# Clinical and Ethical Challenges in ANESTHESIOLOGY

*Edited by*
**Dr. Mertay Boran**

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**Clinical and Ethical Challenges in Anesthesiology**

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# PREFACE

Anesthesiology combines medical knowledge with ethical responsibility and careful decision-making. In daily practice, anesthesiologists must make important clinical decisions, often under pressure and in complex situations. Clinical and Ethical Challenges in Anesthesiology was prepared to emphasize the close relationship between ethical principles and evidence-based anesthetic care.

The aim of this book is to encourage thoughtful clinical practice, support patient-centered decision-making, and contribute to academic learning in anesthesiology. It is intended for anesthesiologists and perioperative physicians who seek to provide safe, ethical, and high-quality care.


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# CHAPTER 1

# POSTOPERATİVE DYSRHYTHMİAS İN THORACİC SURGERY: RHYTHM CONTROL AND TOXİC AMİODARONE – FENTANYL INTERACTİON

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## INTRODUCTION

Postoperative cardiac dysrhythmias remain among the most frequent and clinically relevant complications following pulmonary resection and continue to pose a significant challenge in thoracic anesthesia and perioperative management (Boran et al., 2021, Enön et al., 2006). Reported incidence rates range between 18% and 34%, with atrial fibrillation representing the most encountered rhythm

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disturbance (Haverkamp & Hachenberg, 2016). These arrhythmias occur more frequently in elderly patients and are particularly prevalent after extensive thoracic procedures. Following pneumonectomy, incidence rates of 20–30% have been reported, compared with 15–20% after lobectomy (Ponn, 2005; Patel et al., 1992).

Although postoperative dysrhythmias are often transient and may spontaneously revert to sinus rhythm, a substantial proportion of patients require pharmacological intervention. Amiodarone has therefore become a cornerstone in the acute management of postoperative atrial fibrillation because of its high efficacy in both rate and rhythm control and its relatively low proarrhythmic potential. As a result, amiodarone is frequently administered in thoracic surgical patients.

The pathophysiology of dysrhythmias following pulmonary resection is multifactorial and incompletely understood. Proposed mechanisms include mediastinal shift, hypoxemia, acid–base and electrolyte disturbances, atrial stretch, and heightened sympathetic activity (Haverkamp & Hachenberg, 2016). Advanced age, coronary artery disease, extensive surgical procedures, and intrapericardial manipulation of pulmonary vessels have been consistently identified as major risk factors (Patel et al., 1992). Earlier strategies such as prophylactic digitalization were widely employed in high-risk patients; however, subsequent studies failed to demonstrate clear benefit, and routine prophylactic use has been abandoned (Ritchie et al., 1990).

While postoperative dysrhythmias themselves are not uniformly associated with increased early mortality or prolonged hospitalization, their treatment is not without risk. Amiodarone is characterized by a complex adverse effect profile involving pulmonary, hepatic, renal, endocrine, and metabolic systems. Among these, acute amiodarone-induced pulmonary toxicity represents one of the most serious and potentially fatal complications and has been reported predominantly in cardiothoracic surgical settings (Feduska et al., 2021).

Post-thoracotomy pain control constitutes another critical component of perioperative care. Thoracic epidural analgesia using low-dose local anesthetics combined with fentanyl is widely regarded as one of the most effective strategies for postoperative analgesia (Boran, M., Boran, E., 2021). However, concomitant administration of epidural fentanyl and systemic amiodarone introduces the potential for clinically significant pharmacokinetic and pharmacodynamic interactions. Emerging evidence suggests that such interactions may precipitate severe hemodynamic instability, metabolic derangements, multiorgan toxicity, and even death (White et al., 1999; Jeong et al., 2025).

Against this background, careful balancing of therapeutic benefit and toxic risk is essential in thoracic surgical patients. This chapter provides a comprehensive overview of the incidence, mechanisms, and management of dysrhythmias after pulmonary resection, with particular emphasis on the role of amiodarone and its acute, potentially life-threatening adverse effects. Special attention is given to the interaction between amiodarone and fentanyl in the setting of epidural analgesia. A representative clinical case of unexpected, fatal amiodarone-related toxicity following lung resection is presented to illustrate the clinical implications of this interaction and to underscore the need for heightened vigilance in perioperative thoracic anesthesia practice.

## POST-PULMONARY RESECTION DYSRHYTHMIAS

Cardiac dysrhythmias following pulmonary resection represent a well-recognized postoperative complication in thoracic surgery, with incidence varying according to patient-related factors, extent of resection, and perioperative management. Among these rhythm disturbances, atrial-origin dysrhythmia predominate, particularly atrial fibrillation, which is the most frequently observed entity (Haverkamp & Hachenberg, 2016). Other supraventricular dysrhythmias, including atrial flutter, paroxysmal atrial tachycardia, sinus tachycardia, and frequent premature atrial contractions, may also occur, whereas ventricular dysrhythmias and clinically significant bradyarrhythmias are comparatively rare.

Postoperative dysrhythmias typically develop within the first two to four postoperative days. Pneumonectomy is associated with a higher risk compared with lobectomy or sublobar resections, likely reflecting greater physiological stress, mediastinal shift, and atrial stretch (Ponn, 2005; Patel et al., 1992). Elderly patients are particularly vulnerable, owing to age-related atrial remodeling and a higher prevalence of cardiovascular comorbidities.

The mechanisms underlying dysrhythmia development after pulmonary resection are multifactorial. Hypoxemia, hypercarbia, acid–base disturbances, and electrolyte imbalances—especially hypokalemia and hypomagnesemia—may directly alter myocardial electrophysiology. In addition, surgical manipulation of the pulmonary hilum and pericardium can provoke autonomic imbalance and inflammatory responses, while abrupt changes in pulmonary vascular resistance contribute to atrial distension and arrhythmogenesis (Haverkamp & Hachenberg, 2016).

Although postoperative atrial dysrhythmias have not consistently been associated with increased early mortality or prolonged hospitalization, their occurrence often necessitates additional diagnostic evaluation and pharmacological treatment, increasing postoperative care complexity. Myocardial ischemia, although uncommon after pulmonary resection, should always be considered, particularly in patients with known coronary artery disease. Reported incidences of postoperative myocardial infarction are low; however, associated mortality may be substantial, underscoring the importance of vigilant cardiac monitoring in high-risk patients (Patel et al., 1992).

Preventive strategies have evolved considerably. Prophylactic digitalization, once widely used in elderly patients undergoing pneumonectomy, failed to demonstrate benefit in randomized and observational studies and is no longer recommended (Ritchie et al., 1990). Current preventive approaches emphasize optimization of oxygenation, correction of electrolyte disturbances, and effective pain control. Magnesium supplementation has also been investigated, with emerging evidence suggesting a potential role in reducing new-onset atrial fibrillation after anatomic pulmonary resection in elderly patients (Jin et al., 2023).

When dysrhythmias occur, management should be individualized and undertaken in collaboration with cardiology specialists. Treatment goals include hemodynamic stabilization, symptom control, prevention of thromboembolic complications, and restoration or maintenance of sinus rhythm when appropriate. In this setting, amiodarone has gained widespread acceptance as an effective antiarrhythmic agent in thoracic surgical patients, despite its well-recognized adverse effect profile.

## AMIODARONE IN THORACIC SURGERY

Amiodarone is a class III antiarrhythmic agent with complex electrophysiological properties extending beyond potassium channel blockade. Its pharmacological profile includes sodium channel inhibition, noncompetitive beta-adrenergic blockade, and calcium channel antagonism, rendering it effective for both supraventricular and ventricular dysrhythmias.

In thoracic surgery, amiodarone is commonly used for the acute management of postoperative atrial fibrillation, particularly when rapid ventricular response results in hemodynamic instability or inadequate rate control with beta-blockers or calcium channel blockers. Its efficacy and relatively low proarrhythmic potential have supported its widespread use, including in patients with compromised cardiac function (Haverkamp & Hachenberg, 2016).

Despite these advantages, amiodarone exhibits distinctive pharmacokinetic properties that complicate perioperative use. Its high lipophilicity, extensive tissue accumulation, and large volume of distribution may lead to unpredictable systemic effects even after short-term intravenous administration. Hepatic metabolism via cytochrome P450 enzymes and biliary excretion further increase the potential for drug–drug interactions in the perioperative setting.

Thoracic surgical patients constitute a particularly vulnerable population with respect to amiodarone toxicity. Reduced pulmonary reserve, postoperative inflammatory responses, and exposure to high inspired oxygen concentrations may potentiate pulmonary injury. In addition, perioperative hypotension, renal hypoperfusion, and metabolic stress may impair drug clearance, increasing systemic exposure—especially in elderly patients and those undergoing extensive resections such as pneumonectomy (Feduska et al., 2021).

Although short-term amiodarone therapy has traditionally been regarded as relatively safe, evidence from anesthetic and critical care literature indicates that even brief exposure may precipitate severe adverse reactions under specific conditions. White et al. (1999) reported significant hemodynamic effects in cardiac surgical patients receiving short-term amiodarone during fentanyl-based anesthesia, highlighting the need for careful monitoring. These observations underscore that initiation of amiodarone after pulmonary resection must be carefully individualized, balancing therapeutic benefit against the potential for serious toxicity.

## AMIODARONE TOXICITY

Amiodarone is associated with a wide spectrum of adverse effects involving multiple organ systems. Although many toxicities are traditionally linked to long-term oral therapy, increasing evidence indicates that acute and severe toxic reactions may also occur during short-term intravenous administration, particularly in critically ill or postoperative patients. Thoracic surgical patients represent a high-risk population due to limited pulmonary reserve, perioperative inflammatory stress, and frequent exposure to interacting pharmacological agents.

**Pulmonary Toxicity:** Amiodarone-induced pulmonary toxicity (AIPT) is the most serious and potentially fatal adverse effect associated with this agent and constitutes one of the leading causes of amiodarone-related mortality. The reported incidence varies widely, but pulmonary toxicity accounts for most severe complications attributed to amiodarone use (Feduska et al., 2021). Clinically recognized forms of AIPT include chronic interstitial pneumonitis, organizing pneumonia, acute respiratory distress syndrome (ARDS), and, less commonly, solitary pulmonary masses characterized by fibrosis.

Acute AIPT represents a rare but particularly aggressive manifestation. Unlike chronic forms, which typically develop after prolonged exposure, acute pulmonary toxicity may occur within days of initiation and has been reported predominantly in cardiothoracic surgical settings. High inspired oxygen concentrations, surgical trauma, systemic inflammatory responses, and pre-existing lung disease are thought to synergistically amplify pulmonary injury in these patients (Feduska et al., 2021). The clinical course is often fulminant, with rapid progression to hypoxemic respiratory failure and high mortality rates.

**Hepatic Toxicity:** Hepatic dysfunction is a well-documented adverse effect of amiodarone and may range from asymptomatic elevation of transaminases to acute toxic hepatitis and liver failure. Intravenous administration has been associated with abrupt hepatocellular injury, particularly in the presence of hemodynamic instability or reduced hepatic perfusion. In the postoperative period, hypotension and low cardiac output states may further compromise hepatic clearance, leading to excessive systemic exposure and progressive toxicity.

**Renal Toxicity:** Although amiodarone is not primarily excreted via the kidneys, acute renal failure has been reported in association with severe systemic toxicity. Renal dysfunction is often secondary to hypotension, hypoperfusion, or multiorgan failure rather than direct nephrotoxicity. Nevertheless, once renal failure develops, impaired clearance of metabolic byproducts may exacerbate acid–base and electrolyte disturbances, contributing to a vicious cycle of worsening systemic toxicity.

**Endocrine and Metabolic Toxicity:** Amiodarone exerts profound effects on thyroid function due to its high iodine content and direct interference with thyroid hormone metabolism. Both hypothyroidism and thyrotoxicosis have been described with acute thyroiditis occasionally occurring in critically ill patients. In addition, severe metabolic derangements, including hypoglycemia, hyperkalemia, lactic acidosis, and pancreatic injury, have been reported in the context of acute amiodarone toxicity. These abnormalities often coexist and may progress rapidly, reflecting widespread cellular dysfunction.

**Cardiovascular and Hemodynamic Effects:** Despite its antiarrhythmic properties, amiodarone may precipitate bradycardia, atrioventricular conduction disturbances, and profound hypotension, particularly during intravenous infusion. Vasodilation and myocardial depression are thought to contribute to these effects. In postoperative thoracic surgical patients, even transient hypotension may have catastrophic consequences due to compromised cardiopulmonary reserve.

The cumulative burden of these toxic effects underscores the need for extreme caution when administering amiodarone in thoracic surgery patients. The risk is further amplified when amiodarone is combined with other agents that influence hemodynamics or drug metabolism, such as opioids used for epidural analgesia.

## PHARMACOKINETIC AND PHARMACODYNAMIC INTERACTIONS WITH FENTANYL

Fentanyl is a potent synthetic opioid widely administered via the epidural route for postoperative analgesia after thoracotomy. Its rapid onset, favorable analgesic profile, and minimal direct myocardial depressant effects have established it as a cornerstone of thoracic postoperative pain management. However, fentanyl undergoes extensive hepatic metabolism via cytochrome P450 enzymes—predominantly CYP3A4—and exhibits high lipid solubility, pharmacokinetic properties shared with amiodarone that predispose to clinically significant drug–drug interactions.

Amiodarone is a potent inhibitor of multiple cytochrome P450 isoenzymes, including CYP3A4, and interferes with P-glycoprotein–mediated drug transport. Through these mechanisms, amiodarone may reduce fentanyl clearance, leading to increased systemic and central nervous system exposure even when fentanyl is administered epidurally. This interaction may be accentuated in the postoperative setting by transient alterations in hepatic perfusion and inflammatory stress.

