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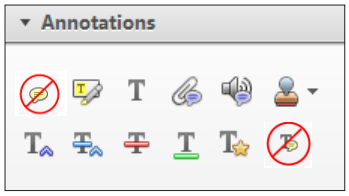

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Designing a new scoring system (QualyP Score) correlating the management of cardiopulmonary bypass to postoperative outcomes

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Abstract

Aim: The aim of this study was to ascertain if a score, directly derived from CPB records, could correlate to major postoperative outcomes.

Methods: An additive score (QualyPscore) was created from 10 parameters: peak lactate value during CPB, peak VCO_2i, lowest DO_2i/VCO_2i, peak respiratory quotient, CPB time, cross-clamp time, lowest CPB temperature, circulatory arrest, ultrafiltration during CPB, number of packed red cells transfused intraoperatively. The PerfSCORE was calculated, as well. Multivariable logistic regression models were built to detect the independent predictors of: peak lactates >3 mmol/L during the first three postoperative days; the incidence of acute kidney injury network (AKIN) 1-2-3; respiratory insufficiency; mortality.

Results: The mean score was 4.8±2.6 (0-10). A QualyPscore ≥1 was predictive of postoperative acidosis (OR=1.595). A score ≥2 was predictive of AKIN 2 (OR=1.268) and respiratory insufficiency (OR=1.526). A score ≥5 was predictive of AKIN 3 (OR=1.848) and mortality (OR=1.497).

Conclusions: QualyPscore may help to provide a quality marker of perfusion, emphasizing the need for goal-directed perfusion strategies.

Keywords

perfusion; quality; risk score

Introduction

Since the first successful clinical applications of cardiopulmonary bypass (CPB) in the early 1950s, the role of extracorporeal circulation has shifted progressively from a mere substitution of the heart and lungs towards the more complex field of organ perfusion.

Therefore, numerous investigations have been performed to individuate which parameters might better associate with an improved organ perfusion during CPB.[1–4] Consequently, the application of the physiological concepts of metabolic needs to the setting of CPB promoted the concept of the so-called "goal-directed" perfusion.[2] However, several surveys proved that the scientific data available at present are not yet sufficient to serve as evidence-based guidelines.[5,6] The present study aims to evaluate the quality of organ perfusion during CPB and to structure a scoring system to assess

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this quality by a comprehensive evaluation of flow-dependent parameters.

Methods

This is a retrospective analysis of prospectively collected data from a single institution. The local Ethics Committee approved the study.

Inclusion criteria were age ≥18 years and surgery on CPB and aortic cross-clamping.

Exclusion criteria were surgery for aortic dissection, implantation of a ventricular assist device, heart transplantation, off-pump surgery, surgery on cardiopulmonary bypass without aortic cross-clamping, congenital heart disease, minimally-invasive surgery, chronic renal failure under replacement treatment and chronic respiratory insufficiency requiring domiciliary oxygen support.

Surgical technique and cardiopulmonary bypass

CPB and surgical techniques were standardized and did not change during the study period. In all patients, surgery was performed through a median sternotomy. The CPB circuit and perfusion conduct were standardized for all patients and consisted of a phosphorylcholine-coated tubing set (Soring Group, Saluggia, Vercelli, Italy), a Stöckert roller pump (Stöckert Instrumente, Munich, Germany) and a hollow-fiber membrane oxygenator.

Heparin was given at a dose of 300 IU/kg to achieve a target activated clotting time over 480 sec. Systemic temperature varied according to the kind of surgery, never falling below 25°C in case of circulatory arrest.

The priming solution consisted of 500 ml of Emagel (Piramal Healthcare UK Ltd, Morpeth, Northumberland, UK) and 800 ml of Ringer's acetate. Pump priming was reduced to an average of 800-1000 mL after aortic cannulation and retropriming.

Myocardial protection was always achieved with intermittent hyperkalaemic blood cardioplegia. Theoretical CPB flow was calculated, establishing a rate of 2.7 L/min/m^2 and indexing it to an ideal body mass index of 25 kg/m^2. Protamine was administered at the end of the operation to fully reverse heparin. Blood recovery with an autotransfusion device (Autotrans Dideco, Mirandola, Modena, Italy) was performed intraoperatively in all cases. A level of haemoglobin lower than 7 g/dl during CPB and before admission to the ICU suggested blood transfusion.

