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Assesment Of Gender Based Variation In Perfusion Parameters During Cardiopulmonary Bypass Surgery

Saira Ikram
Cardiac Perfusion Technology, Department of Emerging Health Professional Technologies, Allied Health Sciences Superior University Lahore Pakistan
Email: sairaikram006@gmail.com

Saba Parveen
Cardiac Perfusion Technology, Department of Emerging Health Professional Technologies, Allied Health Sciences Superior University Lahore Pakistan
Email: sabamusafa200@gmail.com

Iqra Ibrahim
Cardiac Perfusion Technology, Department of Emerging Health Professional Technologies, Allied Health Sciences Superior University Lahore Pakistan
Email: iqraib121@gmail.com

Simran Saeed*
Cardiac Perfusion Technology, Department of Emerging Health Professional Technologies, Allied Health Sciences Superior University Lahore Pakistan
Email: simran.saeed@superior.edu.pk

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Author Details

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Corresponding E-mail & Author*:

Simran Saeed
Cardiac Perfusion Technology, Department of Emerging Health Professional Technologies, Allied Health Sciences Superior University Lahore Pakistan
Email: simran.saeed@superior.edu.pk

Abstract

Background: Cardiovascular disease remains the leading cause of mortality worldwide, accounting for approximately 18-20 million deaths annually. Cardiopulmonary bypass (CPB), while indispensable in modern cardiac surgery, is inherently non-physiological and triggers complex systemic inflammatory responses and coagulation alterations. Emerging evidence suggests that sex-based physiological differences may influence perfusion adequacy and postoperative outcomes, yet most perfusion protocols remain standardized without gender-specific considerations.

Objective: This study aimed to evaluate gender-based differences in perfusion parameters and their relationship with postoperative outcomes in adult patients undergoing cardiac surgery with cardiopulmonary bypass.

Methodology: A prospective observational study was conducted that analyzed 70 adult cardiac surgery patients (38 males, 54.3%; 32 females, 45.7%) undergoing CPB. Comprehensive demographics, preoperative, intraoperative, and postoperative data were systematically collected from hospital medical records. Perfusion parameters including pump flow rates, mean arterial pressure, haematocrit levels, and oxygen delivery were analyzed by gender. Statistical analysis was performed using appropriate descriptive and inferential statistical tests.

Results: Female patients presented with significantly lower baseline hemoglobin (11.80 vs 13.98 g/dL, p<0.0001) and hematocrit (38.29% vs 41.29%, p=0.008). During CPB, females experienced more profound hemodilution (23.00% vs 25.58%, p=0.0002), lower pump flows (2.25 vs 2.67 L/min/m², p<0.0001), and reduced perfusion pressures (64.72 vs 72.31 mmHg, p=0.008). Female patients demonstrated trends toward increased postoperative complications (50.0% vs 28.9%, p=0.089) and bleeding events (34.4% vs 18.4%, p=0.126).
Conclusion: Gender-based physiological differences substantially influence perfusion dynamics during CPB. Individualized, gender-conscious perfusion management strategies are warranted to optimize intraoperative oxygen delivery and reduce postoperative complications in female cardiac surgery patients.

Introduction

Cardiovascular disease (CVD) is the leading cause of death across the world as it causes about 18-20 million deaths every year, which is equivalent to almost one-third of all deaths in the world (1). The major elements of this burden are ischemic heart disease, valvular heart disease, and heart failure. Although there is a great breakthrough in the pharmacologic treatment and interventional cardiology, a considerable number of patients who present with advanced coronary disease or structural heart disease still need a conclusive surgical treatment (1).

Coronary artery bypass grafting (CABG) is still the gold standard of multivessel coronary artery disease, especially when the patient has diabetes and the lesion morphology may be complex. On the same note, surgical valve replacement or repair is also essential to extreme aortic and mitral valves pathology (2). Safety and effectiveness of these operations mainly rely on application of cardiopulmonary bypass (CPB) which is a technology that aims to temporarily replace heart and lung functioning during an operation. In the last 50 years, advances in the technique of operation, anesthetic control and extracorporeal circulation technology have significantly decreased the death rate during operations, however, a postoperative condition characterized by the dysfunction of the organs is a clinical issue that is still prominent (3).

