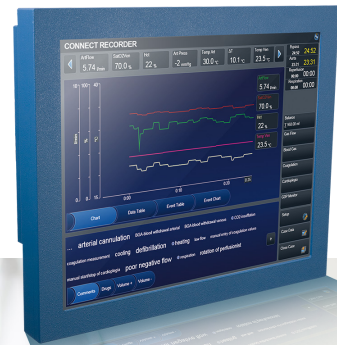


## GDP®

## Goal-Directed Perfusion



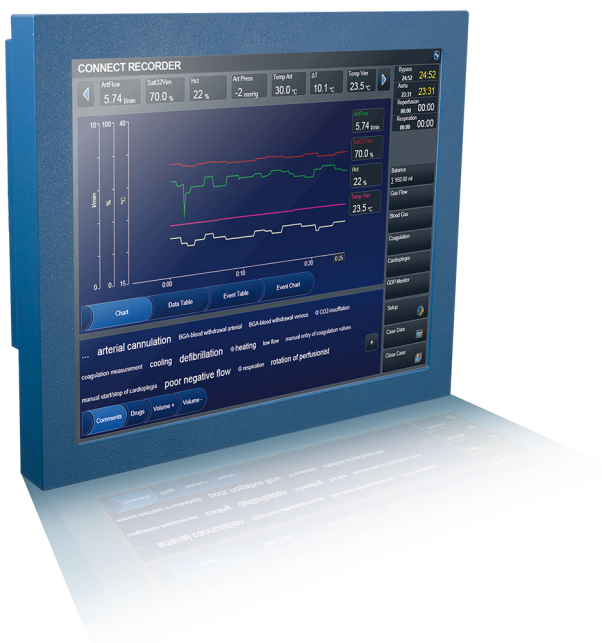
## SCIENTIFIC PUBLICATIONS

### Abstract Book

# GDP®

## Goal-Directed Perfusion

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# Purpose of the Abstract Book

1

The LivaNova GDP Abstract Book is intended to provide a comprehensive overview of the much-discussed Goal-Directed Perfusion (GDP) Therapy and how it can influence the work of perfusionists now and into the future.

The Book includes a general overview of the GDP Therapy concept, its implementation through the LivaNova Connect™ GDP Monitor and the list of papers published so far on the therapy.

It provides a list of relevant publications and scientific abstracts covering three main areas:

- **GDP & ACUTE KIDNEY INJURY (AKI)**
- **GDP AND AKI ECONOMIC CONSIDERATIONS**
- **GDP & NEUROLOGICAL IMPACT**

# Goal-Directed Perfusion and GDP Monitor Introduction

2

## GDP Therapy - Clinical information

Acute kidney injury (AKI) is a serious complication of cardiac surgery, affecting a considerable proportion of patients and increasing post-operative morbidity and mortality<sup>1</sup>. Various factors, including age, pre-operative renal function, hemodynamic state, and duration and complexity of surgery, have been associated with post-operative AKI.<sup>2</sup>

An association between the nadir hematocrit (HCT) value during cardiopulmonary bypass (CPB) and post-operative AKI was first reported in 1994.<sup>3</sup> Numerous retrospective studies subsequently confirmed this finding, and some authors have hypothesized that insufficient oxygen delivery ( $DO_2$ ) may be the mechanism underlying the link between severe hemodilution on CPB and poor renal outcomes.<sup>4-7</sup>

Subsequent retrospective studies<sup>8,9</sup> have confirmed the association between nadir  $DO_2$  on CPB and post-operative AKI, with the identification of a "critical  $DO_2$ " in the range of 260 to 272 mL/min/m<sup>2</sup> for patients undergoing moderately hypothermic (>32°C) CPB. Based on these observations, the concept of goal-directed perfusion (GDP), aimed at maintaining the  $DO_2$  on CPB above the critical value, was introduced.<sup>9</sup>

The current guidelines of the American Society of Extracorporeal Technology include measurement of  $DO_2$  within the standard measurements for assessing arterial pump flow rate.<sup>10</sup>

It is not only the  $DO_2$  that plays a role in the GDP Therapy concept.

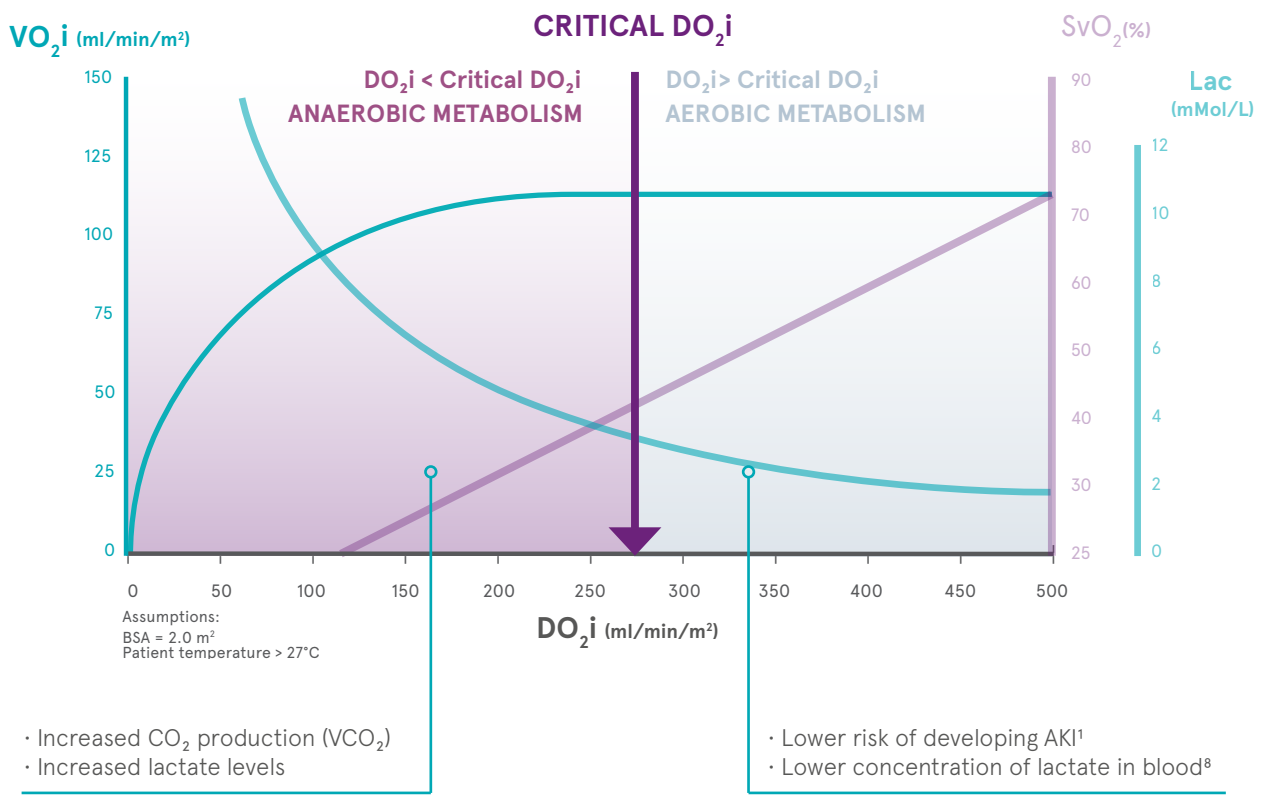
It was also identified that  $DO_2$  levels < 260 mL/minute/m<sup>2</sup> during CPB were associated with increased lactate formation<sup>11</sup> and that hyperlactatemia was associated with decreased  $DO_2$  levels and an increased  $CO_2$  production ( $VCO_2$ ) during CPB, with critical values settled at a  $VCO_2$  > 60 mL/minute/m<sup>2</sup> and a  $DO_2/VCO_2$  ratio < 5.0.<sup>12</sup>

These data generate the hypothesis that, when the  $DO_2$  during CPB falls below a critical value (in the range of 260 to 270 mL/minute/m<sup>2</sup>), organ dysoxia may be triggered, with consequent tissue acidosis leading to increased  $VCO_2$ , and that this mechanism may be a determinant of impaired post-operative renal function.<sup>9</sup>

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**AEROBIC AND ANAEROBIC METABOLISM DURING PERFUSION**



In recent years, perfusion clinicians have been raising another question:  
**Can GDP Therapy affect other CPB morbidities?**

In order to find a scientific answer to this question, many clinicians have started studying this topic, particularly focussing on cerebral perfusion and its neurological aspects.

# Goal-Directed Perfusion and Connect™ GDP Monitor

LivaNova, alongside leading clinicians who have studied the clinical benefits and improved patient outcomes associated with the application of Goal-Directed Perfusion, is at the forefront of creating global awareness on the advantages of this therapy. Furthermore, LivaNova implements and transparently provides the GDP formulas patented by Dr. Marco Ranucci into the Connect – GDP Monitor.

With the GDP Monitor the perfusionist may view advanced parameters such as  $VCO_{2i}$ ,  $O_2ER$  and the metabolic ratio  $DO_{2i}/VCO_{2i}$ . Such parameters are relevant for optimal perfusion management where the metabolic needs of each patient during cardiac procedures is effectively respected. <sup>1,2, 3, 7</sup>



## DO<sub>2i</sub>

**DO<sub>2</sub> = OXYGEN DELIVERY** (ml/min), or oxygen supply, is the amount of oxygen delivered to the body from arterial blood flow. It is calculated from cardiac output/ pump flow and arterial oxygen content.

**DO<sub>2i</sub> = INDEXED OXYGEN DELIVERY** (ml/min/m<sup>2</sup>) is the oxygen delivery divided by the Body Surface Area (BSA).

## VO<sub>2i</sub>

**VO<sub>2</sub> = OXYGEN CONSUMPTION** (ml/min), or oxygen uptake, is the volume of oxygen consumed by the tissues. Under aerobic metabolic conditions, oxygen is consumed to generate energy so VO<sub>2</sub> corresponds to the metabolic rate. VO<sub>2</sub> can be derived from cardiac output/pump flow and the difference between arterial and venous oxygen contents.

**VO<sub>2i</sub> = INDEXED OXYGEN CONSUMPTION** (ml/min/m<sup>2</sup>) is the oxygen consumption divided by the Body Surface Area (BSA).

## VCO<sub>2i</sub>

**VCO<sub>2</sub> = CARBONDIOXIDE PRODUCTION** (ml/min), is the amount of carbon dioxide produced by the tissues and removed by the lungs or the oxygenator.

**VCO<sub>2i</sub> = INDEXED CARBON DIOXIDE PRODUCTION** (ml/min/m<sup>2</sup>), is the carbon dioxide production divided by the Body Surface Area (BSA).

## VO<sub>2i</sub> / DO<sub>2i</sub>

**VO<sub>2i</sub> / DO<sub>2i</sub> = OXYGEN EXTRACTION RATIO (O<sub>2</sub>ER)** is the ratio of oxygen consumption and oxygen delivery  $VO_{2i}/DO_{2i}$ , and represents the fraction of oxygen taken up by the tissues.

## DO<sub>2i</sub> / VCO<sub>2i</sub>

**DO<sub>2i</sub> / VCO<sub>2i</sub> = Indexed oxygen delivery divided by indexed carbon dioxide production.** It is reported in the literature as a marker correlated to Acute Kidney Injury (AKI) and Hyperlactatemia (HL)<sup>1</sup>.

# Goal-Directed Perfusion & AKI

## List of publications

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**1. OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS AND ACUTE RENAL FAILURE AFTER CORONARY OPERATIONS**

**Ranucci M. et al.**

*Ann Thorac Surg.* 2005 Dec;80(6):2213-20.

