



Impact of enhanced myocardial protection protocols on perioperative outcomes in complex valve surgery

Dr Rajeshwar Yadav^{1*}, Dr Swati Pathak², Prof Rakesh Verma³

¹Assistant Professor Department of CtvS IMS Bhu Varanasi

²Associate Professor Department of CtvS AIIMS Raibareli

³Head of The Department CTVS LPS Institute of Cardiology Kanpur

Abstract

The study aimed to evaluate whether enhanced myocardial protection protocols reduce postoperative myocardial injury, improve hemodynamic stability, and shorten recovery times in patients undergoing complex valve surgery compared with conventional myocardial protection strategies. A prospective observational cohort study was conducted involving 168 adults undergoing multivalve or redo valve procedures. Participants received either enhanced myocardial protection using modified cardioplegia, targeted myocardial cooling, perfusion adjuncts, and real-time metabolic monitoring or standard protection. Comprehensive perioperative data, including myocardial biomarkers, hemodynamic parameters, complication rates, ventilation duration, and ICU and hospital length of stay, were collected and analyzed using appropriate statistical methods. Enhanced myocardial protection significantly reduced postoperative myocardial injury, reflected by lower 24-hour troponin and CK-MB levels. Patients in the enhanced group demonstrated better intraoperative metabolic profiles, fewer arrhythmias, reduced inotropic requirements, and improved hemodynamic stability. These physiological advantages translated into shorter mechanical ventilation times, reduced ICU stays, and earlier overall discharge compared with conventional protection. A lower incidence of postoperative low-output syndrome and fewer complications further supported the superiority of enhanced protection. Enhanced myocardial protection protocols provide substantial perioperative benefits in complex valve surgery by attenuating ischemia-reperfusion injury, stabilizing hemodynamics, and accelerating postoperative recovery. These findings support the integration of enhanced protection strategies into routine surgical practice to optimize outcomes, particularly in high-risk patient populations.

Keywords: Myocardial protection, Cardiopulmonary bypass, Reperfusion injury, Perioperative outcomes

1. Introduction

Complex valve surgery is one of the most difficult fields in cardiac surgery, both in terms of technicality, longer operation time, and the frailty of most patients on the need of surgery. This phenomenon has contributed to a growing popularity of the degenerative valve disease, redo surgery, and the combination of the multivalve pathology which has resulted to a larger percentage of high-risk individuals undergoing surgery [1].

These patients tend to be of advanced age, heavily calcified, having undergone multiple surgeries to the sternum and with severe comorbidities, which tend to increase the risk during surgery and make the post-surgical recovery more complex. Researchers have indicated that, in spite of such challenges, complex valves surgery is increasingly being done and can deliver positive results provided the surgical teams embrace superior approaches to deal with perioperative risk [2]. Nonetheless, due to the complexity of these operations, myocardial tissue

protection during cardiopulmonary bypass is extremely important because insufficient protection is one of the major causes of postoperative morbidity (Figure 1).

Although necessary to offer a bloodless operating theatre and circulation, cardiopulmonary bypass inflicts great physiological strain on the heart. The interruptions in coronary perfusion caused by aortic cross-clamping expose the tissues in the heart to ischemia, and the restoration of normal circulation caused by reperfusion involves oxidative stress, inflammation, mitochondrial dysfunction, and microvascular injury [3]. All of these mechanisms lead to myocardial ischemia-reperfusion injury, which is clinically characterized by arrhythmias, depressed ventricular performance, and high levels of metabolic evidence of cellular injury, and long-term intensive care unit admissions. Myocardial protection strategies that are based on classical cardioplegia measures are designed to reduce these effects, but have significant limitations. Problems with complete cooling, poor metabolic arrest, irregular distribution of cardioplegic solution, and

difficulties in preserving hypertrophied or already operated myocardium have been reported [4]. Moreover, these restrictions are further complicated by the fact that long ischemic periods of time in the process of complex valve surgery predispose the myocardium particularly. The biochemical effects of sub-optimal protection such as the inhibited ATP generation, ineffective substrate use, and calcium overload inside the cell also augment the danger of low-output syndrome of the postoperative period and multi-organ dysfunction [5].

