotic phenomena. It serves as a powerful didactic lesson, underscoring the intricate, multi-faceted, and often compartmentalized nature of the coagulation system.[11] The subsequent management of this patient required a delicate and precarious navigation of a treacherous therapeutic tightrope, demanding a constant and dynamic balancing of three competing, high-stakes risks: preventing the propagation and embolization of the newly formed DVT, avoiding a catastrophic hemorrhage in a patient with profoundly impaired clotting, and, most critically, protecting her dual mechanical heart valves from the life-terminating threat of acute thrombosis. The clinical decisions made were not merely an application of standard algorithms, which are ill-suited for such a paradoxical scenario, but rather a bespoke strategy grounded in a deep, first-principles understanding of pathophysiology.[12]

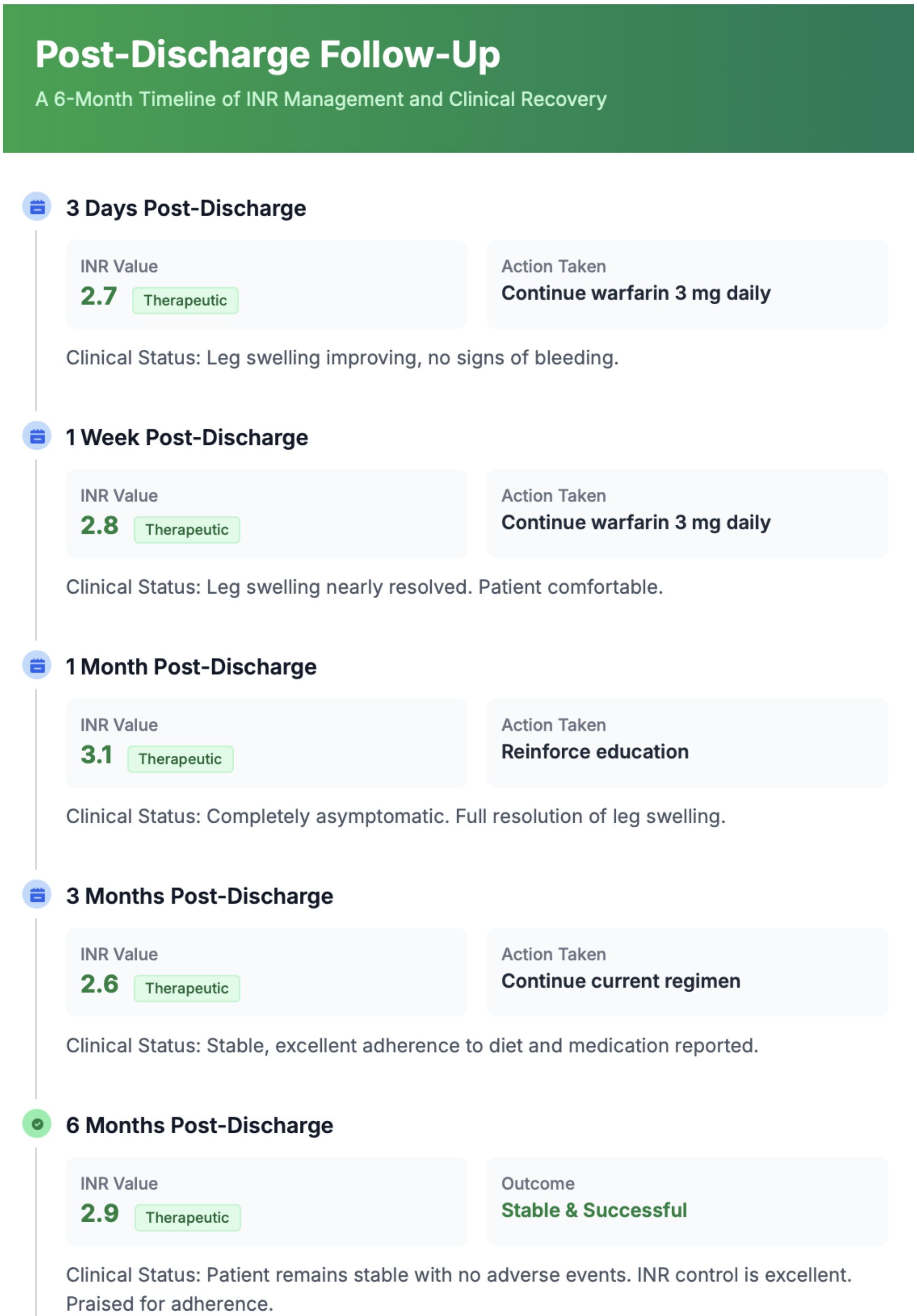


Figure 1. Post-discharge follow-up and INR management.