Data collection and definitions

Baseline characteristics and intra- and postoperative data from all patient have been recorded in an institutional database. In particular:

(a) Intraoperative records: re-operation; type of operation (coronary artery bypass graft (CABG), valvular, CABG and valvular, other); priming volume; CPB time; cross-clamp time; lowest temperature during CPB; circulatory arrest; diuresis during CPB; need for ultrafiltration during CPB; number of PRCs transfused; peak arterial lactate concentration during CPB; lowest haemoglobin (Hb) and haematocrit (Hct) values during CPB; arterial and venous blood samples for oxygen and carbon dioxide derived estimates (see next paragraph).

(b) Postoperative records (during the first three postoperative days): peak lactates; estimates of renal function (peak sCr level; lowest eGFR; acute kidney injury (AKI) stage according to the AKIN criteria;[7]; need for renal replacement therapy); estimates of pulmonary function (lowest PaO_2/FiO_2 ratio; duration of ventilation; respiratory failure, defined as either one of the following: ventilation >48 hours, need for re-intubation or for post-extubation non-invasive mechanical ventilation with continuous positive airway pressure (CPAP) hood (StarMed spa, Mirandola, Modena, Italy) [required if PaO_2/FiO_2<200 mmHg after having excluded any other cause of respiratory failure, such as pneumothorax, pleural effusion, pulmonary embolism]); in-hospital mortality.

Blood samples and calculations

As an institutional protocol, blood gas analysis was performed every 20 minutes from the institution All blood gas data were corrected for temperature, according to standard equations.

The estimates of oxygen- and carbon dioxide-derived parameters have been calculated according to Ranucci and associates.[1] In particular:

$$DO_2i\ [mL/min/m^2] = 10 \times \text{pump index } [L/min/m^2] \times \text{arterial } O_2 \text{ content } [mL/100mL];$$

$$VO_2i\ [mL/min/m^2] = 10 \times \text{pump index } [L/min/m^2] \times (\text{arterial} - \text{venous } O_2 \text{ content}) [mL/100\ mL];$$

$$\text{Oxygen content } [mL/100\ mL] = Hb\ [mg/dL] \times 1.34 \times SO_{2(\text{arterial/venous})}[\%] + pO_{2(\text{arterial/venous})}[mmHg] \times 0.003.$$

As far as the VCO_2i calculation is concerned, expiratory CO_2 tension (eCO_2, mmHg) was measured at the site of the oxygenator exhaled gas port with a ventilator-integrated capnograph. Gas volumes and flows are expressed in STPD (standard temperature and pressure

dry); adequate corrections according to body temperature pressure saturated (BTPS) conditions were applied [Appendix A]. Therefore, VCO_2i was calculated as follows:

VCO_2i [mL/min/m^2] = (eCO_2 [mmHg] x gas flow into the oxygenator [L/min] x 10000)/(760 x body surface area)

Aim of the study and design of the score

The main aim of our study was to design a score that might correlate the estimate of an adequate perfusion to the occurrence of adverse outcomes after surgery on CPB. We named it the QualyP Score.

According to reference values already established in the current literature, ten parameters were included to design this additive score. In particular: peak lactates during CPB, peak VCO_2i, lowest DO_2i/VCO_2i, respiratory quotient, CPB time, cross-clamp time, lowest CPB temperature, circulatory arrest, ultrafiltration during CPB, number of packed red cells transfused intraoperatively (during CPB and before admission to the ICU) (Table 1).

The major outcome was considered to be postoperative acidosis (defined as peak lactate >3 mmol/L during the first three postoperative days, even on a single blood sample); secondary outcomes were incidences of different degrees of renal failure (AKIN 1-2-3); respiratory failure; mortality. To avoid any interference to the assessment of postoperative hyperlactataemia, Ringer lactate was never administered during the study period and postoperative blood samples were performed at least two hours from any RBC transfusion.

Statistical analysis was performed by the SPSS program for Windows, version 15.0 (SPSS Inc, Chicago, IL). Continuous variables are presented as mean ± standard deviation (SD) and categorical variables are presented as absolute numbers and/or percentages. For all statistical tests, a p-value <0.05 was considered significant.

All parameters recorded in our database, including the QualyP score, were tested for the association with the postoperative outcomes with a binary logistic regression analysis. To avoid over-fitting, all factors being significantly associated ($p<0.05$) with any outcome were used to build multivariate stepwise forward logistic regression models to establish their independent predictors.