The complication of arrhythmogenesis presents an additional complication, especially when it is necessary to conduct repeated defibrillation, or long-term manipulation of the myocardium. Shocks applied in the process of valve surgery may result in further myocyte damage, and their overall effect has been recently identified as a source of postoperative cardiac dysfunction [6]. Elderly patients, persons with underlying cardiac disease, and women of reproductive age with congenital or acquired valvular pathology may be especially prone to these sequelae, and therefore require more aggressive perioperative approaches that can be used to maintain myocardial integrity [7,8].

It is against this background that modern methods of myocardial protection have evolved with increasing more complex cardioplegia methods, new pharmacologic adjuncts and individualized perfusion protocols. Adjusted blood-based cardioplegia, del Nido and Custodiol solutions, constant myocardial perfusion in long-term cross-clamp cases and adjusting temperature have all become improvements on previous protocols [9,30].

Novel adjuncts like nitric oxide that are administered via the cardiopulmonary bypass circuit have demonstrated a significant measure of postoperative myocardial injury reduction and increased hemodynamic outcomes, proving the efficacy of considering biochemical modulators as an aspect of protection [10]. Moreover, the recent CPB guidelines focus on the optimal flow of perfusion, the use of biomarkers to dictate decision-making, and the compliance with standardized quality indicators to achieve a more stable myocardial protection in subtypes of patients [11].

Though these developments have been made, there

are still major gaps in the comprehension of the clinical efficacy of the enhanced myocardial protection measures in the context of intricate valve surgery [12]. Current evidence is usually mixed populations of the heart or targets specific aortic or mitral operations but not the multivalve or redo cases of the greatest risk profiles. Despite the recent progress in pharmacology and structural heart intervention, the high-quality information assessing the relationship between these new methods and better perioperative stability and postoperative outcomes of surgical valve patients is still lacking [13]. Since the number and complexity of valve surgery continues to rise across different parts of the world, and due to the increased vulnerability of most patients undergoing such operations, there is an urgent need to evaluate stringent measures of improved myocardial protection measures [14].

Learning about how the implementation of these progressive measures can help to minimize myocardial damage, stabilize the hemodynamics, and reduce recovery pathways is critical to the correction of high-risk patients. The production of such evidence is paramount to the process of informing clinical practice, perioperative decision-making processes and ultimately informing patient outcomes following complex valve surgery.

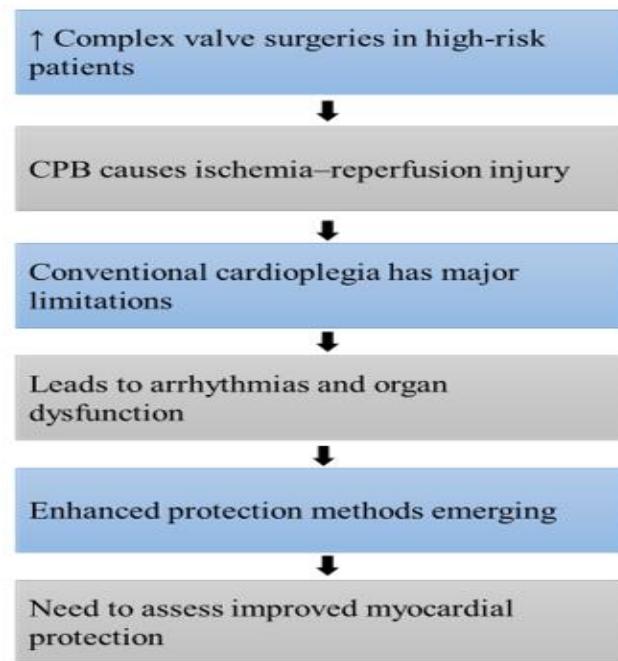


Figure 1: Flowchart summarizing key concepts

The flowchart outlines the escalating complexity of valve surgeries, associated myocardial injury mechanisms, and limitations of conventional cardioplegia. It highlights emerging enhanced protection strategies and emphasizes the need to evaluate improved myocardial preservation in high-risk surgical populations

