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Low cardiac output syndrome after cardiac surgery: A retrospective analysis

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Abstract. Low cardiac output syndrome is a prevalent complication observed after cardiac surgery, related to elevated rates of mortality and morbidity. The study aimed to pinpoint independent risk factors for low cardiac output through the analysis of post-cardiac surgery data. This is a single-centre, two-year retrospective study from January 2021 to December 2022, including all patients admitted to the A1 general intensive care unit for postoperative management of cardiac surgery. Variables from preoperative, intraoperative, and postoperative data were collected and evaluated with the statistical package for the social sciences, with a significance level set at $p < 0.05$. Overall, the median age was 44 years (22-80), with 60% being female. The prevalence of low cardiac output syndrome after cardiac surgery was 44% (n = 85). Significant risk factors for low cardiac output syndrome were identified: low preoperative left ventricular function (ejection fraction <40%), preoperative atrial fibrillation, impaired preoperative renal function, multiple valve replacement, prolonged extracorporeal circulation, and clamping time. Patients who experienced low cardiac output syndrome had longer hospital stays and a higher incidence of postoperative complications, including atrial fibrillation and kidney injury, as well as a higher mortality rate (7% versus 0%). Identification and treatment of low cardiac output syndrome can improve myocardial recovery and decrease mortality. A better understanding of its physiopathological mechanisms may help develop potential preventive strategies

Keywords: cardiopulmonary bypass; risk factors; inotrope; circulatory support; mortality rate

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Introduction

Low cardiac output syndrome (LCOS) is a significant complication observed in patients who have undergone cardiac surgery. Although definitions differ among studies, the most common include decreases in the cardiac index to < 2.2 L/min/m^2 requiring inotropic agents or mechanical circulatory support to keep the systolic pressure > 90 mmHg as well as the cardiac index > 2.2 L/min/m^2 [1].

J.L. Pérez Vela *et al.* [2] conducted a multicentre, prospective cohort analysis and found an incidence of 7.5% for LCOS after cardiac surgery. A.E. Duncan *et al.* [3] reported a higher incidence of 10% in a North American study involving 59,810 patients. LCOS was associated with significant morbidity and mortality, reaching up to 40%. Additionally, it required an extended intensive care unit (ICU) stay, increased resource utilization, and a heightened occurrence of respiratory, and neurological complications, and kidney injury, necessitating prolonged mechanical ventilation.

Several LCOS risk factors were identified in the literature. In a retrospective multicentre cohort study involving 781 patients, F. Biancari *et al.* [4] demonstrated that elderly age, diabetes, kidney injury, and malnutrition were clinically associated with a high LCOS risk. Q. Qing *et al.* [5] developed an individualised nomogram prediction model for LCOS after cardiac surgery. The results indicated that global longitudinal strain was a significant factor associated with LCOS after cardiac surgery.

Biologically, anaemia, elevated Brain Natriuretic Peptide (BNP) and pro-BNP were identified in cohort studies [6-8]. Surgically, the main factors identified were urgent surgery, longer Cardiopulmonary bypass (CPB) and cross-clamp times [9]. Research conducted in Lille also identified morning surgery as a risk factor for postoperative cardiac complications after aortic valve replacement, highlighting the circadian expression of specific genes. This result was not found in a recent cohort of 9700 patients with several types of surgery [10, 11]. The literature extensively describes the outcome of LCOS, indicating its association with heightened postoperative complications, prolonged stays in the ICU and on mechanical ventilation, and mortality rates up to 50-80% in the case of refractory LCOS [4]. However, the long-term outcome of LCOS is still poorly studied [12].

Several studies have been conducted to investigate LCOS after cardiac surgery. However patient outcomes and LCOS risk factors after cardiac surgery in Morocco remain unknown due to the limited access to cardiac surgery, the young age of patients, the high incidence of rheumatic heart disease and the poorly studied long-term LCOS outcomes. Recent advances illustrate the potential of expanding cardiac surgery with acceptable in-hospital mortality. The study aimed to identify independent risk factors influencing the outcome of LCOS after adult cardiac surgery by analysing preoperative, intraoperative, and postoperative data.