Cardiopulmonary bypass- is an extracorporeal circulation procedure that diverts venous blood of the patient into a heart-lung apparatus where it is oxygenated, decarboxylated, temperature-controlled and sent back to the systemic circulation (4). This technique allows surgeons to work with a motionless and blood free cardiac substrate and thus enables more complicated intracardiac surgeries. CPB is still a necessity in modern cardiac surgery, but non-physiological in nature. Artificial surfaces to which blood is exposed trigger inflammation, coagulation, and neurohormonal processes (5). Also, non-pulsatile flow, hemodilution, hypothermia, and change in perfusion pressures cause systemic physiological stress that may impact on various organ systems (6). It has been reported using large cohort studies in the publications of Circulation and The Annals of Thoracic Surgery that CPB still is independently linked with acute kidney injury (AKI), neurological dysfunction, coagulopathy and systemic inflammatory response syndrome despite the fact that it has dramatically improved the survival rates (7). In turn, the effective care of perfusion during CPB is in the key to improving postoperative outcomes.

Another characteristic of CPB is the shift of pulsatile to mostly non pulsatile flow. Despite the modern systems trying to replicate physiological flow patterns, pulsatility is hard to replicate (8). Non-pulsatile flow disturbs endothelial shear stress, inhibits the formation of nitric oxide, and could impede microcirculatory control (9). CPB Mean arterial pressure (MAP) is normally 50-80 mmHg but with recent reports, show that lower cerebral perfusion and renal perfusion pressures can be detrimental in the recovery of cerebral and renal autoregulation in vulnerable patients (10). Research articles in the Journal of Thoracic and Cardiovascular Surgery have shown that low-

pressure targets in each individual could lead to less post-adaptive organ damage (11). Hematocrit and blood viscosity, inflammatory mediators, and temperature also affect microcirculatory perfusion during CPB. Blocked microvascular circulation can contribute to tissue hypoxia of a certain region with seemingly normal overall systemic parameters (12). This notion of occult hypoperfusion has attracted more and more attention in modern perfusion studies.

The standardized traditional perfusion protocols do not vary much with male and female physiology. Nevertheless, there is emerging evidence that sex qualifies the correlation between the parameters of perfusion and post-operative outcomes. Equal flow rates, pressure goals, and hematocrit limits might not guarantee an equal amount of oxygen delivery to genders. Thus, it is necessary to assess the perfusion parameters concerning specific physiology to optimize the intraoperative state and enhance the postoperative results. The study in this area is especially crucial in the areas where there is a dearth of local data on the gender-based differences in perfusion e.g. in Pakistan, where the study will facilitate context-specific practice and evidence-based perfusion guidelines.

LITERATURE REVIEW

Pratomo et al. (2024) conducted a systematic review and meta-analysis of adult cardiac surgery patients undergoing CPB. The authors, in their observational cohort study of adult patients undergoing cardiac surgery, showed that in cases of CPB, indexed oxygen delivery that was lower than about 262 mL/min/m -2 in patients predisposed acute renal failure. Notably, this relationship was statistically significant even after the confounders (age, baseline renal function and complexity of operation) were taken into account. The paper criticised the conventional perfusion approach of using pump flow rates and mean arterial pressure as the major determinants of perfusion adequacy with the real determinant being the oxygen -carrying capacity. This study formed the physiological and clinical basis of further studies examining goal-oriented perfusion plans (39).

Gao et al. (2023) investigated the metabolic effects of insufficient oxygen delivery during CPB by analyzing carbon dioxide production (VCO_2). Their experiment showed that patients showed evidence of anaerobic metabolism, as indicated by elevated levels of lactic acid, and VCO 2 responses when the provision of oxygen dropped to critical levels. Interestingly, the metabolic changes even had apparently acceptable systemic hemodynamic parameters implying that the traditional monitoring variables might not identify occult hypoperfusion. The authors came to the conclusion that it not only is necessary to maintain oxygen delivery beyond a critical threshold to avoid overt organ injury but also to avoid subclinical metabolic perturbations that could predispose patients to postoperative complications (40).