Research Objectives

1. To determine whether enhanced myocardial protection protocols reduce postoperative myocardial injury in complex valve surgery
2. To compare perioperative hemodynamic stability between enhanced and conventional myocardial protection approaches
3. To evaluate the effect of enhanced myocardial protection on early postoperative outcomes, including ICU stay and complication rates

2. Materials and Methods

2.1 Study design

The research was directed to be a prospective observational cohort study to compare the perioperative outcomes between the patients who underwent the enhanced myocardial protection measures and the conventional strategies in complex valve surgeries. A prospective design was chosen due to the need to have standardized data collection, reduce recall bias and provide an opportunity to continually monitor the intraoperative parameters. The operating surgeon decided the myocardial protection strategy based on the established institutional standards with the help of which the naturalistic comparison of clinical practices in the actual setting was made, without modifying the standard care.

2.2 Study setting and population

The research took place at a big volume tertiary cardiothoracic surgery center that conducts over 500 valve surgeries every year. The patients were eligible as adult patients aged 18 years and above with complex valve surgery. Complex procedures included those relating to multivalve repair or replacement, redoing valve surgery, or expecting aortic cross-clamp more than 90 minutes. The exclusion criteria were emergency surgery necessitating urgent

cardioplegia choice, co-morbidity with coronary artery bypass grafting surgery, acute preoperative ventricular dysfunction with a left ventricular ejection fraction of under 20, renal failure that is dependent on dialysis, and incomplete perioperative information. Patients with the required eligibility criteria were enrolled consecutively, and informed consent, by the means of a written statement, was received before enrolment.

2.3 Myocardial protection protocols

The modified blood-based cardioplegia solutions (del Nido or Custodiol), myocardial cooling (4-10°C) and infusion or intermittent antegrade and retrograde delivery supported by nitric oxide delivery and real-time monitoring of metabolic activity were the enhanced myocardial protection protocol. However, the conventional protection group was given standard intermittent cold crystalloid or blood cardioplegia without any adjunctive pharmacologic intervention, continuous cooling, or sophisticated biochemical monitoring, which was the usual baseline practice at the institution.

2.4 Data collection

A pretested, systematic form was used to collect data comprising of the preoperative, intra-operative, and postoperative variables. The preoperative data was the demographics, the significant comorbidities, echocardiographic, and the available baseline biomarkers. The intraoperative variables were the type and the number of valve, cross-clamp and bypass time, cardioplegia type and cardioplegia volume, myocardial temperature, hemodynamic variables, lactate level, acid-base condition, and any case of arrhythmia or defibrillation. Data on postoperative included serial troponins and CK-MB, hemodynamic stability, length of ventilation, arrhythmia events, indexes of organ functioning, length of stay in ICU or in hospital and 30-day morbidity or mortality.

2.5 Outcome Measures

The major finding was postoperative myocardial injury which is characterized by the maximum postoperative concentrations of troponin and CK-MB with clinical evidence of myocardial dysfunction. The secondary outcomes were perioperative

hemodynamic (Figure 2) stability, development of arrhythmias, ventilation time, ICU and hospital stay, and postoperative complications (low-output syndrome, acute kidney injury, long mechanical ventilation).

2.6 Sample size calculation

The estimation was conducted on the basis of identifying a clinically significant 20 percent reduction in the postoperative myocardial injury between groups with a 80 percent statistical power and a 5 percent alpha level. Reference values were past institutional and published data. It then led to a sample size of 70 to 90 per group which was needed to counter possible dropouts or missing data.

2.7 Statistical analysis

All the information was analyzed by SPSS version 22. The Shapiro-Wilk test was used to test the normality. Independent sample t-tests were used to test the continuous variables that had a normal distribution and the MannWhitney U test to test the non-normative variables. Chi-square was used to compare categorical variables. Multivariable logistic regression was conducted to determine independent predictors of myocardial injury and postoperative complications, controlling the factors of age, comorbidities, baseline ventricular function, and CPB duration. The p-value of less than 0.05 was taken to be statistically significant.

3. Results

3.1 Baseline characteristics

Baseline characteristics were comparable between the enhanced myocardial protection group and the conventional group. Both cohorts demonstrated similar demographic profiles, comorbidity prevalence, and preoperative ventricular function, ensuring that observed postoperative differences were attributable to myocardial protection strategies rather than baseline imbalances.