Materials and Methods

This is a single-centre two-year retrospective study from January 2021 to December 2022, including 190 patients admitted to the A1 intensive care unit for postoperative management of cardiac surgery. Criteria for inclusion encompassed adult individuals subjected to cardiac surgery with CPB, regardless of the specific surgical procedure. Exclusion criteria included pregnant females, children, and individuals lacking complete data, such as echocardiographic measurements or perioperative hemodynamic information. Additionally, those undergoing surgical interventions for penetrating cardiac injury or pericardial effusion were excluded from the study.

LCOS was defined following the most common definition from previous reports: decrease in the cardiac index to < 2.2 L/min/m^2 requiring inotropic agents or mechanical circulatory support to maintain the systolic pressure > 90 mmHg and the cardiac index > 2.2 L/min/m^2 [1]. Vasoconstricting medication to improve peripheral vascular resistance was not considered an LCOS. All pre- and in-hospital patient records were reviewed, and data were collected using standardised forms. Baseline variables were divided into three groups pre-operative factors, intra-operative factors, and post-operative factors:

- Preoperative variables: gender (male and female), age, comorbidities, heart rate (sinus or atrial fibrillation), preoperative echocardiographic parameters; preoperative ejection fraction (> 40% or ≤ 40%), left ventricular diameter diastolic (LVDD), left ventricular diameter systolic (LVDS).
- Intraoperative variables: type of intervention (isolated or multiple valve replacement, coronary artery bypass graft (CABG), cardiopulmonary bypass (CPB) and cross-clamp times.
- Postoperative variables: inotropic use, EF at 0 h, 4 h and 24 h, complications (acute pulmonary oedema, kidney injury, neurological, respiratory, infectious complications), duration of mechanical ventilation, length of stay in the intensive care unit, and mortality rate.

Statistical Package for the Social Sciences (SPSS), and Statistics software at the Laboratory of Epidemiology and Public Health of Fez, Morocco were used to analyse the data. Descriptive statistics were employed to calculate frequencies, with mean and standard deviation utilised for continuous variables. Univariate proportions were assessed using the chi-squared test, and statistical significance was determined at p-values < 0.05. Predictive factors of mortality were studied with a logistic regression model with multivariate analysis to compare patients who developed with those who did not. The study adhered to the ethical norms of the Declaration of Helsinki [13] and was approved by the Hassan II University Hospital's ethics committee (No. 18/2023). Informed consent was deemed unnecessary given the retrospective nature of the study. The study did not use information that could be employed for the identification of individuals who participated in the research.

Results and Discussion

In general, 85 of 190 patients (44%) had LCOS, confirmed by a low cardiac index of less than 2,2 L/min/m^2. Patient characteristics were divided into 3 groups: preoperative, intraoperative, and postoperative.

Preoperative data analysis in cardiac surgery

This study observed a higher proportion of women compared to men, resulting in a gender ratio of 1.7. The median age recorded was 44 years (22-80).

Comorbidities: the main comorbidities were atrial fibrillation (N: 83, 44%), smoking (N: 29, 16.3%) and hypertension (N: 26, 13%) (Table 1).

Table 1. Patient comorbidities

Variables	Frequency (%)
Cardiac history	
Hypertension	26 (13%)
Atrial fibrillation	83 (44%)
Endocarditis	9 (4.7%)
History of cardiac surgery	8 (5%)
Diabetes	12 (6.3%)
Kidney failure	8 (5%)
Smoking	29 (16.3%)

Source: compiled by the authors

Preoperative echocardiographic parameters: 145 patients had preserved ejection fraction, while 17 patients had preoperative low ejection fraction, 17 patients (8.9%) had a left ventricular dilatation, the median of the right ventricular end-diastolic area was 48 mm ± 7 and the median of pulmonary artery systolic pressure was 33 mmHg (Table 2).