To avoid multi-co-linearity, variables affected by mathematical coupling were separately entered in different models. In case of inter-correlation, the best single independent variable was chosen.

Results

Demographics, preoperative variables and intraoperative details are shown in Table 2.

Table 1. QualyP Score: values with literature references.

Variables	0	1	2
Peak lactates during CPB [mmol/L][1]	<3	≥3	–
Peak VCO2i [ml/min/m^2][2]	<60	≥60	–
Peak DO2i/VCO2i[2]	≥5	<5	–
Peak VCO2i/VO2i[2]	<0.9	≥0.9	–
CPB time [min][3]	<126	127–177	>177
Aortic cross-clamping time [min][3]	<90	91–131	>131
Lowest temperature on CPB [°C][4]	34-36	28-33	<28
Circulatory arrest[5]	No	Yes	–
Ultrafiltration for low urine output during CPB[6]	No	Yes	–
Number of PRCs transfused[7]	0	1–2	>2

CPB= cardiopulmonary bypass; VCO_2i= indexed CO_2 production; DO_2i= indexed O_2 delivery; VO_2i= indexed O_2 consumption; PRC= packed red blood cells.

[1]Maillet J-M, Le Besnerais P, Cantoni M, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. Chest 2003;123:1361-1366.

[2]Ranucci M, Isgrò G, Romitti F, Mele S, Biagioli B, Giomarelli P. Anaerobic metabolism during cardiopulmonary bypass: predictive value of carbon dioxide derived parameters. Ann Thorac Surg 2006;81:2189-2195.

[3]Data derived from an interim analysis of the first 100 patients. 0 = duration until the median time; 1 = duration until 1 standard deviation from the median; 2 = duration over 1 standard deviation from the median.

[4]Marx, John (2006). Rosen's emergency medicine: concepts and clinical practice. Mosby/Elsevier. p. 2239.

[5]Goldstone AB, Bronster DJ, Anyanwu AC, Goldstein MA, Filsoufi F, Adams DH, Chikwe J. Predictors and outcomes of seizures after cardiac surgery: a multivariable analysis of 2,578 patients. Ann Thorac Surg 2011;91:514-518.

[6]Parolari A, Pesce LL, Pacini D, Mazzanti V, Salis S, Sciacovelli C, Rossi F, Alamanni F; Monzino Research Group on Cardiac Surgery Outcomes. Risk factors for perioperative acute kidney injury after adult cardiac surgery: role of perioperative management. Ann Thorac Surg 2012;93:584-591.

[7]Jegger D, Revelly JP, Horisberger J, von Segesser LK, Ruchat P. Establishing an association between a peri-operative perfusion score system (PerfSCORE) and post-operative patient morbidity/mortality during CPB cardiac surgery. Perfusion 2007;22:311-316.

Mean QualyP Score was 4.8±2.6 (0-10).

Postoperative acidosis

Among all 187 patients, a peak postoperative lactate concentration >3 mmol/L was observed in 78 patients (41.7%).

When recorded variables were tested for association with postoperative acidosis, only 11 factors were entered into the multivariate model. Among these, QualyP Score proved to be an independent predictor of postoperative acidosis (OR 1.595, 95% CI 1.356-1.876) (Table 3). The C-statistic of the model was 0.798.

The AUC for QualyP Score was 0.780, with a cut-off value of 1 (sensibility 98.7%; specificity 98.2%).

Table 2. Demographics, preoperative characteristics and operative details.