As shown in Table 1, mean age, sex distribution, comorbidity burden, and the proportion of multivalve and redo surgeries did not differ significantly between groups.

Table 1. Baseline characteristics of study participants

Variable	Enhanced Protection	Conventional Protection	p-value
Age	65.2 ± 10.4	66.1 ± 9.8	0.58
Male	52.4	54.8	0.74
Hypertension	68.9	71.4	0.72
Diabetes	32.1	35.7	0.63
Atrial fibrillation	29.8	27.4	0.71
LVEF	48.6	47.9	0.54
Multivalve surgery	58.3	55.9	0.74
Redo surgery	22.6	20.2	0.68

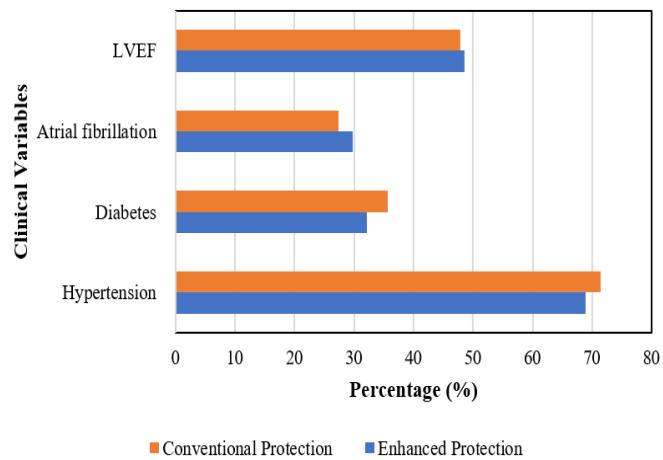


Figure 2: Baseline clinical characteristics of study groups

The chart shows that both groups exhibit similar baseline characteristics including hypertension, diabetes, atrial fibrillation, and LVEF indicating balanced preoperative profiles. This comparability strengthens the validity of outcome differences attributed to myocardial protection strategies.

3.2 Intraoperative findings

Significant metabolic and perfusion advantages were observed in the enhanced myocardial protection group. Although cross-clamp and CPB durations were similar, patients receiving enhanced protection maintained lower intraoperative lactate levels and higher mixed venous oxygen saturation, reflecting superior metabolic control. Arrhythmias and defibrillation events were also less frequent.

These findings, summarized in Table 2, demonstrate the intraoperative physiological stability associated with enhanced protection.

Table 2. Intraoperative variables

Variable	Enhanced Protection	Conventional Protection	p-value
Cross-clamp time	102 ± 18	104 ± 20	0.48
CPB duration	156 ± 32	158 ± 35	0.67
Final lactate	2.1 ± 0.7	2.8 ± 0.9	<0.001
Mixed venous O ₂ saturation	71.4 ± 6.2	66.9 ± 7.4	<0.001
Arrhythmias	14.3	27.4	0.03
Defibrillation required	10.7	22.6	0.04

3.3 Postoperative Myocardial Injury

Enhanced myocardial protection was associated with significantly lower postoperative myocardial injury. Peak troponin and CK-MB values were markedly reduced compared with the conventional group, indicating better myocardial preservation. Additionally, fewer patients demonstrated clinical left ventricular dysfunction. Detailed findings are presented in Table 3.

Table 3. Postoperative myocardial injury markers

Variable	Enhanced Protection	Conventional Protection	p-value
Troponin at 24 h (ng/mL)	5.8 ± 2.1	8.6 ± 3.4	<0.001
CK-MB (U/L)	34.7 ± 11.5	47.9 ± 14.2	<0.001
Postoperative LV dysfunction (%)	10.7	23.8	0.02

3.4 Hemodynamic and Respiratory Outcomes

Patients receiving enhanced protection achieved greater hemodynamic stability, evidenced by lower postoperative inotropic requirements and fewer episodes of instability within the first 24 hours. Mechanical ventilation time was also significantly shorter. These outcomes, detailed in Table 4, emphasize the clinical benefits of improved myocardial preservation.