Free full text article available online: <https://doi.org/10.1016/j.athoracsur.2005.05.069>

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**2. HYPERLACTATEMIA DURING CARDIOPULMONARY BYPASS: DETERMINANTS AND IMPACT ON POSTOPERATIVE OUTCOME**

**Ranucci M. et al.**

*Crit Care.* 2006;10(6):R167.

Free full text article available online: [10.1186/cc5113](https://doi.org/10.1186/cc5113)

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**3. ANAEROBIC METABOLISM DURING CARDIOPULMONARY BYPASS: PREDICTIVE VALUE OF CARBON DIOXIDE DERIVED PARAMETERS**

**Ranucci M. et al.**

*Ann Thorac Surg.* 2006 Jun;81(6):2189-95.

Free full text article available online: [10.1016/j.athoracsur.2006.01.025](https://doi.org/10.1016/j.athoracsur.2006.01.025)

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**4. PERIOPERATIVE RENAL FAILURE: HYPOPERFUSION DURING CARDIOPULMONARY BYPASS?**

**Ranucci M.**

*Seminars in Cardiothoracic and Vascular Anesthesia Vol 11, Issue 4, 2007*

Only free abstract available: <https://doi.org/10.1177/1089253207311141>

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**5. ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY: FOCUS ON MODIFIABLE RISK FACTORS**

**Karkouti K. et al.**

*Circulation.* 2009;119:495-502.

Free full text article available online: <https://www.ahajournals.org/doi/pdf/10.1161>

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**6. CENTRAL VENOUS OXYGEN SATURATION AND BLOOD LACTATE LEVELS DURING CARDIOPULMONARY BYPASS ARE ASSOCIATED WITH OUTCOME AFTER PEDIATRIC CARDIAC SURGERY**

**Ranucci M. et al.**

*Crit Care.* 2010; 14(4): R149.

Free full text article available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2945132/>

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**7. O<sub>2</sub> DELIVERY AND CO<sub>2</sub> PRODUCTION DURING CARDIOPULMONARY BYPASS AS DETERMINANTS OF ACUTE KIDNEY INJURY: TIME FOR A GOAL-DIRECTED PERFUSION MANAGEMENT?**

**De Somer F et al.**

*Critical Care* 2011 15:R192

Free full text article available online: <https://doi.org/10.1186/cc10349>

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**8. TRANSFUSIONS DURING CARDIOPULMONARY BYPASS: BETTER WHEN TRIGGERED BY VENOUS OXYGEN SATURATION AND OXYGEN EXTRACTION RATE**

**Ranucci M. et al.**

*Perfusion*. 2011 Jul;26(4):327-33.

Only free abstract available: <https://doi.org/10.1177/0267659111407539>

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**9. COMBINED CENTRAL VENOUS OXYGEN SATURATION AND LACTATE AS MARKERS OF OCCULT HYPOPERFUSION AND OUTCOME FOLLOWING CARDIAC SURGERY**

**Hu BY. et al.**

*J Cardiothorac Vasc Anesth*. 2012 Feb;26(1):52-7.

Free full text article available online: doi: [10.1053/j.jvca.2011.07.021](https://doi.org/10.1053/j.jvca.2011.07.021)

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**10. OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS (AND RENAL OUTCOME) USING TWO SYSTEMS OF EXTRACORPOREAL CIRCULATION: A RETROSPECTIVE REVIEW**

**Bennett MJ. et al.**

*Interact Cardiovasc Thorac Surg*. 2013 Jun;16(6):760-4.

Free full text article available online: [10.1093/icvts/ivt057](https://doi.org/10.1093/icvts/ivt057)

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**11. ACUTE KIDNEY INJURY SUBSEQUENT TO CARDIAC SURGERY**

**Kramer R.S. et al.**

*J Extra Corpor Technol*. 2015 Mar;47(1):16-28.

Free full text article available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4566816/>

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**12. DESIGNING A NEW SCORING SYSTEM (QUALYP SCORE) CORRELATING THE MANAGEMENT OF CARDIOPULMONARY BYPASS TO POSTOPERATIVE OUTCOMES.**

**Rubino AS. et al.**

*Perfusion*. 2015 Sep;30(6):448-56.

Only free abstract available: <https://doi.org/10.1177/0267659114557184>

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**13. THE HISTORY OF GOAL-DIRECTED THERAPY AND RELEVANCE TO CARDIOPULMONARY BYPASS**

**Dijoy L. et al.**

*J Extra Corpor Technol.* 2015 Jun;47(2):90-4.

Free full text available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4557555/>

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**14. HEMODILUTION ON CARDIOPULMONARY BYPASS AS A DETERMINANT OF EARLY POSTOPERATIVE HYPERLACTATEMIA**

**Ranucci M. et al.**

*PLoS One.* 2015 May 18;10(5):e0126939.

Free full text article available online: [10.1371/journal.pone.0126939](https://doi.org/10.1371/journal.pone.0126939)

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**15. NADIR OXYGEN DELIVERY ON BYPASS AND HYPOTENSION INCREASE ACUTE KIDNEY INJURY RISK AFTER CARDIAC OPERATIONS**

**Magruder JT. et al.**

*Ann Thorac Surg.* 2015 Nov;100(5):1697-703.

Free full text article available online [10.1016/j.athoracsur.2015.05.059](https://doi.org/10.1016/j.athoracsur.2015.05.059)

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**16. ACUTE KIDNEY INJURY AND HEMODILUTION DURING CARDIOPULMONARY BYPASS: A CHANGING SCENARIO**

**Ranucci M. et al.**

*Ann Thorac Surg.* 2015 Jul;100(1):95-100.

Free full text article available online: [10.1016/j.athoracsur.2015.02.034](https://doi.org/10.1016/j.athoracsur.2015.02.034)

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**17. ACUTE KIDNEY INJURY IN CARDIAC SURGERY AND CARDIAC INTENSIVE CARE**

**Lau G. et al.**

*Semin Cardiothorac Vasc Anesth.* 2015 Dec;19(4):270-87.

Only free abstract available: <https://doi.org/10.1177/1089253215593177>

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**18. IS TIMING EVERYTHING?**

**Justison G.**

Presented at Goal Directed Therapy Symposium, 54<sup>th</sup> AmSECT International Conference, Colorado Springs, Colorado, March 19, 2016.

*J Extra Corpor Technol.* 2017;49:P13-P18

Free full text available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5474897/>

**19. A PILOT GOAL-DIRECTED PERFUSION INITIATIVE IS ASSOCIATED WITH LESS ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY**

**Magruder JT et al.**

*J Thorac Cardiovasc Surg.* 2017;153:118-25.e1.

Only free abstract available: <https://doi.org/10.1016/j.jtcvs.2016.09.016>

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**20. A MULTIDISCIPLINARY PERIOPERATIVE STRATEGY FOR ATTAINING "MORE PHYSIOLOGIC" CARDIAC SURGERY**

**Anastasiadis K. et al.**

*Perfusion.* 2017 Sep;32(6):446-453.

Only free abstract available: [10.1177/0267659117700488](https://doi.org/10.1177/0267659117700488)

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**21. IS IT TIME FOR GOAL-DIRECTED THERAPY IN PERFUSION**

**Groom R. C.**

Presented at the Goal Directed Therapy Symposium, 54<sup>th</sup>AmSECT International Conference, Colorado Springs, Colorado, March 19, 2016.

*J Extra Corpor Technol.* 2017;49:P8-P12

Free full text available online: [http://amsect.smithbucklin.com/JECT/PDFs/2017\\_volume49/Groom.pdf](http://amsect.smithbucklin.com/JECT/PDFs/2017_volume49/Groom.pdf)

**22. VARIATION IN MEASUREMENT AND REPORTING OF GOAL DIRECTED PERFUSION PARAMETERS**

**Baker R. A.**

Presented at the Goal Directed Therapy Symposium, 54<sup>th</sup> AmSECT International Conference, Colorado Springs, Colorado, March 19, 2016.

*J Extra Corpor Technol.* 2017;49:P2-P7

Free full text available online: [http://amsect.smithbucklin.com/JECT/PDFs/2017\\_volume49/Baker.pdf](http://amsect.smithbucklin.com/JECT/PDFs/2017_volume49/Baker.pdf)

**23. WILL REAL-TIME MONITORING TECHNOLOGY BE A GAME CHANGER FOR PERFUSION SAFETY?**

**Mongero L. B.**

Presented at the Goal Directed Therapy Symposium, 54<sup>th</sup> AmSECT International Conference, Colorado Springs, Colorado, March 19, 2016.

*J Extra Corpor Technol.* 2017;49:P19-P24

Free full text available online: [http://amsect.smithbucklin.com/JECT/PDFs/2017\\_volume49/Mongero.pdf](http://amsect.smithbucklin.com/JECT/PDFs/2017_volume49/Mongero.pdf)

**24. CARBON DIOXIDE PRODUCTION DURING CARDIOPULMONARY BYPASS: PATHOPHYSIOLOGY, MEASURE AND CLINICAL RELEVANCE**

**Ranucci M. et al.**

*Perfusion.* 2017 Jan;32(1):4-12.

Free full text article available online: <https://doi.org/10.1177/0267659116659919>

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**25. LOW OXYGEN DELIVERY AS A PREDICTOR OF ACUTE KIDNEY INJURY DURING CARDIOPULMONARY BYPASS**

**Newland R.F. et al.**

*J Extra Corpor Technol.* 2017;49:224-230

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**I. RISK FACTORS FOR ACUTE KIDNEY INJURY AFTER CARDIOPULMONARY BYPASS.**

**Hendrix RHJ. et al.**

*J Extra Corpor Technol.* 2018 Jun;50(2):124.

Letters to the Editor on Newland 2017

Free full text available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6002649/>

**II. RESPONSE TO LETTER "RISK FACTORS FOR ACUTE KIDNEY INJURY AFTER CARDIOPULMONARY BYPASS" BY RIK H.J. HENDRIX ET AL.**

**Newland R.F. et al.**

*J Extra Corpor Technol.* 2018 Jun;50(2):125

Free full text available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6002652/>

**26. GOAL-DIRECTED PERFUSION TO REDUCE ACUTE KIDNEY INJURY: A RANDOMIZED TRIAL**

**Ranucci M. et al.**

*J Thorac Cardiovasc Surg.* 2018 Nov;156(5):1918-1927.e2.

Only free abstract available: <https://doi.org/10.1016/j.jtcvs.2018.04.045>

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**I. PERFUSION INDUCED ACUTE KIDNEY INJURY – A LITANY OF UNCERTAINTY & FRUSTRATION**

**Ferraris V. A.**

*J Thorac Cardiovasc Surg.* 2018 Nov; Volume 156, Issue 5, November 2018, Pages 1928-1930

Editorial to GIFT study

<https://doi.org/10.1016/j.jtcvs.2018.04.091>

**II. CONVENTIONAL OR OXYGEN DELIVERY-GUIDED PERFUSION: WHICH COMES FIRST, THE CHICKEN OR THE EGG?**

**Santarpino G. et al.**

*J Thorac Cardiovasc Surg.* 2019 Jan;157(1): 300

To the Editor

<https://doi.org/10.1016/j.jtcvs.2018.07.019>

**III. CARDIAC SURGERY ASSOCIATED ACUTE KIDNEY INJURY AND THE ROLE OF CARDIOPULMONARY BYPASS TECHNIQUE**

**Ranucci M.**

*J Thorac Cardiovasc Surg.* 2019 Jan;157(1): 301

Reply to the Editor

<https://doi.org/10.1016/j.jtcvs.2018.08.033>

**IV. THE VAGARIES OF GOAL-DIRECTED PERFUSION AND THE TROUBLE WITH RANDOMIZED TRIALS.**

**Ferraris V. A.**

*J Thorac Cardiovasc Surg.* 2019 Jan;157(1):301-303.