The core of this clinical dilemma lies in the profound dissonance between the systemic anticoagulant effect of warfarin, as crudely quantified by the INR, and the potent, localized prothrombotic forces that were fiercely active within the microenvironment of the patient's lower extremity veins.[13] To truly comprehend this paradox, one must first deconstruct the pharmacology of warfarin and the meaning of the INR itself. Warfarin, a vitamin K antagonist, exerts its effect by inhibiting the enzyme vitamin K epoxide reductase complex 1 (VKORC1). This action prevents the essential post-translational gamma-carboxylation of glutamic acid residues on the N-termini of several key hemostatic proteins, rendering them functionally inactive. This includes the pro-coagulant clotting factors II (prothrombin), VII, IX, and X, which form the backbone of the common and extrinsic coagulation pathways. Concurrently, warfarin also inhibits the synthesis of the endogenous, vitamin K-dependent anticoagulant proteins, Protein C and Protein S, a nuance of profound importance in states of anticoagulation instability. The laboratory test used to monitor this effect is the prothrombin time (PT), which measures the time to fibrin clot formation after the addition of thromboplastin (tissue factor) and calcium to a plasma sample. The INR is simply a standardized version of the PT, designed to harmonize results across different laboratories and thromboplastin reagents. Crucially, the PT/INR assay is designed to assess the functional integrity of the extrinsic pathway (initiated by tissue factor and involving Factor VII) and the final common pathway (involving Factors X, V, II, and fibrinogen). A markedly elevated INR of 7.78, as seen in this patient, therefore indicates a profound depression of these specific pathways, particularly the extrinsic pathway, which is highly sensitive to the level of Factor VII, the vitamin K-dependent clotting factor with the shortest half-life. However, and this is the central point of failure in a simplistic interpretation, it does not signify a complete abrogation of the entire coagulation cascade. It provides a valuable, but ultimately incomplete, snapshot of a much larger and more complex biological system. The formation of a thrombus in our patient, despite this impressive systemic laboratory derangement, can be robustly and elegantly explained by the enduring principles of Virchow's triad—venous stasis, a hypercoagulable state, and endothelial injury—which remained potently and synergistically active, creating a localized prothrombotic storm powerful enough to overwhelm the systemic, warfarin-induced calm.[14]

The triad of factors described by Rudolf Virchow in the 19th century remains the cornerstone of our understanding of thrombogenesis. In this patient, each component of the triad was not merely present but was amplified by her underlying comorbidities, creating a formidable prothrombotic milieu that was uniquely resistant to the systemic effects of warfarin. The patient's complex underlying cardiac condition was a powerful and relentless driver of the first and perhaps most critical element of the triad: venous stasis. Her formal diagnosis of heart failure with a mildly reduced ejection fraction (HFmrEF, LVEF 43.7%), objectively confirmed by a significantly elevated NT-proBNP level, represents a state of chronic circulatory insufficiency. This condition, a sequela of her long-standing rheumatic heart disease, results in reduced cardiac output and, critically, elevated cardiac filling pressures. These elevated pressures are transmitted backward from the failing left ventricle to the left atrium and pulmonary circulation, and from the right ventricle to the right atrium and the entire systemic venous system. This leads directly to elevated systemic venous pressures, which in turn impede the return of blood from the periphery. The hemodynamic consequence in the dependent venous capacitance vessels of the lower extremities is a dramatic reduction in blood flow velocity, leading to sluggish, near-static columns of blood, particularly within the valve pockets of the deep veins of the calf—the precise location where her DVT was identified. These valve sinuses are natural areas of flow separation and eddy current formation, and when forward flow is compromised, they become stagnant pools. This stasis is far from a benign state; it creates a localized microenvironment of hypoxia and acidosis, and, most importantly, it allows for the accumulation and concentration of activated clotting factors and inflammatory cells, preventing their clearance and dilution by flowing blood. It effectively creates a "prothrombotic soup" in which the biochemical reactions of coagulation can proceed unchecked. Furthermore, her persistent atrial fibrillation and severely enlarged left atrium contribute significantly to this global circulatory stasis, impairing diastolic filling and overall cardiac efficiency, thereby exacerbating the already poor venous return from the legs. This profound and chronic state of venous stasis acted as the foundational element, the fertile soil upon which a thrombus could be built and propagated.[15,16]

Figure 2. Deconstructing the anticoagulation paradox.