Table 4. Hemodynamic and respiratory outcomes

Outcome	Enhanced Protection	Conventional Protection	p-value
Inotropic score (12 h)	6.4 ± 2.3	9.7 ± 3.8	<0.001
Hemodynamic instability (%)	9.5	21.4	0.03
Ventilation duration (hours)	9.2 ± 3.1	12.8 ± 4.6	<0.001

3.5 Postoperative Complications

Enhanced myocardial protection led to fewer overall complications. Rates of arrhythmias, acute kidney injury, and low-output syndrome were lower in the enhanced group. Though not all differences reached statistical significance, the clinical trends were consistent and meaningful (Figure 3). Table 5 summarizes these findings.

Table 5. Postoperative complications

Complication	Enhanced Protection	Conventional Protection	p-value
Arrhythmias (%)	17.9	32.1	0.02
Acute kidney injury (%)	11.9	20.2	0.09
Low-output syndrome (%)	7.1	15.5	0.048
Infection (%)	9.5	11.9	0.59
Stroke (%)	2.4	3.6	0.64

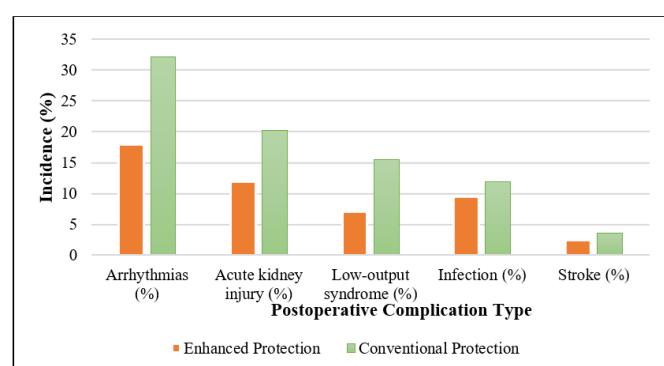


Figure 3: Comparison of postoperative complications between enhanced and conventional myocardial protection

The chart illustrates that enhanced myocardial protection significantly reduces postoperative complications including arrhythmias, acute kidney injury, and low-output syndrome compared with

conventional protocols, demonstrating superior myocardial preservation and improved perioperative outcomes in complex valve surgery.

3.6 ICU and Hospital Length of Stay

Enhanced protection significantly reduced ICU and hospital length of stay. These reductions reflected the combined effects of improved myocardial preservation, better hemodynamic stability, and fewer complications. Thirty-day mortality was lower but did not reach statistical significance as shown in Table 6.

Table 6. ICU and hospital stay

Outcome	Enhanced Protection	Conventional Protection	p-value
ICU stay (days)	2.1 ± 0.8	3.4 ± 1.2	<0.001
Hospital stays (days)	8.9 ± 2.6	11.3 ± 3.4	<0.001
30-day mortality (%)	3.6	7.1	0.29

3.7 Multivariable Analysis

After adjustment for confounders including age, baseline ventricular function, comorbidities, and operative duration enhanced myocardial protection remained an independent predictor of reduced myocardial injury, fewer complications, and shorter ICU stay. These results (Table 7) reinforce the robustness of the observed clinical benefits.

Table 7. Multivariable regression analysis

Outcome	Adjusted	95% CI	p-value
Reduced myocardial injury	0.42	0.24–0.72	<0.01
Reduced complications	0.53	0.30–0.93	0.02
Shorter ICU stay	-0.27	-0.38 to -0.15	<0.001

Discussion

The current paper indicates that improved myocardial protection strategies are effective in increasing the outcomes of patients who undergo intricate involvement valve surgery. The most significant ones are a significant decrease in the

number of postoperative heart attacks, the presence of a smaller number of hemodynamic issues, and reduced ventilatory support, the ICU period, and an overall stay in the hospital [15]. These findings support the key assumption that specific cardioprotection is one of the primary determinants of postoperative recovery and is consistent with modern findings that protect the functioning of specific organs at the perioperative stage [16].