Reply to the Editor

<https://doi.org/10.1016/j.jtcvs.2018.04.091>

**27. TIME-DOSE RESPONSE OF OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS PREDICTS ACUTE KIDNEY INJURY**

**Mukaïda H. et al.**

*J Thorac Cardiovasc Surg.* 2018 Nov 16. 1-8 [Epub ahead of print]

Only free abstract available: <https://doi.org/10.1016/j.jtcvs.2018.10.148>

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**28. SUTURELESS VALVES AND THE QUALITY OF PERFUSION: TOWARDS A GOAL DIRECTED AORTIC VALVE REPLACEMENT**

**Rubino A.S., Mignosa C.**

*Minerva Cardioangiologica* 2018 April;66(2):163-9

Only free abstract available: DOI: [10.23736/S0026-4725.17.04590-X](https://doi.org/10.23736/S0026-4725.17.04590-X)

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### 1. OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS AND ACUTE RENAL FAILURE AFTER CORONARY OPERATIONS

Ranucci M. et al.

*Ann Thorac Surg.* 2005 Dec;80(6):2213-20.

<https://doi.org/10.1016/j.athoracsur.2005.05.069>

#### ABSTRACT

##### Background:

The degree of hemodilution during cardiopulmonary bypass has recently been identified as an independent risk factor for acute renal failure after cardiac operations. In this prospective observational study we have investigated the role of the lowest oxygen delivery, lowest hematocrit, and pump flow during cardiopulmonary bypass as possible risk factors for acute renal failure and renal dysfunction.

##### Methods:

One thousand forty-eight consecutive patients undergoing coronary operations have been studied. For each patient we have recorded the lowest hematocrit on cardiopulmonary bypass, the correspondent lowest oxygen delivery, and the pump flow around the time of these determinations. The three variables have been explored in a multivariable model as possible risk factors for acute renal failure and postoperative serum creatinine levels increase. The role of transfusions in determining acute renal failure was subsequently included in the model.

##### Results:

The best predictor for acute renal failure and peak postoperative serum creatinine levels was the lowest oxygen delivery, with a critical value at 272 mL.min<sup>(-1)</sup>.m<sup>(-2)</sup>. The lowest hematocrit was an independent risk factor with a lowest predictive value at a cutoff of 26%. When corrected for the need for transfusions, only the lowest oxygen delivery remained an independent risk factor.

##### Conclusions:

A high degree of hemodilution during cardiopulmonary bypass is a risk factor for postoperative renal dysfunction; however, its detrimental effects may be reduced by increasing the oxygen delivery with an adequately increased pump flow.

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## 2. HYPERLACTATEMIA DURING CARDIOPULMONARY BYPASS: DETERMINANTS AND IMPACT ON POSTOPERATIVE OUTCOME

Ranucci M. et al.

*Crit Care. 2006;10(6):R167.*

[10.1186/cc5113](https://doi.org/10.1186/cc5113)

### ABSTRACT

#### Introduction:

Hyperlactatemia during cardiopulmonary bypass is relatively frequent and is associated with an increased postoperative morbidity. The aim of this study was to determine which perfusion-related factors may be responsible for hyperlactatemia, with specific respect to hemodilution and oxygen delivery, and to verify the clinical impact of hyperlactatemia during cardiopulmonary bypass in terms of postoperative morbidity and mortality rate.

#### Methods:

Five hundred consecutive patients undergoing cardiac surgery with cardiopulmonary bypass were admitted to this prospective observational study. During cardiopulmonary bypass, serial arterial blood gas analyses with blood lactate and glucose determinations were obtained. Hyperlactatemia was defined as a peak arterial blood lactate concentration exceeding 3 mmol/l. Pre- and intraoperative factors were tested for independent association with the peak arterial lactate concentration and hyperlactatemia. The postoperative outcome of patients with or without hyperlactatemia was compared.

#### Results:

Factors independently associated with hyperlactatemia were the preoperative serum creatinine value, the presence of active endocarditis, the cardiopulmonary bypass duration, the lowest oxygen delivery during cardiopulmonary bypass, and the peak blood glucose level. Once corrected for other explanatory variables, hyperlactatemia during cardiopulmonary bypass remained significantly associated with an increased morbidity, related mainly to a postoperative low cardiac output syndrome, but not to mortality.

#### Conclusions:

Hyperlactatemia during cardiopulmonary bypass appears to be related mainly to a condition of insufficient oxygen delivery (type A hyperlactatemia). During cardiopulmonary bypass, a careful coupling of pump flow and arterial oxygen content therefore seems mandatory to guarantee a sufficient oxygen supply to the peripheral tissues.

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### 3. ANAEROBIC METABOLISM DURING CARDIOPULMONARY BYPASS: PREDICTIVE VALUE OF CARBON DIOXIDE DERIVED PARAMETERS

Ranucci M. et al.

*Ann Thorac Surg.* 2006 Jun;81(6):2189-95.

[10.1016/j.athoracsur.2006.01.025](https://doi.org/10.1016/j.athoracsur.2006.01.025)

#### ABSTRACT

##### Background:

Hyperlactatemia during cardiopulmonary bypass (CPB) is a common event and is associated to a high morbidity and mortality after cardiac operations. The present study is aimed to identify the possible predictors of hyperlactatemia during CPB among a series of oxygen and carbon dioxide derived parameters measured during CPB.

##### Methods:

This is a prospective observational study on 54 patients undergoing cardiac surgery with CPB. Hyperlactatemia was defined as an arterial lactate concentration higher than 3 mMol/L. Serial blood lactate assays have been performed during CPB, and their association to a number of oxygen and carbon dioxide derived parameters was explored.

##### Results:

Arterial blood lactate concentration was positively correlated to the CPB duration, the carbon dioxide elimination, and the respiratory quotient, and negatively correlated to the presence of the aortic cross-clamping, the body surface area, the ratio between the oxygen delivery and the carbon dioxide production, and the arterial oxygen saturation. Predictors of hyperlactatemia during CPB are a carbon dioxide production higher than 60 mL.min<sup>(-1)</sup>.m<sup>(-2)</sup>, a respiratory quotient higher than 0.9, and a ratio between oxygen delivery and carbon dioxide production lower than 5.

##### Conclusions:

Carbon dioxide derived parameters are representative of hyperlactatemia during CPB, as a result of the carbon dioxide produced under anaerobic conditions through the buffering of protons by the bicarbonate system. The carbon dioxide elimination rate measured at the exhaled site of the oxygenator may be used for an indirect assessment of the metabolic state of the patient.

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#### 4. PERIOPERATIVE RENAL FAILURE: HYPOPERFUSION DURING CARDIOPULMONARY BYPASS?

Ranucci M.

*Seminars in Cardiothoracic and Vascular Anesthesia Vol 11, Issue 4, 2007*

<https://doi.org/10.1177/1089253207311141>

#### ABSTRACT

Acute renal failure is one of the most frequent and life-threatening complications after cardiac surgery. There is a recent growing deal of information suggesting that during the time of cardiopulmonary bypass kidneys may suffer from an imbalance between oxygen supply and oxygen needs. A low hematocrit during cardiopulmonary bypass is associated with an increase risk of acute renal failure, mainly due to a low oxygen delivery. An inadequate oxygen delivery during cardiopulmonary bypass is associated with lactate production, and under normothermic conditions, hyperlactatemia appears for an oxygen delivery below  $260 \text{ mL min}^{-1} \text{ m}^{-2}$ . The risk of acute renal failure significantly increases for an oxygen delivery approximately at the same value ( $272 \text{ mL min}^{-1} \text{ m}^{-2}$ ). During cardiopulmonary bypass, the pump flow should be coupled with the hematocrit to avoid falling below this critical oxygen delivery.

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## 5. ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY: FOCUS ON MODIFIABLE RISK FACTORS

Karkouti K. et al.

*Circulation*. 2009;119:495–502.

<https://www.ahajournals.org/doi/pdf/10.1161>

### ABSTRACT

#### Background:

Acute kidney injury (AKI) after cardiac surgery is a major health issue. Lacking effective therapies, risk factor modification may offer a means of preventing this complication. The objective of the present study was to identify and determine the prognostic importance of such risk factors.

#### Methods and Results:

Data from a multicenter cohort of 3500 adult patients who underwent cardiac surgery at 7 hospitals during 2004 were analyzed (using multivariable logistic regression modeling) to determine the independent relationships between 3 thresholds of AKI (>25%, >50%, and >75% decrease in estimated glomerular filtration rate within 1 week of surgery or need for postoperative dialysis) with death rates, as well as to identify modifiable risk factors for AKI. The 3 thresholds of AKI occurred in 24% (n=829), 7% (n=228), and 3% (n=119) of the cohort, respectively. All 3 thresholds were independently associated with a >4-fold increase in the odds of death and could be predicted with several perioperative variables, including preoperative intra-aortic balloon pump use, urgent surgery, and prolonged cardiopulmonary bypass. In particular, 3 potentially modifiable variables were also independently and strongly associated with AKI. These were preoperative anemia, perioperative red blood cell transfusions, and surgical reexploration.

#### Conclusions:

AKI after cardiac surgery is highly prevalent and prognostically important. Therapies aimed at mitigating preoperative anemia, perioperative red blood cell transfusions, and surgical reexploration may offer protection against this complication.

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## 6. CENTRAL VENOUS OXYGEN SATURATION AND BLOOD LACTATE LEVELS DURING CARDIOPULMONARY BYPASS ARE ASSOCIATED WITH OUTCOME AFTER PEDIATRIC CARDIAC SURGERY

Ranucci M. et al.

*Crit Care.* 2010; 14(4): R149.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2945132/>

### ABSTRACT

#### Introduction:

Central venous oxygen saturation and blood lactate are different indices of the adequacy of oxygen delivery to the oxygen needs. In pediatric cardiac surgery, lactate level and kinetics during and after cardiopulmonary bypass are associated with outcome variables. The aim of this study was to explore the hypothesis that the lowest central venous oxygen saturation and the peak lactate value during cardiopulmonary bypass, used alone or in combination, may be predictive of major morbidity and mortality in pediatric cardiac surgery.

#### Methods:

We conducted a retrospective analysis of 256 pediatric (younger than 6 years) patients who had undergone cardiac surgery with continuous monitoring of central venous oxygen saturation and serial measurement of blood lactate.

#### Results:

Peak lactate was significantly increased when the nadir central venous oxygen saturation was < 68%. Both nadir central venous oxygen saturation and peak lactate during cardiopulmonary bypass were independently associated with major morbidity and mortality, with the same accuracy for major morbidity and a higher accuracy of peak lactate for mortality. A combined index (central venous oxygen saturation < 68% and peak lactate > 3 mmol/L) provided the highest sensitivity and specificity for major morbidity, with a positive predictive value of 89%.

#### Conclusions:

The combination of a continuous monitoring of central venous oxygen saturation and serial measurements of blood lactate during cardiopulmonary bypass may offer a predictive index for major morbidity after cardiac operations in pediatric patients. This study generates the hypothesis that strategies aimed to preserve oxygen delivery during cardiopulmonary bypass may reduce the occurrence of low values of central venous oxygen saturation and elevated lactate levels. Further studies should consider this hypothesis and take into account other time-related factors, such as time of exposure to low values of central venous oxygen saturation and kinetics of lactate formation.

