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What are the minimal criteria of goal-directed perfusion (GDP) in adult cardiac surgery?

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ABSTRACT

Introduction: Nowadays, many cardiac surgery teams are adopting the goal-directed perfusion (GDP) strategy in their practice to maintain optimal perfusion during cardiac surgeries and improve patient outcomes. Furthermore, it plays an indispensable role as a quality control tool to monitor both perfusionists' practice and equipment (in addition to disposables used in the surgery.

Objectives: To identify the role and the elements of GDP that facilitate better surgical outcomes. In addition, to compare between GDP and the traditional conventional perfusion strategy (CP) in terms of perfusion adequacy and surgical outcomes. Finally, to recognize challenges that may prevent the effective application of GDP and finding possible applicable solutions.

Methods: A systematic literature review was conducted from three different databases PubMed, SpringerLink, and ScienceDirect. The selected studies were in English from the USA and Europe with a time frame starting from 2005.

Results: The findings highlight the crucial role of the GDP strategy in protecting and preserving end-organ function after on-bypass cardiac surgery procedures. Furthermore, a clear understanding of the GDP implementation component and criteria was obtained. Alternatively, a satisfactory GDP level can be achieved by the optimal utilization of available resources.

Discussion: Dismantling the GDP strategy into practically recognized components to ease the implementation at different levels of perfusion practice.

Conclusion: The GDP approach involves the intensive monitoring of respiratory-related parameters to enhance surgical outcomes. The process includes blood preservation, optimal flow and intraoperative parameters management. Monitoring is the key element of GDP, which can be applied by using the sophisticated technology or the proper use of existing resources to develop protocols within the international guidelines and recommendations. Achieving an optimal perfusion requires concerted efforts of organizational, safety, and practical measurements.

Keywords: acute kidney Injury (AKI), cardiac surgery, cardiopulmonary bypass (CPB), goal-directed perfusion (GDP), hemodilution, oxygen delivery (DO2)

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1. INTRODUCTION

Since the initial times of adopting cardiac surgery procedures as modalities of treatment, the question about the adequacy of perfusion on cardiopulmonary bypass (CPB) has been raised and systematically researched. Consequently, the awareness of goal-directed perfusion (GDP) has been intensified and deliberately applied in many cardiac surgery settings as an evidence-based clinical practice that optimizes the adequacy and quality of perfusion supplied while simultaneously providing a significantly predictive and preventive approach to preserve end-organ functions from possible post-cardiac surgery complications such as acute kidney injury (AKI). The aims of this study are firstly to recognize the significance of using GDP in adult cardiac surgery, to identify the criteria needed to practice it optimally as well as the limitations that prevent its application in the field with possible alternative suggestions to confront these limitations.

Principally, the simplest way to describe GDP as a strategy is by the dynamic monitoring of respiratory-based parameters, basically oxygen delivery (DO2), oxygen consumption (VO2), and carbon dioxide production (VCO2), which enhances the adequacy of perfusion delivered.[1] Raising awareness of the GDP concept began in the late 1980s when Dr. William C. Shoemaker reported a trend of decreased mortality following high-risk surgeries accompanied by high parameter readings.[2] Based on his findings, many researchers were motivated to examine the different effects and influences of respiratory-based parameters on the outcomes of cardiac surgery. Statistically, the incidence of AKI in adult cardiac surgery is about 30%. For this reason, its consideration as a critical indicator of end-organ dysfunction in cardiac surgery has been appealed by many investigators.[3] What is more, the routinely monitored kidney function test as well as highly sensitive kidney tissues toward hypoxia facilitate the detection of postoperative complications related to extracorporeal circulation (ECC).

In 2005, Dr. Marco Ranucci performed a landmark research that examined the relationship between hemodilution and AKI in post-cardiac surgery patients, which articulated the minimal tolerable on bypass DO2-index (DO2i) limit that can reduce the incidence of AKI by targeting it above 272 ml/min/m2.[4] Therefore, his findings inspired many researchers in their studies, which facilitated the consideration of GDP as a golden standard for perfusion practice instead of traditional conventional perfusion (CP) practice.

In fact, international organizations and regulatory perfusion societies are continuously developing their standards and guidelines based on clinical evidence, which promote both the quality of perfusion delivered on bypass and the outcomes of cardiac surgery. Thus, the GDP strategy is extensively introduced within the international guidelines. For example, the American Society of Extracorporeal Technology (AmSECT) appraised the standards and guidelines for perfusion practice document in 2013 based on clinical evidence and previously accepted perfusion practices. The major points addressed blood preservation measurements along with continuous blood gas monitoring as standards of practice and relatively placed guidelines for both.[5]

On the one hand, fulfilling an effective application of the GDP strategy necessitates a dedicated type of monitoring technology with specific procedures for preserving the patient's blood. On the other hand, logistics disabilities can negatively impact the convenient level of GDP practice in many less fortunate and limited resourced cardiac surgery departments. In truth, the increasing awareness of GDP implementation has encouraged many institutes to develop tools and programs that can facilitate the application of GDP in the absence of resources, either by rising some self-developed calculators, in-hospital programs, mobile applications, or by using a preoperatively DO2i-estimated tool as developed by the division of cardiac surgery in Boston, USA to successfully achieve GDP.[6]

2. METHODOLOGY

To achieve the study objectives, a systematic literature review was conducted. First, the method of literature selection will be described. In addition, the findings of the literature will be discussed in the Results section.

2.1 Literature review

To identify the relevant literature, the systematic literature strategy was conducted using three search engines: PubMed, SpringerLink, and ScienceDirect. Based on the objectives of the study questions, the following terms were formed: Goal-directed perfusion, Oxygen delivery, Monitoring, Adult cardiac surgery, End-organ protection, AKI in cardiac surgery, Optimal perfusion, Extracorporeal circulation effects, Cardiopulmonary bypass.