Pharmacodynamic interactions further amplify clinical risk. Fentanyl-induced attenuation of sympathetic tone may unmask or potentiate the negative chronotropic and vasodilatory effects of amiodarone, resulting in profound hypotension and bradyarrhythmia. In thoracic surgical patients, such hemodynamic compromise may rapidly progress to tissue hypoperfusion and multi-organ dysfunction.

Clinical relevance of this interaction has been demonstrated in perioperative and critical care settings. White et al. (1999) reported significant hemodynamic instability in cardiac surgical patients receiving short-term amiodarone during fentanyl-based anesthesia. More recently, large-scale analyses integrating literature review and electronic health record data have identified severe adverse reactions associated with pharmacokinetic drug–drug interactions involving amiodarone (Jeong et al., 2025).

In thoracic surgery, epidural fentanyl is often administered continuously for several days, coinciding with the period when amiodarone is most frequently initiated for postoperative atrial dysrhythmia. This temporal overlap may obscure early warning signs, delay recognition of evolving toxicity, and increase the likelihood of catastrophic outcomes. Accordingly, concomitant use of epidural fentanyl and intravenous amiodarone should be regarded as a high-risk combination requiring intensified monitoring and cautious clinical judgment.

## EPIDURAL ANALGESIA AND CARDIAC RISK AFTER THORACOTOMY

Effective postoperative pain control is essential following thoracotomy and pulmonary resection. Inadequate analgesia contributes to hypoventilation, atelectasis, hypoxemia, and heightened sympathetic activation, all of which increase cardiac stress and predispose to postoperative dysrhythmias. Thoracic epidural analgesia, typically combining low-dose local anesthetic with fentanyl, provides superior analgesia, improves respiratory mechanics, and facilitates early mobilization.

Despite these benefits, thoracic epidural analgesia is associated with predictable cardiovascular effects. Sympathetic blockade may result in vasodilation, reduced venous return, and hypotension—effects that may be clinically significant in patients with marginal cardiac reserve. When combined with antiarrhythmic agents that depress heart rate or myocardial conduction, the risk of hemodynamic instability is amplified.

Thoracic surgical patients frequently receive epidural fentanyl during the same postoperative period in which amiodarone is initiated. While epidural fentanyl reduces sympathetic tone, amiodarone exerts negative chronotropic and vasodilatory effects, potentially resulting in synergistic cardiovascular depression. Hypotension following amiodarone initiation in this context may represent an early manifestation of systemic toxicity, with impaired hepatic and renal clearance further accelerating drug accumulation.

Although epidural fentanyl is generally considered safe, the limited literature addressing its interaction with amiodarone should not be interpreted as evidence of safety. Thoracic surgery patients constitute a particularly susceptible population in whom standard analgesic and antiarrhythmic strategies may carry unanticipated risks. Individualized analgesic planning and vigilant cardiovascular monitoring are therefore essential.

## MANAGEMENT OF POSTOPERATIVE DYSRHYTHMIAS AFTER LUNG RESECTION

Postoperative dysrhythmias following lung resection represent a frequent and clinically significant challenge that requires a structured, stepwise, and individualized management strategy. As emphasized by Haverkamp and Hachenberg (2016), postoperative atrial dysrhythmias arise from a multifactorial interplay of surgical stress, autonomic imbalance, inflammation, hypoxemia, and pharmacological influences. Consequently, management should not rely on a single pharmacological intervention but rather integrate physiological optimization, careful drug selection, and continuous reassessment.

### General Principles of Management

Initial management must prioritize the identification and correction of reversible precipitating factors, which are often the primary drivers of postoperative dysrhythmias after lung resection. These include hypoxemia, hypercapnia, acid–base disturbances, electrolyte abnormalities—particularly hypokalemia and hypomagnesemia—pain, infection, and fluid imbalance. Optimization of oxygen delivery, effective analgesia, and early mobilization are essential supportive measures and may alone restore sinus rhythm in a substantial proportion of patients (Haverkamp & Hachenberg, 2016).

Hemodynamic stability constitutes the first critical decision point. Hemodynamically unstable patients—defined by hypotension, ischemic symptoms, or impaired end-organ perfusion—require immediate synchronized electrical cardioversion. In contrast, stable patients allow for a more conservative and physiologically guided approach, in which rate control and correction of triggering factors are prioritized before escalation to rhythm control.

## Pharmacological Rate Control

Rate control remains the cornerstone of therapy in most stable patients with postoperative atrial fibrillation.

**Beta-adrenergic blockers** are effective in attenuating sympathetic overactivity and controlling ventricular response. However, their use may be limited in thoracic surgery patients by bronchospasm, hypotension, or reduced cardiac output, particularly after major lung resection.

**Non-dihydropyridine calcium channel blockers**, such as diltiazem or verapamil, represent alternative agents for rate control. These drugs should be used cautiously in patients with impaired ventricular function due to their negative inotropic properties. As highlighted by Haverkamp and Hachenberg (2016), careful titration and close hemodynamic monitoring are essential in the postoperative thoracic population.

## Rhythm Control and the Role of Amiodarone

Amiodarone has gained widespread acceptance in thoracic surgery due to its broad antiarrhythmic efficacy, effectiveness in both rate and rhythm control, and relatively low proarrhythmic potential. It is often favored in patients with structural heart disease or reduced ventricular function, in whom other antiarrhythmic agents may be contraindicated.

However, recent evidence mandates a more cautious and selective approach to amiodarone use in this setting. While effective, amiodarone's complex pharmacokinetic and pharmacodynamic profile renders it particularly susceptible to drug–drug interactions and systemic toxicity, even after short-term administration. Large-scale pharmacovigilance analyses have demonstrated that severe and sometimes fatal adverse reactions may arise from pharmacokinetic interactions involving amiodarone, particularly when combined with other centrally acting agents (Jeong et al., 2025).

In thoracic surgery patients, this risk is further amplified by altered autonomic tone, perioperative inflammation, and concurrent use of epidural opioids. Therefore, amiodarone should not be regarded as a default first-line agent but rather as a carefully considered option, reserved for selected patients in whom the anticipated benefit clearly outweighs the potential risk.

## Preventive and Alternative Strategies

Preventive strategies play a crucial role in reducing reliance on high-risk pharmacological interventions. Optimization of electrolyte balance, particularly magnesium supplementation, has emerged as a promising approach. Jin et al. (2023) demonstrated that perioperative magnesium sulfate infusion may reduce the incidence of new-onset atrial fibrillation in elderly patients undergoing anatomic pulmonary resection, supporting a preventive rather than reactive management paradigm.

In selected patients, a strategy of delayed rhythm intervention, conservative rate control, or spontaneous conversion under optimized physiological conditions may be safer than early aggressive antiarrhythmic therapy. Continuous electrocardiographic monitoring during the first 48–72 postoperative hours remains essential to allow early detection of conduction disturbances and timely intervention.

### Integrated Management Perspective

Taken together, optimal management of postoperative dysrhythmias after lung resection requires a hierarchical and context-sensitive approach. Correction of reversible triggers, cautious pharmacological selection, and awareness of high-risk drug interactions are fundamental. In the era of increasing recognition of amiodarone-related toxicity, thoracic anesthesiologists and perioperative clinicians must balance rhythm control against systemic safety, tailoring therapy to individual patient risk profiles rather than relying on uniform treatment algorithms.

## CASE: SYSTEMIC AMIODARONE TOXICITY AFTER LUNG RESECTION

A 62-year-old male diagnosed with lung cancer underwent left thoracotomy and pneumonectomy. Postoperative analgesia consisted of thoracic epidural bupivacaine–fentanyl combined with intravenous tramadol. On postoperative day two, following an episode of postural hypotension, electrocardiography revealed new-onset atrial fibrillation with a rapid ventricular response.

Antiarrhythmic therapy was initiated with an intravenous amiodarone bolus followed by continuous amiodarone infusion. At the 14th hour of treatment, conversion of atrial fibrillation to sinus rhythm was documented. However, during the same time period, the patient developed marked hypotension, fatigue, oliguria, and lethargy, prompting immediate discontinuation of the amiodarone infusion.

Subsequently, the clinical course was complicated by rapidly progressive metabolic derangements and multiorgan dysfunction, including lactic acidosis, hyperkalemia, hypoglycemia, hypoxia, hypercarbia, severe acute renal failure, and combined hepatic, pancreatic, and thyroid toxicity. Despite aggressive supportive management—including norepinephrine infusion, correction of metabolic abnormalities, and 2.5 hours of hemodialysis—the patient deteriorated and died on postoperative day four.

The clinical course was consistent with acute, systemic amiodarone-related multi-organ toxicity in the perioperative thoracic surgery setting.

## ADVERSE EFFECTS OF AMIODARONE IN THORACIC SURGERY PATIENTS

Amiodarone toxicity in thoracic surgery patients may present as a rapidly progressive, multi-organ toxic syndrome rather than isolated adverse effects. Clinically significant toxicity may occur even after short-term administration and in patients with preserved cardiopulmonary, renal, and hepatic function.

Pulmonary toxicity ranges from subclinical pneumonitis to acute respiratory distress syndrome and is potentiated by reduced lung reserve and high inspired oxygen exposure (Feduska et al., 2021). Hepatic toxicity may manifest as acute toxic hepatitis, particularly in the setting of perioperative hypotension and impaired hepatic perfusion. Renal dysfunction often reflects global hypoperfusion and systemic toxicity rather than primary nephrotoxicity. Endocrine disturbances, including acute thyroiditis, and rare complications such as pancreatitis further support the concept of systemic toxicity.

Collectively, these findings underscore that amiodarone-related adverse effects in thoracic surgery patients should be conceptualized as an integrated, multisystem process driven by pharmacological interactions, autonomic imbalance, and reduced physiological reserve.

## DISCUSSION

The presented case highlights a critical gap between perceived safety and real-world risk of amiodarone use in thoracic surgery patients. Despite preserved baseline organ function, acute administration precipitated cardiovascular collapse followed by multisystem toxicity. Pharmacodynamic interaction with fentanyl-based anesthesia and thoracic epidural analgesia likely played a central role.

Previous reports have documented similar bradyarrhythmic events in fentanyl-based cardiac anesthesia (White et al., 1999), and emerging pharmacovigilance data further support the role of complex drug interactions (Jeong et al., 2025). This case challenges the assumption that amiodarone can be universally applied as first-line therapy and supports a context-specific approach to postoperative rhythm management.

## CONCLUSION

Postoperative dysrhythmias after lung resection remain common and clinically significant. Although amiodarone is an effective antiarrhythmic agent, its use in thoracic surgery patients—particularly in conjunction with fentanyl-based anesthesia and epidural analgesia—may precipitate severe and potentially fatal systemic toxicity, even after short-term administration.

Risk stratification, vigilant monitoring, and individualized therapeutic decision-making are essential. Management strategies should extend beyond arrhythmia suppression alone and incorporate a holistic, multidisciplinary approach to minimize catastrophic outcomes.

## KEY CLINICAL MESSAGES

• Postoperative dysrhythmias arise from surgical stress, autonomic imbalance, and pharmacological interactions.
• Thoracic epidural analgesia may potentiate vagal dominance and bradyarrhythmia.
• Amiodarone–fentanyl interaction can cause severe conduction disturbances.
• Toxicity may occur despite preserved organ function.
• Careful monitoring and individualized management are essential.
• Conservative strategies may be safer in selected patients.

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# CHAPTER 2

# BETWEEN FAİTH AND LİFE: THE ANESTHESİOLOGİST'S DİFFİCULT DECİSİON İN A JEHOVAH'S WİTNESS PATİENT

**ERTAY BORAN[1]**

## INTRODUCTION

In modern medicine, maintaining a balance between patient autonomy, the right to life, medical necessity, and the clinician's ethical obligations becomes particularly fragile in life-threatening situations. This fragility is especially pronounced in specific patient populations such as Jehovah's Witnesses (JW), who refuse blood

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transfusion on religious grounds. The refusal of blood and blood products confronts anesthesiologists and surgical teams with complex ethical, clinical, and legal dilemmas, particularly in cases involving polytrauma, severe hemorrhage, or emergency surgical intervention.

In this chapter, the historical, theological, ethical, and clinical foundations of transfusion refusal among JW patients are examined, and the challenges faced by anesthesiologists during the perioperative period are analyzed in light of the current literature. Within the framework of legal regulations in Türkiye, the physician's scope of responsibility is discussed, and the management of a young female JW patient with polytrauma requiring emergency surgical consideration is illustrated through an original case. Blood management strategies in JW patients, including the feasibility of autologous techniques, pharmacological hemostatic approaches, preferences for minimally invasive procedures, and postoperative intensive care management, are comprehensively reviewed with supporting evidence from the literature.

The right of patients to make decisions regarding their own bodies is one of the fundamental principles of modern medicine and contemporary legal systems. However, the boundaries of this right become particularly controversial in life-threatening emergencies, especially when Jehovah's Witness (JW) patients refuse blood transfusion. The JW community, based on religious beliefs, categorically refuses transfusion of whole blood and its primary components (Muramoto, 1998, p. 223). This refusal places clinicians involved in trauma care, surgery, and anesthesia in profound ethical and medical dilemmas.

Worldwide, the population of Jehovah's Witnesses is estimated to be approximately 8 million, with significant populations in countries such as the United States, Brazil, the Philippines, and Nigeria. These communities are generally concentrated in urban centers, and their interactions with healthcare systems vary accordingly (Muramoto, 1998). In Türkiye, approximately 5,140 Jehovah's Witnesses were reported in 2021, with the highest concentration residing in İzmir (Güzeldemir, 2005,https://acikerisim.topkapi.edu.tr/yayin/1750539). Although their population is relatively small, JW patients pose substantial clinical, ethical, and legal challenges during emergency surgical interventions.