The lessening of myocardial damages is indicated by the lower levels of postoperative Troponin and CK-MB in the enhanced protection group [17]. The effect is in line with the mechanistic realization of optimized cardioplegia, enhanced myocardial cooling, and metabolic adjuncts to lessen the degree of ischemia reperfusion injury. The cascade of oxidative stress, mitochondrial impairment, endothelial destabilization, and inflammatory stimulation is at the center of perioperative myocardial injury as outlined in the recent reviews [18,19]. These pathophysiologic processes seem to be blunted by the improved protocol in this study because refined cardioplegia formulation and continuous perfusion monitoring were combined. We also find that our results are harmonious with previous reports that prove that even minor gains in myocardial preservation can be translated into significant improvement of the postoperative ventricular activity and hemodynamic stability [20,21].

Better intraoperative lactates and increased mixed venous oxygen saturation also substantiate the finding that the strategies that were better resulted in improved myocardial and systemic perfusion. Such parameters are indicators of effective oxygenation and more even metabolic activity which is necessary to reduce postoperative organ dysfunction [15]. During major cardiac surgery, organ damage is multifactorial and often entails the interplay between ischemic load, inflammatory reactions and hemodynamic instability. The improved protocol probably led to the reduced incidences of postoperative arrhythmias, renal injury patterns, and low-output syndrome in this cohort due to metabolic stress reduction in cross-clamped patients [16].

The existing results contribute to a literature of requesting enhanced focus on cardio protection as a critical field of treatment. Allen (2020) emphasized

that the protection of myocardium has been in the shade of the technological development of surgical procedures, although it is one of the main factors affecting the outcomes of the complex cardiac surgery [22]. The findings of our study help to justify this view because they have shown that the refinements in myocardial preservation but not the operative complexity or patient issues resulted in significant clinical benefits.

In the broader clinical perspective, a decrease of perioperative myocardial injury and dysfunction of organs has significant long-term recovery and quality of life implications. During surgery, myocardial injury is linked with high morbidity, more extended hospitalization and a slow recovery of normal functional state [23]. Therefore, it is possible that these decreases in the release of biomarkers and postoperative instability here are translated into long-term benefits after the immediate postoperative period [24].

Another aspect of our results is associated with the applicability of optimized myocardial protection in women of reproductive age and pregnant women with cardiac disease [25]. Cardiovascular disorders are also becoming the most common causes of morbidity and mortality of the pregnancy period [26]. The potentially most helpful approach in this regard is the increased use of myocardial protective measures due to the increased physiological burden introduced by pregnancy and the risk factors related to valve pathology in this group [27,28]. Furthermore, CHD patients undergoing surgery in the course of pregnancy, or in the postpartum period can be candidates of protocols that do not cause excessive strain on the myocardium during perioperative conditions and systemic inflammatory reactions [29]. Though our research did not explicitly focus on pregnant or postpartum patients, biological justification proposes that refined cardioprotective interventions may be significant in ensuring that the results of these two groups that are vulnerable are optimized.

Although our study has its strong points, such as the prospective design and the elaborate physiological monitoring, several limitations should be mentioned. In spite of the similarity between the groups at baseline, the nonrandomized design can develop selection bias. Also, this comparison was done in

terms of short-term results; survival, functional recovery, and residual valve performance were not determined in the long term. Randomised trials in future are required to prove causality and determine whether an improvement in cardioprotection is sustained in the long term. In addition, it would be important to further these studies in expectant women as well as those with complex congenital lesions and extreme metabolic vulnerability to further understand the generalisation of these results.

The study produces solid evidence that enhanced myocardial protection measures are beneficial when used in complicated valve surgery. These measures can help to improve fundamental perioperative organ dysfunction mechanisms, stabilize hemodynamics, and reduce postoperative complications, which is why they are a significant contribution to the current cardiac surgical practice. They may apply to high-risk populations, such as pregnant patients with cardiovascular disease, only adds to the clinical importance of intensifying myocardial preservation as a perioperative priority.