The literature selection was based on the time frame of 2005 and after because it was believed in the impact of the valuable findings of Marco Ranucci's landmark research, which basically introduced the concept of GDP globally. Only English-language articles were selected using the snowball sampling technique according to the following inclusive criteria (Figure 1):

- Research findings from 2005 and after
- Application of GDP in adult cardiac surgery
- AKI prevention in cardiac surgery
- Optimal perfusion in cardiac surgery

To meet the objectives of the study question, as it has a wide and complex association, the following exclusive criteria were applied:

- GDP in neonatal and pediatric surgeries
- Cerebral oxygen consumption
- Off-pump cardiac surgery
- Animal trials
- Invasive oxygen consumption monitoring (liver, carotid, myocardial)

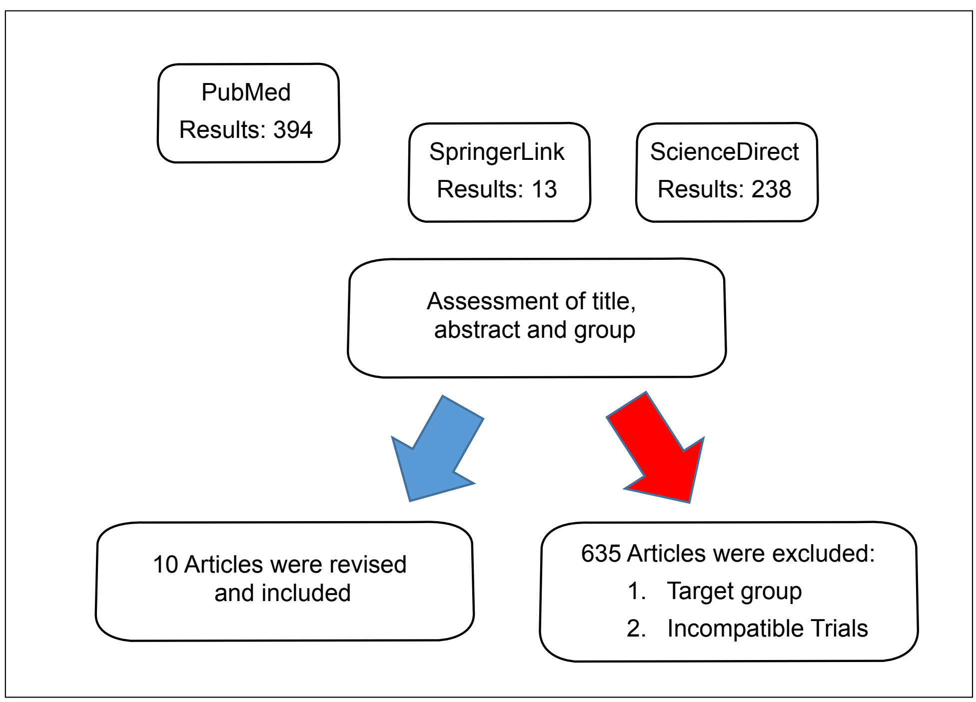

Figure 1. Research strategy
Source: Authors

The selected articles were chosen to consolidate the cutoff monitoring limits of the required parameters with the effect of CPB on end-organ function by comparing GDP and CP in terms of perfusion adequacy. Moreover, the aim was to recognize best perfusion practice based on international guidelines and recommendations and to identify the role of GDP as a quality control measurement. Furthermore, to describe the consistency of optimal perfusion components that enable better surgical outcomes, and to determine possible tools to confront the lack of dedicated monitors in the field, which can ease the application of GDP. Finally, the available free articles related to the study were assessed to evaluate the accessibility of the topic at different levels of practice.

3. RESULTS

The results define the criteria of GDP and present the advantages of adopting it in the clinical area. A comparison was made between GDP and traditional CP strategies in terms of optimal perfusion and quality of perfusion delivered. Finally, the possible GDP strategy to prevent challenges with associated solutions for a successful GDP application is shown.

3.1 Rising of the concept

William C. Shoemaker was one of the early medical pioneers who integrated the concept of monitoring some vital parameters in order to improve the medical outcomes of patients, which was widely implemented in emergency and intensive care medicine, termed as goal-directed therapy (GDT). In his initial record (1988), he described a relationship between monitoring some critical parameter values and mortality reduction. Furthermore, he expressed these high parameter values associated with better surgical outcomes as “supranormal” values, which reflected the elevated levels of cardiac index, oxygen delivery, and maximal oxygen consumption observed in the survivors.[2]

3.2 Definition

Although there is no clear formal definition of GDP in the literature, many researchers define it as the optimal perfusion goal to be achieved by using intensive monitoring during CPB to reduce mortality and postoperative complications.[2] On the other hand, many researchers focused more on which parameters should be monitored and carefully responded to. Justison described GDP as enhancing the current knowledge of adequate perfusion and using respiratory-based parameters to provide a whole new level of detail about what is happening to the patient at a tissue level.[1] In conclusion, all of these definitions consider monitoring DO2, VO2, and VCO2 as prime on-bypass parameters, and when contemporaneously added to other parameters such as pump flow, pH, blood gases, blood pressure, lactate levels, temperature, and urine output, the GDP strategy will be achieved effectively and surgical outcomes can be enhanced.

3.3 Criteria and elements

3.3.1 Oxygen delivery (DO2)

The prominent role of oxygen delivery (DO2) monitoring comes from its ability to represent the actual amount of oxygen delivered to body tissues and vital organs. In other words, it reflects the adequacy of perfusion supplied during CPB.
The AmSECT (2013)[5] Guidelines included the following equations to address the calculation formula of DO2 on bypass:

$$DO_2 (mL/min/m^2) = 10 \times \text{pump flow } (L/min/m^2) \times \text{arterial } O_2 \text{ content } (mL/100\ mL),$$

where arterial O2 content is calculated as follows:

$$\text{Arterial } O_2 \text{ content } (mL/100\ mL) = Hb\ (mg/dL) \times 1.36 \times Hb \text{ saturation } (\%) + 0.003 \times O_2 \text{ tension } (mmHg). \text{ (Hb: hemoglobin).}$$[5]