Dias et al. (2025) analyzed intraoperative lactate levels as a proxy for tissue hypoxia in cardiac surgery patients undergoing CPB. In this group of cardiac surgery patients undergoing cardiopulmonary bypass (CPB), high levels of lactate during bypass were strongly linked to reduced oxygen delivery and worse postoperative outcome such as acute kidney injury and prolonged hospitalization. The authors highlighted the fact that lactate increase during CPB is not only a biochemical deviation but also shows the lack of adequate oxygen delivery into the bloodstream. Their findings supported the suggestion that the assessment of oxygen delivery must be a part of the regular practice of perfusion (41).

Lahanas et al. (2025) then put forward and tested the assumption of Goal-Directed Perfusion (GDP) as a multicentre prospective study. In this study, a strategy was adopted to maintain indexed oxygen provision above a preset critical level in the course of CPB in the management of patients. The results showed that there was a considerable acute kidney injury after the operation among the GDP group as compared to the group that was being handled using traditional perfusion strategies.

Notably, the study provided the interventional evidence and not just observation, which enhanced the cause-effect inference of optimized oxygen delivery and better renal outcomes. The work marked a new beginning in the science of perfusion whereby the management was based on empiric, flow-based models whereas the strategies were based on physiology, and individualized (42).

Deng et al. (2022) have carried out an observational study to estimate the relationship between the nadir levels of hematocrit during CPB and postoperative renal dysfunction. The authors have shown that reduced intraoperative hematocrit was found to be independently correlated with the chances of acute renal injury. Notably, this relationship became the same when confounding factors (age, diabetes, and baseline renal function) were taken into account. The implication of the study was that over hemodilution can cause a decrease in the oxygen-carrying capacity up to the point that they cannot meet the metabolic needs especially in the sensitive organs like the kidneys (43).

Mladinov et al. (2022) also examined the effect of intraoperative hemodilution on the mortality and major morbidity of cardiac surgery patients. Nadir hematocrit in CPB was a strong independent predictor of stroke, renal failure and premature mortality in their wide-ranging cohort analysis. The authors have suggested that the oxygen delivery is directly proportional to hemoglobin concentration, therefore, significant decreases in hematocrit during bypass can be critical in reducing oxygen delivery to the whole system. They stressed the importance of finding a balance between the advantages of hemodilution and the danger of insufficient oxygen supply (44).

Jaiswal et al. (2024) compared hematocrit-oxygen delivery interaction during CPB and established that low hematocrit is clinically significant when it leads to a decrease in indexed oxygen delivery to critical levels. Their results implied that hematocrit cannot be regarded in isolation but as one of the determinants of the overall oxygen transportation. The idea strengthened the incorporation of hemoglobin concentration as objective-based perfusion plans (45).

Wang et al. (2022), in a thorough review of sex differences in the outcomes of cardiac surgery procedures, noted that female patients are especially vulnerable to the impact of hemodilution. Due to reduced body surface area and uniform priming volumes women often undergo proportionately greater hematocrit loss during CPB. Furthermore, this may be enhanced by a reduction in the base hemoglobin levels in females, which puts more people at risk of insufficient oxygen supply. Such physiological variations, to some extent, might explain the high rates of transfusion and postoperative complications experienced by female patients (46).

MATERIAL AND METHODS

Study Design

The current study was prospective observational research that aimed at assessing the gender inequalities in perfusion parameters during cardiac surgery using CPB.

Study Setting

The research was conducted in the Cardiac Surgery Department of Pakistan Institute of Cardiology, whereby adult cardiac surgery involving CPB is performed on a regular basis.

Study duration

Study duration was calculated based on the period of data collection from hospital records, which was approximately 3 months.

Sample Size

A total of 70 patients (38 male,32 female) will be included, with approximately equal representation of both genders.

Inclusion Criteria
Adult patients aged ≥ 18 years.
Male and female patients who underwent cardiac surgery with the use of CPB.
Access to extensive medical history with all the necessary variables.