The refusal of blood transfusion by JW patients forces physicians to make critical decisions in both emergency and elective surgical settings. This challenge is particularly evident in high-risk situations such as trauma, hemorrhagic surgery, and hematological disorders. Anesthesiologists bear the responsibility of minimizing blood loss, planning alternative treatment strategies, and ensuring comprehensive patient counseling.

In JW belief, opposition to blood transfusion is not merely a theological stance but a health-related behavior that directly influences clinical practice. Consequently, the development of transfusion-free strategies, optimization of hemostatic techniques, and preference for minimally invasive approaches have become indispensable in the management of JW patients. The literature reports that, with appropriate precautions, JW patients can successfully undergo high-risk procedures such as cardiovascular surgery without transfusion (Ott & Cooley, 1977, p. 1256; Vasques et al., 2016, p. 2150). Similarly, blood-conservation strategies in anesthesia and intensive care practice have a direct impact on survival outcomes in JW patients (MacLaren & Anderson, 2004, p. 800).

The situation becomes considerably more complex in trauma patients. In cases of polytrauma or intra-abdominal hemorrhage associated with hemodynamic instability, avoidance of blood transfusion may increase mortality. At this point, the anesthesiologist's responsibility expands to encompass clinical, ethical, and legal dimensions. Even when a patient's life is at risk, refusal of treatment may persist. In Türkiye, Article 21 of the Patient Rights Regulation mandates respect for patient preferences, whereas Article 24 permits medical intervention without consent in cases of life-threatening emergency (Özdilek, 2006, p. 87). These seemingly contradictory norms place physicians in a critical decision-making position (Güzeldemir, 2005, p. 4; Özbilen, 2013, p. 29).

This chapter aims to address the challenges encountered in the anesthetic and surgical management of JW patients from clinical, ethical, and legal perspectives. By evaluating the available literature, a practical framework for clinical decision-making is proposed, and the theoretical discussion is contextualized through an original case presented at the end of the chapter.

## METHODS

This study is designed as a narrative literature review. During the analytical process, the sources were classified into three main domains:

I. Clinical and Perioperative Management: Studies focusing on blood management, transfusion alternatives, intensive care practices, and surgical outcomes were reviewed, including Crowe & DeSimone (2019), Vasques et al. (2016), MacLaren & Anderson (2004), and Ott & Cooley (1977).

II. Ethical and Faith-Based Refusal: The bioethical dimensions of transfusion refusal in the context of Jehovah's Witness beliefs were primarily based on Muramoto (1998).

III. Legal Framework: Issues related to patient information, legal validity of medical interventions, and situations in which consent is not required were examined based on the works of Özdilek (2006), Güzeldemir (2005), and Özbilen (2013).

The scope of the study is not limited to literature analysis; ethical, clinical, and legal interpretations are further discussed through an original case, which is integrated into the analytical framework.

## Historical, Theological, and Ethical Foundations of Blood Transfusion Refusal in Jehovah's Witnesses

### Basis of Blood Transfusion Refusal Among Jehovah's Witnesses

Jehovah's Witnesses constitute a unique community that generates distinctive clinical and ethical debates within healthcare systems worldwide. Their refusal of blood transfusion based on religious beliefs creates significant technical and ethical challenges for clinicians, particularly in high-risk areas such as anesthesia, surgery, and intensive care. The JW community's stance against blood transfusion is grounded in religious interpretation and continues to directly influence clinical decision-making despite advances in modern medicine (Muramoto, 1998, pp. 223–225).

This situation poses particular difficulties in clinical settings involving a high risk of major blood loss, such as trauma, cardiovascular surgery, and emergency surgical interventions. While anesthesiologists are obligated to respect the patient's decision, they are simultaneously required to engage in complex decision-making processes guided by ethical, professional, and legal responsibilities when the patient's life is at risk. Consequently, the boundary between religious belief and medical necessity becomes a critical and practical question in clinical care.

### Theological Background: The Spiritual Significance of Blood

According to Jehovah's Witness doctrine, blood is regarded as "life itself." This belief is based on interpretations of passages from the Old Testament and views the extracorporeal use of blood as an act contrary to divine will. The JW community categorically rejects the transfusion of whole blood and its major components, including packed red blood cells, plasma, and platelets.

Muramoto (1998, pp. 224–226) emphasizes that theological consistency has played a central role in the continued strict opposition to transfusion within the JW faith, despite developments in modern medicine. Nevertheless, over time, the community has adopted more flexible approaches regarding certain options, such as blood fractions, recombinant factors, and autologous techniques. This flexibility has allowed clinicians to broaden blood management strategies and has enabled some patients to experience less complicated perioperative courses.

**Impact of Religious Refusal on Clinical Practice**

The refusal of blood transfusion should be regarded by clinicians not merely as a "preference" but as an integral component of an individual's religious and moral identity. This perspective necessitates heightened sensitivity in the physician–patient relationship and throughout the informed consent process. Crowe and DeSimone (2019, pp. 474–475) emphasize that optimal clinical care for JW patients can only be achieved through comprehensive information-sharing, individualized planning, and systematic implementation of transfusion alternatives.

Religious refusal generates particularly profound dilemmas in emergency situations requiring rapid decision-making, such as polytrauma. Two fundamental principles confront the clinician: the obligation to preserve life and the obligation to respect patient autonomy and religious belief. This conflict exposes clinicians to ethical and legal risk. Özbilen (2013, p. 29) notes that exceptions permitting medical intervention without consent must be applied under very strict conditions; otherwise, such interventions may be deemed unlawful.

## PERIOPERATIVE BLOOD MANAGEMENT AND ANESTHETIC APPROACHES

In JW patients, refusal of blood and blood products renders perioperative blood management a matter of vital importance for anesthesiologists. Blood loss during surgical and anesthetic procedures leads to reductions in both intravascular volume and oxygen-carrying capacity, precipitating hemodynamic instability. When transfusion is not an option, compensation for these effects requires the combined use of pharmacological and non-pharmacological methods (Crowe & DeSimone, 2019). Accordingly, anesthesiologists, as integral members of the surgical team, must meticulously plan strategies aimed at minimizing blood loss.

### Preoperative Blood Management

Preoperative preparation is the primary determinant of success in transfusion-free surgery for JW patients. Optimization of hemoglobin levels, correction of coagulation parameters, and enhancement of hematopoietic capacity are strongly recommended prior to surgery (Lawson & Ralph, 2015). Elective procedures should not be performed before completion of preoperative optimization, as this approach represents one of the most important factors in reducing mortality.

### Erythropoietin and Iron Therapy

Erythropoietin (EPO) is a frequently used pharmacological agent in JW patients to increase hemoglobin levels and enhance oxygen-carrying capacity prior to surgery. Particularly in JW patients with chronic disease or a predisposition to anemia, EPO can significantly reduce the need for transfusion. EPO therapy is more effective when administered in combination with iron, folate, and vitamin B12; iron deficiency should be corrected preoperatively, as it limits the efficacy of EPO (Crowe & DeSimone, 2019).

### Correction of Coagulation Parameters

In JW patients, where blood products cannot be used, coagulopathy represents a serious risk factor. During the preoperative period, antifibrinolytic agents—particularly tranexamic acid and aprotinin—are effective tools for reducing blood loss (Lawson & Ralph, 2015). These agents increase the predictability of intraoperative blood loss in high-risk surgical procedures.

### Intraoperative Blood Management

Strategies aimed at minimizing blood loss during surgery are of critical importance in JW patients. The role of the anesthesiologist extends beyond maintaining hemodynamic stability and includes developing a multidisciplinary approach in collaboration with the surgical team.

### Collaboration Through Surgical Techniques

Surgical techniques that reduce blood loss must be coordinated with anesthetic management. The cardiovascular surgical series conducted by Ott and Cooley (1977) involving 542 JW patients demonstrated that minimal dissection, low-pressure bypass techniques, and meticulous hemostasis significantly reduce blood loss.

### Controlled Hypotension

Controlled reduction of mean arterial pressure decreases bleeding within the surgical field. As transfusion is not possible in JW patients, this method assumes vital importance. However, it must be applied cautiously in patients at risk of ischemia (Lawson & Ralph, 2015).

### Acute Normovolemic Hemodilution (ANH)

ANH involves the removal of a predetermined volume of blood prior to surgery while maintaining normovolemia with crystalloid or colloid solutions. JW patients accept ANH only when performed as a “closed-circuit autologous procedure.” This method reduces erythrocyte loss during surgery and results in higher postoperative hemoglobin levels (Crowe & DeSimone, 2019).

**Cell Salvage Systems**

Cell salvage allows blood lost during surgery to be collected and reinfused into the same patient. In JW patients, this technique is considered acceptable when the blood remains in continuity with the patient’s circulation and is regarded as an autologous process. Crowe and DeSimone (2019) describe this method as one of the most effective tools in transfusion-free surgery.

**Antifibrinolytic Agents**

Tranexamic acid and aprotinin reduce intraoperative blood loss. Their use is particularly critical in JW patients, for whom transfusion is not an option (Lawson & Ralph, 2015).

4.3. Postoperative Blood Management and Intensive Care

In the postoperative period, control of blood loss and maintenance of hematological stability are of critical importance in JW patients. Bloodless intensive care unit (ICU) protocols are based on minimal blood sampling, optimizing oxygen-carrying capacity, and aggressive management of hemostasis (MacLaren & Anderson, 2004).

**Minimal Blood Sampling**

Unnecessary laboratory testing should be avoided in JW patients, as each blood sample may further reduce existing hemoglobin and hematocrit levels (MacLaren & Anderson, 2004).

**Hemodynamic Stability and Oxygen-Carrying Capacity**

Preservation of oxygen-carrying capacity in the postoperative period is vital. High-fraction oxygen therapy, appropriate fluid management, and pharmacological support constitute the primary strategies.

### Pharmacological Hemostasis

Aprotinin, tranexamic acid, and desmopressin may be used to reduce postoperative bleeding. These agents are fundamental components of transfusion-free care in JW patients (Crowe & DeSimone, 2019).

### Outcomes and Experience with Transfusion-Free Surgery

Surgical outcomes in JW patients can be improved through appropriate blood management strategies. The meta-analysis by Vasques et al. (2016) demonstrated that mortality following cardiovascular surgery in JW patients did not differ significantly from transfused patient populations. Similarly, the series reported by Ott and Cooley (1977) confirmed that successful outcomes can be achieved through meticulous blood management. Advances in pharmacological agents and surgical technology have enabled JW patients to safely undergo many major surgical procedures (Lawson & Ralph, 2015). However, blood management remains particularly challenging in trauma and emergency surgical cases.

Refusal of blood transfusion in JW patients extends beyond a purely medical decision and assumes ethical and legal dimensions. In Türkiye, patient rights legislation protects patient autonomy and informed consent while simultaneously obligating physicians to preserve life and fulfill their duty of care (Özbilen, 2013, pp. 26–31). In the context of JW patients, a delicate balance must be maintained between these competing obligations. Physicians must respect religious beliefs while remaining fully aware of medical necessity and legal responsibilities in emergency situations (Güzeldemir, 2005, pp. 4–6).

## LEGAL NATURE OF MEDICAL INTERVENTION AND CONSENT

In Turkish law, medical intervention is defined as an act directed toward bodily integrity, and its legality is generally established through patient consent. In JW patients, refusal of blood transfusion represents the opposite of consent; that is, the patient has explicitly refused permission. Özbilen (2013, pp. 27–28) emphasizes that such refusal constitutes a fundamental expression of the patient's will regarding bodily integrity, and violation of this will may result in criminal liability.

### Importance of Informed Consent

Güzeldemir (2005, pp. 4–6) defines informed consent not merely as the communication of medical risks but as a process that provides all information necessary for patients to make decisions freely. In JW patients, this process is particularly critical with respect to refusal of transfusion and the scope of alternative treatments. During this process, the physician should explain the possible consequences of refusing transfusion (shock, organ failure, death), present alternative treatment methods in detail, clarify which products are accepted and rejected, and jointly determine procedures to be applied in emergency scenarios. Whenever possible, this process should be supported by written documentation and included in the patient's medical record (Güzeldemir, 2005, p. 5).

### Emergency Situations and Authority to Intervene

Under Turkish law, medical intervention without patient consent may be performed in emergency situations (Patient Rights Regulation, Article 24). However, in JW patients, the presence of a previously documented written refusal renders the emergency exception inapplicable (Özdilek, 2006, pp. 88–90).

The permissibility of transfusion in an unconscious JW patient may be evaluated under three scenarios:

I. Written refusal present: The physician may not intervene; acting otherwise results in legal liability (Özbilen, 2013, p. 27).

II. Verbal refusal known, no written documentation: The physician should act in accordance with ethical committee and professional guidance. A gray area exists; however, respect for the patient's religious will remains essential.

III. No prior declaration: The emergency exception may be applied; however, if there is reason to suspect that the patient may be a JW, intervention should be planned with caution.

Within this framework, emergency management represents not only a clinical decision but also a legal and ethical responsibility matrix (Muramoto, 1998, pp. 229–231).

## Criminal and Civil Liability of the Physician

Transfusion performed against patient consent carries risks in both criminal and civil law. Özbilen (2013, p. 29) notes that medical intervention performed without consent may be classified as intentional bodily harm. Also, physicians are obligated to fulfill their duty of care by minimizing complications that may arise in JW patients (Güzeldemir, 2005, p. 6).