As can be seen from the previous formulas, the DO2 value depends on two independent factors: pump flow and Hb. On the other hand, oxygen saturation depends on oxygen tension (partial pressure) and both are well maintained by the intraoperative high oxygen supply of the CBP gas blender.[6]
The crucial role of monitoring BSA indexed oxygen delivery (DO2i) that results from dividing DO2 on BSA comes from the fact that it reflects the actual oxygen delivered to tissues or precisely reveals the actual functional impact of hemoglobin plus pump flow. On the other hand, the classical measurement of oxygen saturation from blood gases or monitors reflects the oxygen concentration in the blood without taking metabolic or tissue needs into account.[1]

Pump flow

CPB blood flow conditions are very dynamic and dependent on many systematic stipulations. The major aim is essentially to deliver adequate perfusion that meets the physiological needs of tissues and organs at different temperatures. In fact, the wide range of the cardiac index reflects the different flows based on core temperature, while BSA values are calculated individually for each case using the patient’s height and weight based on institutional preference formulas (Table 1). In practice, the standard formula for calculating adult bypass pump flow is:

Flow (L/min/m2) = Cardiac index (2.0-2.8 L/min) x BSA (m^2).[7]

Table 1: Temperature-related cardiac index in Deep Hypothermic Circulatory Arrest (DHCA.)[7]

Core temp *°C*	Cardiac index *M²*	*Approx *DHCA*
37-35	2.2-2.5	5 min
<35-32	2.0-2.2	
<32-28	1.8-2.0	
<28-24	1.6-1.8	20 min
<24-20	1.0-1.5	
<20	0.5-0.8	45 min

*90% probability of absence of structural or functional damage.
(*Source*: Kirklin JW, Barratt-Boyes GB, eds. Cardiac Surgery. Churchill- Livingstone, New York, 1993:61-127.)

Broadly speaking, the GDP strategy recommends elevated flow to overcome low critical DO2 values as an immediate perfusionist response until other measurements are made.[4,8] Apart from temperature-based flows applied in special procedure protocols, the fluctuating pump flows used to overcome some surgical conditions and occurrences of improving the bloodless surgical field or elevated cannula pressure, it will induce transient low DO2 values if not used carefully. However, adverse on-bypass variables such as high arterial cannula pressure or low operating volumes can be challenging to achieve an acceptable DO2 level through pump flow.

Hemoglobin

Hemoglobin is a large molecule made up of proteins and iron. It consists of four folded chains of a protein called globin. Each of these globin molecules is bound to a red pigment molecule called heme, which contains an ion of iron (Fe^{+2}). In fact, each iron ion in the heme can bind to one oxygen molecule. Therefore, each hemoglobin molecule can transport a total of four oxygen molecules. Oxyhemoglobin is the fully loaded hemoglobin by oxygen in the lungs, which moves within the arteries and arterioles to deliver the oxygen to the body tissues, where it becomes deoxyhemoglobin after the release of oxygen molecules into the tissues.[9] Clinically, the indispensable role of hemoglobin in DO2 makes the orientation toward optimizing its function critically recognized in the guidelines of CPB use. Therefore, testing the lowest acceptable level of on-bypass hemoglobin in the presence of priming hemodilution, cardioplegia administration, and CPB hemolysis is determined by its function represented in DO2. Again, recommendations to reduce allogenic blood transfusion are strongly emphasized by many surgical teams, as it can also lead to postoperative complications such as AKI. Although the minimal acceptable DO2i level that can prevent AKI in cardiac surgery is above 272 ml/min/m2 with an Hb level of 7.0–8 gm/dl, blood transfusion guidelines have clearly stated that the trigger of blood transfusion on-bypass should be assessed and discussed based on the clinical features and DO2 levels and should be applied when the value is less than 7.0 g/dl (Table 2).[1]

Table 2: Guidelines for blood transfusion in cardiac surgery.[10]

Recommendations	Class[a]	Level[b]
Implementation of a PBM protocol for the bleeding patient is recommended.	I	C
The use of PRBCs of all ages is recommended, because the storage time of the PRBCs does not affect the outcomes.	I	A
The use of leucocyte-depleted PRBCs is recommended to reduce infectious complications.	I	B
Pooled solvent detergent FFP may be preferred to standard FFP to reduce the risk of TRALI.	IIb	B
Perioperative treatment algorithms for the bleeding patient based on viscoelastic POC tests should be considered to reduce the number of transfusions.	IIa	B
It is recommended that one transfuse PRBCs on the basis of the clinical condition of the patient rather than on a fixed haemoglobin threshold.	I	B
A haematocrit of 21-24% may be considered during CPB when an adequate DO_2 (>273 ml O_2/min/m²) level is maintained.	IIb	B
Platelet concentrate should be transfused in bleeding patients with a platelet count below 50 (10/1) or patients on antiplatelet therapy with bleeding complications.	IIa	C

Consequently, the GDP strategy tends to preserve blood as a baseline standard for cardiac surgery by using the blood conservation measurements of autologous priming on biocompatible circuits, shortening CPB lines, using on-bypass hemoconcentrators, and effectively using autotransfusion systems (ATS) to optimize the quality of perfusion.[5]

3.3.2 VO2, Oxygen extraction ratio (O2ER) and VCO2

Whole body oxygen consumption (VO2) is universally considered as a measure of the body's metabolic activity and an indicator of tissue perfusion adequacy during CPB.[11] Considering the linear relationship between DO2 and VO2 on bypass, the main goal is to deliver adequate perfusion in order to reduce tissue oxygen demand. For this reason, monitoring VO2 levels is vital to determine the adequacy of perfusion and metabolic activity in one side and the effectiveness of non-CPB measurements such as anesthesia agents together. The formula used to calculate VO2 is:

$$VO2 = CO \times (CaO2 - CvO2)$$

where CaO2 refers to arterial oxygen content and CvO2 refers to venous oxygen content.