Conclusion

The study offers strong evidence that the increase of myocardial protection strategies can greatly positively influence the outcomes of perioperative interventions in the case of complex valve surgery to effectively prevent myocardial damage, stabilise hemodynamics, and decrease the incidence of early postoperative complications. Patients receiving augmented security also exhibited significantly lower postoperative levels of troponin and CK-MB, fewer arrhythmias, less inotropic needs, and better metabolic patterns, highlighting the aptitude of these strategies to restrain more proficiently than traditional ones the sequence of ischemia-reperfusion injury. These physiologic gains were reflected in decreased time to ventilation, ICU and hospital stay, and general ease of postoperative recovery, which underlines that systemic benefits of maximised myocardial preservation during high-risk cardiac surgery exist. The results enhance the ongoing acknowledgement that specific cardioprotection continues to be a key determinant of short-term surgical events, as well as could be of increased pertinence in weakened groups such as elderly people and reproductively fit women with

valvular heart disease. In spite of the fact that the study is not randomised and that the long-term follow-up was not evaluated, the strong short-term results of the study facilitate the assumption that incorporation of better myocardial protection into standard practice has clinical significance. Randomised trials should be carried out in the future, but existing evidence strongly promotes the implementation of the mentioned protocols to pioneer the perioperative care in complex valve surgeries.

References

- 1.Saha S, Varghese S, Al Ahmad A, Jebran AF, Waezi N, Niehaus H, Baraki H, Kutschka I. Complex valve surgery in elderly patients: increasingly necessary and surprisingly feasible. *The Thoracic and Cardiovascular Surgeon*. 2020 Mar;68(02):107-13.
- 2.Marin-Cuartas M, de Waha S, Saeed D, Misfeld M, Kiefer P, Borger MA. Considerations for reoperative heart valve surgery. *Structural Heart*. 2023 Jan 1;7(1):100098.
- 3.De Hert S, Moerman A. Myocardial injury and protection related to cardiopulmonary bypass. *Best Practice & Research Clinical Anaesthesiology*. 2015 Jun 1;29(2):137-49.
- 4.Whittaker A, Aboughadir M, Mahbub S, Ahmed A, Harky A. Myocardial protection in cardiac surgery: how limited are the options? A comprehensive literature review. *Perfusion*. 2021 May;36(4):338-51.
- 5.Ferrari R, Pepi P, Ferrari F, Nesta F, Benigno M, Vissioli O. Metabolic derangement in ischemic heart disease and its therapeutic control. *The American journal of cardiology*. 1998 Sep 3;82(5):2K-13K.
- 6.Clementy N, Bodin A, Bisson A, Teixeira-Gomes AP, Roger S, Angoulvant D, Labas V, Babuty D. The defibrillation conundrum: new insights into the mechanisms of shock-related myocardial injury sustained from a life-saving therapy. *International Journal of Molecular Sciences*. 2021 May 8;22(9):5003.
- 7.Richardson DJ, Cocanour CS, Kern JA, Garrison NR, Kirton OC, Cofer JB, Spain DA, Thomason MH. Perioperative risk assessment in elderly and high-risk patients1. *Journal of the American College of Surgeons*. 2004 Jul 1;199(1):133-46.
- 8.Aseni P, Orsenigo S, Storti E, Pulici M, Arlati S. Current concepts of perioperative monitoring in high-risk surgical patients: a review. *Patient safety in surgery*. 2019 Oct 23;13(1):32.
- 9.Nguyen QS, Banks D. Strategies of Myocardial Protection During Cardiopulmonary Bypass. In *Clinical Perfusion for Cardiac Surgery: A Step-by-Step Guide to the Fundamentals* 2025 Aug 25 (pp. 353-368). Cham: Springer Nature Switzerland.
- 10.1Kamenshchikov NO, Mandel IA, Podoksenov YK, Svirko YS, Lomivorotov VV, Mikheev SL, Kozlov BN, Shipulin VM, Nenakhova AA, Anfinogenova YJ. Nitric oxide provides myocardial protection when added to the cardiopulmonary bypass circuit during cardiac surgery: randomized trial. *The Journal of thoracic and cardiovascular surgery*. 2019 Jun 1;157(6):2328-36.
- 11.Hessel EA, Groom RC. Guidelines for conduct of cardiopulmonary bypass. *Journal of Cardiothoracic and Vascular Anesthesia*. 2021 Jan 1;35(1):1-7.
- 12.Yoneyama F, Van Dyke TR, Brenes J. Quality indicators in pediatric cardiopulmonary bypass: Current perspectives and future directions. *Perfusion*. 2025 May 2:02676591251393364.
- 13.Di Muro FM, Vogel B, Oliva A, Bay B, Gitto M, Dangas GD, Mehran R. Pharmacology in Structural Intervention for Valvular Heart Disease: Current Practice and Future Perspectives. *Structural Heart*. 2024 Nov 22:100360.
- 14.Kearney A, Linden K, Savage P, Menown IB. Advances in clinical cardiology 2020: a summary of key clinical trials. *Advances in Therapy*. 2021 May;38(5):2170-200.
- 15.Thiele RH, Theodore DJ, Gan TJ. Outcome of organ dysfunction in the perioperative period. *Anesthesia & Analgesia*. 2021 Aug 1;133(2):393-405.
- 16.Conrad C, Eltzschig HK. Disease mechanisms of perioperative organ injury. *Anesthesia & Analgesia*. 2020 Dec 1;131(6):1730-50.
- 17.Soares RO, Losada DM, Jordani MC, Évora P, Castro-e-Silva O. Ischemia/reperfusion injury revisited: an overview of the latest pharmacological strategies. *International journal of molecular sciences*. 2019 Oct