Despite a high INR suggesting profound hypocoagulability, this patient possessed multiple layers of a potent hypercoagulable state that are not captured, or are entirely invisible, to the prothrombin time assay (Figure 2). This unmeasured prothrombotic drive stemmed from two primary sources: her prosthetic hardware and her chronic inflammatory state. Firstly, the very presence of two mechanical prosthetic heart valves represents a permanent, non-endothelialized, foreign surface within the high-flow environment of the circulation. Blood is exquisitely designed to clot upon contact with any surface other than healthy endothelium. When blood elements, particularly platelets and Factor XII (Hageman factor), encounter the pyrolytic carbon and metallic components of the St. Jude valves, they are immediately activated. This initiates the contact activation pathway, also known as the intrinsic pathway of coagulation. This cascade, proceeding through Factors XII, XI, IX, and VIII, leads to the activation of Factor X and the subsequent generation of thrombin, entirely independent of the tissue factor-driven extrinsic pathway. This is a critical distinction, because the PT/INR test is fundamentally insensitive to the activity of the intrinsic pathway's initial stages. Therefore, a patient with mechanical valves has a continuous, low-level prothrombotic stimulus that is perpetually active but "invisible" to standard warfarin monitoring. While therapeutic warfarin doses suppress the final common pathway and can partially mitigate this risk, they do not abolish the initial contact activation.[17] This results in a continuous, low-grade generation of thrombin and a persistent state of platelet activation, effectively priming the entire circulatory system for thrombosis.

Secondly, both her underlying severe rheumatic heart disease (RHD) and her chronic heart failure are well-established states of chronic, low-grade systemic inflammation, which itself is a potent prothrombotic stimulus. These conditions are characterized by elevated circulating levels of pro-inflammatory cytokines, such as Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-6 (IL-6), as well as other acute-phase reactants. These inflammatory mediators are not innocent bystanders; they actively skew the hemostatic balance toward thrombosis through multiple mechanisms. They potently upregulate the expression of tissue factor on the surface of circulating monocytes and on endothelial cells throughout the vasculature, effectively "lighting the fuse" of the extrinsic pathway at a local level. They also downregulate the body's crucial endogenous anticoagulant pathways, such as the thrombomodulin-protein C system, and impair fibrinolysis by increasing the production of plasminogen activator inhibitor-1 (PAI-1). This inflammation-driven hypercoagulability provides a powerful and relentless stimulus for thrombosis that is largely independent of the vitamin K-dependent factors suppressed by warfarin. While inflammatory markers were not specifically reported in this case, it is virtually certain that a patient with this constellation of diseases would have an elevated C-reactive protein (CRP) level, a marker that is independently and strongly associated with an increased risk of VTE. This inflammatory layer adds another dimension of hypercoagulability that is not reflected in the INR.[18]

The third component of the triad, endothelial dysfunction or injury, completed the perfect storm for thrombosis. The same elevated venous pressures and stasis from chronic heart failure that set the hemodynamic stage also inflict chronic mechanical stress and stretch on the delicate venous endothelium of the lower limbs. This physical strain, combined with the constant exposure to the circulating inflammatory mediators described above, leads to a state of profound endothelial dysfunction. A healthy endothelium is a masterful, active anticoagulant surface, constantly producing vasodilators like nitric oxide and prostacyclin, which inhibit platelet aggregation, and expressing surface molecules like thrombomodulin and heparin-like proteoglycans, which actively suppress coagulation.[19] In this patient, this protective shield was lost. The normal antithrombotic phenotype of the venous endothelium was replaced by a prothrombotic one. This pathological transformation is characterized by the reduced production of nitric oxide and prostacyclin, coupled with the increased surface expression of adhesion molecules, such as P-selectin and E-selectin, which act like molecular velcro, snagging passing platelets and leukocytes from the sluggish blood flow. Most critically, these "activated" endothelial cells begin to express tissue factor on their own surfaces, turning the vein wall itself into a potent initiator of coagulation. This localized, activated endothelium in the deep veins of her right leg became a highly receptive surface for thrombus initiation and growth. In summary, while the systemic circulation, as measured by a global laboratory test, appeared profoundly anticoagulated, the local microenvironment in the patient's lower limb veins was a cauldron of thrombotic risk. The potent local triad of profound venous stasis (concentrating reactants), a powerful inflammatory and contact-activated hypercoagulable state (providing the biochemical fuel), and an activated endothelial surface (providing the ignition point) provided a stimulus more than sufficient to overwhelm the systemic depression of the extrinsic coagulation pathway and initiate robust thrombus formation in the deep veins of her leg.[20]