Moreover, the oxygen extraction ratio (O2ER) is the ratio of the body's oxygen consumption (VO2) compared to the systemic oxygen delivery (DO2), which reflects the perfusion supply efficiency against the tissue demand status as in the formula:

$$O2ER = VO2 / DO2.$$

Clinically, elevating on-bypass O2ER values of more than 27% reflected perfusion insufficiency with possible end-organ dysfunction.[2]

However, monitoring on-bypass VO2 and O2ER levels to determine flow insufficiency and hypoxia, along with using VCO2 as an additional indicator of metabolic hypoxia, can be vitally implemented in cardiac surgery. de Somer et al. concluded that when DO2 falls below a critical value (in the range of 260–270 mL/min/m2) during CPB, organ hypoxia can be triggered, with consequent tissue acidosis leading to increased VCO2. This mechanism could be a determinant factor in impaired postoperative renal function.[12] On-bypass VCO2 can be detected from the oxygenator gas outlet either by using VCO2 monitoring systems or by connecting it to the anesthesia machine.

3.3.3 Monitoring principles

Adequate perfusion on bypass depends on many intraoperative variables. In addition, vigorous parameter monitoring provides the basis for predicting and preventing end-organ hypoxia. For this reason, international guidelines, within their regulatory standards, imposed recommendations for the use of dedicated monitoring to enhance surgical outcomes.5 While the CP strategy tends to monitor flow, pressures, blood gases, lactate and urine output (UOP), the GDP strategy adds the special perfusion-related parameters of DO_2, VO2, O_2ER, and VCO_2 to optimize perfusion and tissue oxygenation. Clinically, traditional CP techniques achieve high DO_2 in almost 50% of cases, while the GDP approach achieves high DO_2 in more than 90% of cases, with a consequent reduction in the rate of AKI by about 40%.[13] The key difference between the two strategies lies in preserving end-organ function and preventing AKI, which is superior in GDP than in traditional CP. Table 3 shows the main parameters monitored for each strategy.

Table 3: Parameters monitored for the differences between CP and GDP.

Parameters	CP	GDP
BSA flow	Yes	Yes
Hemoglobin, Hct	Yes	Yes
Hemodynamic pressures (MAP, CVP, SVR)	Yes	Yes
CBP pressures (oxygenator, cardioplegia, etc.)	Yes	Yes
Arterial blood gases	Yes	Yes
Venous blood gases	Yes	Yes
UOP	Yes	Yes
Lactate	Yes	Yes
DO_2	No	Yes
VO_2	No	Yes
O_2ER	No	Yes
VCO_2	No	Yes

Source: Authors

In fact, rapid science and technology development has availed many state-of-the-art monitors, which have been widely integrated into CBP machines. Consequently, real-time monitoring technologies such as CONNECT software (LivaNova, Mirandola, Italy) and Spectrum Medical (Gloucester, England) successfully facilitated the application of GDP in cardiac surgery by saving perfusionists' time for long and distracting calculations. Basically, both technologies effectively contributed to the quality of perfusion delivered as well as helped perfusion researchers to assess the oxygenators and consumables used on CPB by reflecting the real performance variable values. Furthermore, numerous studies have exploited the extensive databases of both technologies to refine their results.

Finally, some variances in algorithmic programming between the two modalities produced some differences in results, but both provide a sophisticated level of parameter monitoring.[14]

3.3.4 Blood conservation measurements

Effective patient blood management is the first step in applying the GDP strategy. Therefore, many international regulatory guidelines have been enforced to enhance competent approaches that save the bypass patient's blood. From the preparation phase of CBP to the intraoperative phase, the aim is to avoid hemodilution and optimize the function of blood components in general, mainly hemoglobin.[10]

Preparation phase

Basically, blood management considers the reduction of hemodilution as the main goal, which is initially activated after careful review of the patient's records, general condition, and calculations of the blood flow necessary to deliver adequate DO2. In fact, hemodilution is advantageous to a certain extent because it reduces blood viscosity, which will be beneficial for microcirculatory perfusion, but it also has undesirable negative effects on the concentration of coagulation factors and blood cells during and after ECC, which may possibly reduce postoperative hemostasis and organ function. For this reason, minimizing priming and operating fluid on ECC is vital to promote the quality of perfusion delivered.[15] Preparing the least suitable oxygenator, preferably with an integrated filter, based on the target flow of the case is essential to reduce the priming required. Furthermore, reconstructing the CPB circuits by removing unnecessary additional lengths and purge lines from the circuits as well as minimizing the tube size have a great impact on the priming volume and hemolysis reduction.[5]

Intraoperative phase

Providing a satisfactory level of perfusion on bypass is predisposed to many factors such as avoiding on-bypass hemodilution and maintaining adequate pressure, which are essential for this. First, autologous priming techniques (antegrade and retrograde) should be considered to eliminate the excess volumes in the oxygenator and circuit, which will reduce the dilution effect on the blood component and thus improve the function of the blood on ECC.[5] Next, cardioplegia volume is considered to be the main cause of on-bypass hemodilution. Therefore, accurate volumes are required to be delivered during the initial dose and re-administration shots with proper volume venting. Dynamic volume and circulation management uses convectional hemoconcentrator techniques to eliminate excess volume while taking the coagulation status into account.[10] Nonetheless, the purposeful removal of extra volume from the circulation is subject to close monitoring of the coagulation and electrolyte status to overcome possible heparin insufficiency or electrolyte disturbances occurring during the process. On the other hand, the use of new initiatives such as miniaturized extracorporeal circulation (MECC) or minimally invasive extracorporeal circulation (MiECC), aimed at supporting Hb function intraoperatively, when combined with low-volume cardioplegia solutions, results in a remarkable reduction in the operating volume, cardioplegia volume, and overall surgical complications.[16] The use of autotransfusion systems (ATS) in cardiac surgery has been proven to have a valuable blood preservation effect. For this reason, many departments use it in their built-in cardiac surgery protocols by applying it during the case instead of the pump suction. Moreover, the salvaged and processed blood from ATS can be retransfused after surgery, which can directly reduce the need for allogenic blood transfusion while improving overall surgical outcomes (Table 4).[10]

Table 4: Patient blood management on CPB.[10]