Table 2. Preoperative echocardiographic parameters

Parameters	Frequency (%)
Left ventricular ejection fraction	
> 60%	145 (76%)
40 % a 60%	37 (19.4%)
< 40%	7 (3.6%)
LEVDD >56 mm	17 (8.9%)
Right ventricular end-diastolic area (mm)	48 ± 7
Pulmonary artery systolic pressure (mmHg)	33

Notes: LEVDD – left ventricular end-diastolic diameter
Source: compiled by the authors

No significant difference in gender was observed, patients with LCOS were not older. Atrial fibrillation was statistically different between the two groups. Patients with low ejection fraction (EF< 40%) were at greatest risk (7 patients in the group with LCOS in comparison with none in the group without LCOS, $p < 0.01$). Other clinical and echocardiographic parameters, such as diabetes, history of cardiac surgery, New York Heart Association (NYHA) status [14], left ventricular end-diastolic diameter, and pulmonary artery systolic pressure, exhibited no significant differences between the LCOS and Non-LCOS patient groups (all $p > 0.05$) (Table 3).

Table 3. Preoperative data of patients with LCOS

		Groupe with LCOS N =	Groupe without LCOS N =	p
Female / male		**65/40**	**49/36**	**0.5**
Age (yr.)		**47 ± 12**	**42 ± 11**	**0.113**
		History		
Cardiac history	Hypertension	20	6	> 0.05
	Atrial fibrillation	20	63	**0.01**
	Endocarditis	3	4	> 0.05
Cardiac surgery		2	6	> 0.05
Diabetes		10	2	0.26
Chronic renal failure		2	6	0.22
Smoking		12	17	> 0.05
NYHA III et IV		20	31	0.22
EF < 40%		7	0	**<0.01**

Continued Table 3

	Groupe with LCOS N =	Groupe without LCOS N =	p
LVEDD > 56 mm	8	17	>0.05
PAPS > 35 mmHg	47	70	>0.05

Notes: PASP – pulmonary artery systolic pressure; LVEDD – left ventricular end-diastolic diameter
Source: compiled by the authors

Intraoperative data collection and analysis in cardiac surgery

Types of cardiac surgery and inotropic agents: the most common surgery was valve replacement, mainly isolated valve replacement (42%), 20% of patients underwent multiple valve replacement and 18% coronary Artery Bypass Graft. Dobutamine was the main agent used (89%) in patients with LCOS, the *Median* of *time* receiving inotropes was 31 hours (Table 4), 100% of patients with LCOS used at least one inotrope (+/– one vasopressor), The use of multiple inotropes (or vasopressors) was higher in LCOS group.

Table 4. Inotropes used for LCOS

	N (%)
Number of used inotropes (all patients):	
0	105 (56%)
1	68 (35%)
≥ 2	17 (7.3%)
The main drug used:	
Dobutamine	75 (92%)
Milrinone	10 (11%)
Adrenaline	9 (10.5%)
Dose of dobutamine (µg · kg-1.min-1)	
Minimal-initial	8.2 +- 2.3
Maximal	14.0 +- 3.4
Median duration of treatment (hours):	31 [8 - 54]

Source: compiled by the authors

Cardiopulmonary bypass and cross-clamp times: the median duration of cardiopulmonary bypass was 80 minutes (± 35), and the median duration of aortic cross-clamping was 55 minutes (+/– 30). When studying the patient characteristics during surgery, patients who underwent multiple valve surgery replacement had more risk of developing LCOS. A significant correlation was observed between prolonged cardiopulmonary bypass (CPB) (> 1 h 30 hour, p = 0.05) and/or aortic clamping time (> 1 hour, p = 0.02) and the occurrence of a low output cardiac surgery (Table 5).