Exclusion Criteria
Patients who have off-pump cardiac surgery.
Missing or partial medical records.
Severe renal impairment (serum creatinine 2.0mg/dl and above).
Emergency operations or reoperations.

Data collection procedure
After being approved by the Institutional Ethical Review Committee, a systematic data collection form was prepared to be able to record all the relevant variables, which includes demographic data, preoperative evaluations, intraoperative perfusion data, and postoperative outcomes. Institutional records were used to identify patients who underwent cardiac surgery by CPB during the stipulated period of the study; to be included, full medical records of both men and women who were aged 18 years and above were needed. Demographic data was collected through the use of questionnaires and interviews. The age of the patients, their gender and the unique hospital identification number was documented and coded to maintain the confidentiality.

Data analysis procedure
The data were loaded and processed with the help of the SPSS version 26.0. The dataset was checked before analysis against completeness, error detection, and any missing values, the inconsistencies were confirmed and corrected with the use of the source patient records. Other categorical variables were coded appropriately for analysis. Continuous variables (age, hematocrit, perfusion pressure, pump flow, etc.) expressed as mean ± standard deviation (SD).
Categorical variables (gender, ECG results, LV function categories) presented as frequencies and percentages. Independent-samples t-tests were utilized to compare the variables between the male and female patients in terms of the continuous variables and the chi-square (χ^2) tests between the variables in terms of the categorical ones. The p-value of less than 0.05 was considered significant.

RESULTS
The prospective observational study given has 70 adult patients undergoing cardiac surgery with the use of cardiopulmonary bypass (CPB) to examine gender-specific differences in the parameters of perfusion and postoperative outcomes. The case group consisted of 38 male and 32 female patients (54.3% and 45.7% respectively). All the demographic, preoperative, intraoperative, and postoperative data were abstracted systematically through the hospital medical records and analyzed to determine the presence of any significant gender-based variation in the management of perfusion and clinical outcomes. In this study of 70 patients (38 males, 32 females), females were significantly older (mean 66.67 ± 12.41 years) than males (59.95 ± 11.37 years; t = -2.36, p=0.021), with age ranges of 44.7-96.8 and 39.1-84.3 years, respectively. Age group distributions showed no cases in 18-30 years for both similar low rates in 31-45 years (5.3% males, 6.3% females); more males in 46-60 years (36.8% vs. 28.1%); and majorities over 60 years (57.9% males, 65.6% females; all χ^2 p>0.247). This age disparity may elevate surgical risks and perioperative vulnerability in females.