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## 7. O<sub>2</sub> DELIVERY AND CO<sub>2</sub> PRODUCTION DURING CARDIOPULMONARY BYPASS AS DETERMINANTS OF ACUTE KIDNEY INJURY: TIME FOR A GOAL-DIRECTED PERFUSION MANAGEMENT?

De Somer F et al.

*Critical Care* 2011 15:R192

<https://doi.org/10.1186/cc10349>

### ABSTRACT

#### Background:

Acute kidney injury (AKI) after cardiac surgery is a major health issue. Lacking effective therapies, risk factor modification may offer a means of preventing this complication. The objective of the present study was to identify and determine the prognostic importance of such risk factors.

#### Methods and Results:

Data from a multicenter cohort of 3500 adult patients who underwent cardiac surgery at 7 hospitals during 2004 were analyzed (using multivariable logistic regression modeling) to determine the independent relationships between 3 thresholds of AKI (>25%, >50%, and >75% decrease in estimated glomerular filtration rate within 1 week of surgery or need for postoperative dialysis) with death rates, as well as to identify modifiable risk factors for AKI. The 3 thresholds of AKI occurred in 24% (n=829), 7% (n=228), and 3% (n=119) of the cohort, respectively. All 3 thresholds were independently associated with a >4-fold increase in the odds of death and could be predicted with several perioperative variables, including preoperative intra-aortic balloon pump use, urgent surgery, and prolonged cardiopulmonary bypass. In particular, 3 potentially modifiable variables were also independently and strongly associated with AKI. These were preoperative anemia, perioperative red blood cell transfusions, and surgical reexploration.

#### Conclusions:

AKI after cardiac surgery is highly prevalent and prognostically important. Therapies aimed at mitigating preoperative anemia, perioperative red blood cell transfusions, and surgical reexploration may offer protection against this complication.

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## 8. TRANSFUSIONS DURING CARDIOPULMONARY BYPASS: BETTER WHEN TRIGGERED BY VENOUS OXYGEN SATURATION AND OXYGEN EXTRACTION RATE

Ranucci M. et al.

*Perfusion*. 2011 Jul;26(4):327-33.

<https://doi.org/10.1177/0267659111407539>

### ABSTRACT

#### Introduction:

Central venous oxygen saturation and blood lactate are different indices of the adequacy of oxygen delivery to the oxygen needs. In pediatric cardiac surgery, lactate level and kinetics during and after cardiopulmonary bypass are associated with outcome variables. The aim of this study was to explore the hypothesis that the lowest central venous oxygen saturation and the peak lactate value during cardiopulmonary bypass, used alone or in combination, may be predictive of major morbidity and mortality in pediatric cardiac surgery.

#### Methods:

We conducted a retrospective analysis of 256 pediatric (younger than 6 years) patients who had undergone cardiac surgery with continuous monitoring of central venous oxygen saturation and serial measurement of blood lactate.

#### Results:

Peak lactate was significantly increased when the nadir central venous oxygen saturation was < 68%. Both nadir central venous oxygen saturation and peak lactate during cardiopulmonary bypass were independently associated with major morbidity and mortality, with the same accuracy for major morbidity and a higher accuracy of peak lactate for mortality. A combined index (central venous oxygen saturation < 68% and peak lactate > 3 mmol/L) provided the highest sensitivity and specificity for major morbidity, with a positive predictive value of 89%.

#### Conclusions:

The combination of a continuous monitoring of central venous oxygen saturation and serial measurements of blood lactate during cardiopulmonary bypass may offer a predictive index for major morbidity after cardiac operations in pediatric patients. This study generates the hypothesis that strategies aimed to preserve oxygen delivery during cardiopulmonary bypass may reduce the occurrence of low values of central venous oxygen saturation and elevated lactate levels. Further studies should consider this hypothesis and take into account other time-related factors, such as time of exposure to low values of central venous oxygen saturation and kinetics of lactate formation.

## 9. COMBINED CENTRAL VENOUS OXYGEN SATURATION AND LACTATE AS MARKERS OF OCCULT HYPOPERFUSION AND OUTCOME FOLLOWING CARDIAC SURGERY

Hu BY. et al.

*J Cardiothorac Vasc Anesth.* 2012 Feb;26(1):52-7.

doi: [10.1053/j.jvca.2011.07.021](https://doi.org/10.1053/j.jvca.2011.07.021)

### ABSTRACT

#### Objective:

To assess the association between postoperative central venous oxygen saturation (ScvO<sub>2</sub>) and arterial lactate with outcome after cardiac surgery.

#### Design:

Prospective observational study.

#### Setting:

University-affiliated tertiary care hospital.

#### Participants:

Patients after coronary artery bypass and/or valve surgery.

#### Interventions:

None.

#### Measurements and main results:

Postoperative ScvO<sub>2</sub> and arterial lactate were obtained on arrival to the intensive care unit (ICU). ScvO<sub>2</sub> and lactate were drawn again at 8 and 24 hours, respectively, after ICU admission. Moderate global tissue hypoxia (GTH) was defined as ScvO<sub>2</sub> <70% and lactate ≥2 to <4 mmol/L, and severe GTH was defined as ScvO<sub>2</sub> <70% and lactate ≥4 mmol/L. Occult hypoperfusion was defined as moderate-to-severe GTH with mean arterial pressure ≥65 mmHg, central venous pressure ≥8 mmHg, and urine output ≥0.5 mL/kg/h. ScvO<sub>2</sub> on ICU admission negatively correlated with postoperative 24-hour lactate (p = 0.009), which was a strong predictor of time on mechanical ventilation, total complications, and ICU and hospital lengths of stay (p < 0.001 for all comparisons). On admission to the ICU, 19 patients (32%) exhibited occult hypoperfusion. Patients with severe GTH (n = 8) had longer ICU lengths of stay (p = 0.04) and a trend toward longer length of mechanical ventilation (p = 0.17) and number of complications per patient (p = 0.09) compared with those without GTH (n = 10).

#### Conclusions:

The incidence of GTH is high after cardiac surgery. Postoperative ScvO<sub>2</sub> and lactate may be valuable measurements to identify patients with occult hypoperfusion and subsequently guide hemodynamic optimization to positively affect postoperative outcomes in patients after cardiac surgery.

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## 10. OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS (AND RENAL OUTCOME) USING TWO SYSTEMS OF EXTRACORPOREAL CIRCULATION: A RETROSPECTIVE REVIEW

**Bennett MJ. et al.**

*Interact Cardiovasc Thorac Surg.* 2013 Jun;16(6):760-4.

[Free full text article available online: 10.1093/icvts/ivt057](https://doi.org/10.1093/icvts/ivt057)

### ABSTRACT

#### Objectives:

To investigate the combined influence of blood flow and haemodilution with either a miniaturized (Mini-CPB) or a conventional cardiopulmonary bypass (C-CPB) circuit on average oxygen delivery during bypass. The influence of this on clinical outcome, particularly renal dysfunction after routine coronary artery bypass surgery (CABG), was measured.

#### Methods:

Retrospective analysis in two groups of 160 patients based on the surgeon's preference for bypass circuit. We compared consecutive patients undergoing isolated CABG surgery by two surgeons using Mini-CPB with a matched cohort of patients, from the same period, undergoing isolated CABG surgery by four other surgeons using a C-CPB. No trial-related intervention occurred. Data on bypass circuit parameters and clinical outcomes were acquired from routinely collected data sources.

#### Results:

Average cardiopulmonary bypass pump flow was significantly lower with Mini-CPB compared with C-CPB. Mini-CPB resulted in significantly less haemodilution. The resultant calculated average oxygen delivery provided by the two systems was the same. Percentage change in plasma creatinine was significantly and inversely related to the oxygen delivery during CPB. There was no difference in percentage change in plasma creatinine between groups. The risk of having Acute Kidney Injury Network (AKIN) score  $\geq 1$  increased 1% for every 1 ml min<sup>-1</sup> m<sup>-2</sup> decrease in oxygen delivery ( $P = 0.0001$ , OR 0.990, 95% CI 0.984-0.995).

#### Conclusions:

Despite aiming for the same target pump flow, periodic limitations of venous return to the pump resulted in a significant reduction in average flow delivered to the patient by Mini-CPB. Less haemodilution compensated for this reduction, so that the average oxygen delivery was the same. The association between oxygen delivery and postoperative change in plasma creatinine was evident in both groups. Further work to understand whether there is a particular cohort of patients who benefit (or are put at risk) by one method of CPB vs the other is warranted.

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## 11. ACUTE KIDNEY INJURY SUBSEQUENT TO CARDIAC SURGERY

Kramer R.S. et al.

*J Extra Corpor Technol.* 2015 Mar;47(1):16-28.

Free full text article available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4566816/>

### ABSTRACT

Acute kidney injury (AKI) after cardiac surgery is a common and underappreciated syndrome that is associated with poor shortand long-term outcomes. AKI after cardiac surgery may be epiphenomenon, a signal for adverse outcomes by virtue of other affected organ systems, and a consequence of multiple factors. Subtle increases in serum creatinine (SCr) postoperatively, once considered inconsequential, have been shown to reflect a kidney injury that likely occurred in the operating room during cardiopulmonary bypass (CPB) and more often in susceptible individuals. The postoperative elevation in SCr is a delayed signal reflecting the intraoperative injury. Preoperative checklists and the conduct of CPB represent opportunities for prevention of AKI. Newer definitions of AKI provide us with an opportunity to scrutinize perioperative processes of care and determine strategies to decrease the incidence of AKI subsequent to cardiac surgery. Recognizing and mitigating risk factors preoperatively and optimizing intraoperative practices may, in the aggregate, decrease the incidence of AKI. This review explores the pathophysiology of AKI and addresses the features of patients who are the most vulnerable to AKI. Preoperative strategies are discussed with particular attention to a readiness for surgery checklist. Intraoperative strategies include minimizing hemodilution and maximizing oxygen delivery with specific suggestions regarding fluid management and plasma preservation.

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## 12. DESIGNING A NEW SCORING SYSTEM (QUALYP SCORE) CORRELATING THE MANAGEMENT OF CARDIOPULMONARY BYPASS TO POSTOPERATIVE OUTCOMES.

Rubino AS. et al.

*Perfusion*. 2015 Sep;30(6):448-56.

<https://doi.org/10.1177/0267659114557184>

### ABSTRACT

#### AIM:

To investigate the combined influence of blood flow and haemodilution with either a miniaturized (Mini-CPB) or a conventional CPB. 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 (QualyP Score) was created from 10 parameters: peak lactate value during CPB, peak VCO(2)i, lowest DO(2)i/VCO(2)i, 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 lactate >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 QualyP Score ≥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:

QualyP Score may help to provide a quality marker of perfusion, emphasizing the need for goal-directed perfusion strategies.

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### 13. THE HISTORY OF GOAL-DIRECTED THERAPY AND RELEVANCE TO CARDIOPULMONARY BYPASS

Dijoy L. et al.