Table 5. Intraoperative data of patients with LCOS

	Groupe with LCOS N=	Groupe without LCOS N=	P
Surgical procedures			
Isolated valve	36	44	> 0.05
Multiple valves	7	31	< **10^{-3}**
Coronary artery bypass graft	32	2	> 0.05
Urgent timing	9	14	> 0.05
Duration			
Cardiopulmonary bypass (> 1 h 30)	38	54	**0.05**
Crosscalmp time (> 1 h)	35	50	**0.02**

Notes: CABG – coronary artery bypass graft
Source: compiled by the authors

Postoperative data assessment in cardiac surgery

Patients with LOSC had higher postoperative complication rates, including postoperative atrial fibrillation (AF) (18 vs 12), the average time to onset was 1.4 days from the surgery, Amiodarone was the only antiarrhythmic used, atrial fibrillation (AF) duration was 24.0 hours; 60% of cases resolved within 36 hours. LCOS group also had a higher incidence of kidney injury (6 vs 0), longer post-operative

ICU stay (4.5 vs 2 days), and increased mortality rate (7% vs 0 deaths). Among the 190 patients studied, all who expired had LCOS (Table 6).

Post-operative left ventricular systolic function (EF≤ 40%) at three times 0 h, 4 h and 24 h after surgery were higher in patients with LCOS P<0.05 (Table 7).

Table 6. Postoperative data of patients with LCOS

	Groupe with LCOS	Groupe without LCOS
Postoperative troponin levels (ng/mL)	3.9	2.7
Postoperative atrial fibrillation (N)	18	12
Postoperative kidney injury (N)	6	0
ICU stay (days)	4.5	2
Mortality rate (%)	7	0

Source: compiled by the authors

Table 7. Dynamic of ejection fraction

Parameters		Groupe with LCOS N =	Groupe without LOSC N =	p
Preoperative low FE (≤ 40%)		7	0	**< 0.01**
EF: 0 h	> 40%	35	100	**< 0.01**
	≤ 40%	50	5	
EF: 4 h	> 40%	30	100	**< 0.01**
	≤ 40%	55	5	
EF: 24 h	> 40%	30	102	**< 0.01**
	≤ 40%	55	3	

Source: compiled by the authors

Predictors of LCOS after cardiac surgery

The outcome of patients with LCOS was assessed. In univariate analysis, statistically significant differences ($p < 0.05$) were observed between the groups "with LCOS" and "without LCOS". The preoperative risk factors ncluded atrial fibrillation and low preoperative ejection fraction. Intraoperative risk factors comprised longer cardiopulmonary bypass and cross-clamp times, as well as multiple valve surgery. The patients' risk factors for LCOS are detailed in Table 8.

Table 8. Risk factors for LCOS

Risk factor	Groupe with LCOS n = 85	Groupe without LOSC n = 105	p
Atrial fibrillation	30	63	**$\leq 10^{-3}$**
EF < 40%	7	0	**≤0.01**
CBP time (>1 h 30)	38	54	**0.05**
Cross clamp time (>1 h)	35	50	**0.02**
Surgery:			
Isolated valve	36	44	
Multiple valves	7	31	**$\leq 10^{-3}$**
CABG	32	2	

Notes: CABG – coronary artery bypass graft; CPB – cardiopulmonary bypass
Source: compiled by the authors

The analysis of 190 patients revealed a notable incidence of LCOS in this study, especially in those with pre-existing ventricular dysfunction and those who underwent high-risk procedures, such as multiple valve replacement and had prolonged CPB and cross-clamp time. Compared to the group without LCOS, patients with LCOS, stay longer in hospital, develop more complications, and have poor outcomes.

LCOS is a frequent and serious complication in patients who have undergone cardiac surgery. Definitions differ among studies, as, based on hemodynamic parameters or the use of inotropes or circulatory assistance, the most common includes decreases in the cardiac index to < 2.2 L/min/m^2 requiring inotropes or mechanical circulatory support to keep the systolic pressure > 90 mmHg as well as the cardiac index > compiled by the authors 2.2 L/min/m^2. [1, 2, 15]. The LCOS incidence after cardiac surgery in this study was 44%, which is higher than incidences reported in several studies varying from 13 to 30% [16, 17].