Recommendations	Class[a]	Level[b]
Implementation of institutional measures to reduce haemodilution by fluid infusion and CPB during cardiac surgery to reduce the risk of bleeding and the need for transfusions is recommended.	I	C
The use of a closed extracorporeal circuit may be considered to reduce bleeding and transfusions.	IIb	B
The use of a biocompatible coating to reduce perioperative bleeding and transfusions may be considered.	IIb	B
The routine use of cell salvage should be considered to prevent transfusions.	IIa	B
(Modified) ultrafiltration may be considered as part of a blood conservation strategy to minimize haemodilution.	IIb	B
Retrograde and antegrade autologous priming should be considered as part of a blood conservation strategy to reduce transfusions.	IIa	A
Normothermia during CPB (temperature >36°C) and maintenance of a normal pH (7.35–7.45) may contribute to a reduced risk of postoperative bleeding.	IIb	B

3.4 End-organ protection in cardiac surgery

Surgical outcomes are characterized by end-organ function postoperatively, which depends on many factors. Likewise, controlling these factors can significantly improve the outcomes.

de Somer et al. categorized these end-organ dysfunction factors into two major categories: predisposing and perioperative. Predisposing factors include all chronic diseases and medical conditions that are difficult to control and that negatively impact overall surgical outcomes. In contrast, perioperative variables such as systemic inflammatory response, hemodilution, hypoperfusion, and microembolization can be effectively controlled by using the evidence-based GDP strategy through the proper management of CPB parameters and consumables.[15]

3.5 Acute kidney injury in cardiac surgery

Acute kidney injury (AKI) resulting from cardiac surgery is a recognized complication with high mortality and morbidity rates. Numerous studies have been carried out to identify the predisposing factors associated with CPB and also to determine the possibility of predicting and preventing this complication.17 AKI is a condition in which the kidney functions partially or completely loses its ability to work, as evidenced by the reduction in glomerular filtration rate (GFR) and serum creatinine (SCr) over a period of time. Table 5 summarizes the different diagnostic criteria of AKI based on three models, namely RIFLE (Risk, Injury, Failure, Loss End-Stage Kidney Disease), AKIN (Acute Kidney Injury Network), and KDIGO (Kidney Disease: Improving Global Outcome).

Table 5: Rifle, AKIN, and KDIGO diagnostic criteria of AKI.[17]

	RIFLE	Stages	AKIN	Stages	KDIGO	Urine output
Definition	SCr >1.5 baseline over 7 days		SCr >1.5 baseline over 48 h or↑SCr of 0.3 mg/dl over 48 h		SCr >1.5 baseline over 7 days or↑SCr of 0.3 mg/dl over 48 h	Urine output
Class risk	↑SCr×1.5 or↓GFR >25%	Stage 1	SCr >1.5 baseline or>0.3 mg/dl increase	Stage 1	SCr >1.5 baseline or>0.3 mg/dl increase	<0.5 mL/kg/h×6 h
Injury	↑SCr×2 or↓GFR >50%	Stage 2	SCr >2 baseline	Stage 2	SCr >2 baseline	<0.5 mL/kg/h x 12 h
Failure	↑SCr×3 or↓GFR >75%	Stage 3	SCr >3 baseline or↑SCr to 4.0 mg/dl (with an acute increase of at least 0.5 mg/dl) or↑of RRT	Stage 3	SCr >3 baseline or↑SCr to 4.0 mg/dl or↑of RRT	<0.5 mL/kg/h×24 h
Loss	Persistent acute renal failure with complete loss of kidney function >4 weeks					
ESKD	RRT required for >3 months					

Statistically, the overall incidence of AKI during cardiac surgery is about 30%. Furthermore, the severity of AKI can be asymptomatic or mild to moderate recoverable incidence, but it can also progress morbidly to acute renal failure (ARF), which is a serious complication of cardiac surgery. This occurs in 1–5% of patients. With dialysis treatment, the mortality rate can reach up to 50%.[4] In addition to the high morbid-mortality associated with AKI, the extended length of stay and increased costs of care are also crucial aspects that must be managed by healthcare facilities.
The key in controlling the incidence of AKI is early diagnosis and possible interventions to effectively predict and prevent its occurrence in cardiac surgery procedures.

3.5.1 Prediction and prevention of AKI in cardiac surgery

Unfortunately, the highly sensitive nature of the kidneys to hypoxia is a criticism of the use of ECC, especially in long procedures. Renal ischemia on CPB can be triggered by many factors including decreased oxygen-carrying capacity, non-pulsatile flow, prolonged cross-clamp time, metabolic acidosis, reperfusion injury, tubular oxidative stress, exogenous and endogenous toxins, metabolic abnormalities, and neurohormonal activation.18 Prevention of AKI is a wide-ranging process that should be started before surgery and crystallized intraoperatively.

After recognizing disease severity, risk factors, comorbidities, and other chronic conditions that can cause AKI, plenty of measurements should be performed to predict and prevent cardiac surgery-associated AKI. Preoperatively, discontinuation of nephrotoxic and hypotensive medications such as non-steroidal drugs, angiotensin receptor, and converting enzyme blockers should be considered. Medications that can cause lactic acidosis, such as metformin, should also be discontinued.[18]
Although autoregulation of renal flow occurs down to a pressure of about 80 mmHg the optimal on-bypass pressure to maintain the kidney function is still controversial, yet pump flow is a pressure-dependent variable.19 An individualized precise revision should be performed preoperatively based on the patient's blood pressure chart to determine their own "normal" range as a referral baseline on bypass which can be helpful. Fundamentally, ECC produces two harmful effects that suppress the kidney function: hemodilution and the inflammatory process. Based on this, minimizing priming volume as well as using biocompatible circuits have a great protective aspect against hemodilution and inflammatory response on CPB.[15]

The peak benefit of minimizing hemodilution is supporting both renal pressure and the oxygen delivery by preserving blood catecholamines and hemoglobin, thereby moderating the need for pharmacological blood pressure support on bypass. Correspondingly, the preserved blood component promotes the hormonal function of the renal system that reduces its activation trigger on bypass and eventually reduces the kidney's oxygen demand. Into the bargain, metabolic support also is a primary consideration on bypass, avoiding hyperglycemia as well as metabolic acidosis along with maintaining optimal albumin levels minimize possible kidney injury.[18]