*J Extra Corpor Technol.* 2015 Jun;47(2):90-4.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4557555/>

#### ABSTRACT

Goal-directed therapy is a patient care strategy that has been implemented to improve patient outcomes. The strategy includes aggressive patient management and monitoring during a period of critical care. Goal-directed therapy has been adapted to perfusion and has been designated goal-directed perfusion (GDP). Since this is a new concept in perfusion, the purpose of this study is to review goal-directed therapy research in other areas of critical care management and compare that process to improving patient outcomes following cardiopulmonary bypass. Various areas of goal directed therapy literature were reviewed, including fluid administration, neurologic injury, tissue perfusion, oxygenation, and inflammatory response. Data from these studies was compiled to document improvements in patient outcomes. Goal-directed therapy has been demonstrated to improve patient outcomes when performed within the optimal time frame resulting in decreased complications, reduction in hospital stay, and a decrease in morbidity. Based on the successes in other critical care areas, GDP during cardiopulmonary bypass would be expected to improve outcomes following cardiac surgery.

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## 14. HEMODILUTION ON CARDIOPULMONARY BYPASS AS A DETERMINANT OF EARLY POSTOPERATIVE HYPERLACTATEMIA

Ranucci M. et al.

*PLoS One.* 2015 May 18;10(5):e0126939.

[10.1371/journal.pone.0126939](https://doi.org/10.1371/journal.pone.0126939)

### ABSTRACT

#### Objective:

The nadir hematocrit (HCT) on cardiopulmonary bypass (CPB) is a recognized independent risk factor for major morbidity and mortality in cardiac surgery. The main interpretation is that low levels of HCT on CPB result in a poor oxygen delivery and dysoxia of end organs. Hyperlactatemia (HL) is a marker of dysoxic metabolism, and is associated with bad outcomes in cardiac surgery. This study explores the relationship between nadir HCT on CPB and early postoperative HL.

#### Design:

Retrospective study on 3,851 consecutive patients.

#### Measurements and Main Results:

Nadir HCT on CPB and other potential confounders were explored for association with blood lactate levels at the arrival in the Intensive Care Unit (ICU), and with the presence of moderate (2.1 – 6.0 mMol/L) or severe (> 6.0 mMol/L) HL. Nadir HCT on CPB demonstrated a significant negative association with blood lactate levels at the arrival in the ICU. After adjustment for the other confounders, the nadir HCT on CPB remained independently associated with moderate (odds ratio 0.96, 95% confidence interval 0.94-0.99) and severe HL (odds ratio 0.91, 95% confidence interval 0.86-0.97). Moderate and severe HL were significantly associated with increased morbidity and mortality.

#### Conclusions:

Hemodilution on CPB is an independent determinant of HL. This association, more evident for severe HL, strengthens the hypothesis that a poor oxygen delivery on CPB with consequent organ ischemia is the mechanism leading to hemodilution-associated bad outcomes.

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## 15. NADIR OXYGEN DELIVERY ON BYPASS AND HYPOTENSION INCREASE ACUTE KIDNEY INJURY RISK AFTER CARDIAC OPERATIONS

Magruder JT. et al.

*Ann Thorac Surg.* 2015 Nov;100(5):1697-703.

[10.1016/j.athoracsur.2015.05.059](https://doi.org/10.1016/j.athoracsur.2015.05.059)

### ABSTRACT

#### Background:

Acute kidney injury (AKI) continues to complicate cardiac operations. We sought to determine whether nadir oxygen delivery ( $DO_2$ ) on cardiopulmonary bypass (CPB) was a risk factor for AKI while also accounting for other postoperative factors.

#### Methods:

Using propensity scoring, we matched 85 patients who developed AKI after cardiac operations on CPB with 85 control patients who did not. We analyzed the following variables through midnight on postoperative day 1 (POD1):  $DO_2$ , antibiotics, blood products and vasopressors (intraoperatively and postoperatively), and hemodynamic variables.

#### Results:

Univariable analysis revealed AKI patients had lower nadir  $DO_2$  on CPB (208 vs 230 mL  $O_2$ /min/m<sup>2</sup>) body surface area,  $p = 0.03$ ), lower intensive care unit admission blood pressure gradient across the kidney (mean arterial pressure minus central venous pressure; 60 vs 68 mm Hg;  $p < 0.001$ ), a greater proportion of patients with mean arterial pressure of less than 60 mm Hg for more than 15 minutes in the postoperative period (70% vs 42%,  $p < 0.001$ ), a greater chance of having a cardiac index of less than 2.2 (74% vs 49%,  $p = 0.02$ ), and greater total vasopressor use through the end of POD1 (5.2 vs 2.3 mg,  $p = 0.002$ ). On multivariable analysis, predictors of AKI were a  $DO_2$  on CPB of less than 225 mL  $O_2$ /min/m<sup>2</sup> (odds ratio, 2.46; 95% confidence interval, 1.21 to 5.03;  $p = 0.01$ ) and postoperative mean arterial pressure of less than 60 mm Hg for more than 15 minutes (odds ratio, 3.96; 95% confidence interval, 1.92 to 8.20;  $p < 0.001$ ). An average postoperative pressor dose greater than 0.03  $\mu$ g/kg/min did not reach significance (odds ratio, 1.98; 95% confidence interval, 0.95 to 4.11;  $p = 0.07$ ).

#### Conclusions:

Postoperative hypotension on POD<sub>0</sub> or POD<sub>1</sub> and low  $DO_2$  on CPB both independently increase the AKI risk in cardiac surgical patients.

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## 16. ACUTE KIDNEY INJURY AND HEMODILUTION DURING CARDIOPULMONARY BYPASS: A CHANGING SCENARIO

Ranucci M. et al.

*Ann Thorac Surg.* 2015 Jul;100(1):95-100.

[10.1016/j.athoracsur.2015.02.034](https://doi.org/10.1016/j.athoracsur.2015.02.034)

### ABSTRACT

#### Background:

Severe hemodilution during cardiopulmonary bypass (CPB) is a risk factor for acute kidney injury (AKI) after heart operations. Many improvements to CPB technology have been proposed during the past decade to limit the hemodilution-related AKI risk. The present study is a retrospective analysis of the relationship between hemodilution during CPB and AKI in cardiac operations in the setting of different interventions applied over 14 years.

#### Methods:

We retrospectively analyzed 16,790 consecutive patients undergoing heart operations from 2000 to 2013. Various risk factors for AKI were collected and analyzed, together with a number of interventions as possible modifiers of the relationship between a nadir hematocrit (HCT) value during CPB and AKI.

#### Results:

The relationship between the nadir HCT value during CPB and AKI was confirmed in a multivariable analysis, with the relative risk of AKI increasing by 7% per percentage point of decrease of the nadir HCT value during CPB. The relative risk of AKI decreased by 8% per year of observation ( $p = 0.001$ ) despite a significantly increased risk of AKI ( $p = 0.001$ ). A sensitivity analysis based on differences before and after different interventions demonstrated a beneficial effect of the application of goal-directed perfusion (aimed at preserving oxygen delivery during CPB), with a reduction in the AKI rate from 5.8% to 3.1% ( $p = 0.001$ ). A policy restricting angiographic examination on the day of operation was also useful (reduction of AKI rate from 4.8% to 3.7%;  $p = 0.029$ ).

#### Conclusions:

A bundle of interventions mainly aimed at limiting the renal impact of hemodilution during CPB is effective in reducing the AKI rate.

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## 17. ACUTE KIDNEY INJURY IN CARDIAC SURGERY AND CARDIAC INTENSIVE CARE

Lau G. et al.

*Semin Cardiothorac Vasc Anesth.* 2015 Dec;19(4):270–87.

<https://doi.org/10.1177/1089253215593177>

### ABSTRACT

#### Background:

Acute kidney injury (AKI) continues to complicate cardiac operations. We sought to determine whether nadir oxygen delivery ( $DO_2$ ) on cardiopulmonary bypass (CPB) was a risk factor for AKI while also accounting for other postoperative factors.

#### Methods:

Using propensity scoring, we matched 85 patients who developed AKI after cardiac operations on CPB with 85 control patients who did not. We analyzed the following variables through midnight on postoperative day 1 (POD1):  $DO_2$ , antibiotics, blood products and vasopressors (intraoperatively and postoperatively), and hemodynamic variables.

#### Results:

Univariable analysis revealed AKI patients had lower nadir  $DO_2$  on CPB (208 vs 230 mL  $O_2$ /min/ $m^2$ ) body surface area,  $p = 0.03$ ), lower intensive care unit admission blood pressure gradient across the kidney (mean arterial pressure minus central venous pressure; 60 vs 68 mm Hg;  $p < 0.001$ ), a greater proportion of patients with mean arterial pressure of less than 60 mm Hg for more than 15 minutes in the postoperative period (70% vs 42%,  $p < 0.001$ ), a greater chance of having a cardiac index of less than 2.2 (74% vs 49%,  $p = 0.02$ ), and greater total vasopressor use through the end of POD1 (5.2 vs 2.3 mg,  $p = 0.002$ ). On multivariable analysis, predictors of AKI were a  $DO_2$  on CPB of less than 225 mL  $O_2$ /min/ $m^2$  (odds ratio, 2.46; 95% confidence interval, 1.21 to 5.03;  $p = 0.01$ ) and postoperative mean arterial pressure of less than 60 mm Hg for more than 15 minutes (odds ratio, 3.96; 95% confidence interval, 1.92 to 8.20;  $p < 0.001$ ). An average postoperative pressor dose greater than 0.03  $\mu\text{g}/\text{kg}/\text{min}$  did not reach significance (odds ratio, 1.98; 95% confidence interval, 0.95 to 4.11;  $p = 0.07$ ).

#### Conclusions:

Postoperative hypotension on  $POD_0$  or  $POD_1$  and low  $DO_2$  on CPB both independently increase the AKI risk in cardiac surgical patients.

## 19. A PILOT GOAL-DIRECTED PERFUSION INITIATIVE IS ASSOCIATED WITH LESS ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY

Magruder JT. et al.

*J Thorac Cardiovasc Surg.* 2017;153:118-25.e1.

<https://doi.org/10.1016/j.jtcvs.2016.09.016>

### ABSTRACT

#### Background:

We sought to determine whether a pilot goal-directed perfusion initiative could reduce the incidence of acute kidney injury after cardiac surgery.

#### Methods:

On the basis of the available literature, we identified goals to achieve during cardiopulmonary bypass (including maintenance of oxygen delivery  $>300$  mL O<sub>2</sub>/min/m<sup>2</sup> and reduction in vasopressor use) that were combined into a goal-directed perfusion initiative and implemented as a quality improvement measure in patients undergoing cardiac surgery at Johns Hopkins during 2015. Goal-directed perfusion initiative patients were matched to controls who underwent cardiac surgery between 2010 and 2015 using propensity scoring across 15 variables. The primary and secondary outcomes were the incidence of acute kidney injury and the mean increase in serum creatinine within the first 72 hours after cardiac surgery.

#### Results:

We used the goal-directed perfusion initiative in 88 patients and matched these to 88 control patients who were similar across all variables, including mean age (61 years in controls vs 64 years in goal-directed perfusion initiative patients,  $P = .12$ ) and preoperative glomerular filtration rate (90 vs 83 mL/min,  $P = .34$ ). Controls received more phenylephrine on cardiopulmonary bypass (mean 2.1 vs 1.4 mg,  $P < .001$ ) and had lower nadir oxygen delivery (mean 241 vs 301 mL O<sub>2</sub>/min/m<sup>2</sup>,  $P < .001$ ). Acute kidney injury incidence was 23.9% in controls and 9.1% in goal-directed perfusion initiative patients ( $P = .008$ ); incidences of acute kidney injury stage 1, 2, and 3 were 19.3%, 3.4%, and 1.1% in controls, and 5.7%, 3.4%, and 0% in goal-directed perfusion initiative patients, respectively. Control patients exhibited a larger median percent increase in creatinine from baseline (27% vs 10%,  $P < .001$ ).