This study identified factors contributing to the LCOS risk, which include atrial fibrillation, low preoperative ejection fraction, prolonged CBP and cross-clamp times and multiple valve replacement, consistent with other

studies [16-18]. Compared to the group without LCOS, the incidence of complications, ICU stay, and mortality rates are higher. J. Wang *et al.* [18], in an observational study of 212 patients, demonstrated the following pre-operative parameters with low cardiac output: atrial fibrillation, kidney failure, hyponatremia, high central venous pressure and low ejection fraction. N.T. Luan [17] identified the following independent risk factors in a descriptive study on 60 patients undergoing valve replacement surgery: pre-operative low EF, prolonged time to extracorporeal and clamp aorta.

The most common parameters used in clinical practice for assessment of Left ventricular ejection fraction (LVEF) are visually estimated (eyeballing) ejection fraction or manually traced biplane Simpson's rule. A low LVEF is a significant predictor of LCOS after cardiac surgery. K.B. Rana *et al.* [19] found in their prospective study of 200 patients undergoing CABG a relation between pre-operative left ventricular dysfunction and LCOS after surgery, which was significantly different in patients with pre-operative ejection fraction < 40%, compared to ejection fraction ≥ 40%. P. Amabili *et al.* [20] used the systolic global longitudinal strain to evaluate left ventricular function and determine that GLS was a significant risk factor for LCOS after cardiac surgery, while analysis of myocardial strain appears to improve the prediction of LCOS. In this study, pre-operative low EF frequency was 8.2% in LCOS patients, while no patient had pre-operative low EF in the group without LCOS.

Several studies showed the relationship between pre-operative right ventricular dysfunction and postoperative LCOS. P.C. Ting *et al.* [21] recognised the right ventricular global longitudinal strain (RVGLS) as a factor independently associated with a heightened need for postoperative vasoactive inotropic support. E.L. Posada-Martinez *et al.* [6] also conducted a prospective observational study involving 75 patients with severe aortic stenosis and preserved ejection fraction (EF) to examine the correlation between right ventricular free wall longitudinal strain (RVFWSL) and LCOS, they identified a RVFWSL < 17.3% as a predictor of LCOS. Consistent with prior research, this study established a reduced left ventricular ejection fraction as a notable predictor of LCOS.

L. Hong *et al.* [22] developed machine learning (ML) techniques to predict LCOS in patients after cardiac surgery using ML approaches, predictive parameters included LVEF, lactate level, LVEDD, mean artery blood pressure, age, and blood loss during surgery were used to validate the predictive algorithms. Regarding age, it was not identified as a factor, which contrasts with other studies. L. Zhao *et al.* [23], in a retrospective study involving 117 patients aged over 60 years, demonstrated that age over 70 years is an independent factor for the development of LCOS. Most patients in this study are young with rheumatic valve disease and they have several risk factors for developing postoperative LCOS, compared to most elderly patients who had undergone coronary bypass surgery with few risk factors of LCOS.

Atrial fibrillation has been recognised as an independent risk factor for postoperative LCOS. However, the surgical correction of valvulopathy along with atrial fibrillation enhances the long-term prognosis for these patients. Additionally, preoperative ejection fraction was related to a significantly increased postoperative LCOS risk [2, 3]. Surgeon experience with ageing has also been reported as a factor in decreasing LCOS and improving outcomes in cardiac surgery [24]. In Morocco, the number of cardiac surgeons is extremely limited, this factor cannot be studied. CBP time was identified as an independent predictor of LCOS which is consistent with several other studies [2, 16]. Protocols aiming to optimise CPB time could improve postoperative cardiac function.

Regarding the surgical procedure, A.E. Duncan *et al.* [3] identified the combined procedure (valve + bypass) as a surgical risk factor, while isolated valve surgery (aortic valve) was a protective factor. Multiple valve surgery was identified as a surgical risk factor in this study. Patients who developed LCOS are more likely to suffer postoperative complications, require longer intensive care unit stays, with increased risk of postoperative kidney injury, several studies have confirmed the association between low postoperative cardiac output and a high incidence of postoperative complications. LCOS is a factor for higher in-hospital mortality, varying from 12% to 33%, increasing to 40-80% in refractory LCOS requiring hemodynamic support [2, 4]. Among the 85 patients with LCOS, six (7%) died perioperatively.