3.5.2 GDP for AKI prevention

In general, confronting the negative effect of ECC on the kidneys is recognized by the GDP strategy in two ways: blood preservation measurements to reduce hemodilution and homogenously harmless circuit utilization to reduce the inflammatory response. Additionally, the GDP strategy establishes the baseline least tolerable parameter levels and prolongation to prevent AKI as well promote perfusion delivered to other body organs.[19]

Starting by Ranucci et al. results of reducing the hemodilution to prevent AKI by maintaining the level of DO2i above 272ml/min/m2,4 orientation of the more intensive oxygenation parameters was raised. Initially, monitoring of arterial blood gases, venous blood gases, Hb level, and serum lactate level became adeptly merged with related calculations of DO2i, VO2i, and O2ER. The studies continued again to realize the cutoff limits cohered to AKI. de Somer et al. recognized that adding of VCO2 monitoring is also valuable to prevent AKI on the ratio of DO2/VCO2 > 5.3 and a nadir DO2i level more than 262 ml/min/m2 in hypothermic procedures.12 Based on their research findings, the full crystallization of GDP as a systematic approach was incessantly empowered and supported by many institutions, boosting valuable guidelines to be imposed based on evidence-based practice. Encouraging autologous priming techniques, utilization of heparin-coated biocompatible circuits, using leukocyte filters with hemoconcentrators, applying ATS systems, and developing new perfusion initiatives like the modified short circuits of the MiECC system have a great impact of demolishing the inflammatory response of ECC.[5,10]Avoiding nephrotoxic antifibrinolytics to minimize the renal dysfunction is crucially highlighted. Besides, recommendations toward using aminocaproic acid and tranexamic acid as safe alternatives for aprotinin are highly advised to protect kidneys from its undesirable effect.[17]

The question related to the time relation of low DO2i reading and incidence of AKI was lately answered by Rasmussen et al. when he concluded that either short (1-5 minutes) or at least 30 minutes exposure to low DO2i reading were independently associated with the need for renal replacement therapy.[8]

3.6 Optimal perfusion concept

The terminology of optimal perfusion on CPB does not have a definite definition; moreover, the postoperative condition is the basic ascertaining way for CPB perfusion adequacy. Perfusion could be considered adequately delivered if the patient survives without life-threatening complications or persistent clinically manifested organ dysfunction.[20]

A comprehensive two-part summary review conducted by Murphy et al. compared between acknowledged CPB protocols that used to deliver an optimal perfusion level on CPB by reviewing related evidence-based practice of CPB management.[20]

On-bypass mean arterial pressure (MAP) has a special consideration during cardiac surgery as it has a direct impact on the physiological needs of the body. Two major trends of controlling on-bypass MAP (high MAP and low MAP) are used. Furthermore, both strategies have their own benefits and drawbacks. For this reason, optimal MAP on bypass should be individually determined based on the underling case's condition.[20]

Pump flow rate has an indispensable role in transporting adequate tissue oxygenation. Besides, the flow rate calculations are based on many intra-surgical variables. While the cardiac index and the BSA are the essential components of the calculations, the temperature also has a great implication.

For example, while normothermic procedures necessitate a cardiac index of 2.2–2.5 L/min, hypothermic procedures necessitate a remarkable reduction of the flow by reducing it up to 1.4–1.8 L/min to overcome hypertension intraoperatively. Pulsatile and non-pulsatile pump flow differentiation is still not clearly acquired. Although many research have been conducted to recognize the difference between both flows, the results remain uncertain.[20]

Hemodilution is necessary on ECC for improving the microcirculation, but excessive hemodilution induces a demolished level of DO_2 impairing the tissue perfusion and causing postoperative complications, thus avoiding excessive hemodilution on CPB enhances the surgical outcomes.[15] In addition, a precise blood gas management should be applied to avoid metabolic acidosis and end-organ damage.

Finally, achieving an optimal perfusion level is dependent on many factors, a multipart process should be integrated, which requires the collaboration of both; the healthcare team and the facility in coherent to the inventiveness of evidence-based science.[20]

3.7 Challenges, suggestion, and alternative solutions for GDP application

GDP as a strategy tends to improve surgical outcomes by extensive monitoring for the respiratory-based parameters, which requires a dedicated type of high-tech monitors. In view of that, the lack of logistic support at some departments may limit the application of GDP effectively. Barriers that limit the application of the GDP strategy are not mentioned in the literature clearly; however, it can be recognized more at less fortunate limited resourced departments. The expected causes can be financial incapability, also lack of recognition of the significance of GDP strategy or because of personal preference of using old traditional monitoring strategies.

Providentially, many departments have overcome these limitations by emerging their self-developed calculators or programs to assist an effective on-bypass monitoring approach, while others have developed a simple quick reference tool to estimate the target DO2i level by correcting the flow based on two variables; the Hb and the flow.6 Using the same modalities can empower the application of GDP at these limited resourced departments, while instigating evidence-based protocols to successfully grant GDP application.

4. DISCUSSION

The findings of the literature represented the crucial role of GDP as a confidently driven perfusion strategy based on the orientation of preserving end-organ function and enhancing surgical outcomes. They reveal that GDP is inspired from evidence-based science, which consists of four major components: patient blood management, oxygen delivery, monitoring principles, and optimal perfusion.

4.1 Patient blood management (PBM)

Both AmSECT and EACTS guidelines and recommendations urged on the maximum preservation of the patient's blood prior to initiating the CPB, with attention to post-hemodilutional status of the hemoglobin, and emphasized it as a whole team consideration to reduce possible allogenic blood transfusion.[5,10] What is more, the international guidelines regarding on-bypass PBM recommended that the hemodilution resulting from priming circuits should be reduced by efficient reconstruction and minimizing tube sizing without compromising the flow needed. Additionally, using the oxygenators with integrated filters accompanied with biocompatible circuits achieves a convenient method of reducing hemodilution, hemolysis, and ECC inflammatory response.[15,17] Cardioplegia volume as a major cause of intraoperative hemodilution can be controlled by proper volume administration and using hemoconcentration techniques.