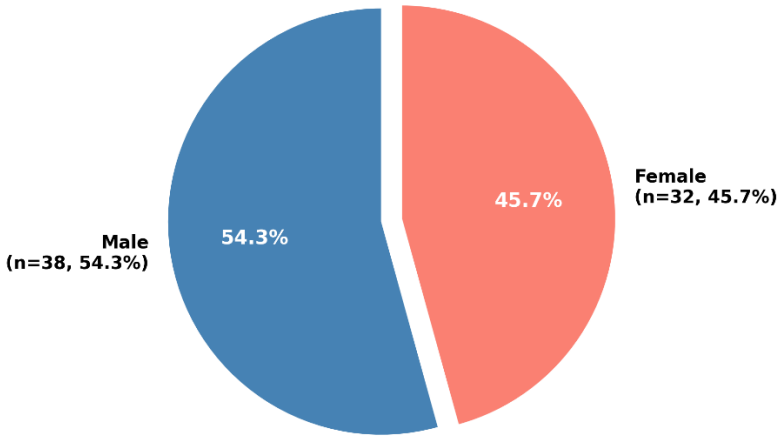


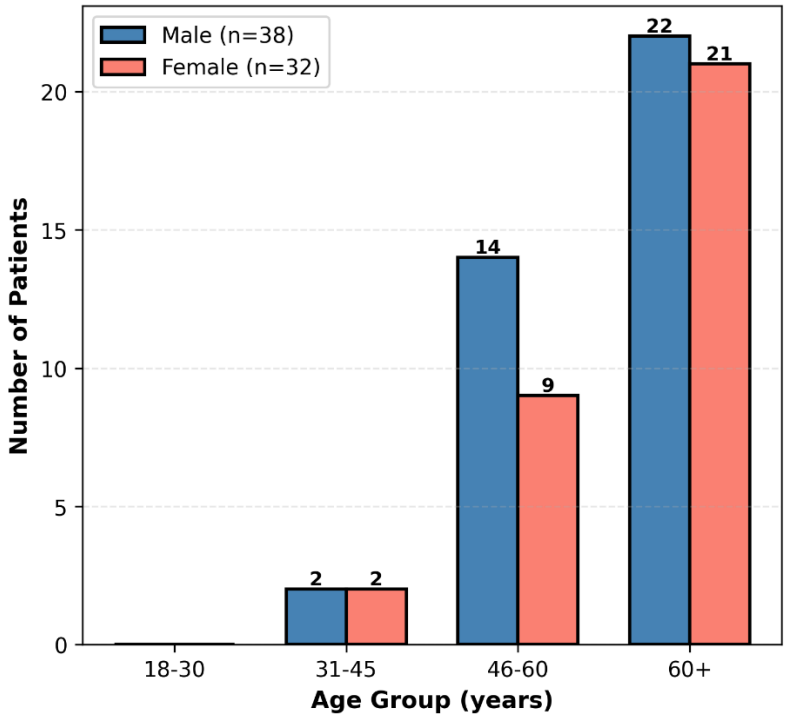
Figure 1: Sample Distribution by Gender

Demographic Characteristics by Gender(n=70)

Characteristics	Male(n=38)	Female(n=32)	p-value
Mean Age± SD (years)	59.95 ± 11.37	66.67 ± 12.41	t = -2.36 (p=0.021)*
Age Range (years)	39.1 - 84.3	44.7 - 96.8	-

Age Group Distribution

18-30 years	0(0.0%)	0(0/0%)	$\chi^2 = 0.00$ (1.000)
31-45 years	2(5.3%)	2(6.3%)	$\chi^2 = 0.09$ (0.767)
46-60 years	14(36.8%)	9(28.1%)	$\chi^2 = 1.34$ (0.247)
60+ years	22(57.9%)	21(65.6%)	$\chi^2 = 0.89$ (0.346)