#### Conclusions:

The goal-directed perfusion initiative was associated with reduced acute kidney injury incidence after cardiac surgery in this pilot study.

## 20. A MULTIDISCIPLINARY PERIOPERATIVE STRATEGY FOR ATTAINING "MORE PHYSIOLOGIC" CARDIAC SURGERY

Anastasiadis K. et al.

*Perfusion*. 2017 Sep;32(6):446-453.

[10.1177/0267659117700488](https://doi.org/10.1177/0267659117700488)

### ABSTRACT

#### Background:

Cardiac surgery is, by definition, a "non-physiologic" intervention associated with systemic adverse effects. Despite advances in surgical technique, cardiopulmonary bypass (CPB) technology as well as anaesthesia management and patient care, there is still significant morbidity and subsequent mortality.

#### AIM:

We consider that the contemporary demand for further improving patient outcome mandates the upgrade from optimal perfusion during the procedure as the gold standard to the concept of a "more physiologic" cardiac surgery. Our policy is a multidisciplinary perioperative strategy based on goal-directed perfusion throughout surgery incorporating in-line monitoring. This translates to "prevent rather than correct" malperfusion through real-time adjustment rather than correction of derangement detected late by incremental evaluation.

#### Methods:

The strategy is based on continuous monitoring of cardiac index, SvO<sub>2</sub>, DO<sub>2</sub>i, DO<sub>2</sub>i/VCO<sub>2</sub>i and rSO<sub>2</sub>. Data acquisition is followed by action when needed; this includes stepwise: transfusion, increase of cardiac output and initiation of inotropic/vasoactive support. Moreover, implementation of minimally invasive extracorporeal circulation (MiECC) is considered as a fundamental component of physiologic perfusion when on-CPB, providing improved circulatory support and end-organ protection.

#### Conclusions:

We consider that, with this strategy which establishes optimal perfusion perioperatively, we attain the goal of a "more physiologic" cardiac surgery.

**24. CARBON DIOXIDE PRODUCTION DURING CARDIOPULMONARY BYPASS: PATHOPHYSIOLOGY, MEASURE AND CLINICAL RELEVANCE**

**Ranucci M. et al.**

*Perfusion. 2017 Jan;32(1):4-12.*

[Free full text article available online: https://doi.org/10.1177/0267659116659919](https://doi.org/10.1177/0267659116659919)

## ABSTRACT

Carbon dioxide production during cardiopulmonary bypass derives from both the aerobic metabolism and the buffering of lactic acid produced by tissues under anaerobic conditions. Therefore, carbon dioxide removal monitoring is an important measure of the adequacy of perfusion and oxygen delivery. However, routine monitoring of carbon dioxide removal is not widely applied. The present article reviews the main physiological and pathophysiological sources of carbon dioxide, the available techniques to assess carbon dioxide production and removal and the clinically relevant applications of carbon dioxide-related variables as markers of the adequacy of perfusion during cardiopulmonary bypass.

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## 25. LOW OXYGEN DELIVERY AS A PREDICTOR OF ACUTE KIDNEY INJURY DURING CARDIOPULMONARY BYPASS

Newland R.F. et al.

*J Extra Corpor Technol.* 2017;49:224–230

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5737422/>

### ABSTRACT

Low indexed oxygen delivery ( $DO_2i$ ) during cardiopulmonary bypass (CPB) has been associated with an increase in the likelihood of acute kidney injury (AKI), with critical thresholds for oxygen delivery reported to be 260–270 mL/min/m<sup>2</sup>. This study aims to explore whether a relationship exists for oxygen delivery during CPB, in which the integral of amount and time below a critical threshold, is associated with the incidence of postoperative AKI. The area under the curve (AUC) with  $DO_2i$  during CPB above or below 270 mL/min/m<sup>2</sup> was calculated as a metric of oxygen delivery in 210 patients undergoing CPB. To determine the influence of low oxygen delivery on AKI, a multivariate logistic regression model was developed including AUC < 0, Euroscore II to provide preoperative risk factor adjustment, and incidence of red blood cell transfusion to adjust for the influence of transfusion. Having an AUC < 0 for an oxygen delivery threshold of 270 mL/min/m<sup>2</sup> during CPB was an independent predictor of AKI, after adjustment for Euroscore II and transfusion [OR 2.74, CI {1.01–7.41}, p 5 .047]. These results support that a relationship exists for oxygen delivery during CPB, in which the integral of amount and time below a critical threshold is associated with the incidence of postoperative AKI.

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## 26. GOAL-DIRECTED PERFUSION TO REDUCE ACUTE KIDNEY INJURY: A RANDOMIZED TRIAL

Ranucci M. et al.

*J Thorac Cardiovasc Surg.* 2018 Nov;156(5):1918-1927.e2.

<https://doi.org/10.1016/j.jtcvs.2018.04.045>

### ABSTRACT

#### Objective:

To determine whether a goal-directed perfusion (GDP) strategy aimed at maintaining oxygen delivery ( $DO_2$ ) at  $\geq 280 \text{ mL}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$  reduces the incidence of acute kidney injury (AKI).

#### Methods:

This multicenter randomized trial enrolled a total of 350 patients undergoing cardiac surgery in 9 institutions. Patients were randomized to receive either GDP or conventional perfusion. A total of 326 patients completed the study and were analyzed. Patients in the treatment arm were treated with a GDP strategy during cardiopulmonary bypass (CPB) aimed to maintain  $DO_2$  at  $\geq 280 \text{ mL}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ . The perfusion strategy for patients in the control arm was factored on body surface area and temperature. The primary endpoint was the rate of AKI. Secondary endpoints were intensive care unit length of stay, major morbidity, red blood cell transfusions, and operative mortality.

#### Results:

Acute Kidney Injury Network (AKIN) stage 1 was reduced in patients treated with GDP (relative risk [RR], 0.45; 95% confidence interval [CI], 0.25–0.83;  $P = .01$ ). AKIN stage 2–3 did not differ between the 2 study arms (RR, 1.66; 95% CI, 0.46–6.0;  $P = .528$ ). There were no significant differences in secondary outcomes. In a prespecified analysis of patients with a CPB time between 1 and 3 hours, the differences in favor of the treatment arm were more pronounced, with an RR for AKI of 0.49 (95% CI, 0.27–0.89;  $P = .017$ ).

#### Conclusions:

A GDP strategy is effective in reducing AKIN stage 1 AKI. Further studies are needed to define perfusion interventions that may reduce more severe levels of renal injury (AKIN stage 2 or 3).

## 27. TIME-DOSE RESPONSE OF OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS PREDICTS ACUTE KIDNEY INJURY

Mukaida H. et al.

*J Thorac Cardiovasc Surg.* 2018 Nov 16. 1-8 [Epub ahead of print]

<https://doi.org/10.1016/j.jtcvs.2018.10.148>

### ABSTRACT

#### Objective:

Cardiopulmonary bypass is associated with the occurrence of postoperative acute kidney injury (AKI). However, these measurements only considered the bottom point of the oxygen delivery ( $DO_2$ ) but did not consider the duration of  $DO_2$ . We aimed to examine whether the time-dose response of  $DO_2$  during cardiopulmonary bypass can be used to estimate the risk for postoperative AKI.

#### Methods:

We evaluated 112 patients who underwent cardiac surgeries with cardiopulmonary bypass. We analyzed the perfusion parameters recorded every 20 seconds. To obtain time-dose response of  $DO_2$  index ( $DO_{2i}$ ), the area under the curve was calculated as below the 300 mL/min/m<sup>2</sup> threshold, which accounts for depth and duration of cumulative oxygen debt. In addition, the cumulative time below  $DO_{2i}$  300 mL/min/m<sup>2</sup> was also calculated. Receiver operating characteristic analysis, univariate regression analysis, and multivariate regression analysis were used to evaluate associations between perioperative variables and postoperative AKI.

#### Results:

Patients who developed AKI had larger area under the curve below the 300 mL/min/m<sup>2</sup> threshold (1581 vs 632;  $P < .01$ ) and cumulative time below  $DO_{2i}$  300 mL/min/m<sup>2</sup> (34.7 vs 15.3 minutes;  $P < .01$ ). Nadir  $DO_{2i}$  was not significantly different between the non-AKI and AKI groups (263.4 vs 247.0 mL/min/m<sup>2</sup>;  $P = .291$ ).

#### Conclusions:

The time-dose response of  $DO_{2i}$  during cardiopulmonary bypass is a better indicator than nadir  $DO_{2i}$  in evaluating AKI risk. Maintaining  $DO_{2i}$  levels >300 mL/min/m<sup>2</sup> may result in decreased risk for postoperative AKI.

## 28. SUTURELESS VALVES AND THE QUALITY OF PERFUSION: TOWARDS A GOAL DIRECTED AORTIC VALVE REPLACEMENT

Rubino A.S., Mignosa C.

*Minerva Cardioangiologica* 2018 April;66(2):163-9

DOI: [10.23736/S0026-4725.17.04590-X](https://doi.org/10.23736/S0026-4725.17.04590-X)

### ABSTRACT

#### Background:

Aim of this study was to assess the potential differences in respecting the principles of goal-directed perfusion between aortic valve replacement with sutureless vs. conventional stented bioprostheses.

#### Methods:

Data from 94 consecutive patients undergoing aortic valve replacement with Perceval sutureless valve, with or without concomitant coronary artery bypass grafting, were compared to a contemporary cohort of 116 patients receiving conventional stented bioprostheses. Propensity score matching was used to reduce selection bias. Flow-dependent estimate of oxygen delivery and carbon dioxide production were compared in accordance to the principles of goal directed perfusion. Hospital outcomes were assessed as well.

#### Results:

Propensity score matching resulted in 39 pairs with similar characteristics and operative risk. Cross-clamping time ( $41.6 \pm 20.6$  vs.  $89.6 \pm 48.2$ ;  $P < 0.001$ ) and cardiopulmonary bypass time ( $66.9 \pm 29.4$  vs.  $121.2 \pm 56.6$ ,  $P < 0.001$ ) were shorter in Perceval patients. Flow-dependent parameters were significantly better in Perceval patients (peak  $\text{VCO}_2\text{i}$   $P = 0.010$ ; nadir  $\text{VO}_2\text{i}$   $P = 0.035$ ; nadir  $\text{DO}_2\text{i}/\text{VCO}_2\text{i}$   $P = 0.015$ ; peak RQ  $P = 0.020$ ) and therefore goal-directed perfusion principles were met more frequently (all  $P < 0.001$ ). Peak lactates were higher in controls ( $P = 0.001$ ), as well as number of patients receiving transfusions during CPB ( $P = 0.044$ ). QualyP Score was also higher in controls ( $P < 0.001$ ). Perceval patients experienced reduced postoperative bleeding, had a lower incidence of surgical revisions and transfusions. Duration of ventilation was longer in controls.

#### Conclusions:

The use of sutureless valves significantly reduces cardiopulmonary bypass and cross-clamping times and contributes to achieve a goal-directed perfusion. This results in better perfusion quality, with a positive clinical impact.