The International Guidelines highlighted the role of CPB closed circuits, MECC and MiECC strategies, both of which consider shrinking the circuit's surface area with an effective integration of vacuum-assisted devices that confirmed effective elimination of excessive hemodilution, hemolysis, and air contact, considering the adoption of low-volume cardioplegia modalities.[10]

Autologous priming, either antegrade or retrograde, as a standard protocol of evacuating excess priming volume is greatly presented with consideration of patient's hemodynamics.

Applying such a strategy still necessitates the conscientious collaboration between the anesthetist and the perfusionist.10 Nevertheless, integration of ATS machines within the procedures will reduce the amount of blood loss by re-concentration and avoiding a suction traumatic effect on the vacuumed blood.[10]

Transfusing allogenic blood can be considered when Hb is less than the transfusion trigger, which can be detected simply by inadequate DO2i levels or when Hb < 7gm/dl.[10] Also, Dijoy et al. recommended conserving on-bypass Hct within the range above 23–24% to avoid postoperative morbidity and mortality.[2] Here again, precautions regarding the risk–benefit ratio for blood transfusion complications should be weighed particularly when considering the long-stored blood nature of shifting the blood-oxygen association curve to the left, which reduces blood-oxygen released to the tissues and eventually reduces actual DO_2 as recognized by many experts. Finally, EACTS recommended preserving normothermic temperature management > 36°C with normal pH values to reduce the risk of postoperative bleeding by facilitating a coagulation-friendly environment.[10]

4.2 Oxygen delivery (DO2)

The significance of oxygen delivery in cardiac surgery comes from the predictive nature of precisely monitored values of indexed DO2 for postoperative end-organ dysfunction, essentially AKI. Ranucci et al. identified the DO2i-AKI predisposing cutoff limit in normothermic coronary procedures at the level less than 272ml/min/m².[4] On the other hand, de Somer et al. added the variable of VCO2 to Nader's lowest DO2i in hypothermic cardiac procedures, concluding that a DO2i level less than 262 mL/min/m² accompanied with a nadir DO2/VCO2 ratio <5.3 was independently associated with higher AKI incidence.[12] The variance between the DO2i results of both studies resulted from temperature-related effects on the hemoglobin's viscosity and oxygen association curve during hypothermia. Both researchers documented the reduction in hemodilution principally, in addition to the quick elevation of the flow to confront on-bypass low DO_2i levels.

Nonetheless, protective measurements after maximum PBM by preoperatively calculating the optimal flow based on a CI of 2.2–2.5L/min to avoid an on-bypass initial drop are significantly helpful in determining the size of the arterial cannula needed to achieve the targeted DO2 limit within a safe perfusion pressure.[2] Finally, assessing the quality of CPB consumables and the perfusionist's practice based on DO2 monitoring can effectively realize the differences between oxygenators, circuits, and perfusion trends used.[21] Also, it consists of a quality control tool to assess the area of practice necessities for further improvement accordingly (Figure 2).

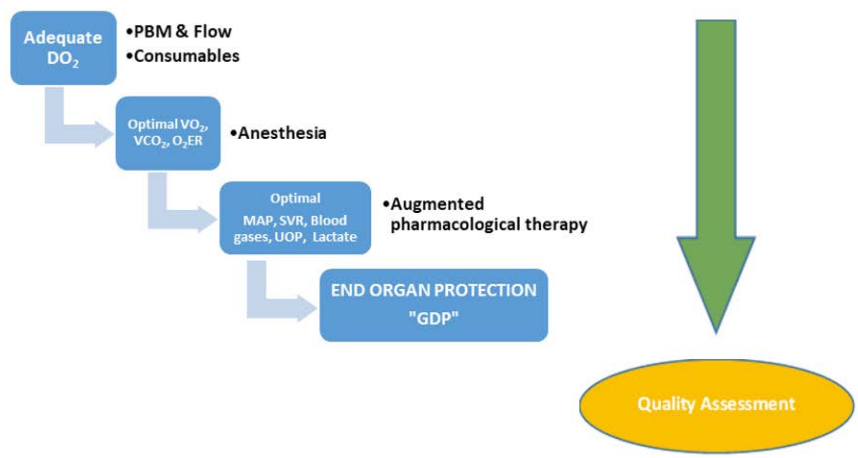

Figure 2. GDP as a quality control tool.
Source: Authors

4.3 Monitoring principles

Monitoring configures the extensive understanding needed to assess the reliability of all measures taken on-bypass. The central difference in monitoring principles between CP and GDP comes from the idea of dynamically changing pump flow in GDP to achieve satisfactory DO2 levels, while the CP approaches maintain a fixed flow based on a previously estimated BSA calculation. Correspondingly, basic parameter monitoring such as temperature, MAP, CVP, SVR, pH, blood gases, Hb, UOP, and lactate levels are actively implemented to enhance tissue perfusion by considering adequate DO2i as the main perfusion goal. On the other hand, the CP strategy tends to monitor these variables based on fixed non-linked matter that target the normal level of each parameter separately.

Related to this, Magruder et al. concluded that when the traditional perfusion strategy failed to deliver adequate DO2 in almost half of the cases, GDP achieved 90% in the same group with a 40% reduction of AKI incidence in the GDP group.[13]

The seventh standard of AmSECT regulatory guidelines and standards (2013) recommended using inline uninterrupted oxygen and gas monitors to improve the application of GDP strategies as a safe practice within the field because its ability to detect and respond to low parameter readings.[5] Furthermore, continuous monitoring provides a holistic representation of the parameter levels through body tissue necessities as CPB comprises many variables that can directly affect the efficiency of perfusion delivered. In advance, the newly applied monitors enrich collecting, recording, and mining the correlated data fortifying the research field. Irrevocably, developing GDP-based in-house checklists and protocols is importantly settled to assist perfusionists' improvement in their practice at all departmentally equipped levels. Sery et al. (2019) developed a quick reference tool based on the two variables Hb and flow to avoid prolonged low DO2i readings by targeting DO2i of 280 ml/min/m2.[6]

Integrating such a tool into the practice can be highly promoted in less fortunate departments to avoid unnecessary prolonged duration of uncorrected low DO2 levels resulting from long distractive calculations and the absence of monitors. Likewise, using some simple programs of excel sheets and self-developed calculators to calculate the needed values of DO2 and VO2 are usefully advocated after sampling within a recognized sampling time frame to offer sufficient monitoring. Besides, VCO2 can be easily determined by connecting the oxygenator's exhaust outlet to the anesthesia machine. Engaging such strategies merged with internationally recognized GDP protocols of PBM, CPB management, sampling, and responsive interventions within controlled time frames will expediently reinforce effective GDP application within the available resources. Figure 3 shows an example of GDP application in the absence of dedicated monitors.