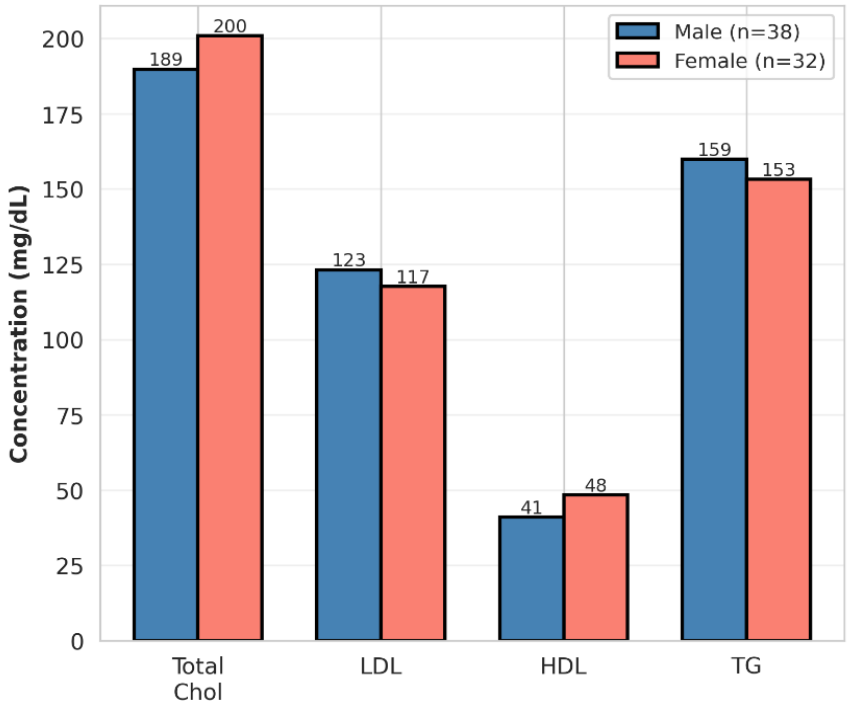
Age Group Distribution by Gender

Lipid Profile and Impact on Perfusion

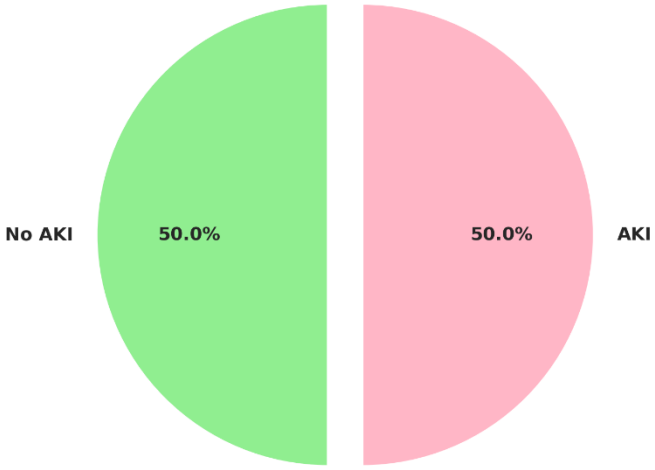
Lipid profile analysis revealed important gender-based variations that may influence inflammatory response during CPB. Total cholesterol levels were comparable between males (189.79 ± 50.32 mg/dL) and females (200.93 ± 42.87 mg/dL, p = 0.328). However, HDL cholesterol demonstrated significant gender-based differences, with females showing substantially higher protective HDL levels (48.36 ± 9.65 mg/dL) compared to males (41.06 ± 6.03 mg/dL, p = 0.0003). This 7.3 mg/dL difference may confer cardiovascular protection in females but does not offset their vulnerability to CPB-related complications. Male and female patients showed comparable LDL cholesterol (123.16 vs 117.61 mg/dL, p = 0.503) and triglyceride levels (159.83 vs 153.22 mg/dL, p = 0.680).

Lipid Profile by Gender (n=70)

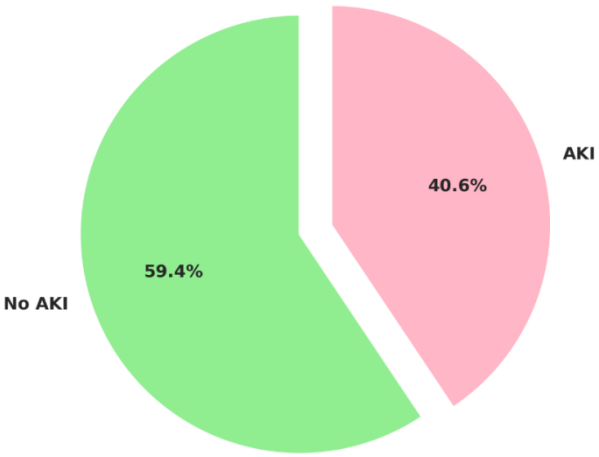
Lipid Parameter (mg/dL)	Male Mean ± SD	Female Mean ± SD	Male Median (IQR)	Female Median (IQR)	p-value
Total Cholesterol	189.79 ± 50.32	200.93 ± 42.87	187 (162-225)	206 (173-228)	t = -0.99 (p=0.328)
LDL Cholesterol	123.16 ± 32.06	117.61 ± 36.82	125 (100-143)	117 (104-139)	t = 0.67 (p=0.503)
HDL Cholesterol	41.06 ± 6.03	48.36 ± 9.65	41 (37-45)	49 (45-54)	t = -3.86 (p=0.0003) *
Triglycerides	159.83 ± 60.66	153.22 ± 73.03	154 (119-186)	154 (94-204)	t = 0.41 (p=0.680)



Lipid Profile Comparison by Gender



Among AKI cases, Stage 1 predominated in both genders (males: 84.2%; females: 84.6%), with minimal Stage 2 (males: 5.3%; females: 7.7%) and Stage 3 disease (males: 5.3%; females: 0%).