Variables	n=187
Age [years]	64.2±13.2
Gender (M)	114 (61.0%)
Height [cm]	163.6±9.1
Weight [Kg]	72.1±12.7
BSA [m^2]	1.80±0.19
BMI [Kg/m^2]	26.9±4.0
Smoker or previous smoke habit	70 (37.4%)
COPD	32 (17.2%)
Systemic hypertension	134 (71.7%)
Diabetes (any kind)	52 (27.8%)
Chronic renal insufficiency *(not requiring preoperative dialysis)*	19 (10.2%)
Previous cerebrovascular accidents	14 (7.5%)
Peripheral vascular disease	21 (11.2%)
Unstable angina	23 (12.3%)
Myocardial infarction in the last 90 days before surgery	19 (10.2%)
Myocardial infarction >90 days before surgery	30 (16.0%)
Previous coronary angioplasty/stenting	20 (10.7%)
NYHA class 3/4	94 (50.3%)
Preoperative inotropes	2 (1.1%)
EuroSCORE II	3.12±3.88
Baseline serum creatinine [mg/dL]	1.1±0.6
Baseline estimated glomerular filtration rate [ml/min/1.73 m^2]	78.6±27.4
Baseline haemoglobin [g/dL]	12.9±1.7
Baseline haematocrit [%]	38.9±4.7
Baseline PaO^2/FiO^2 ratio [mmHg]	395.8±106.2
Re-operation	9 (4.8%)
CABG	46 (24.6%)
Valvular	78 (41.7%)
CABG + valvular	32 (17.1%)
Other kind of surgery	32 (17.1%)
Priming volume [ml]	941.8±197.4
CPB time [min]	121.4±47.9
AoX time [min]	88.7±39.2
Lowest temperature during CPB	31.8±2.7
Circulatory arrest	18 (9.6%)
Diuresis during CPB [ml]	1046.8±772.7
Ultrafiltration during CPB	9 (4.8%)
Number of PRCs transfused	0.3±0.7
Peak arterial lactates [mmol/L]	2.0±1.2
Lowest Hb during CPB [g/dl]	7.2±1.2
Lowest Hct during CPB [%]	21.2±3.1
Lowest DO^2i [$ml/min/m^2$]	270.4±37.3
Lowest VO^2i [$ml/min/m^2$]	54.5±15.2
Peak VCO^2i [$ml/min/m^2$]	68.1±24.1

BSA: body surface area (Mosteller); BMI: body mass index; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass: AoX: aortic cross-clamping; PRCs: packed red blood cells; Hb: haemoglobin; Hct: haematocrit; DO^2i: indexed delivery of oxygen; VO^2i: indexed consumption of oxygen; VCO^2i: indexed carbon dioxide production.

Renal failure – AKIN 1

Forty-nine patients (26.2%) experienced AKI stage 1. However, we could not find any statistical correlation with the incidence of AKI stage 1, even at univariate binary logistic analysis.

Renal failure – AKIN 2

Sixteen patients (8.6%) fulfilled the criteria to be included in AKI stage 2. Among all the tested variables, QualyP Score was found to be an independent predictor of AKIN 2 (OR 1.268, 95% CI 1.018-1.581) (Table 4). The C-statistic of the model was 0.836.

The AUC for QualyP Score was 0.647, with a cut-off value of 2 (sensibility 93.8%; specificity 89.5%)

Renal failure – AKIN 3

AKIN stage 3 occurred in only 11 patients (5.9%). At multivariate analysis, QualyP Score was an independent predictor of AKIN 3 (OR 1.848, 95% CI 1.230-2.778) (Table 4). The C-statistic of the model was 0.902.

The area under the curve (AUC) for the QualyP Score was 0.794, with a cut-off value of 5 (sensibility 90.0%; specificity 49.1%).

Respiratory failure

Among all patients, 21 (11.2%) experienced respiratory failure. Several independent risk factors have been revealed (Table 5). In particular, QualyP Score emerged as an independent predictor (OR 1.526, 95% CI 1.123-2.073), with a cut-off value of 2 (sensibility 95.2% and specificity 89.2%).

Mortality

Seven patients died during hospitalization, accounting for an overall mortality of 3.7%.

At multivariate analysis, the QualyP Score was an independent predictor of mortality (OR 1.497, 95% CI 1.054-2.127), with a cut-off value of 5 (sensibility 85.7%; specificity 50.6%).

However, the PerfSCORE was also an independent risk factor for mortality, but only in models where the QualyPScore was not included (Table 6).

Discussion

The main aim of cardiopulmonary bypass during cardiac operations is to warrant an adequate perfusion to all the organs so that they can maintain their normal functions when the heart is arrested. Accordingly, it is

Table 3. Multivariate models for postoperative acidosis.

Variables	p univariate	p multivariate	OR	95% CI
EuroSCORE II	***.002***	***.006***	***1.197***	***1.052–1.361***
CPB time	***<.001***	***.035***	***1.017***	***1.001–1.034***
AoX time	<.001	.605		
PRCs transfusions during CPB	.018	.280		
NIDDM	.044	.105		
Dislipidaemia	.041	.659		
Surgery type: other	.003	.871		
Circulatory arrest	.001	.117		
Peak RQ	.023	.369		
PerfSCORE	<.001	.164		
QualyP Score	***<.001***	***<.001***	***1.595***	***1.356–1.876***

CPB: cardiopulmonary bypass; AoX: aortic cross-clamping; PRCs: packed red blood cells; NIDDM: non-insulin-dependent diabetes mellitus; RQ: respiratory quotient.