The physician's duty of care encompasses not only preservation of life but also respect for the patient's religious beliefs. Achieving this balance is an inseparable component of both ethical and legal responsibility.

## Patient Rights and Freedom of Religion

In Türkiye, patient rights include constitutional protection of respect for religious beliefs. Refusal of blood transfusion by JW patients represents a concrete expression of this constitutionally protected freedom. Güzeldemir (2005, pp. 4–5) emphasizes the critical role of thorough information and documentation in preventing legal disputes.

Key considerations in the documentation process include: scope and duration of consent, scope of refusal (specific products rejected), explanation of alternative treatment options, procedures to be applied in emergency situations, meticulous preparation of these documents provides both legal and ethical protection for physicians.

**Achieving Ethical and Legal Balance**

In the management of JW patients, ethical principles (autonomy, beneficence, non-maleficence) and legal principles (consent, duty of care, emergency exception) must be applied concurrently (Muramoto, 1998, pp. 227–229). Respect for autonomy entails acknowledgment of the patient's religious integrity, while physicians must not neglect their obligation to preserve life. This dual responsibility necessitates careful evaluation of clinical and legal decisions.

**Practical Legal Recommendations**

Based on the literature and national legislation, the following recommendations are proposed for the management of JW patients:

- Obtain a clear, written refusal declaration.
- Document the refusal in the patient file and operative records.
- Clearly specify which products are refused.
- Define emergency scenarios within the documentation.
- Record all discussions in detail.
- Explain alternative treatment options to the patient.

- Apply the emergency exception cautiously in unconscious JW patients without prior refusal documentation.
- Maintain the duty of care at every stage (Güzeldemir, 2005; Özbilen, 2013; Özdilek, 2006).

**International Ethical and Legal Perspective**

From an international perspective, refusal of blood transfusion by competent JW patients is widely recognized as a lawful expression of autonomy, bodily integrity, and freedom of religion. These rights are protected by the Universal Declaration of Human Rights (United Nations, 1948, Article 18), the International Covenant on Civil and Political Rights (United Nations, 1966, Article 18), and the European Convention on Human Rights (Council of Europe, 1950, Articles 8 and 9). International human rights law consistently emphasizes that medical interventions require free and informed consent, and forced treatment in a competent adult constitutes a violation of bodily integrity (Council of Europe, 1997).

Ethically, this legal framework aligns with contemporary bioethics, which affirms that respect for autonomy remains valid even in life-threatening circumstances. Beneficence does not justify overriding a competent patient's informed refusal; rather, it obligates clinicians to pursue all reasonable alternatives consistent with the patient's values. In this context, patient blood management strategies developed for JW patients have contributed to broader advances in perioperative safety and ethical clinical practice (World Health Organization, 2010).

## CASE REPORT: A JEHOVAH'S WITNESS PATIENT WITH POLYTRAUMA

A 28-year-old female patient presented to the emergency department with suspected polytrauma following a traffic accident in which she was ejected from the vehicle. Evaluation revealed an ischium–pubis fracture, right-sided pneumothorax, pulmonary contusion, and suspected intra-abdominal hemorrhage. Tube thoracostomy was performed in emergency department. Her vital signs remained stable, and diagnostic peritoneal lavage (DPL) was positive. Based on these findings, emergency surgical intervention was planned. During the evaluation, the patient declared that she was a Jehovah's Witness and provided written refusal of all blood and blood products. Given the patient's religious refusal of blood transfusion, a multidisciplinary discussion involving anesthesiology, general surgery, orthopedic surgery, and legal consultation was initiated. The patient was informed in detail about the life-threatening nature of her condition, the risks associated with refusal of transfusion, and alternative blood conservation strategies. A written informed refusal document was obtained and placed in the medical record. Emergency surgical intervention was planned with strict blood conservation principles.

Although the initial positive DPL suggested the need for emergency surgery, a repeat DPL performed under sedation and analgesia yielded a negative result, and the intervention was therefore limited to drain placement only. The patient remained hemodynamically and laboratorily stable and was discharged without complications on the third postoperative day.

This case represents an important example for evaluating the ethical, legal, and clinical decision-making process adopted by the anesthesiologist in a Jehovah's Witness patient with polytrauma, in whom there was a risk of blood loss and a potential need for emergency intervention.

**DISCUSSION**

The presented case highlights the complexity of managing Jehovah's Witness patients with polytrauma, where life-threatening hemorrhage intersects with absolute refusal of blood transfusion. In such scenarios, anesthesiologists and surgeons are required to integrate clinical expertise with ethical sensitivity and legal awareness.

Polytrauma creates an environment in which blood loss may progress rapidly and surgical decisions must be made within minutes, significantly increasing mortality risk in JW patients. In the presented case, the negative result of a second diagnostic peritoneal lavage and the limitation of surgical intervention to minimally invasive techniques contributed to a favorable clinical course.

Crowe and DeSimone (2019) reported that mortality increases substantially in trauma patients managed without transfusion. An optimal management model for JW patients with polytrauma includes:

Preoperative Period: detailed documentation of faith-based refusal (Crowe & DeSimone, 2019), clarification of acceptable blood fractions, consideration of erythropoietin, iron, and folate supplementation (MacLaren & Anderson, 2004)

Intraoperative Management: application of blood-sparing surgical techniques (Lawson & Ralph, 2015), consideration of cell salvage when appropriate, maintenance of hemodynamic stability, cautious use of hypotensive anesthesia

Postoperative Management: intensive care monitoring supporting blood conservation (MacLaren & Anderson, 2004), enhancement of anemia tolerance, optimization of oxygen-carrying capacity

Ethical and Legal Process: comprehensive informed consent (Güzeldemir, 2005), legal recognition of written refusal declarations (Özbilen, 2013; Özdilek, 2006), ethical decision-making guided by autonomy and beneficence (Muramoto, 1998

Key clinical lessons include the importance of reassessing pathology, prioritizing minimally invasive approaches, ensuring readiness of transfusion-alternative strategies, and emphasizing multidisciplinary decision-making.

The literature demonstrates that transfusion-free strategies can be successfully applied in elective and high-risk surgeries; however, trauma settings present unique challenges due to uncontrolled bleeding and limited preparation time. Early identification of JW status, prompt multidisciplinary collaboration, and implementation of blood conservation techniques are essential to improve outcomes.

Pharmacological agents such as tranexamic acid play a crucial role in reducing hemorrhage, particularly in trauma patients. Similarly, meticulous surgical technique and avoidance of unnecessary organ resection are critical components of transfusion-free management. Intensive care strategies focusing on oxygen delivery optimization and erythropoiesis stimulation further contribute to patient recovery.

From an ethical perspective, respect for patient autonomy remains paramount, even in life-threatening situations. The presented case underscores that respecting a patient's informed refusal does not equate to abandonment of care; rather, it necessitates the application of alternative therapeutic strategies within the boundaries of patient preference.

Legally, the presence of a written refusal document clarifies the physician's responsibilities and limits the applicability of emergency intervention without consent. This documentation serves as a protective measure for both patient and physician and reduces the risk of legal conflict.

## CONCLUSION

The management of Jehovah's Witness patients represents one of the most challenging intersections of medicine, ethics, and law. Refusal of blood transfusion requires anesthesiologists and surgical teams to adopt comprehensive blood conservation strategies while maintaining respect for patient autonomy and religious beliefs.

This chapter demonstrates that, with meticulous planning, interdisciplinary cooperation, and adherence to ethical and legal principles, even high-risk cases such as polytrauma can be managed successfully without blood transfusion. Documentation of informed refusal, clear communication, and familiarity with national legal frameworks are indispensable components of safe and ethical practice.

Ultimately, the anesthesiologist's role extends beyond technical expertise to include ethical judgment and legal responsibility. Balancing the duty to preserve life with respect for patient autonomy is not only a professional obligation but also a reflection of modern, patient-centered medicine.

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# CHAPTER 3

# NEUROLOGİCAL CHANGES DURİNG OPEN CARDİAC SURGERY: NEUROMONİTORİNG

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## INTRODUCTION

Neurological injury that may develop after successful cardiac surgery can markedly reduce patients' quality of life and constitutes one of the leading causes of perioperative mortality. Therefore, preservation of cerebral function and early detection of neurological

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complications during cardiac surgery are of paramount importance. Among diagnostic approaches, assessment of cerebral blood flow occupies a central role. Maintaining cerebral perfusion pressure within optimal limits is considered one of the fundamental goals of cardiopulmonary bypass. However, continuously fluctuating hemodynamic conditions during cardiac surgery and the presence of extracorporeal circulation may lead to significant alterations in cerebral blood flow (Demirci et al., 2007: 97–100).

Neurological injury occurring during coronary artery bypass surgery is thought to result from regional or global cerebral hypoperfusion secondary to hypoperfusion or embolic events. A better understanding of the mechanisms regulating cerebral blood flow during the perfusion process is critical for reducing morbidity and mortality related to neurological dysfunction in the perioperative period (Newman et al., 2001: 395–400; Harvey, 2018: 21–39; Shaw et al., 1989: 633–646).

Electroencephalography (EEG) is one of the principal neurophysiological methods that enables monitoring of changes in cerebral electrical activity. Transcranial Doppler ultrasonography (TCD) allows evaluation of alterations in cerebral blood flow and detection of embolic signals. The bispectral index (BIS) quantitatively reflects the degree of cerebral cortical synaptic suppression and is widely used to estimate the hypnotic effect of anesthesia (Karadeniz et al., 2008: 107–108). Nevertheless, the sensitivities of these neuromonitoring modalities may vary across different stages of surgery, and each has its own specific advantages and limitations. Consequently, contemporary practice has shifted away from the search for a single ideal monitoring method toward multimodal neurological monitoring strategies that combine different techniques (Edmonds et al., 1996: 16–22; Thudium et al., 2018: 28–33).

In this study, based on the effectiveness of multimodal neuromonitoring in the early detection of neurological injury, we aimed to evaluate the comparative advantages of various neurological monitoring systems across different stages of surgery. Within this framework, cerebral perfusion monitoring accompanied by TCD, together with EEG and BIS parameters, was performed throughout all phases of coronary artery bypass surgery, with the objective of identifying neurological events that may occur during the perioperative period.

## METHODS

This prospective observational thesis study was conducted with approval obtained from the Training and Planning Coordination Unit of our hospital. A total of 22 patients aged between 30 and 65 years, classified as American Society of Anesthesiologists (ASA) physical status I–II and scheduled for elective coronary artery bypass grafting (CABG), were included in the study.

Patients with active neurological disease; a history of active or previous cerebrovascular events; head trauma; depression, dementia, or psychiatric disorders; previous cardiac surgery; left ventricular ejection fraction ≤40%; concomitant valvular disease; uncontrolled hypertension; peripheral vascular disease; diabetes mellitus (type I or II); atherosclerotic stenosis or plaque in any cerebral vessel demonstrated by Doppler or other methods; carotid artery stenosis or plaque detected by carotid Doppler ultrasonography; renal dysfunction (creatinine >1.5 mg/dL); hepatic dysfunction (SGOT >40 IU/L, SGPT >40 IU/L); hematological dysfunction (severe anemia, hematocrit <30%); significant metabolic or endocrine disorders; or an inadequate temporal bone window were excluded from the study.

All patients were evaluated one day prior to surgery. Detailed information regarding the planned surgical procedure, anesthesia technique, and study protocol was provided, and written informed consent was obtained. Patients continued their routine cardiac medications until the morning of surgery. For premedication, 5–10 mg oral diazepam was administered on the night before surgery, and 0.1 mg/kg intramuscular morphine hydrochloride was given 30 minutes before surgery.

Upon arrival in the operating room, standard monitoring was established prior to induction (electrocardiography, pulse oximetry, and invasive arterial blood pressure monitoring). Two peripheral venous access lines were inserted. In addition to routine cardiac anesthesia monitoring, all patients were monitored with electroencephalography (EEG) and bispectral index (BIS). Cerebral blood flow velocity measurements were obtained using transcranial Doppler (TCD), with simultaneous EEG and BIS recordings.

Before EEG and BIS monitoring, the skin of the forehead, temporal, and postauricular regions was cleaned with an alcohol swab and dried. EEG recordings were obtained from electrodes placed over the frontotemporal scalp using a two-channel EEG module (Inc. S/5 monitor EEG module, Datex-Ohmeda, Madison, WI, USA). Four electrodes (Aspect Zipprep) were used: two electrodes were placed bilaterally over the temporal areas (At1 and At2), with Fpz as the reference and Fp1 as the ground electrode. The 95% spectral edge frequency (SEF), mean frequency (MF), and amplitude (ampl) parameters were continuously monitored.

For BIS monitoring, a BIS module (BIS Inc. S/5 monitor module, Datex-Ohmeda, Madison, WI, USA) and a BIS sensor (BIS™ Quatro, Aspect Medical Systems Inc., Newton, MA, USA) were used. Electrode 1 was placed on the midline of the forehead approximately 5 cm above the nasal bridge; electrode 3 was positioned on the right temporal region at the midpoint between the hairline and the lateral canthus; electrode 4 was placed just above the eyebrow; and electrode 2 was placed between electrodes 1 and 4.

After electrode placement, gentle pressure was applied for 5–10 seconds to ensure adequate contact with the scalp.

Middle cerebral artery blood flow velocity measurements were performed using an HP Sonos 1000 Doppler ultrasound system (Hewlett Packard, USA) with a 2-MHz probe. Measurements were obtained through the left temporal window at the point providing the optimal image over the zygomatic arch. Gel was applied between the probe and scalp to improve image quality. During the initial measurement, the middle cerebral artery was identified and the optimal imaging depth was determined. For subsequent measurements, the same vessel segment and depth (50–55 mm) were used for each patient.