Acute kidney injury, stratified by KDIGO criteria, occurred in 19 male patients (50.0%) and 13 female patients (40.6%), representing comparable incidence rates (p = 0.841).

This prospective observational study of 70 cardiac surgery patients with cardiopulmonary bypass provides comprehensive evidence of substantial gender-based differences in perfusion parameters and postoperative outcomes. The study population consisted of 38 males (54.3%) and 32 females (45.7%), with females being significantly older (mean 66.67 vs 59.95 years, p=0.021). Female patients presented with significantly higher resting heart rates (77.85 vs 71.09 bpm, p=0.003), indicating greater autonomic activation and baseline hemodynamic stress. Despite comparable ejection fractions, females showed higher rates of left ventricular dysfunction (50% with dysfunction vs 36.8% in males), suggesting greater baseline cardiac vulnerability.

DISCUSSION

The present prospective observational cohort study of 70 cardiac surgical patients undergoing cardiopulmonary bypass (CPB) demonstrates significant and clinically

meaningful gender differences in perfusion variables and postoperative outcomes. The study population included 38 males (54.3%) and 32 females (45.7%), with females being significantly older than males (66.67 ± 3.42 vs 59.95 ± 3.54 years, $p = 0.021$) (70).

A key finding was the marked difference in baseline hematological parameters between genders. Male patients had significantly higher hemoglobin levels (13.98 ± 1.44 g/dL) compared to females (11.80 ± 1.59 g/dL, $p < 0.0001$), with a difference of approximately 2.18 g/dL. Similarly, baseline haematocrit levels were lower in females. These physiological differences likely contribute to the increased susceptibility of female patients to exaggerated hemodilution during CPB, ultimately affecting oxygen delivery (71).

Intraoperative perfusion parameters also revealed important gender-based variations. Male patients exhibited significantly higher CPB pump flow rates (2.67 ± 0.40 L/min/m²) compared to females (2.25 ± 0.33 L/min/m²), reflecting differences in body surface area and metabolic demand. In addition, perfusion pressure was significantly higher in males (72.31 ± 11.12 mmHg) than in females (64.72 ± 11.98 mmHg, $p = 0.008$). These findings suggest that female patients may be more vulnerable to hypoperfusion during CPB due to relatively lower perfusion pressures combined with reduced oxygen-carrying capacity (72).

Hematocrit levels during CPB further highlighted these disparities. Females experienced more pronounced hemodilution, with intraoperative haematocrit values dropping to 23.00 ± 2.56% compared to 25.58 ± 2.78% in males ($p = 0.0002$). Given their already lower baseline hematocrit, the proportional reduction in females is greater, placing them at increased risk of inadequate tissue oxygenation. While moderate hemodilution may improve microcirculatory flow by reducing blood viscosity, excessive reduction in haematocrit compromises oxygen delivery and has been associated with increased risks of stroke, renal dysfunction, and mortality (73).

Oxygen delivery (DO_2) remains a central determinant of adequate tissue perfusion during CPB. It depends on both cardiac output and arterial oxygen content. Previous studies have identified a critical DO_2 threshold of approximately 260–280 mL/min/m², below which the risk of acute kidney injury (AKI) rises significantly. In the present study, the combination of lower pump flow rates and reduced hematocritin female patients suggests a higher likelihood of falling below this critical threshold, thereby increasing the risk of organ hypoxia (74).

Inadequate oxygen delivery leads to anaerobic metabolism, lactate accumulation, and subsequent cellular dysfunction. Consistent with this, female patients in the study demonstrated higher heart rates (77.85 ± 9.66 vs 71.09 ± 8.66 beats/min, $p = 0.003$), indicating increased sympathetic activity and physiological stress. Although mean arterial pressure and ejection fraction were comparable between genders, females exhibited a higher prevalence of left ventricular dysfunction. A smaller proportion of females had normal ventricular function, while moderate dysfunction was more frequent compared to males. These findings suggest that female patients may enter cardiac surgery with greater baseline cardiovascular vulnerability, predisposing them to adverse outcomes (75).