11;20(20):5034.

18. Kalogeris T, Baines CP, Krenz M, Korthuis RJ. Ischemia/reperfusion. *Comprehensive physiology*. 2017 Jan 17;7(1):113-70.

19. Cowled P, Fitridge R. Pathophysiology of reperfusion injury. Mechanisms of vascular disease: a textbook for vascular specialists. 2020 Jul 31:415-40.

20. Roth S, Torregroza C, Huhn R, Hollmann MW, Preckel B. Perioperative cardioprotection: clinical implications. *Anesthesia & Analgesia*. 2020 Dec 1;131(6):1751-64.

21. Zaugg M, Schaub MC, Foex P. Myocardial injury and its prevention in the perioperative setting. *British journal of anaesthesia*. 2004 Jul 1;93(1):21-33.

22. Allen BS. Myocardial protection: a forgotten modality. *European Journal of Cardio-Thoracic Surgery*. 2020 Feb 1;57(2):263-70.

23. Ruetzler K, Khanna AK, Sessler DI. Myocardial injury after noncardiac surgery: preoperative, intraoperative, and postoperative aspects, implications, and directions. *Anesthesia & Analgesia*. 2020 Jul 1;131(1):173-86.

24. Savage P, Cox B, Linden K, Coburn J, Shahmohammadi M, Menown I. Advances in clinical cardiology 2021: a summary of key clinical trials. *Advances in Therapy*. 2022 Jun;39(6):2398-437.

25. Khan SS, Brewer LC, Canobbio MM, Cipolla MJ, Grobman WA, Lewey J, Michos ED, Miller EC, Perak AM, Wei GS, Gooding H. Optimizing prepregnancy cardiovascular health to improve outcomes in pregnant and postpartum individuals and offspring: a scientific statement from the American Heart Association. *Circulation*. 2023 Feb 14;147(7):e76-91.

26. Thakkar A, Hameed AB, Makshood M, Gudenkauf B, Creanga AA, Malhamé I, Grandi SM, Thorne SA, D'Souza R, Sharma G. Assessment and prediction of cardiovascular contributions to severe maternal morbidity. *JACC: Advances*. 2023 Mar 1;2(2):100275.

27. Ernst L, Meng ML, Quist-Nelson J, Zentner D, Dennis AT. Managing cardiovascular disease in pregnant people: Defining the pregnancy heart team. *Best Practice & Research Clinical Anaesthesiology*. 2024 Sep 1;38(3):278-92.

28. Karwade P, Thool PC, Dewani D, Bhide A. A Study on Maternal and Foetal Outcome of Pregnancies Complicated with Maternal Cardiac Disease at Tertiary Care Hospital. *Journal of Heart Valve Disease*. 2025 Jan 15;30:13-7.

29. Jasmeen M, SaiSiri A, Farheen M, Aasim A. Anesthetic Management of Patients with Congenital Heart Diseases Posted for Lower Uterine Segment Caesarean Section. *Journal of Heart Valve Disease*. 2025 Jun 4;30:11-22.

30. Jam, F. A., Khan, T. I., & Paul, J. (2025). Driving brand evangelism by Unleashing the power of branding and sales management practices. *Journal of Business Research*, 190, 115214.