From appropriate Doppler flow waveforms, maximum velocity (Vmax), minimum velocity (Vmin), and mean velocity (Vmean) were measured. The maximum-to-minimum velocity ratio (Vmax/Vmin), pulsatility index (PI), and resistive index (RI) were automatically calculated by the device software. Cerebral blood flow velocity measurements were compared according to predefined time points. During cardiopulmonary bypass (CPB), hematocrit values were standardized between 20% and 28% in all patients due to the effect of hematocrit on cerebral blood flow. $PaCO_2$ levels were maintained in accordance with values measured outside CPB using the alpha-stat pH management strategy.

A standardized anesthesia protocol was applied to all patients. Anesthesia induction was achieved with fentanyl 10 µg/kg, midazolam 0.1 mg/kg, and pancuronium bromide 0.1 mg/kg. Anesthesia maintenance was provided with fentanyl infusion at 0.15–0.30 µg/kg/min and midazolam infusion at 0.2–0.4 mg/kg/min; additional doses of pancuronium bromide (0.03 mg/kg) were administered as required. The fraction of inspired oxygen ($FiO_2$) was set at 0.50. Mechanical ventilation was adjusted to maintain normocapnia ($PaCO_2$: 35–45 mmHg) with a tidal volume of 6–8 mL/kg and a respiratory rate of 8–12 breaths per minute.

Radial artery cannulation was performed for arterial blood gas sampling and invasive arterial pressure monitoring, and internal jugular vein cannulation was used for central venous pressure monitoring. Throughout the operation, electrocardiography, heart rate, arterial blood pressure, end-tidal $CO_2$, peripheral oxygen saturation, rectal and nasopharyngeal body temperature, and urine output were continuously monitored. Arterial blood gas analyses were performed concurrently with measurement time points, and $PaCO_2$ levels were maintained within the normocapnic range (35–40 mmHg).

A standard CPB technique was applied in all patients. Prior to CPB, anticoagulation was achieved with 300–400 U/kg heparin to maintain an activated clotting time (ACT) >450 seconds, and heparinization was monitored with ACT measurements at 30-minute intervals. During CPB, a Medos Hilite 7000 membrane oxygenator and circuit were used. Flow rates of 1.6–2.4 L/m$^2$/min were provided using a roller pump (Jostra), and nonpulsatile perfusion pressure was maintained between 40 and 80 mmHg. In patients with systolic arterial pressure exceeding 130 mmHg despite adequate anesthesia depth, nitroglycerin and/or sodium nitroprusside infusion was administered as needed. Body temperature was maintained between 30 and 32 °C during CPB.

The oxygenator priming solution consisted of approximately 1500 mL Ringer’s lactate, 2.5 mg/kg mannitol, and 0.5 mg/kg heparin. Ventilation was suspended during the aortic cross-clamp period. Crystalloid cardioplegia solution used to achieve hyperkalemic and hypothermic cardiac arrest was prepared by adding one ampoule of bicarbonate to a plegisol solution containing 16 mEq potassium per liter. Subsequent blood cardioplegia administered every 20 minutes was prepared to contain 100 mL crystalloid cardioplegia solution, 300 mL blood mixed with priming solution from the pump, and 12.5 mEq potassium per liter. Hematocrit levels were maintained between 20% and 28% by hemodilution. Patients were weaned from CPB when rectal body temperature exceeded 36 °C.

EEG, BIS, and TCD measurements were performed at ten different time points during surgery: (1) before induction, (2) after induction before surgical incision, (3) after sternotomy, (4) during harvesting of the left internal mammary artery, (5) during total bypass at the cooling phase when 34 °C was reached, (6) during cooling at 33 °C, (7) during cooling at 32 °C, (8) during rewarming when 33 °C was reached and at the end of total bypass, (9) after removal of the cross-clamp, and (10) at the end of surgery. The cross-clamp period was defined as the interval between placement and removal of the cross-clamp. At each measurement time point, nasopharyngeal and rectal temperatures, heart rate, systolic, diastolic, and mean arterial pressures were recorded, and arterial blood gas samples were obtained simultaneously. Blood gas analyses included pH, $PaCO_2$, $PaO_2$, oxygen saturation, hematocrit, and hemoglobin values.

In the postoperative period, clinical evaluation included documentation of general neurological examination findings, time to extubation, length of stay in the intensive care unit, and any complications.

ProspeStatistical analyses were performed using SPSS version 11.5. Descriptive statistics were expressed as median (minimum–maximum). Repeated-measures analysis of variance was applied, with Bonferroni correction used for pairwise comparisons. One-way analysis of variance was used to evaluate time-dependent changes in measurements, the Oneway ANOVA test was applied for between-group comparisons, and post hoc tests were used for multiple comparisons. A p value <0.05 was considered statistically significant.

## RESULTS

A total of 22 patients were included in this prospective thesis study. The patients' demographic characteristics and surgery-related data (age, sex, body weight, body mass index, ASA classification, cross-clamp time, perfusion time, and duration of surgery) are summarized in Table 1.

**Table 1. Demographic characteristics of the patients**

| Parameter | n | Mean ± SD | Range |
|---|---|---|---|
| Age (years) | 22 | 54.5 ± 5.5 | 45–64 |
| Weight (kg) | 22 | 77.9 ± 9.2 | 59–94 |
| Body mass index (kg/m²) | 22 | 1.8 ± 0.11 | 1.59–2.10 |
| ASA I / II / III | 22 | – | – |
| Sex (Male) | 22 | – | – |
| Cross-clamp time (min) | 22 | 55.9 ± 14.7 | 24–86 |
| Perfusion time (min) | 22 | 88.9 ± 26.7 | 45–142 |
| Duration of surgery (min) | 22 | 242.3 ± 37.4 | 170–300 |

Nineteen of the patients included in the study were smokers. Five patients had no comorbidities, whereas hyperlipidemia was present in one patient and hypertension in 16 patients.

Evaluation of intraoperative hematocrit values revealed a significant decrease only at the initiation of cardiopulmonary bypass (mean hematocrit at induction: 44.6; mean hematocrit at pump entry: 24.2; $p<0.05$). No significant changes were observed at other measurement time points compared with the preceding values. $PCO_2$ values did not differ significantly from previous measurements at any time point. pH values were maintained between 7.35 and 7.45 throughout all measurement periods, with no significant differences between measurements.

When changes in mean arterial pressure (MAP) over the measurement time points were evaluated, a significant decrease in MAP was observed after induction ($p<0.05$). The increases in MAP during sternotomy and left internal mammary artery (LIMA) dissection were not statistically significant. At the fifth measurement during the cardiopulmonary bypass (CPB) period, a significant decrease in MAP compared with the preceding measurement was detected ($p<0.05$). No significant differences were observed in the other measurements obtained during CPB. The increase in MAP observed at the end of surgery was not significant compared with the preceding measurement.

When maximum flow velocity (Vmax) values measured from the middle cerebral artery were compared across measurement time points, a significant decrease was detected at the second measurement after induction. Although the decrease persisted at the third and fourth measurements, it was not significant compared with the preceding measurements. At entry into CPB (fifth measurement), the decrease in Vmax values was significant. No significant changes were observed at the sixth, seventh, and eighth measurements during CPB. At the end of total bypass (ninth measurement), a significant increase in Vmax values was observed. At the tenth measurement at the end of surgery, the increase persisted but was not significant compared with the preceding measurement and exceeded the pre-CPB values.

Analysis of changes in mean flow velocity (Vmean) measured from the middle cerebral artery showed a significant decrease only at the second measurement after induction ($p<0.05$). Although the decrease continued at the third and fourth measurements, it was not statistically significant. The increase observed at the fifth measurement compared with the preceding measurement was not significant. No significant changes were detected at the sixth, seventh, and eighth measurements during CPB. The increase observed at the ninth measurement was statistically significant ($p<0.05$).

Comparison of middle cerebral artery Vmax values with MAP measurements demonstrated that both parameters exhibited concordant changes throughout all surgical stages. Similarly, pulsatility index (PI) and resistive index (RI) measurements showed parallel changes at all stages.

Evaluation of electroencephalographic spectral edge frequency (SEF) changes revealed a significant decrease only at the second measurement after induction. Although the decrease continued at the third, fourth, fifth, sixth, and seventh measurements, it was not significant compared with previous measurements. The increases observed at the eighth, ninth, and tenth measurements were not statistically significant.

Analysis of bispectral index (BIS) values showed a significant decrease only at the second measurement after induction. Although the decrease persisted at the third, fourth, fifth, sixth, and seventh measurements, it did not reach statistical significance. The increases observed at the eighth, ninth, and tenth measurements were not significant compared with the preceding measurements.

In the comparative evaluation of TCD data with EEG-SEF and BIS values, significant decreases were observed in all parameters during the first four measurements after induction ($p<0.05$). At entry into CPB, a significant decrease in TCD Vmax values was observed ($p<0.05$), whereas the decreases in EEG-SEF and BIS measurements were not statistically significant. During the period of weaning from total CPB, significant increases were observed in Vmax and Vmean values, while the increases in EEG-SEF and BIS values were not significant. After coronary artery bypass graft surgery, all neuromonitoring parameters returned to baseline values and showed concordant trends. No neurological deficits were detected in any patient during the postoperative period.

## DISCUSSION

Despite an overall reduction in mortality and morbidity, neurological injury associated with cardiopulmonary bypass (CPB) remains a significant clinical problem. Neurological complications following cardiac surgery constitute one of the leading causes of postoperative morbidity.

Brain injury related to cardiac surgery is generally considered to be based on three principal pathophysiological mechanisms: (a) hypo- or hyperperfusion, (b) embolization, and/or (c) systemic inflammatory response. The first two mechanisms can be detected using neurophysiological monitoring methods. Monitoring cerebral blood flow, oxygenation, and neural function enables early detection of neurophysiological imbalance or embolic events and allows timely intervention (Newman et al., 2001; Scolletta et al., 2015).

Maintaining cerebral perfusion pressure within optimal limits is one of the primary objectives of cardiopulmonary bypass. During cardiac surgery, variable hemodynamic conditions and extracorporeal circulation may lead to marked fluctuations in cerebral blood flow. Although cerebral autoregulatory mechanisms attempt to compensate for these changes to a certain extent, preservation of regional cerebral perfusion is of critical importance. In addition to surgery-related risks, patient-related factors—such as the presence of extracranial or intracranial atherosclerotic disease—also play a decisive role in the development of postoperative neurological injury (Murkin, 2004). In this context, assessment of cerebral blood flow occupies a central position among diagnostic approaches.

Currently, a large proportion of cardiac surgical procedures are performed under hypothermic CPB to ensure myocardial and cerebral protection. However, in patients undergoing hypothermic CPB, there are periods of normothermic perfusion before bypass, during the rewarming phase, and after weaning from bypass. During normothermic perfusion, cerebral metabolism and cerebral blood flow may exhibit significant changes; the balance between oxygen delivery and demand may be disrupted, thereby increasing the risk of postoperative neurological injury (Boran, 2007; Karadeniz et al., 2005).

Continuous monitoring of cerebral function and cerebral blood flow during cardiac surgery enables early recognition of neurological injury and implementation of preventive measures. For this purpose, various neurophysiological monitoring techniques are employed in cardiovascular surgical practice (Murkin, 2004; Kowalczyk et al., 2016).

The main methods used in central nervous system monitoring include electroencephalography (EEG; including BIS and entropy), evoked potentials, near-infrared spectroscopy (NIRS), transcranial Doppler ultrasonography (TCD), jugular bulb oximetry, transcranial cerebral oximetry, and intracranial pressure monitoring (Edmonds et al., 1996; Lewis et al., 2018).

The incidence of neurological complications following coronary artery bypass surgery largely depends on the adequacy of perioperative and postoperative diagnostic methods. Neurophysiological monitoring techniques offer important advantages in the early detection of these complications.

EEG records the electrical potentials generated by cerebral cortical neurons and is highly sensitive to changes in cerebral perfusion and oxygenation. It also plays an important role in monitoring the hypnotic effects of anesthetic agents. Although EEG is sensitive in detecting altered synaptic function, it has limitations in the specific diagnosis of pathology. Therefore, additional monitoring modalities are required. In this regard, TCD stands out as a method well suited for intraoperative monitoring, as it provides continuous information on cerebral blood flow and enables detection of embolic events. BIS, in addition to monitoring the hypnotic component of anesthesia, may serve as an auxiliary parameter for detecting the onset of severe cerebral ischemia (Boran, 2007; Karadeniz et al., 2008).

In this study, the relationships between different neurological monitoring methods and changes in cerebral blood flow, as well as their relative advantages during various stages of coronary artery bypass surgery, were evaluated comparatively. Cerebral blood flow measured by TCD was used as the reference diagnostic method, and EEG and BIS data were compared with these measurements.

In the literature, TCD-based evaluations define cerebral hypoperfusion as a decrease in middle cerebral artery flow velocity to less than 20% of the pre-incision baseline value, and cerebral hyperperfusion as an increase exceeding 200% (Murkin, 2004; Karadeniz et al., 2005). In EEG monitoring, a reduction of more than 50% from baseline in amplitude or SEF values, and a BIS value below 20, are considered indicative of ischemia (Murkin, 2004;

Karadeniz et al., 2008). In our study, no changes below these threshold values were observed in any patient.

The ability of TCD to reflect cerebral blood flow has been investigated in several comparative studies. Comparisons with the xenon-133 clearance method have shown that middle cerebral artery velocity measurements do not directly represent cerebral blood flow; however, changes in velocity parallel changes in blood flow (Trivedi et al., 1997). Studies using the thermodilution method have demonstrated that TCD is an appropriate technique for monitoring changes in cerebral blood flow during cardiac surgery (Linden et al., 1991).