Table 4. Multivariate models for postoperative AKIN 2 – AKIN 3.

Variables	p univariate	p multivariate	OR	95% CI
AKIN2				
Age	***.002***	***.008***	***1.119***	***1.029–1.216***
Baseline Hb	.011	.054		
Baseline Hct	.040	.553		
QualyP Score	***.043***	***.034***	***1.268***	***1.018–1.581***
BSA	.026	.194		
Lowest Hb during CPB	.023	.334		
Lowest Hct during CPB	.031	.358		
PerfSCORE	.108			
AKIN 3				
IDDM	.038	.897		
Previous PCI/stent	.010	.077		
Surgery: CABG+valvular	.003	.052		
Baseline sCr	***.001***	***.001***	***27.575***	***3.617–210.237***
QualyP Score	***.002***	***.003***	***1.848***	***1.230–2.778***
EuroSCORE II	.006	.815		
Baseline eGFR	.005	.928		
CPB time	.001	.584		
AoX time	***.002***	***.001***	***1.031***	***1.012–1.051***
PerfSCORE	.061			

Hb: haemoglobin; Hct: haematocrit; BSA: body surface area; CPB: cardiopulmonary bypass.
IDDM: insulin-dependent diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; sCr: serum creatinine; eGFR: estimated glomerular filtration rate; AoX: aortic cross-clamping.

necessary that the pump flows and gas exchange during CPB should be modulated to allow a normal oxygen delivery and an adequate elimination of carbon dioxide.

Great attention has been posed in the past on the haemoglobin concentration, given that the degree of haemodilution during CPB is associated with postoperative complications.[3,8] Furthermore, the avoidance of extreme haemodilution is strictly correlated to the efforts made to avoid the transfusion of packed red cells, which is associated with an increased occurrence of infections and mortality.[4]

In 2007, Jegger developed a score to study the association between CPB and clinical outcomes, demonstrating that the PerfSCORE was an independent parameter to predict morbidity.[9]

However, that score included only the raw values of pO_2 and pCO_2, not considering the role played by pump flow to ensure the major part of oxygen delivery,

Table 5. Multivariate models for postoperative respiratory failure.

Variables	p univariate	p multivariate	OR	95% CI
Obesity	***.018***	***.006***	***7.138***	***1.762-28.913***
IDDM	.047	.755		
Chronic renal insufficiency	***.001***	***.014***	***6.075***	***1.432-25.777***
Unstable angina	.022	.079		
Recent myocardial infarction	***.006***	***.018***	***7.268***	***1.413-37.393***
Age	.047	.181		
EuroSCORE II	.001	.250		
PerfSCORE	.006	.503		
QualyP Score	***.004***	***.007***	***1.526***	***1.123–2.073***
Ultrafiltration during CPB	.005	.979		
CPB time	<.001	.001	1.041	1.017–1.067
AoX time	.009	.044	.970	.942–.999
PRCs transfused during CPB	.024	.288		

IDDM: insulin-dependent diabetes mellitus; CPB: cardiopulmonary bypass; AoX: aortic cross-clamping; PRCs: packed red blood cells.

Table 6. Multivariate models for postoperative mortality.

Variables	p univariate	p multivariate	OR	95% CI
Age	***.009***	***.036***	***1.221***	***1.031-1.472***
EuroSCORE II	.002	.089		
QualyP Score	***.007***	***.024***	***1.497***	***1.054-2.127***
Ultrafiltration during CPB	***<.001***	***.002***	***39.530***	***3.907-399.966***
Intraoperative PRCs transfusions	.037	.480		
PerfSCORE	***.002***	***.034***	***1.695***	***1.041–2.757***
CPB time	.044	.390		
Lowest Hb during CPB	.018	.947		
Lowest Hct during CPB	.029	.838		
Lowest DO2i	.040	.759		
Lowest VO2i	.042	.987		

CPB: cardiopulmonary bypass; PRCs: packed red blood cells; Hb: haemoglobin; Hct: haematocrit; DO_2i: indexed delivery of oxygen; VO_2i: indexed consumption of oxygen.

whereas the possibility to calculate the metabolic needs during CPB could be extremely useful in the daily clinical practice.