The extreme INR of 7.78, while paradoxical, warrants a deeper pharmacological consideration beyond its face value. The detailed clinical history, which revealed a period of poor oral intake followed by a sudden change in diet, is the most likely culprit for this profound INR derangement. Critically, the patient's normal liver function tests ruled out compounding factors like acute cardiac hepatopathy, confirming this to be a pure, albeit extreme, warfarin effect. However, this case also shines a bright light on a critical and often underappreciated nuance of warfarin's pharmacology: its differential effect on pro-coagulant and anticoagulant proteins due to their varying half-lives. This is particularly relevant in the context of this patient's documented "INR lability".

Warfarin blocks the production of both pro-coagulant factors and the natural anticoagulant Proteins C and S. However, these proteins are cleared from the circulation at vastly different rates. Protein C, a vital natural anticoagulant, has a very short biological half-life of approximately 8 hours. In stark contrast, Factor II (prothrombin), the most abundant pro-coagulant factor, has a very long half-life of around 60 hours. This disparity is most famously discussed during warfarin initiation, where the rapid drop in Protein C before the pro-coagulant factors have declined can create a transient prothrombotic state. However, this same principle applies to any period of significant instability. In this patient, her documented INR lability suggests a hemostatic system in constant flux. During her period of illness and poor oral intake, the effect of her stable warfarin dose was dramatically potentiated. In this phase, her levels of the short-lived anticoagulant Protein C would have plummeted rapidly. This could have created a transient, paradoxical prothrombotic window where the balance between anticoagulation and pro-coagulation was unfavorably tipped toward clotting, even as her INR (driven primarily by the 6-hour half-life of Factor VII) began its steep ascent. It is plausible, even likely, that the initial nidus of her DVT formed during this vulnerable period of hemostatic imbalance. The subsequent, critically high INR of 7.78 was therefore a lagging indicator of a process that may have been initiated days earlier when the dynamics of her coagulation system were dangerously unstable. This perspective reframes "INR lability" not just as a fluctuating number, but as a period of profound biological disequilibrium with windows of heightened, rather than diminished, thrombotic risk.[17,18]

The moment of diagnosis, confirming an acute DVT in the face of an INR of 7.78, represented the most critical juncture in this patient's care. Standard treatment paradigms were inadequate for this contradictory picture. The immediate management decision—to withhold warfarin but pointedly avoid the administration of active reversal agents—was a contrarian choice that required a sophisticated, multi-faceted risk assessment. This decision was, however, perfectly aligned with the principles outlined in the

American College of Chest Physicians (ACCP) guidelines, which recommend for patients with an INR >4.5 without significant bleeding that warfarin simply be held. The justification for this conservative strategy was threefold: First was the absence of major, life-threatening bleeding. The patient exhibited extensive ecchymoses and a clear bleeding tendency, but she was hemodynamically stable and showed no signs of intracranial, gastrointestinal, or other critical hemorrhage. In this context, aggressive reversal with Vitamin K or Prothrombin Complex Concentrate (PCC) would have been a disproportionate and dangerous response. These agents are not without risk, and PCCs themselves carry a significant risk of inducing thrombosis, which would only add fuel to the fire. Second, and most important, was the catastrophic and overriding risk of mechanical valve thrombosis. This was the paramount concern that governed all subsequent decisions. For a patient with two mechanical valves, particularly in the mitral position, acute valve thrombosis is a swift and often fatal event, leading to acute obstructive shock, heart failure, and massive embolism. Rapidly reversing her anticoagulation with Vitamin K or PCC could easily "overshoot" the target, causing the INR to plummet precipitously and creating a profound rebound hypercoagulable state. The iatrogenic risk of causing a catastrophic valve thrombosis far outweighed the theoretical risk of extension or embolization from her existing DVT. Protecting the valves was the non-negotiable primary objective. Third was the reassuring nature of the thrombus itself. The venous Doppler ultrasound confirmed that the DVT, while acute, was non-occlusive and, critically, was confined to the distal (infrapopliteal) veins of the calf. While any DVT carries some embolic risk, isolated distal DVTs are associated with a significantly lower risk of causing clinically significant pulmonary embolism compared to large, occlusive thrombi in the proximal (popliteal, femoral, or iliac) veins. This anatomical finding provided a crucial "margin of safety," affording the clinical team the confidence to pursue a conservative "watch and wait" approach to her anticoagulation, allowing the INR to drift down naturally while prioritizing the protection of her prosthetic valves.