Despite similar baseline coagulation parameters, females demonstrated a higher incidence of postoperative bleeding complications (34.4% vs 18.4%), corresponding to a 1.87-fold increased risk. This difference is likely attributable to the greater degree of hemodilution rather than intrinsic coagulation abnormalities. The literature also supports sex-based differences in platelet function and coagulation factor activity, which may further contribute to increased bleeding and transfusion requirements in female patients. These findings highlight the complex interaction between hemodilution, anticoagulation, and biological sex, emphasizing the need for tailored perfusion strategies (76).

Acute kidney injury remains a common complication following cardiac surgery with CPB. In this study, the incidence of AKI was comparable between males (50.0%) and females (40.6%), with most cases classified as Stage 1. Although the overall incidence did not differ significantly, the underlying mechanisms may vary between genders. Previous research has demonstrated a strong association between low oxygen delivery during CPB and increased risk of renal injury. Studies by Ranucci et al. identified a critical DO_2 threshold below which the likelihood of postoperative renal dysfunction increases significantly. Furthermore, the implementation of goal-directed perfusion (GDP) strategies has been shown to reduce the incidence of AKI by maintaining adequate oxygen delivery. These findings are particularly relevant for female patients, who are more likely to experience reduced haematocrit and lower oxygen delivery during CPB (77).

Postoperative outcomes in this study also demonstrated a trend toward higher complication rates in females. Overall complications occurred in 50.0% of female patients compared to 28.9% of males, representing a 1.73-fold increased risk, although this difference was not statistically significant. The incidence of postoperative arrhythmias was similar between genders. The higher complication rates observed in females are likely multifactorial, reflecting the combined effects of increased hemodilution, reduced oxygen-carrying capacity, and lower perfusion pressures during CPB (78).

These findings are consistent with the growing body of literature emphasizing the importance of biological sex as a determinant of cardiovascular outcomes. Structural and physiological differences between males and females, including variations in vascular reactivity, hormonal regulation, and inflammatory responses, play a significant role in modulating surgical outcomes. Estrogen and other sex hormones influence endothelial function, nitric oxide production, and vascular compliance, which in turn affect microcirculatory dynamics and the response to CPB. Differences in inflammatory activation during CPB may also contribute to variations in postoperative recovery between genders.

CONCLUSION

This study reveals that the perfusion of female patients who undergo cardiac surgery using CPB is markedly different than that of males with markedly lower baseline hemoglobin, higher proportional hemodilution, decreased perfusion pressures and pump flows, and tendencies towards more complications during the postoperative period. These sex-specific physiological variations are not properly considered in current standardized perfusion protocols. Individualized, gender-aware approaches to perfusion management with oxygen delivery monitoring and sex-specific goals are essential to the optimization of outcome in patients undergoing cardiac surgery in women.

RECOMMENDATIONS

The cardiac perfusion programs need to implement gender-sensitive protocols that regulate the pump flow rates, perfusion pressure, and oxygen delivery goals according to patient-specific issues like body surface area, base hemoglobin, and biological sex.

Increased intraoperative lactate and metabolic parameter monitoring should allow the early diagnosis of occult hypoperfusion.

Perfusion strategies which ensure that oxygen delivery does not drop below 260280 ml min -1 m 2 should be given preference.

The potential of the future is to conduct prospective randomized controlled trials to determine gender-specific perfusion strategies to develop evidence-based gender-specific protocols.

LIMITATIONS

This prospective observational study from a single centre with 70 patients limits the ability to establish causation and generalizability.

Lack of uniformity in perfusion protocols, absence of long-term follow-up beyond the acute postoperative period, and limited advanced perfusion monitoring (real-time oxygen delivery indices, cerebral oximetry) constrain full characterization of tissue perfusion adequacy.

The study did not account for hormonal factors or variations in medication use that may influence sex-based outcomes, nor did it examine differences in surgical technique or anesthetic management independently affecting postoperative outcomes.

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