On the other hand, to the best of our knowledge, this is the first study aimed at the evaluation of the quality of organ perfusion by means of the development of a scoring system that incorporates the estimates of oxygen delivery and consumption during CPB.

In fact, several reports suggest that tissue oxygenation and hypoxia could be better evaluated when the flow-dependent estimates of oxygen delivery and consumption are investigated during CPB, as well as estimates of carbon dioxide elimination.[1,10,11] Likewise, the same principles derived from the normal physiology could be applied to the CPB setting, in terms of oxygen- and carbon dioxide-derived estimates of the metabolic needs.[1]

In particular, Ranucci and coworkers demonstrated that the threshold for anaerobic metabolism during CPB establishes when VCO_2i peaks over 60 ml/min/m^2, VCO_2i/VO_2i reaches 0.9 and DO_2i/VCO_2i falls below 5.[1] These models encouraged other researchers to apply these concepts in the field of postoperative renal function after cardiac surgery on CPB. Similarly, equivalent cut-off values were found to be predictive of postoperative renal failure.[2]

However, it is noteworthy that Poullis recently recognized that no markers of quality of perfusion pressure and oxygen delivery during CPB still exist. Accordingly, correlating such evaluations with clinical outcome could prove helpful in providing a marker of quality of perfusion during CPB.[11]

Therefore, the aim of our QualyP Score was to ascertain if it was possible to evaluate the impact of the quality of perfusion provided during CPB on postoperative outcomes. This scoring system was based on cut-off values derived from literature, with adjunctive parameters resulting from an interim analysis of our first 100 patients (Table 1).

As an estimate of global organ metabolism, serum lactate concentration represents the most relevant and reliable marker of tissue hypoperfusion. Accordingly, the development of high lactate concentrations during CPB is typical of a subset of patients at a higher risk of incurring potentially severe complications.[12] In our study, a level of 3 mmol/L was considered the threshold for the establishment of an anaerobic metabolism, as described by Maillet.[13]

In the present study, the QualyP Score was predictive of postoperative acidosis at a low cut-off, equal to 1. Despite high sensitivity and specificity, this value seems quite low to explain, by itself, the development of postoperative anaerobic metabolism. It could be supposed that, not only the perfusion during CPB, but also other mechanisms (e.g. higher metabolic needs during the weaning from ventilation as well as peripheral wash-out in the first postoperative hours) might explain this increase of serum lactate concentration.

It is general knowledge that the pulmonary damage that might develop after CPB usually ends up in the development of atelectasis, infections and a increase in arterio-venous intrapulmonary shunts, with the consequence of a reduced systemic pO_2.[14] Moreover, the kind of anaesthesia and mechanical ventilation,[15,16] the switch from a pulsatile flow to a continuous and linear one during CPB,[17,18] as well as the induction of an ischaemia-reperfusion injury[14] may all contribute to the reduction of postoperative pulmonary function.

Accordingly, the possibility to identify intraoperatively a perfusion disadvantage which might end up in reduced postoperative pulmonary function, would be certainly welcome. Appropriately, the QualyP Score proved to be predictive of the development of respiratory insufficiency in the immediate postoperative period. Therefore, it could be supposed that a precocious identification of patients at high-risk for major complications might be helpful for subsequent postoperative management.

Among all organs, the kidneys are certainly those which mostly suffer from hypoperfusion.[19,20] Accordingly, various degrees of renal dysfunction are often observed in the common practice after cardiac operations on CPB.[21] In particular, the development of postoperative renal failure is one of the most important determinants of unfavorable outcome in cardiac surgery.[21]

It should be considered that some preoperative characteristics could not be modified before surgery, such as age, diabetes, hypertension or preoperative renal dysfunction. However, it is possible to avoid renal hypoperfusion, which is, in particular, one of the major determinants of the need for postoperative replacement therapy.[20]

In our cohort of patients, the QualyP Score was found to be particularly associated with various degrees of postoperative renal dysfunction, in particular, AKI stage 2 and 3. Our results, therefore, confirm the previous findings of de Somer[2] and Ranucci,[20] suggesting that the analysis of a broad spectrum of estimate parameters could be useful in establishing the adequacy of perfusion.