In this study conducted in a Moroccan centre, the main differences found in patients with LCOS compared to literature were the high incidence of LCOS, the age was not identified as a factor, which contrasts with other studies, the other risk factors and the outcome of patients with LCOS were similar to most series, which can be explained by the young age of patients, the high incidence of rheumatic heart disease most often with pre-existing ventricular dysfunction.

Conclusions

This study evaluated the clinical parameters of patients who developed LCOS after cardiac surgery by analysing preoperative, intraoperative, and postoperative data to determine independent risk factors of LCOS after adult cardiac surgery, and how they influenced the outcome of patients after cardiac surgery. The results showed LCOS is a severe complication after cardiac surgery, 44% in this study. Preoperatively low preoperative ejection fraction (EF < 40%), and atrial fibrillation were associated with LCOS, other characteristics in particular gender and age were similar in both groups. During surgery, patients who underwent multiple valve replacement had more risk of developing LCOS, and a significant correlation was observed between prolonged cardiopulmonary bypass and/or aortic clamping time and the occurrence of a low-output cardiac surgery. LCOS profoundly impacts patient outcomes with increased morbidity and mortality, patients with LOSC had higher rates of

postoperative complications including postoperative atrial fibrillation, higher incidence of kidney injury, longer postoperative ICU stay and increased mortality rate. Among the 190 patients studied, all who had expired had low cardiac output syndrome.

LCOS after cardiac surgery is a multifactorial complication resulting in cardiac dysfunction, determine LCOS risk factors may help identify possible preventive strategies, like to preserve kidney function, safe myocardial protection and optimising pre-existing ventricular dysfunction that could improve LCOS after cardiac surgery in high-risk patients. Subsequent investigations should delve deeper into the underlying pathophysiological mechanisms of LCOS in order. The ultimate goal is to leverage this knowledge to improve outcomes and care strategies for patients afflicted with LCOS.

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Conflict of Interest

The authors declare no conflict of interest.

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Синдром низького серцевого викиду після операції на серці: ретроспективний аналіз

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Анотація. Синдром низького серцевого викиду є поширеним ускладненням, що спостерігається після кардіохірургічного втручання, і пов'язаний із підвищеними показниками смертності та захворюваності. Метою даного дослідження було визначити незалежні фактори ризику низького серцевого викиду шляхом аналізу даних після кардіохірургічних втручань. Дане одноцентрове дворічне ретроспективне дослідження проходило з січня 2021 року по грудень 2022 року та включало всіх пацієнтів, які були госпіталізовані до відділення загальної інтенсивної терапії A1 для післяопераційного лікування кардіохірургії. Змінні були зібрані з передопераційних, інтраопераційних та післяопераційних даних і оцінені з використанням статистичного пакету для соціальних наук, з рівнем значущості, встановленим на рівні $p < 0,05$. Загалом медіана віку становила 44 роки (22-80), 60 % – жінки, поширеність синдрому низького серцевого викиду після кардіохірургічного втручання – 44 % ($n = 85$). Виявлено значущі фактори ризику синдрому низького серцевого викиду: низька передопераційна функція лівого шлуночка (викид фракції <40 %), передопераційна фібриляція передсердь, порушення передопераційної функції нирок, множинна заміна клапана, подовження екстракорпорального кровообігу та час затискання. Пацієнти, у яких спостерігався синдром низького серцевого викиду триваліше перебували в лікарні та мали підвищену частоту післяопераційних ускладнень, включаючи фібриляцію передсердь та пошкодження нирок, а також вищий рівень смертності (7 % проти з 0 %). Діагностика та лікування синдрому низького серцевого викиду може поліпшити відновлення міокарда та зменшити смертність; краще розуміння його фізіопатологічних механізмів може допомогти розробити потенційну профілактичну стратегію

Ключові слова: серцево-легеневе шунтування; фактори ризику; інотроп; підтримка кровообігу; смертність