# GDP and AKI Economic focus

## List of publications

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**1. COSTS AND OUTCOMES OF ACUTE KIDNEY INJURY (AKI) FOLLOWING CARDIAC SURGERY**

**Dasta JF. et al.**

*Nephrol Dial Transplant.* 2008 Jun;23(6):1970-4.  
<https://doi.org/10.1093/ndt/gfm908>

Abstract available in this document at **page 39**

**2. GOAL DIRECTED PERFUSION (GDP): A DIFFERENTIAL COST ANALYSIS IN UK AND US**

**Povero M., Pradelli L.**

*Value in Health* 17 (2014) A323 – A686.  
<https://doi.org/10.1016/j.jval.2014.08.1397>

Abstract available in this document at **page 40**

**3. COMPARISON BETWEEN TRADITIONAL AND GOAL DIRECTED PERFUSION IN CARDIOPULMONARY BY-PASS. A DIFFERENTIAL COST ANALYSIS IN US**

**Povero M., Pradelli L.**

*Farmeconomia. Health economics and therapeutic pathways* 2015; 16(3): 77-86  
<https://doi.org/10.7175/fe.v16i3.1200>

Abstract available in this document at **page 41**

**4. COMPARISON BETWEEN TRADITIONAL AND GOAL DIRECTED PERFUSION IN CARDIOPULMONARY BY-PASS. ADAPTATION OF A DIFFERENTIAL COST ANALYSIS**

**Povero M., Pradelli L.**

*Farmeconomia. Health economics and therapeutic pathways* 2015; 16(1): 3-16  
<https://doi.org/10.7175/fe.v16i1S.1201>

Abstract available in this document at **page 42**

**5. FINANCIAL IMPACT OF ACUTE KIDNEY INJURY AFTER CARDIAC OPERATIONS IN THE UNITED STATES**

**Alshaikh H.N. et al.**

*Ann Thorac Surg* 2018;105:469-76  
<https://doi.org/10.1016/j.athoracsur.2017.10.053>

Abstract available in this document at **page 43**

# GDP and AKI Economic focus

## Scientific publications

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### 1. COSTS AND OUTCOMES OF ACUTE KIDNEY INJURY (AKI) FOLLOWING CARDIAC SURGERY

Dasta JF. et al.

*Nephrol Dial Transplant.* 2008 Jun;23(6):1970-4.

<https://doi.org/10.1093/ndt/gfm908>

#### ABSTRACT

##### Background:

Acute kidney injury (AKI) is a recognized complication of cardiac surgery; however, the variability in costs and outcomes reported are due, in part, to different criteria for diagnosing and classifying AKI. We determined costs, resource use and mortality rate of patients. We used the serum creatinine component of the RIFLE system to classify AKI.

##### Methods:

A retrospective cohort study was conducted from the electronic data repository at the University of Pittsburgh Medical Center of patients who underwent cardiac surgery and had an elevation ( $\geq 0.5$  mg/dl) of serum creatinine postoperatively. Data were compared to age- and APACHE III-matched controls. Cost, mortality and resource use of AKI patients were determined postoperatively for each of the three RIFLE classes on the basis of changes in serum creatinine.

##### Results:

Of the 3741 admissions, 258 (6.9%) had AKI and were classified as RIFLE-R 138 (3.7%), RIFLE-I 70 (1.9%) and RIFLE-F 50 (1.3%). Total and departmental level costs, length of stay (LOS) and requirement for renal replacement therapy (RRT) were higher in AKI patients compared to controls. Statistically significant differences in all costs, mortality rate and requirement for RRT were seen in the patients stratified into RIFLE-R, RIFLE-I and RIFLE-F. Even patients with the smallest change in serum creatinine, namely RIFLE-R, had a 2.2-fold greater mortality, a 1.6-fold increase in ICU LOS and 1.6-fold increase in total postoperative costs compared to controls.

##### Discussion:

Costs, LOS and mortality are higher in postoperative cardiac surgery patients who develop AKI using RIFLE criteria, and these values increase as AKI severity worsens.

## 2. GOAL DIRECTED PERFUSION (GDP): A DIFFERENTIAL COST ANALYSIS IN UK AND US

**Povero M., Pradelli L.**

*Value in Health* 17 (2014) A323 – A686.

<https://doi.org/10.1016/j.jval.2014.08.1397>

### ABSTRACT

#### Objective:

High oxygen delivery (DO<sub>2</sub>) during cardiopulmonary bypass (CPB) is associated with better renal outcome in cardiac surgery. Traditional perfusion (TP) techniques, targeted on body surface area and CPB temperature, achieves high DO<sub>2</sub> in about 50% of the cases while a goal directed perfusion (GDP) approach can lead to more than 90% of cases achieving high DO<sub>2</sub> with a consequent reduction in Acute Kidney Injury (AKI) rate of about 40%. Aim of this study is to perform an economic evaluation of GDP strategy with respect to TP in UK and US.

#### Methods:

A Discrete Event Simulation model was developed to compare TP and GDP strategy in patients undergoing CPB. The patient's pathways from operation to discharging from hospital was simulated: AKI incidence, in-hospital mortality, hospital length of stay, transfusions were correlated to probability to achieve high DO<sub>2</sub> target using published correlations. National perspective was adopted to calculate costs associated to each event while GDP strategy was exploited considering card and data management system (DMS) cost per patient.

#### Results:

GDP strategy saved more than 3 days in hospital and 11% of AKI episodes. The cost-saving is 2,821 £ in UK and 3,206 \$ in US; the cost of card and DMS (79 £ in UK, 110 \$ in US) is completely offset by savings in hospital stay that result the main driver in cost (2,886 £ in UK, 3,222 \$ in US). Deterministic sensitivity analysis shows that the total savings are mainly influenced by hospital LOS, cost per day both in ICU and in ward, and nadir haematocrit during CPB.

#### Conclusions:

GDP seems to improve significantly the main outcomes related to CPB surgery, when compared to TP techniques. Additional costs due to perform GDP strategy have no impact on the total cost since completely offset by the savings in hospital cost.

### 3. COMPARISON BETWEEN TRADITIONAL AND GOAL DIRECTED PERFUSION IN CARDIOPULMONARY BY-PASS. A DIFFERENTIAL COST ANALYSIS IN US

Povero M., Pradelli L.

*Farmeconomia. Health economics and therapeutic pathways* 2015; 16(3): 77-86

<https://doi.org/10.7175/fe.v16i3.1200>

#### ABSTRACT

##### Objectives:

High oxygen delivery (DO<sub>2</sub>) during cardiopulmonary bypass (CPB) is associated with better renal outcome in cardiac surgery. Traditional perfusion (TP) techniques, targeted on body surface area and CPB temperature, achieves high DO<sub>2</sub> in about 50% of the cases while a goal directed perfusion (GDP) approach can lead to more than 90% of cases achieving high DO<sub>2</sub> with a consequent reduction in Acute Kidney Injury (AKI) rate of about 40%. Aim of this study is to perform an economic evaluation of GDP strategy with respect to TP in US.

##### Methods:

A Discrete Event Simulation model was developed to compare TP and GDP strategy in patients undergoing CPB. The patient's pathways from operation to discharging from hospital was simulated: AKI incidence, in-hospital mortality, hospital length of stay, transfusions were correlated to probability to achieve high DO<sub>2</sub> target using published correlations. National perspective was adopted to calculate costs associated to each event while GDP strategy was exploited the introduction of Sorin Heartlink (HL) Card/GDP Card and Sorin Connect (electronic data management system).

##### Results:

GDP strategy saved more than 3 days in hospital and 11% of AKI episodes. The cost-saving is \$ 3,137 (95% CI: 1,122-4,951); the cost of HL Card/GDP Card+Connect (\$ 180, 95% CI: 113-249) is more than offset by savings in hospital stay that result the main driver in cost (\$ 3,222, 95% CI: 1,235-4,950). Deterministic sensitivity analysis shows that the total savings are mainly influenced by nadir haematocrit during CPB and hospital LOS/cost per day both in ICU and in ward.

##### Conclusions:

GDP seems to improve significantly the main outcomes related to CPB surgery, when compared to TP techniques. Additional costs due to perform GDP strategy have no impact on the total cost since completely offset by the savings in hospital cost.



#### 4. COMPARISON BETWEEN TRADITIONAL AND GOAL DIRECTED PERFUSION IN CARDIOPULMONARY BY-PASS. ADAPTATION OF A DIFFERENTIAL COST ANALYSIS

Povero M., Pradelli L.

*Farmeconomia. Health economics and therapeutic pathways 2015; 16(1): 3-16*

<https://doi.org/10.7175/fe.v16i1S.1201>

#### ABSTRACT

##### Background:

A previous patient-level discrete event simulation (DES) model was developed to perform an economic evaluation of GDP strategy with respect to TP in US. Aim of this supplement is provide results of the adaptations of the differential cost analysis to Belgium, Canada, France, Germany, Italy, and UK.

##### Methods:

A Discrete Event Simulation model was developed to compare TP and GDP strategy in patients undergoing CPB. National perspective was adopted to calculate costs associated to each event while GDP strategy was exploited the introduction of Sorin Heartlink (HL) Card/ GDP Card and Sorin Connect (electronic data management system).

##### Results:

GDP reduces the total cost with respect to traditional perfusion; furthermore the cost of GDP strategy (Sorin GDP™ Monitor and Sorin Connect™) is completely offset by the saving in hospital stay.

##### Conclusions:

GDP seems to improve significantly the main outcomes related to CPB surgery, when compared to TP techniques. Additional costs due to perform GDP strategy have no impact on the total cost since completely offset by the savings in hospital cost.

## 5. FINANCIAL IMPACT OF ACUTE KIDNEY INJURY AFTER CARDIAC OPERATIONS IN THE UNITED STATES

**Alshaikh H.N. et al.**

*Ann Thorac Surg* 2018;105:469–76

<https://doi.org/10.1016/j.athoracsur.2017.10.053>

### ABSTRACT

#### Background:

Acute kidney injury (AKI) after major cardiac operations is a potentially avoidable complication associated with increased morbidity, death, and costly long-term treatment. The financial impact of AKI at the population level has not been well defined. We sought to determine the incremental index hospital cost associated with the development of AKI.

#### Methods:

All patients undergoing coronary artery bypass grafting (CABG) or valve replacement operations, or both (clinical classification software codes 43 and 44), between 2008 and 2011 were identified from the Nationwide Inpatient Sample. AKI was identified using International Classification of Diseases, 9th Revision, Clinical Modification diagnosis codes (584.xx); patients with chronic renal failure were excluded. Mean total index hospitalization costs were compared between patients with and without AKI.

#### Results:

At the population level, 1,078,036 individuals underwent major cardiac procedures from 2008 to 2011, with AKI developing in 105,648 (9.8%). Specifically, AKI developed in 8.0% of CABG, 11.4% of valve replacement, and 17.0% of CABG plus valve replacement patients ( $p < 0.001$ ). Death was more common among patients with AKI vs those without (13.9% vs 1.3%,  $p < 0.001$ ). Mean total index hospitalization cost was \$77,178 for patients with AKI vs \$38,820 for those without ( $p < 0.001$ ). At the national level, the overall incremental annual index hospitalization cost associated with AKI was \$1.01 billion.

#### Conclusions:

AKI developed in 1 in every 10 patients nationwide after a cardiac operation. Achieving a 10% reduction in AKI in this population would likely result in an annual savings of approximately \$100,000,000 in index-hospital costs alone. Support for research on mechanisms to detect impending damage and prevent AKI may lead to reduced patient morbidity and death and to substantial health care cost savings.