Conversely, we were not able to confirm the results shown by Ranucci[20] and de Somer,[2] particularly for what concerns the predictive role of DO_2i/VCO_2i on the occurrence of postoperative renal dysfunction. On the other hand, our results confirmed our hypothesis that not one single parameter, but the comprehensive evaluation of tissue hypoperfusion which can be measured by oxygen and carbon dioxide derived parameters, is responsible for the occurrence of postoperative complications.

In particular, it should be considered that 3 out of 10 parameters constituting the additive QualyP Score are directly dependent from the pump flow. This suggests that modulation of the pump flow plays a fundamental role in achieving an adequate perfusion during CPB.

Finally, the complex pathophysiology that is generated during cardiac surgery on CPB (e.g. hypothermia, systemic inflammatory response syndrome, endothelial dysfunction, deregulation of the haemocoagulative cascade, linear flow patterns) all contribute to the development of postoperative complications, sometimes irreversibly leading to the most unfavorable outcome.[14]

However, it is still not evident which role is independently played by CPB on postoperative mortality.[22]

In fact, de Somer supposed that the development of different perfusion strategies combined with adequate pharmacological support might improve the incidence of CPB-related morbidity;[22]

however, no statistical models, as well as scores predictive of postoperative outcomes, have been clearly designed especially incorporating flow-dependent parameters.

In this setting, the QualyP Score and the results derived from our study could be analyzed as a potential marker of the quality of perfusion, as well as a predictive model of postoperative mortality.

Limitations of the study

One of the most important limitations of the study is the relatively low incidence of outcomes observed during the study period. This may be accounted for by the small sample size. Furthermore, the overall EuroSCORE II of the study population is quite low and this might have conditioned the results, considering that patients with severe comorbidities (such as chronic renal replacement therapy or domicilial O_2 support) were excluded from the study.

The lack of a validation cohort is another limitation of the study. However, to try to overcome this problem, we have used reference values from well-established papers from the literature whose results have been found to be confirmed elsewhere.

However, all the multivariate models proved to be sufficiently powered, at least to draw some preliminary conclusions. It should also be noted that the high sensitivity of the cut-off values observed for the outcomes of AKIN 3 and mortality are counterbalanced by a relatively low specificity, suggesting that a revision of the scoring system might probably improve the quality of the model itself.

Furthermore, the absence of reference cut-off levels for our QualyP Score prevented a power sample analysis.

On the other hand, one of the main strengths of our study is that our results stem from a single institution design of the study, which guarantees the uniformity of intraoperative and postoperative treatments and, therefore, might counterbalance the potential biases of multicentre studies.

Conclusions

Despite the continuous improvements in the perfusion techniques since the beginning of the experience with CPB, it is still not possible to benchmark the quality of perfusion during cardiac surgery on CPB.

It could be supposed that the technological progress (more biocompatibility of membranes and circuits, filters, pulsatile or modulated flows) might improve the impact of fixed major determinants during cardiac surgery. However, this may not be sufficient alone.

It is evident that the development of monitoring systems could suggest the appropriate warnings and clues during CPB to avoid the development of organ dysfunction as a consequence of an inadequate intraoperative perfusion.

Furthermore, evidence-based medicine is emerging nowadays as a new paradigm for medical practice, including the field of extracorporeal circulation.[5]

In this setting, the development of scoring systems, such as the QualyP Score, might represent an advantage and a first step towards the definition of goal-directed perfusion strategies and quality benchmarking.

Author Note

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

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Appendix A. Conversion equations for volumes of a gas.

From	To	Multiply APTS by
ATPS	STPD	$[(P_A - P_{waterS})/P_S] * (T_S - T_A)$
ATPS	BTPS	$[(P_A - P_{waterS})/ (P_A - P_{waterB})] * (T_B - T_A)$

P_A: ambient pressure; P_{waterS}: partial pressure of water in saturated air; P_S: standard pressure (760 mmHg); T_S: standard temperature in Kelvin (273 K); T_A: ambient temperature in Kelvin (t °C + 273 K); P_{waterB}: partial pressure of water in saturated air in 37 °C = 47 mmHg; T_B: body temperature. Adapted from Brown SP, Miller WC, Eason JM (2006). Exercise Physiology: Basis of Human Movement in Health and Disease. Lippincott Williams & Wilkins. p. 113.