In our study, parameters that could affect cerebral blood flow were standardized as much as possible. The same anesthesia protocol and similar surgical techniques were applied to all patients; pH and $PaCO_2$ values were kept constant; and hematocrit and temperature variables were controlled during the CPB period.

It is well known that the anesthetic agents used have limited effects on cerebral blood flow. Previous studies have shown that pancuronium has no effect on cerebral blood flow, EEG, or BIS, whereas fentanyl and midazolam may cause decreases in these parameters (Boran, 2007). Consistent with these findings, our study demonstrated significant reductions in cerebral flow velocities, EEG, and BIS values during the post-induction period.

When cerebral maximum flow velocity was compared with mean arterial pressure, parallel changes were observed throughout the surgical process, except for two measurement periods. These findings suggest that when $CO_2$, temperature, and hematocrit are kept constant, cerebral blood flow largely depends on mean arterial pressure. Similar results have been reported in previous studies (Demirci et al., 2007; Orihashi et al., 1997).

The pulsatility index (PI) and resistive index (RI) are important TCD parameters that provide information about vascular resistance. In our study, both parameters showed a significant decrease during the CPB period, and these changes were found to be concordant.

The initiation of CPB is characterized by abrupt hemodilution, non-pulsatile flow, and hypothermia, all of which have pronounced effects on EEG. In our study, significant suppression of SEF values was observed after induction; this decrease persisted during CPB, although differences between measurements were not statistically significant. This finding may be related to the limited number of patients included in the study.

Changes in BIS values paralleled those observed in EEG measurements. A significant decrease was observed after induction, with continued reduction during CPB; although not statistically significant, increases were noted during the rewarming and weaning phases. These findings are consistent with the literature (Boran, 2007; Myles, 2009).

Throughout all stages of surgery, EEG and BIS changes were found to be correlated with each other. However, discrepancies between TCD data and EEG/BIS data were observed during transition periods such as entry into CPB and weaning from CPB. This suggests that TCD more sensitively reflects changes in cerebral blood flow, whereas EEG and BIS may be limited during these transitional phases.

In conclusion, although EEG and BIS monitoring demonstrated significant changes following anesthesia induction, they failed to adequately reflect cerebral blood flow alterations during critical periods such as entry into and exit from CPB. In contrast, TCD parameters—particularly maximum velocity, pulsatility index, and resistive index—showed marked changes during these phases. These findings underscore the importance of multimodal neuromonitoring in coronary artery bypass surgery and suggest that the combined use of TCD with EEG and BIS may provide valuable information for evaluating perioperative neurological events. Further randomized studies with larger patient populations are required in this field.

**Key Points / Highlights**

- Neurological complications remain an important cause of morbidity in cardiac surgeries involving cardiopulmonary bypass (CPB).
- Preservation of cerebral blood flow is a fundamental determinant of neurological safety in coronary artery bypass surgery.
- Transcranial Doppler (TCD) is a reliable method that sensitively and continuously reflects intraoperative changes in cerebral blood flow in real time.
- EEG and Bispectral Index (BIS) are effective for monitoring the hypnotic effects of anesthesia but are limited in detecting abrupt changes in cerebral blood flow.
- Entry into and exit from CPB are the most critical phases in terms of cerebral hemodynamics, during which TCD parameters (Vmax, PI, RI) exhibit marked changes.
- Parallel changes between pulsatility index (PI), resistive index (RI), and mean arterial pressure (MAP) may be useful for evaluating cerebral autoregulation.
- Cerebral blood flow during the intraoperative period is largely dependent on systemic hemodynamic variables, particularly MAP.

- Multimodal neuromonitoring provides a more comprehensive assessment of cerebral perfusion and neural function than any single monitoring modality alone.
- Combined use of TCD with EEG and BIS may contribute to early detection of perioperative neurological risks in coronary artery bypass surgery.
- Randomized studies with larger patient cohorts are required to determine optimal neuromonitoring strategies in cardiac surgery.

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# CHAPTER 4

# PULSATİLİTY AND RESİSTİVE İNDİCES İN CARDİAC SURGERY


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## INTRODUCTION

Cardiac surgery, particularly procedures requiring cardiopulmonary bypass (CPB), imposes significant hemodynamic stress on the cerebral circulation, increasing the risk of neurological complications such as stroke, delirium, and cognitive dysfunction (Gupta & Steiner, 2021; Jarry et al., 2024). The complex interplay

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between systemic hemodynamics, cerebral autoregulation, and the mechanical effects of CPB necessitates continuous monitoring of cerebral perfusion to optimize intraoperative management and minimize postoperative neurological sequelae (Abdul-Khaliq et al., 2002; Boran et al., 2007).

Transcranial Doppler (TCD) ultrasonography has emerged as a non-invasive, real-time tool to assess cerebral hemodynamics in this setting. By insonating basal cerebral arteries, particularly the middle cerebral artery (MCA), TCD provides quantitative measurements of blood flow velocity, which can be analyzed using indices such as the pulsatility index (PI) and resistive index (RI) to infer cerebrovascular resistance and indirectly estimate intracranial pressure (Bellner et al., 2004; de Riva et al., 2012; Kaloria et al., 2020). PI is calculated as the difference between systolic and diastolic velocities divided by mean flow velocity, while RI represents the ratio of the difference between systolic and diastolic velocities to systolic velocity (Bellner et al., 2004; Kaloria et al., 2020). Multiple studies have demonstrated that PI correlates more reliably than RI with intracranial pressure fluctuations and cerebrovascular resistance, highlighting its clinical utility during cardiac surgery (Kaloria et al., 2020; de Riva et al., 2012).

TCD monitoring in cardiac surgery is technically performed using a 2-MHz pulsed-wave Doppler probe applied at accessible cranial windows, most commonly the temporal window, to insonate the MCA. Proper probe positioning and insonation angle are critical to ensure accurate flow velocity measurements and reproducibility (Ying-hua et al., 2024; Jarry et al., 2024). Beyond flow assessment, TCD enables detection of microembolic signals, which are particularly relevant during CPB and aortic manipulation, where embolic load can predict difficult separation from bypass and potential postoperative neurological events (Jarry et al., 2024; Ghazy et al., 2016).

In addition to cerebral blood flow monitoring via TCD, intraoperative brain function assessment is crucial in cardiac surgery. Electroencephalography (EEG) provides direct information on cortical neuronal activity, enabling detection of ischemic changes, seizure activity, and depth of anesthesia (Gimson & Smith, 2021; Jarry et al., 2022). Unlike standard clinical EEG applied in neurology, intraoperative EEG systems used in cardiac surgery are adapted for the surgical environment: they utilize a limited number of electrodes integrated into adhesive pads or headbands, positioned to optimize coverage of frontal and temporal regions that remain accessible during draping (Jarry et al., 2022; Jarry et al., 2023). These devices avoid the full 10–20 system, allowing rapid placement and minimizing interference with surgical access.

Processed EEG (pEEG) systems, such as bispectral index (BIS) monitors, transform raw EEG signals into a numerical scale (0–100) reflecting the depth of anesthesia, facilitating real-time titration of anesthetic agents (Jarry et al., 2023; Gimson & Smith, 2021). BIS monitoring has been demonstrated to reduce the incidence of intraoperative awareness and optimize anesthetic administration, which indirectly supports cerebral perfusion by avoiding hypotension from anesthetic overdose (Jarry et al., 2023). In cardiac surgery, processed EEG parameters can also correlate with cerebral ischemia or embolic events when integrated with TCD monitoring, providing complementary hemodynamic and functional information (Jarry et al., 2024; Patel et al., 2025).

The simultaneous use of TCD and EEG-based monitoring provides a multidimensional approach to cerebral protection during cardiac surgery. While TCD evaluates macrovascular flow dynamics and embolic events, EEG and pEEG provide functional insight into cortical neuronal activity. This integration allows clinicians to detect both global and regional cerebral compromise, optimize CPB flow parameters, adjust anesthetic depth, and implement targeted interventions to prevent neurological injury (Gupta & Steiner, 2021; Jarry et al., 2024; Patel et al., 2025). Such a multimodal approach is particularly critical in high-risk populations, including elderly patients, pediatric congenital heart surgery patients, and those with preexisting cerebrovascular disease (Sun et al., 2022; Yang et al., 2016).

**Intraoperative Cerebral Monitoring in Cardiac Surgery Parameters, Indications, and Objectives**

In cardiac surgery, the brain is particularly vulnerable to hypoperfusion, embolic events, and fluctuations in blood pressure associated with cardiopulmonary bypass (CPB), aortic cross-clamping, and reperfusion phases. Consequently, multimodal cerebral monitoring using transcranial Doppler (TCD) and processed EEG (pEEG) or bispectral index (BIS) is increasingly employed to detect and prevent perioperative neurological injury (Gupta & Steiner, 2021; Jarry et al., 2024).

Transcranial Doppler (TCD) is a non-invasive, ultrasound-based technique that measures blood flow velocity in basal cerebral arteries, most commonly the middle cerebral artery (MCA) via the temporal window (Aaslid, 1992; Bellner et al., 2004). Key parameters include pulsatility index (PI) and resistive index (RI), which reflect cerebrovascular resistance and indirectly estimate intracranial pressure (Bellner et al., 2004; Kaloria et al., 2020; de Riva et al., 2012). In cardiac surgery, TCD provides real-time assessment of cerebral perfusion, detection of microemboli during CPB, and guidance for hemodynamic optimization (Boran et al., 2007, Jarry et al., 2024; Ghazy et al., 2016). Abnormal PI or RI values may indicate impaired autoregulation, hyper- or hypoperfusion, or increased risk of postoperative neurological complications (Baufreton et al., 2011; Boran et al., 2007).

EEG and pEEG monitoring focus on cortical neuronal activity, which is particularly sensitive to ischemia. In the operating room, EEG electrodes are applied using headbands or limited electrode arrays designed for rapid placement and minimal interference with surgical access, predominantly over frontal and temporal regions (Jarry et al., 2022; Jarry et al., 2023). pEEG algorithms, including BIS, analyze frequency, amplitude, and phase relationships of EEG signals to generate a numerical index representing anesthetic depth (Gimson & Smith, 2021). This allows anesthesiologists to maintain optimal anesthesia while avoiding hypotension-induced cerebral hypoperfusion. Changes in processed EEG parameters may also indicate cerebral ischemia or embolic events when correlated with TCD findings, enabling immediate intraoperative intervention (Patel et al., 2025; Jarry et al., 2024).

The indications for multimodal cerebral monitoring in cardiac surgery include: High-risk CPB procedures, such as aortic arch repair or complex congenital heart surgery (Abdul-Khaliq et al., 2002; Sun et al., 2022). Patients with pre-existing cerebrovascular disease or impaired cerebral autoregulation (Yang et al., 2016). Advanced age or prolonged CPB duration, which are associated with increased risk of postoperative neurological complications (Patel et al., 2025; Boran et al., 2007). Real-time detection of embolic events or hypoperfusion to guide intraoperative hemodynamic adjustments (Jarry et al., 2024; Ghazy et al., 2016).

The primary objectives of integrating TCD and EEG/pEEG monitoring are: Early detection of cerebral ischemia, hyperemia, or embolic phenomena. Optimization of CPB flow rates, mean arterial pressure, and hematocrit to maintain adequate cerebral perfusion. Guidance of anesthetic depth to balance sedation with preservation of hemodynamic stability. Reduction of postoperative neurological complications, including stroke, cognitive dysfunction, and delirium (Gupta & Steiner, 2021; Jarry et al., 2024).

In summary, the combined use of TCD and EEG/pEEG during cardiac surgery provides complementary hemodynamic and functional data, enabling individualized management to preserve cerebral integrity. This multimodal strategy is particularly valuable in high-risk populations and complex procedures, where cerebral injury can have significant morbidity and mortality (Patel et al., 2025; Sun et al., 2022; Jarry et al., 2024).

## Measurement Techniques, Device Settings, Normal Values, and Intraoperative Changes in Cardiac Surgery

**Transcranial Doppler (TCD) Measurement Techniques:** TCD utilizes a low-frequency (2 MHz) pulsed-wave ultrasound probe to insonate basal cerebral arteries, most commonly the MCA via the temporal bone window (Aaslid, 1992; Bellner et al., 2004). The temporal window is preferred due to thin bone and minimal interference, though the orbital and suboccipital windows may be used for anterior and posterior circulation assessment (de Riva et al., 2012). During cardiac surgery, continuous or intermittent TCD monitoring is employed, depending on the surgical phase and patient risk profile (Boran et al., 2015, Jarry et al., 2024).

Key device parameters include: **Sample volume depth:** Typically 45–65 mm for MCA. **Angle of insonation:** Kept as close to 0° as possible to minimize velocity underestimation. **Gain and filter settings:** Optimized to maximize signal-to-noise ratio while minimizing artifact from CPB pumps or electrocautery.

**Normal TCD Values: Mean flow velocity (MFV):** MCA 55 ± 12 cm/s in adults at rest (Yang et al., 2016). **Pulsatility index (PI):** Normal adult MCA PI ranges 0.6–1.1; values >1.2 may indicate increased cerebrovascular resistance or impaired autoregulation (Bellner et al., 2004; Kaloria et al., 2020). **Resistive index (RI):** Typically 0.55–0.75; elevated RI may reflect elevated intracranial pressure or distal vascular resistance (Czosnyka et al., 1996).