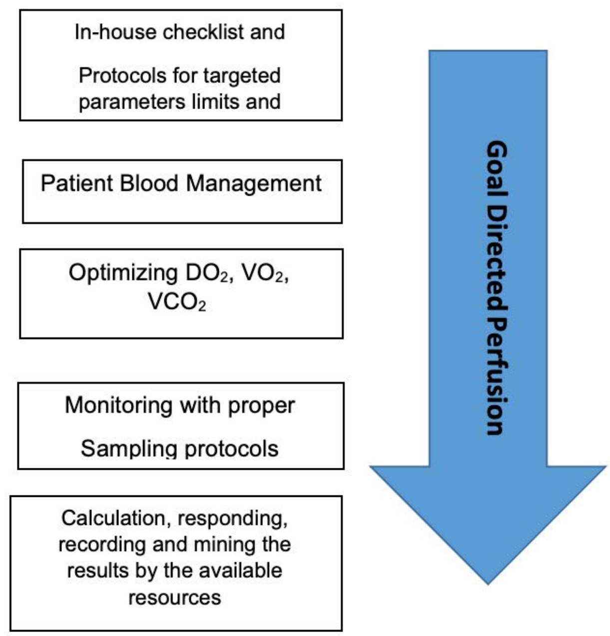

Figure 3: GDP process at limited resourced departments.
Source: Authors

4.4 Optimal perfusion

The main goal of cardiac surgery is to improve the overall health condition for the patient by restoring the organ function with better prognosis and preventing possible health condition deterioration. Optimal perfusion can be promoted by all safe evidence-based measurements, which are proven to deliver adequate perfusion on CPB.[2] Also, optimal perfusion as a concept performs the umbrella that directs all organizational, safety, and practical measurements taken to preserve end-organ function after cardiac surgery.

EACTS highlighted the role of dynamically changing cardiac surgery protocols and modalities besides the wide-ranging variances among the qualifications and resources within cardiac surgery departments in the absence of globally standardized practice in the field that covers all CPB aspects, addressing the regulatory role of evidence-based practice to fulfill the major goal of enhancing postoperative outcomes.[10]

AmSECT divided their 15 regulatory standards into two major groups: administrative and practical. The administrative standards importantly urged the specialized perfusion education program to qualify perfusionists (Standard 2). In addition to that, the standards commended establishing institutionally based protocols (Standard 1), checklists (Standard 4), communication with the surgical team (Standard 5), and quality control managements (Standard 13) to grant best practice. The practical standards organized perfusion-related areas of records (Standard 3), PBM (Standard 9), gas exchange (Standard 10), anticoagulant management (Standard 8), and safety measurements acknowledgment (Standard 6). While Standard 11 specified the determination of required blood flow by evaluating DO2 and VO2 levels in addition to acid–base, ABGs, VBGs, Hb, and temperature variables.[5]

The standards facilitate enforcing a maximum safety assurance process by multiple steps starting by the comprehensible acknowledgement of the patient's health status through the patient's records and result assessment prior to the surgery to recognize the patient's condition and needs. Then, it greatly validated applying different CPB level, flow, temperature and pressure sensors to ensure on-bypass safety. The same safety precautions were identified by de Somer (2013), such as using pre-bypass filters, avoiding old blood transfusion, level sensors and limiting the use of cardiotomy suctions, which can prevent small particle embolization during ECC, which are responsible for possible neurological incidences.[5,15]

On-bypass evidence-based practice tends to target best therapeutic ranges of all variables constructing the optimal perfusion goal. However, augmented preoperative pharmacological management by avoiding nephrotoxic drugs for patients at risk is highly prized to avoid an unwanted ECC effect.[18] In addition, implementing other available surgical and medical techniques of beating heart surgery and trans-catheter aortic valve replacement can be beneficially applied for specific high risk patients' groups. Nevertheless, early initiation of renal replacement therapy for patients at risk of AKI is highly recommended, as it may lower mortality and shorten the ICU length of stay.[18] Intensifying the algorithmic hemodynamic monitoring intraoperatively and postoperatively accompanied with decreased vasopressor use ultimately reduced patients' length of stay and improved overall outcomes.[2] As a final point, the optimal perfusion process, as enthusiastically inspired by the evidence-based science, integrates the international guidelines through organizational regulatory protocols and on-bypass safety precautionary considerations to ensure the best practical management for the needed variables (Figure 4).

Figure 4. Optimal perfusion process.
Source: Authors

5. CONCLUSION

Considering GDP as a golden standard for practicing perfusion in the last decade derived from its ability to prevent postoperative end-organ dysfunction, especially AKI. Directing a therapeutic acceptable DO2i level when intensively merged with the management of other parameters induces the optimal perfusion needed to preserve end-organ function. Therefore, implementing GDP as a quality measurement in cardiac surgery helps to ascertain the excellence of both practice and equipment used. Implementing the evidence-based clinical science through perfusion educational programs, CPB safety assurance protocols, and best on-bypass practical measurements to achieve efficient perfusion indispensably fulfills a successful optimal perfusion concept. Nevertheless, many alternative solutions can be integrated to confront the lack of sophistically dedicated monitoring modalities through the proper utilization of the existing resources based on the clinically practiced guidelines and recommendations that endow successful GDP application.

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