This patient-specific strategy of controlled, gradual normalization of the INR proved highly successful. It created a therapeutic window wherein the immediate, severe bleeding risk was allowed to subside without ever exposing the patient to the unacceptable risk of a subtherapeutic INR and valve thrombosis. The successful outcome serves as a powerful validation of this nuanced, pathophysiology-driven approach. It underscores the critical lesson that in such paradoxical cases, the prosthetic valve must be viewed as the highest-risk site for a life-threatening thrombus, and management of any peripheral thrombotic event must be carefully integrated with, and often subordinated to, the absolute requirement to protect the valves.

While this case represents an extreme and dramatic example, it is not entirely unique. The medical literature contains other reports of thrombotic events occurring at therapeutic or even supratherapeutic INRs, most commonly described in patients with other potent prothrombotic conditions such as active malignancy or high-titer antiphospholipid syndrome. This case compellingly adds severe, multi-valvular heart disease with mechanical prostheses to this list of high-risk states where the INR may fail as a solitary guardian against thrombosis. The long-term management of this patient remains a significant challenge. The root cause of this entire event was her profound INR lability, and therefore, the primary long-term goal must be to maximize her time within the therapeutic range (TTR). The cornerstone of this strategy is intensive and repeated patient education regarding the critical importance of a consistent diet, medication adherence, and recognizing the signs of both bleeding and thrombosis. For such a high-risk patient, consideration must also be given to more frequent INR testing or even the implementation of a patient self-testing (home INR monitoring) program, which has been shown in meta-analyses to improve TTR and clinical outcomes in motivated patients. It must be emphatically stated that there is no role for alternative anticoagulants in this patient. The use of Direct Oral Anticoagulants (DOACs) is strictly and absolutely contraindicated in patients with mechanical heart valves, a fact tragically underscored by the premature termination of the RE-ALIGN trial, which showed an excess of both thromboembolic and bleeding events in patients randomized to dabigatran compared to warfarin. Therefore, the diligent, collaborative, and intelligent management of warfarin remains the only viable long-term strategy for this patient.[19,20]

In summary, this case of acute DVT in a patient with dual mechanical valves and a critically elevated INR serves as an unforgettable illustration of the complexities inherent in long-term anticoagulation. It demonstrates unequivocally that a supratherapeutic INR, while a clear indicator of bleeding risk, does not confer absolute immunity against thrombosis when potent, localized prothrombotic factors related to Virchow's triad are concurrently active. The successful outcome hinged on a deep appreciation of these competing risks, leading to a masterful and conservative strategy of temporarily holding warfarin without active reversal. This case champions the imperative for clinicians to think critically beyond a single laboratory value, to integrate a deep understanding of pathophysiology with clinical context, and to employ a highly individualized, patient-centered approach when confronted with the ultimate anticoagulation tightrope

4. Conclusion

This case of acute deep vein thrombosis in a patient with dual mechanical valves and a critically elevated INR serves as a powerful illustration of the complexities inherent in long-term anticoagulation management. It demonstrates unequivocally that a supratherapeutic INR, while indicating a high risk of bleeding, does not confer absolute immunity against thrombosis, particularly when potent underlying prothrombotic factors related to Virchow's triad are present. The successful management hinged on a deep appreciation of the competing risks, leading to a conservative strategy of temporarily holding warfarin without active reversal. This approach allowed for a controlled normalization of coagulation, mitigating the bleeding risk while paving the way for the safe re-institution of anticoagulation to protect her prosthetic valves. This case highlights the imperative for clinicians to think beyond the INR value and to employ a highly individualized, pathophysiology-driven approach when confronted with the ultimate anticoagulation tightrope.

5. References

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