During CPB, MFV may decrease due to hemodilution, hypothermia, or low perfusion pressures, while PI can increase in response to elevated systemic vascular resistance or cerebral vasoconstriction (Abdul-Khaliq et al., 2002; Baufreton et al., 2011). TCD is particularly sensitive to embolic signals, which appear as high-intensity transient signals (HITS), correlating with neurological complications if persistent (Ghazy et al., 2016; Jarry et al., 2024).

**EEG and Processed EEG (pEEG/BIS) Measurement Techniques:** Intraoperative EEG in cardiac surgery is generally limited to frontal electrode montages using adhesive electrode strips or headbands. This is due to the need for rapid placement, sterility, and avoidance of interference with the surgical field (Jarry et al., 2022). Modern processed EEG devices, including BIS, Narcotrend, and Entropy monitors, convert raw EEG signals into numerical indices ranging from 0 (isoelectric) to 100 (awake), facilitating anesthetic titration (Gimson & Smith, 2021).

**Device Parameters and Interpretation**

**BIS:** Maintains anesthesia typically in the 40–60 range for cardiac surgery.

Electrode impedance: Kept below 5 kΩ for signal reliability. Artifact rejection**:** Automatic detection of electromyographic (EMG) and electrocardiographic artifacts ensures accurate readings.

Intraoperatively, processed EEG indices are influenced by anesthetic depth, cerebral perfusion, hypothermia, and embolic events. Sudden BIS drops may indicate cerebral hypoperfusion or ischemia, especially when correlated with TCD PI elevations or decreased MFV (Jarry et al., 2023; Patel et al., 2025). Conversely, unexpectedly high BIS during CPB may signal inadequate anesthetic delivery or embolic cortical activation.

**Integration of TCD and EEG Monitoring:** Combining TCD and EEG provides a comprehensive assessment of both hemodynamic and functional cerebral status. For example, a patient with elevated MCA PI and decreasing BIS values during aortic cross-clamping may require increased mean arterial pressure, adjustments in CPB flow, or selective cerebral perfusion to prevent ischemia (Jarry et al., 2024; Gupta & Steiner, 2021).

**Summary of Intraoperative Changes**: **TCD:** MFV decreases during low-flow CPB; PI increases with distal resistance; HITS may indicate emboli. **EEG/pEEG:** Anesthetic depth, temperature, and perfusion affect numerical indices; sudden declines signal ischemia risk. **Clinical implication:** Real-time adjustments based on these parameters can reduce postoperative neurological complications, including stroke, delirium, and cognitive dysfunction (Sun et al., 2022; Patel et al., 2025).

## Intraoperative Findings and Clinical Implications in Cardiac Surgery

**Transcranial Doppler Findings:** TCD monitoring during cardiac surgery provides dynamic insights into cerebral hemodynamics. Mean flow velocity (MFV) and pulsatility index (PI) are critical parameters that reflect cerebral perfusion and vascular resistance. In adult cardiac surgery patients, normal MCA MFV ranges from 50–70 cm/s, with a PI of 0.6–1.1 (Yang et al., 2016; Bellner et al., 2004).

During cardiopulmonary bypass (CPB), MFV typically decreases due to hypothermia, hemodilution, and reduced perfusion pressures, whereas PI may increase secondary to elevated cerebrovascular resistance (Abdul-Khaliq et al., 2002; Baufreton et al., 2011). Persistent elevations in PI (>1.2) correlate with postoperative neurological complications, including cognitive dysfunction and stroke (Kaloria et al., 2020; Gupta & Steiner, 2021).

Embolic monitoring via TCD also detects high-intensity transient signals (HITS), indicative of microemboli. A high embolic load during CPB is associated with difficult weaning from bypass, postoperative delirium, and cognitive decline (Ghazy et al., 2016; Jarry et al., 2024).

**EEG and Processed EEG Findings:** Intraoperative EEG, particularly processed indices like BIS, provides real-time information on cortical activity and anesthetic depth. During cardiac surgery, sudden decreases in BIS, when correlated with TCD PI elevations or MFV reductions, suggest cerebral hypoperfusion or ischemia (Jarry et al., 2023; Patel et al., 2025).

Processed EEG can also detect subclinical seizure activity or cortical electrical suppression in patients with embolic or hypoperfusion events (Gimson & Smith, 2021). Maintaining BIS in the target range (40–60) reduces the risk of anesthetic over- or under-dosing and helps prevent postoperative neurocognitive complications (Jarry et al., 2022).

**Integration of TCD and EEG Findings:** The combination of TCD and EEG provides a multi-dimensional assessment of the brain. For instance: Elevated MCA PI with decreasing BIS during aortic cross-clamping may signal ischemic risk, prompting hemodynamic interventions. Stable BIS with decreasing MFV may indicate the need for increased perfusion pressure or selective cerebral perfusion (Jarry et al., 2024; Sun et al., 2022). Detection of HITS correlates with cortical EEG changes, allowing for intraoperative embolic management.

**Clinical Outcomes:** Studies consistently demonstrate that proactive monitoring of cerebral hemodynamics and cortical function reduces postoperative neurological complications. Patients with well-maintained MFV and PI during CPB have lower rates of stroke, delirium, and cognitive dysfunction (Patel et al., 2025; Gupta & Steiner, 2021). Similarly, EEG-guided anesthesia reduces periods of deep cortical suppression or undetected hypoperfusion, further protecting neurological function (Jarry et al., 2023).

**Summary:** TCD and EEG/BIS provide complementary information on hemodynamic and functional cerebral status. Elevated PI, decreased MFV, or abnormal EEG signals are early indicators of ischemia or embolic events. Real-time intervention based on these monitoring tools improves postoperative neurological outcomes.

## MATERİALS and METHODS

### Study Design and Ethical Approval

This prospective observational study was conducted following approval from the institutional ethics committee. This is study derived form thesis. All participants provided written informed consent prior to enrollment. The primary objective was to investigate the relationship between cerebral perfusion parameters derived from transcranial Doppler (TCD), cortical activity assessed via electroencephalography (EEG), anesthetic depth monitored with Bispectral Index (BIS), and systemic hemodynamics in patients undergoing elective coronary artery bypass grafting (CABG) under cardiopulmonary bypass (CPB) (Gupta & Steiner, 2021; Jarry et al., 2024).

### Patient Selection

Twenty-two adult patients, aged 30–65 years, with an American Society of Anesthesiologists (ASA) physical status I–II, scheduled for elective CABG, were included. Exclusion criteria were: prior cerebrovascular events, severe carotid artery stenosis, intracranial pathology, or known neurological disorders that could confound cerebral hemodynamics (Gupta & Steiner, 2021; Jarry et al., 2024). All patients underwent standard preoperative assessment, including routine blood tests, echocardiography, and carotid Doppler imaging to rule out significant cerebrovascular disease.

**Anesthetic and Surgical Management**

A standardized anesthetic protocol was applied to all patients. Induction of anesthesia consisted of intravenous midazolam and fentanyl, titrated to maintain hemodynamic stability, followed by endotracheal intubation and mechanical ventilation. Anesthesia was maintained with total intravenous anesthesia (TIVA) using continuous infusion of midazolam and fentanyl in accordance with institutional guidelines. CPB was performed under moderate hypothermia (32°C) using full-flow bypass, with systemic hemodynamic parameters continuously recorded (Abdul-Khaliq et al., 2002; Sun et al., 2022).

Surgical procedures were performed by the same cardiac surgical team to minimize variability. The left internal mammary artery (LIMA) was dissected for grafting, and CPB was initiated with careful monitoring of systemic perfusion and temperature.

**Neuromonitoring Modalities**

**Transcranial Doppler (TCD)**

Cerebral blood flow velocities were measured in the middle cerebral artery (MCA) using TCD. Pulsatility Index (PI) and Resistance Index (RI) were calculated as markers of cerebrovascular resistance and cerebral perfusion. TCD measurements were obtained at five predefined surgical stages: Before induction of anesthesia (baseline, Time Point 1), Post-induction, prior to surgical incision (Time Point 2), After sternotomy during LIMA dissection (Time Point 3) During total bypass cooling phase at 32°C (Time Point 4), At the end of surgery (Time Point 5)

These time points were selected to capture critical phases of anesthesia induction, surgical manipulation, hypothermic CPB, and recovery, allowing assessment of temporal dynamics in cerebral perfusion (Bellner et al., 2004; Kaloria et al., 2020; de Riva et al., 2012).

## Electroencephalography (EEG) and Bispectral Index (BIS)

Two-channel EEG was used to evaluate cortical synaptic activity. Spectral Edge Frequency (SEF) was derived to quantify changes in cortical activity during anesthesia and surgery (Gimson & Smith, 2021). Concurrent BIS monitoring was employed to provide a processed numerical index of anesthetic depth, facilitating comparison with EEG and cerebral perfusion measures (Jarry et al., 2022).

## Systemic Hemodynamics

Mean arterial pressure (MAP) was continuously recorded via arterial cannulation throughout surgery. MAP measurements were synchronized with TCD, EEG, and BIS data at all five time points, enabling integrated analysis of cerebral perfusion and cortical activity (Sun et al., 2022; Abdul-Khaliq et al., 2002).

## Data Collection and Statistical Analysis

All neuromonitoring and hemodynamic parameters were recorded at the five predefined stages. PI and RI values were analyzed alongside EEG SEF, BIS indices, and MAP to assess correlations and trends across surgical stages.

Statistical analysis was conducted using SPSS software. Repeated-measures analysis of variance (ANOVA) compared parameters across surgical stages. Post hoc testing was applied for pairwise comparisons where appropriate. Pearson correlation coefficients were calculated to evaluate relationships between PI, RI, EEG, BIS, and MAP (Gupta & Steiner, 2021; Bellner et al., 2004; Jarry et al., 2024). Statistical significance was set at $p < 0.05$.

Trends were additionally expressed as percentage changes relative to the previous time point, highlighting intraoperative dynamics in cerebral perfusion, cortical activity, and systemic hemodynamics.

## Outcome Measures

Primary outcomes included intraoperative changes in TCD-derived PI and RI, their correlation with EEG SEF and BIS indices, and their relationship with MAP at all five surgical stages. Secondary outcomes involved assessment of postoperative neurological function, including stroke, delirium, or cognitive dysfunction, and correlation of these events with intraoperative neuromonitoring trends (Jarry et al., 2024; Gupta & Steiner, 2021).

## RESULTS

**CD Parameters (PI and RI):** The Pulsatility Index (PI) and Resistance Index (RI) measured by transcranial Doppler ultrasonography (TCD) demonstrated significant variations throughout the perioperative period. According to one-sample *t*-test results, both PI and RI values were significantly different from zero at all measurement time points ($p = 0.000$), confirming the clinical presence and reliability of these measurements.

The lowest PI and RI values were observed during the cross-clamp period, and these reductions were statistically significant ($p < 0.05$). A strong positive correlation was identified between PI and RI values ($r \approx 0.95–0.97$, $p = 0.000$), indicating that TCD-derived parameters consistently reflect perioperative hemodynamic changes.

**Mean Arterial Pressure (MAP):** Mean arterial pressure (MAP) values were significantly different from zero at all time points based on one-sample *t*-test analysis ($p = 0.000$). Analysis of variance (ANOVA) revealed significant differences particularly during the post-LIMA, cross-clamp, and end-of-surgery periods ($p < 0.05$). Changes in MAP showed a strong correlation with TCD-derived PI and RI values ($r = 0.953–0.974$, $p = 0.000$), demonstrating a close relationship between TCD parameters and systemic hemodynamic status.

**EEG and BIS:** EEG spectral edge frequency (SEF) values decreased in accordance with increasing depth of anesthesia. Although one-sample *t*-test analysis showed that EEG SEF values were significantly different from zero at all time points ($p = 0.000$–0.001), ANOVA *p*-values exceeded 0.05 at several peri-induction time points (1st, 2nd, and 4th measurements), indicating that intergroup differences were not statistically significant ($p = 0.533$–0.584).

Bispectral Index (BIS) values demonstrated a significant decrease during the cross-clamp period ($p = 0.000$). Although BIS values were also significantly different from zero at other time points based on one-sample *t*-tests, cluster analysis revealed that statistically meaningful differences were confined to the cross-clamp period. No significant correlation was observed between TCD parameters and EEG or BIS measurements ($p > 0.05$).

**Correlation Analyses:** Statistically significant correlations were identified between TCD parameters (PI and RI) and MAP ($r \approx$ 0.95–0.97, $p = 0.000$). In contrast, no significant correlations were found between PI or RI and EEG SEF or BIS values ($p > 0.05$). These findings suggest that TCD-derived changes are more closely associated with systemic hemodynamic alterations rather than with neurophysiological monitoring parameters.

**Clinical Findings:** No neurological complications were observed in any patient during the postoperative period. Specifically, no cases of delirium, epilepsy, ischemic or hemorrhagic stroke, alterations in consciousness or personality, or focal neurological deficits were recorded. These findings indicate that the perioperative changes in TCD and hemodynamic parameters were clinically tolerable and not associated with adverse neurological outcomes.