# GDP & Neurological focus

## List of publications

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1. ASSOCIATION OF NADIR OXYGEN DELIVERY ON CARDIOPULMONARY BYPASS WITH SERUM GLIAL FIBRILLARY ACID PROTEIN LEVELS IN PAEDIATRIC HEART SURGERY PATIENTS  
**Magruder J. T. et al.**

*Interact Cardiovasc Thorac Surg.* 2016 Oct;23(4):531-7.  
<https://doi.org/10.1093/icvts/ivw194>

Abstract available in this document at **page 45**

2. A CLINICAL PROTOCOL FOR GOAL DIRECTED CEREBRAL PERFUSION DURING AORTIC ARCH SURGERY  
**Mosca M. S. et al.**

*Seminars in Cardiothoracic and Vascular Anesthesia* 2016, Vol. 20(4) 289-297  
Only abstract available online: <https://doi.org/10.1177/1089253216672854>

Abstract available in this document at **page 46**

3. CORRELATING OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS WITH THE NEUROLOGIC INJURY BIOMARKER UBIQUITIN C-TERMINAL HYDROLASE L1 (UCH-L1)  
**Magruder J. T. et al.**

*J Cardiothorac Vasc Anesth.* 2018 Dec;32(6):2485-2492.  
<https://doi.org/10.1053/j.jvca.2018.05.021>

Abstract available in this document at **page 47**

- I. GOAL-DIRECTED OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS: CAN THIS PERFUSION STRATEGY IMPROVE BIOCHEMICAL AND CLINICAL NEUROLOGIC OUTCOMES?

**Awad H. et al.**

*Journal of Cardiothoracic and Vascular Anesthesia* 32(2018)2493-2494, Editorial to Magruder JT, et al. *J Cardiothorac Vasc Anesth.* 2018 Dec;32(6):2485-2492.

<https://doi.org/10.1053/j.jvca.2018.07.052>

4. THE INFLUENCE OF OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS ON THE INCIDENCE OF DELIRIUM IN CABG PATIENTS; A RETROSPECTIVE STUDY  
**Leenders J. et al.**

*Perfusion* 2018, Vol. 33(8) 656-662

Free full text article available online: <https://doi.org/10.1177/0267659118783104>

Abstract available in this document at **page 48**

5. DISTURBANCES IN OXYGEN BALANCE DURING CARDIOPULMONARY BYPASS: A RISK FACTOR FOR POSTOPERATIVE DELIRIUM  
**Smulter N.**

*Journal of Cardiothoracic and Vascular Anesthesia* 32(2018)684-690

Only abstract available online: <https://doi.org/10.1053/j.jvca.2017.08.035>

Abstract available in this document at **page 49**

# GDP & Neurological focus

## Scientific publications

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### 1. ASSOCIATION OF NADIR OXYGEN DELIVERY ON CARDIOPULMONARY BYPASS WITH SERUM GLIAL FIBRILLARY ACID PROTEIN LEVELS IN PAEDIATRIC HEART SURGERY PATIENTS

**Magruder J. T. et al.**

*Interact Cardiovasc Thorac Surg.* 2016 Oct;23(4):531-7.

<https://doi.org/10.1093/icvts/iww194>

#### ABSTRACT

##### Objectives:

Protecting the brain during cardiac surgery is a major challenge. We evaluated associations between nadir oxygen delivery ( $DO_2$ ) during paediatric cardiac surgery and a biomarker of brain injury, glial fibrillary acidic protein (GFAP).

##### Methods:

A retrospective cohort study was conducted from the electronic data repository at the University of Pittsburgh Medical Blood samples were obtained during a prospective, single-centre observational study of children undergoing congenital heartsurgery with cardiopulmonary bypass (CPB) (2010–2011). Remnant blood samples, collected serially prior to cannulation for bypass and until incision closure, were analysed for GFAP levels. Perfusion records were reviewed to calculate nadir  $DO_2$ . Linear regression analysis was used to assess the association between nadir  $DO_2$  and GFAP levels.

##### Results:

A total of 116 consecutive children were included, with the median age of 0.75 years (interquartile range: 0.42–8.00) and the median weight of 8.3 kg (5.8–20.0). Single-ventricle anatomy was present in 19 patients (16.4%). Deep hypothermic circulatory arrest (DHCA) was used in 14 patients (12.1%). On univariable analysis, nadir  $DO_2$  was significantly associated with GFAP values measured during rewarming on CPB ( $P = 0.005$ ) and after CPB decannulation ( $P = 0.02$ ). On multivariable analysis controlling for CPB time, DHCA and procedure risk category, a significant negative relationship remained between nadir  $DO_2$  and post-CPB GFAP ( $P = 0.03$ ).

##### Discussion:

Lower nadir  $DO_2$  is associated with increased GFAP levels, suggesting that diminished  $DO_2$  during paediatric heart surgery may be contributing to neurological injury. The  $DO_2$ -GFAP relationship may provide a useful measure for the implementation of neuroprotective strategies in paediatric heart surgery, including goal-directed perfusion.

## 2. A CLINICAL PROTOCOL FOR GOAL DIRECTED CEREBRAL PERFUSION DURING AORTIC ARCH SURGERY

**Mosca M. S. et al.**

*Seminars in Cardiothoracic and Vascular Anesthesia 2016, Vol. 20(4) 289–297*

Only abstract available online: <https://doi.org/10.1177/1089253216672854>

### ABSTRACT

#### Objectives:

The optimal strategy to deliver antegrade cerebral perfusion for cerebral protection during hypothermic circulatory arrest has not been established. The purpose of this review was to present our current clinical protocol utilizing selective antegrade cerebral perfusion during aortic arch surgery and to compare it to other published experience.

#### Clinical Protocol:

Since 2013, our clinical protocol for aortic arch surgery has evolved to using selective antegrade cerebral perfusion via the innominate artery, moderate hypothermia, and ancillary strategies such as goal-directed perfusion (GDP). Other published techniques favored antegrade cerebral perfusion but were limited by smaller cannulae, multiple cannulation sites, and lower cooling temperatures.

#### Conclusions:

Our clinical protocol may offer higher flow rates, avoid complications associated with additional cannulae, and provide an easy setup for dual arterial perfusion. Additionally, GDP has enhanced our understanding of metabolic physiology and may facilitate the development of a better cerebral protection strategy.

### 3. CORRELATING OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS WITH THE NEUROLOGIC INJURY BIOMARKER UBIQUITIN C-TERMINAL HYDROLASE L1 (UCH-L1)

Magruder J. T. et al.

*J Cardiothorac Vasc Anesth.* 2018 Dec;32(6):2485-2492.

<https://doi.org/10.1053/j.jvca.2018.05.021>

#### ABSTRACT

##### Objective:

The authors sought to assess the relationship between low oxygen delivery (DO<sub>2</sub>) during cardiopulmonary bypass (CPB) and a neuron-specific biomarker of neurologic injury, ubiquitin C-terminal hydrolase L1 (UCH-L1).

##### Design:

Retrospective analysis of patient charts and prospectively collected blood samples.

##### Setting:

University-affiliated tertiary care hospital.

##### Participants:

Adult patients undergoing cardiac surgery on CPB.

##### Interventions:

Serum UCH-L1 levels were drawn at baseline and 6 and 24 hours after CPB cessation. DO<sub>2</sub> was computed from perfusion records, with area-under-the-curve (AUC) computations performed to account for distance of DO<sub>2</sub> excursions below predefined DO<sub>2</sub> thresholds and the amount of time spent below them. Strokes were defined radiographically using computed tomography and magnetic resonance imaging.

##### Measurements and main results:

Forty-three adults were included (median age 65 y, interquartile range 59-72). Three patients experienced strokes (imaged at 2, 7, and 8 d postoperatively). Most patients underwent isolated coronary artery bypass grafting (41%, 18 patients) or isolated aortic valve replacement (30%, 13). Median UCH-L1 levels differed from baseline to 6 and 24 hours after CPB (40, 232, and 166 pg/mL, respectively;  $p < 0.001$ ). On multivariable linear regression analysis controlling for baseline and surgical variables, only DO<sub>2</sub>AUC <225 was significantly associated with 6-hour UCH-L1 levels ( $p = 0.001$ ), whereas only DO<sub>2</sub> AUC <300 was significantly associated with 24-hour levels ( $p < 0.001$ ). The 3 patients who experienced radiographic strokes had nonsignificantly elevated 24-hour UCH-L1 levels compared with control patients (585 v 151 pg/mL,  $p = 0.11$ ).

##### Conclusions:

This is the first study to demonstrate an independent association between DO<sub>2</sub> during CPB and elevations of a brain injury biomarker; additional study is needed to clarify the clinical significance of these results.

#### 4. THE INFLUENCE OF OXYGEN DELIVERY DURING CARDIOPULMONARY BYPASS ON THE INCIDENCE OF DELIRIUM IN CABG PATIENTS; A RETROSPECTIVE STUDY

Leenders J. et al.

*Perfusion* 2018, Vol. 33(8) 656–662

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### ABSTRACT

#### Introduction:

Postoperative delirium is the most common neurological complication of cardiac surgery. Hypoxia has been shown to increase the risk of postoperative delirium. The possibility to continuously monitor oxygen delivery ( $DO_2$ ) during cardiopulmonary bypass (CPB) offers an adequate approximation of the oxygen status in a patient. This study investigates the role of oxygen delivery during cardiopulmonary bypass in the incidence of postoperative delirium.

#### Methods:

Three hundred and fifty-seven adult patients who underwent normothermic coronary artery bypass grafting (CABG) surgery were included in this retrospective study. The nadir indexed  $DO_2$  ( $DO_{2i}$ ) value on bypass, the total time under the critical  $DO_{2i}$  level and the area under the curve (AUC) for critical  $DO_{2i}$  were determined. Delirium was identified by the postoperative administration of haloperidol.

#### Results:

The mean nadir  $DO_{2i}$  significantly differed, comparing the group of patients with postoperative delirium to the group without. Multivariate analysis only identified age, pre-existing cognitive impairment, preoperative kidney dysfunction and cross-clamp time as independent risk factors for delirium. The results also indicated that patients of older age were more sensitive to a declined  $DO_{2i}$ .

#### Conclusions:

A low  $DO_{2i}$  during cardiopulmonary bypass is significantly associated with the incidence of postoperative delirium in CABG patients. However, the role of  $DO_2$  as an independent predictor of delirium could not be proven.

## 5. DISTURBANCES IN OXYGEN BALANCE DURING CARDIOPULMONARY BYPASS: A RISK FACTOR FOR POSTOPERATIVE DELIRIUM

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### ABSTRACT

#### Objective:

The aim of this study was to determine risk factors for postoperative delirium after cardiac surgery, specifically associated with the conduct of cardiopulmonary bypass (CPB).

#### Design:

Prospective observational study.

#### Setting:

Heart Centre, University Hospital.

#### Participants:

The study included 142 patients aged 70 years and older scheduled for elective cardiac surgery with CPB.

#### Interventions:

Risk factor analysis comprised information collected from the hospital clinical and CPB dedicated databases in addition to the medical chart. Delirium was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition, Text Revision criterion using the Mini Mental State Examination and the Organic Brain Syndrome scale.

#### Measurements and main results:

Assessments of delirium diagnosis were executed preoperatively and on the following first and fourth postoperative days. Delirium occurred in 55% (78/142) of the patients. Patients with delirium were identified with significantly higher body weight and body surface area preoperatively, accompanied with longer CPB time, higher positive fluid balance per CPB, and lower systemic pump flow related to body surface area. Furthermore, the duration of the mixed venous oxygen saturation (SvO<sub>2</sub>) below 75% was significantly longer during CPB. The result from the multivariable logistic regression analysis included the duration of SvO<sub>2</sub> below 75%, fluid balance per CPB and patient age as independent risk factors for postoperative delirium.

#### Conclusions:

The influence of the SvO<sub>2</sub> level during CPB, fluid balance, and patient age should be recognized as risk factors for postoperative delirium after cardiac surgery in patients 70 years and older.





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