**Table 1.** *Perioperative Changes in Parameters Over Time (Mean ± SD) and Statistical Significance (p < 0.05)*

| Parameter | Induction | Post-Induction | LIMA | Cross-Clamp | Endof Surgery | Trend / Interpretation |
|---|---|---|---|---|---|---|
| TCD PI | 0.542 ± 0.070 | 0.529 ± 0.058 (−2.4%) | 0.528 ± 0.099 (−2.6%) | 0.201 ± 0.089* (−63%) | 0.515 ± 0.073 (−5%) | Marked decrease during cross-clamp with subsequent recovery; $p < 0.05$ |
| TCD RI | 0.862 ± 0.168 | 0.859 ± 0.151 (−0.3%) | 0.888 ± 0.251 (+3%) | 0.231 ± 0.136* (−74%) | 0.829 ± 0.172 (−4%) | Critical reduction during cross-clamp; $p < 0.05$ |
| MAP (mmHg) | 110 ± 13 | 83 ± 11* (−24.5%) | 87 ± 9 (−20.5%) | 62 ± 11* (−43.6%) | 74 ± 8* (−32.7%) | Significant changes at cross-clamp and selected time points; $p < 0.05$ |
| BIS | 98 ± 0.09 | 60 ± 0.09 | 46 ± 0.09 | 41 ± 5* | 44 ± 9 | Significant reduction during cross-clamp and end periods; $p < 0.05$ |
| EEG SEF | 22 ± 2 | 12 ± 5 | 11 ± 2 | 9 ± 1.5 | 11 ± 2 | Decrease consistent with anesthesia depth; $p > 0.05$ |

* $p < 0.05$

**Table 2**. *Correlations Between TCD Parameters and MAP, EEG, and BIS (r, p < 0.05)*

| Variable Pair | *r* | *p*-value | Significance |
|---|---|---|---|
| PI – MAP | 0.953 | 0.000 | Yes |
| RI – MAP | 0.974 | 0.000 | Yes |
| PI – EEG | 0.225 | 0.326 | No |
| RI – EEG | 0.078 | 0.737 | No |
| PI – BIS | 0.219 | 0.339 | No |

| Variable Pair | *r* | *p*-value | Significance |
|---|---|---|---|
| RI – BIS | 0.182 | 0.430 | No |
| MAP – EEG | 0.225 | 0.326 | No |
| AP – BIS | 0.099 | 0.669 | No |

## DISCUSSION

In this study, we examined the utility of transcranial Doppler (TCD)–derived Pulsatility Index (PI) and Resistance Index (RI) as surrogate markers of cerebral perfusion during elective cardiac surgery with cardiopulmonary bypass, correlating these indices with mean arterial pressure (MAP) and neurophysiological measures (EEG SEF and BIS). We selected five key intraoperative time points representing perfusion transitions: pre-induction, post-induction, post-sternotomy/LIMA harvest, cross-clamp (non-pulsatile CPB), and end of surgery under native pulsatile flow. In our cohort, PI and RI demonstrated significant perioperative changes, notably at the cross-clamp phase ($p < 0.05$), which was accompanied by substantial reductions in MAP ($p < 0.05$) and BIS ($p < 0.05$). Meanwhile, correlations between TCD indices and MAP were strong (PI–MAP $r \approx 0.95$; RI–MAP $r \approx 0.97$, $p < 0.05$), whereas correlations between TCD indices and EEG or BIS were not significant ($p > 0.05$), indicating that hemodynamic changes in cerebral blood flow velocity were more closely tied to systemic perfusion than to cortical electrophysiological patterns.

**Interpretation of TCD Indices in Cerebral Perfusion**: TCD is a dynamic, non-invasive technique that measures blood flow velocity in basal intracranial arteries, reflecting real-time cerebrovascular hemodynamics (Naqvi et al., 2013). PI and RI—derived from the spectral flow waveform—are widely used as indices of cerebrovascular resistance and pulsatility. PI is calculated as (systolic – diastolic velocity) / mean velocity, whereas RI is calculated as (systolic – diastolic velocity) / systolic velocity. Both parameters variably reflect distal vascular resistance and vascular compliance (de Riva et al., 2012; Naqvi et al., 2013).

The relationship between PI and intracranial pressure (ICP) and cerebral perfusion pressure (CPP) has been investigated in neurosurgical populations: Bellner et al. (2004) demonstrated a very strong correlation between TCD-derived PI and simultaneously measured ICP in neurocritical care patients ($r = 0.938$, $p < 0.0001$), suggesting PI may reflect upstream hydrodynamic changes (Bellner et al., 2004; Kaloria et al., 2020). In patients with intracranial hypertension, PI correlates with opening ICP values more strongly than RI, supporting its relative sensitivity for cerebrovascular resistance and pressure effects (Kaloria et al., 2020). These associations underscore PI's responsiveness to global cerebrovascular conditions, which is relevant in cardiac surgery when systemic hemodynamic fluctuations occur.

However, other studies have cautioned that the relationship between PI and ICP is complex and not linear, as autoregulatory changes, vessel compliance, and systemic blood pressure can influence TCD indices independently of intracranial pressure (de Riva et al., 2012). Importantly, the "PI = f(CVR, compliance, pressure)" equation derived in modeling studies indicates that PI reflects multiple interacting determinants of flow dynamics rather than single mechanistic variables alone. In practice, this means that changes in PI or RI must be interpreted in the context of systemic hemodynamic shifts, rather than in isolation (de Riva et al., 2012).

**Hemodynamic Findings and Cross-Clamp Physiology**: Our data revealed that the cross-clamp phase, characterized by non-pulsatile bypass flow, was the most hemodynamically stressful period for cerebral perfusion, with both PI ($0.201 \pm 0.089$, $p < 0.05$) and RI ($0.231 \pm 0.136$, $p < 0.05$) reaching their lowest values, in conjunction with the lowest MAP (61.8 mmHg, $p < 0.05$). These observations align with physiological principles that continuous non-pulsatile flow during cardiac bypass modifies cerebrovascular impedance and flow patterns, temporarily altering the expected pulsatility of cerebral circulation. Classic TCD literature emphasizes that flow pulsatility is influenced by both peripheral resistance and the mechanical characteristics of flow delivery; non-pulsatile CPB therefore disrupts baseline pulsatility, which is reflected in reduced PI and RI values (Naqvi et al., 2013). Moreover, this physiologic transition from pulsatile to non-pulsatile perfusion underscores the need for continuous monitoring throughout critical surgical epochs.

Our findings of strong correlations between MAP and TCD indices confirm that systemic hemodynamic forces strongly influence cerebral flow dynamics during surgery ($p < 0.05$). This interdependence is well supported by broader TCD research showing that changes in MAP, CPP, and ICP modulate flow velocity and pulsatility; studies in both neurocritical and perioperative settings have shown that PI correlates inversely with CPP when pressure drops, reflecting compensatory cerebrovascular resistance adjustments (Bellner et al., 2004). While our study did not directly measure ICP or CPP, the strong PI–MAP and RI–MAP correlations ($p < 0.05$) suggest that systemic blood pressure fluctuations during anesthesia and CPB have major effects on cerebrovascular resistance and flow patterns.

EEG, BIS, and the Independence of Neurophysiological Measures: EEG SEF and BIS are widely utilized in anesthesia to assess cortical electrical activity and depth of anesthesia. Our results show that BIS values significantly decreased during the cross-clamp ($41 \pm 5$, $p < 0.05$). EEG SEF also declined in parallel, although cluster comparisons between phases did not achieve statistical significance ($p > 0.05$). These patterns indicate suppression of cortical activity consistent with anesthetic depth and diminished cortical perfusion during low MAP and flow states. However, the absence of significant correlations between TCD indices and EEG/BIS ($p > 0.05$) underscores that hemodynamic and cortical electrophysiological changes can occur independently—an important conceptual distinction that supports the need for multimodal monitoring. Neurophysiological indices primarily reflect synaptic and cortical electrical status, whereas TCD indices reflect global flow resistance and velocity changes.

This dissociation aligns with broader literature indicating that processed EEG attributes such as BIS can be influenced by anesthetic depth and sedation rather than direct measures of cerebral perfusion or autoregulatory status. Indeed, reviews of EEG in perioperative neuroscience suggest that while processed EEG can reduce anesthetic dosing and awareness, it may not reliably indicate perfusion adequacy by itself without corroborative circulatory metrics (Bispectral Index discussions). Therefore, combining TCD with EEG/BIS provides complementary rather than redundant information.

**Multimodal Monitoring Compared with Alternative Techniques:** A critical strength of our study is the integration of *multimodal monitoring*: TCD (PI/RI), EEG SEF, BIS, and MAP. This approach reflects contemporary emphasis on comprehensive assessment in complex cardiac surgery, where cerebral perfusion is influenced by hemodynamic factors (MAP, CPB flow), embolic phenomena, anesthetic depth, and autoregulatory capacity. Literature in both cardiac and neurocritical settings supports the value of combined modalities over single measures.

**Near-Infrared Spectroscopy (NIRS)**: NIRS provides continuous, non-invasive assessment of regional cerebral oxygenation and has been widely used in cardiac surgery to detect oxygen desaturation events, particularly in pediatric and adult populations (Patel et al., 2025; Sun et al., 2022). However, NIRS primarily reflects *regional cortical oxygen hemoglobin saturation* and can be confounded by extracerebral tissues and scalp blood flow, limiting its specificity for global cerebral perfusion. While NIRS adds valuable information on oxygenation, it does not provide direct measures of flow resistance or pulsatility like TCD. Therefore, *NIRS and TCD can be synergistic*, but neither fully replaces the other.

**Jugular Venous Oxygen Saturation ($SjvO_2$):** $SjvO_2$ monitoring assesses *global cerebral oxygen balance* and can identify episodes of low perfusion. However, it is invasive, requires catheterization, and offers a temporally averaged indicator rather than *real-time dynamic data*. TCD, by contrast, provides high temporal resolution of velocity and pulsatility changes, enabling clinicians to detect acute shifts in cerebral hemodynamics that might be obscured in $SjvO_2$ metrics.

**Invasive ICP Monitoring**: Although ICP monitoring remains the "gold standard" for certain neurosurgical contexts, it is not indicated routinely in elective cardiac surgery due to its invasiveness and associated risks. Nonetheless, studies in neurocritical care demonstrate strong correlations between TCD PI and ICP (Bellner et al., 2004; Kaloria et al., 2020). These data suggest that TCD PI may serve as a *non-invasive surrogate* for changes in ICP or intracranial compliance when invasive monitoring is inappropriate. However, this surrogate role must be interpreted with caution due to confounding factors such as compliance variability (de Riva et al., 2012).

**Clinical Outcomes and Neurological Safety**: Importantly, none of the patients in our cohort experienced postoperative neurological deficits, including delirium, seizures, ischemic or hemorrhagic strokes, or significant changes in consciousness or motor/sensory function. Taken together with our intraoperative monitoring data—significant TCD changes, MAP correlations, and neurophysiological suppression during cross-clamp—the absence of adverse neurological outcomes suggests that real-time multimodal feedback may facilitate prompt clinical interventions (e.g., MAP optimization, anesthetic titration) that preserve neurological integrity. This observation is consistent with cardiac surgery literature emphasizing the predictive and protective roles of TCD monitoring (Jarry et al., 2024; Ghazy et al., 2016; Gupta & Steiner, 2021). Moreover, studies focusing on cerebral microemboli have shown that real-time TCD detection of high intensity transient signals (HITS) can predict difficult weaning from CPB and correlate with adverse outcomes, highlighting the broader utility of TCD as a monitoring tool (Jarry et al., 2024).

**Integrating Hemodynamic and Monitoring Insights:** The juxtaposition of pulsatile vs. non-pulsatile perfusion has clinical significance in cardiac surgery. During cross-clamp and CPB, cerebral perfusion is supported by non-pulsatile flow, which may alter autoregulatory responses and flow resistance characteristics as measured by PI and RI. Studies comparing on-pump and off-pump CABG show that hypoperfusion is more pronounced and prolonged with non-pulsatile flow, further supporting the value of continuous TCD monitoring in capturing these shifts (TCD intraoperative studies). Our findings that PI and RI dramatically change during the cross-clamp ($p < 0.05$) while partially reverting toward baseline values post-CPB suggest that pulsatility restoration upon reperfusion correlates with recovery of cerebrovascular dynamics. This echoes physiological interpretations that pulsatile flow promotes more physiological shear patterns and may benefit autoregulatory stability.

**Limitations and Future Directions**: While our results align with and are supported by the existing literature, several limitations must be acknowledged. First, our sample size was modest, which may reduce the power to detect smaller correlations, particularly between TCD indices and neurophysiological measures. Second, TCD is operator dependent; acoustic window quality and probe placement can affect signal acquisition. Third, we did not measure ICP or $SjvO_2$ directly; such comparisons could further elucidate cerebral physiology during surgery. Finally, while our study focused on immediate postoperative outcomes, long-term cognitive and neuropsychological outcomes were not assessed.

Future studies should consider larger cohorts, high-risk patients (e.g., with carotid disease or compromised autoregulation), and additional modalities such as NIRS and $SjvO_2$ to expand multimodal monitoring paradigms. Comparative studies of different bypass strategies (on-pump vs. off-pump) and anesthetic protocols might also clarify how specific intraoperative management decisions affect cerebral hemodynamics and outcomes.

## CONCLUSION

In summary, our study demonstrates that: TCD PI and RI change significantly across intraoperative phases, especially during cross-clamp with non-pulsatile CPB ($p < 0.05$). Strong correlations exist between TCD indices and MAP ($p < 0.05$), reflecting the interdependence of systemic and cerebrovascular hemodynamics. EEG SEF and BIS provide complementary neurophysiological information, although they do not correlate directly with TCD indices. No postoperative neurological complications were observed, aligning with literature suggesting that multimodal monitoring enhances intraoperative safety. Compared with alternative modalities, TCD combined with EEG/BIS and systemic hemodynamics offers real-time, non-invasive, continuous assessment of cerebral perfusion and cortical function that is especially valuable during critical phases of cardiac surgery.

These findings elevate the evidence for multimodal intraoperative neuromonitoring in cardiac surgery, positioning TCD PI/RI as central components of a comprehensive cerebral protection strategy that is supported by existing research (Bellner et al., 2004; Kaloria et al., 2020; Jarry et al., 2024; Gupta & Steiner, 2021).

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