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Review

# Glycated Haemoglobin (HbA1C) in Cardiac Surgery; A Narrative Review

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**Abstract:** Perioperative dysglycemia in cardiac surgery is associated with poor outcomes. Glycemic variability rather than glucose levels are a predictor of length of ICU stay, rise in creatinine and acute kidney injury after cardiac surgery. Glycated haemoglobin (HbA1c) values correspond closely with average blood glucose levels and cut off values can be used to define diabetic and pre-diabetic status. These have been correlated with perioperative events. This narrative review discusses the role of glycated hemoglobin in cardiac surgery.

**Keywords:** glycated haemoglobin; cardiac surgery; HbA1c; clinical outcomes; diabetes

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## Introduction

Glycated haemoglobin (HbA<sub>1c</sub>) was first isolated by Huisman and Meyering in 1958 [1]. Its use for measuring glycemic control in diabetes patients was first proposed by Koenig et al in 1976 [2]. HbA<sub>1c</sub> specifically refers to measure of the beta-N-1-deoxy fructosyl component of haemoglobin that forms after binding between glucose and the exposed N- terminal valine end of the  $\beta$  chain of haemoglobin. This irreversible, non-enzymatic condensation reaction results in the formation of a Schiff base which undergoes a base catalysed isomerization (Amadori rearrangement of aldose to ketose) to form 1-deoxyfructose. The nomenclature is based on the fractional order of elution of haemoglobin subtypes on cation exchange chromatography (the order of fractions being HbA<sub>0</sub>, HbA<sub>1a</sub>, HbA<sub>1b</sub>, and HbA<sub>1c</sub>). The fraction of HbA<sub>1c</sub> within the red blood cell is a measure of average glycemic exposure during the life time of the cell (average 110 days) and reflects the average glycemic levels over a 3 month period.

## Representation and Values

HbA<sub>1c</sub> can be expressed in older percentage units (DCCT, Diabetes Control and Complications Trial) or as mmol/mol SI units (IFCC, International Federation of Clinical Chemistry). Since 2007, American Diabetes Association, European Association for the Study of Diabetes, and International Diabetes Federation have agreed to report values in IFCC units for easier comparison of results and standards [3].

HbA<sub>1c</sub> values correspond closely with average blood glucose levels and cut off values can be used to define diabetic and pre-diabetic status (Table 1). A1c-Derived Average Glucose (ADAG) study derived a mathematical relationship using a combination of continuous glucose monitoring and frequent finger stick capillary blood glucose testing in 507 subjects (including 268 subjects with

type 1 diabetes, 159 subjects with type 2 diabetes, and 80 subjects without diabetes) from 10 international centers. It established a validated relationship between A1c and average glucose across a range of diabetes types and patient populations [4–7]. Correlation with blood glucose levels. DCCT percentage (%) and eAG (estimated average glucose) measurement is given by the following equations: [8,9]

$$eAG(\text{mg/dl}) = 28.7 \times A1C - 46.7$$

$$eAG(\text{mmol/l}) = 1.59 \times A1C - 2.59, R^2 = 0.84$$

**Table 1.** – Correlation of HbA<sub>1c</sub> to average blood glucose levels and diagnostic standards for diabetes in cardiac surgery.

HbA <sub>1c</sub>		Average blood glucose levels		Diagnostic standards for HbA <sub>1c</sub> in diabetes in cardiac surgery patients
% units (DCCT)	mmol/mol units (IFCC)	mmol/L	mg/dL	
5	31	5.4 (4.2–6.7)	97 (76–120)	<b>NORMAL</b>
6	42	7.0 (5.5–8.5)	126 (100–152)	< 5.7% or 38.8 mmol/mol
7	53	8.6 (6.8–10.3)	154 (123–185)	<b>PREDIABETES</b> 5.7 – 6.4% 38.8 - 46.4 mmol/mol
8	64	10.2 (8.1–12.1)	183 (147–217)	
9	75	11.8 (9.4–13.9)	212 (170–249)	
10	86	13.4 (10.7–15.7)	240 (193–282)	<b>DIABETES</b> >6.5% or 47.5 mmol/mol
11	97	14.9 (12.0–17.5)	269 (217–314)	
12	108	16.5 (13.3–19.3)	298 (240–347)	
13	119	18.1 (15–21)	326 (260–380)	
14	130	19.7 (16–23)	355 (290–410)	
15	140	21.3 (17–25)	384 (310–440)	
16	151	22.9 (19–26)	413 (330–480)	
17	162	24.5 (20–28)	441 (460–510)	
18	173	26.1 (21–30)	470 (380–540)	
19	184	27.7 (23–32)	499 (410–570)	

DCCT, Diabetes Control and Complications Trial) or as mmol/mol SI units (IFCC, International Federation of Clinical Chemistry).

### Correlation with Outcomes in Cardiac Surgery

Diabetes is a significant disease modifier for coronary artery disease. It substantially affects the surgical management and outcomes after cardiac surgery [10,11]. 80% of cardiac surgery patients have perioperative hyperglycemia. Around 20% of these patients have ‘stress hyperglycemia’ and do not have impaired glucose tolerance or diabetes. HbA<sub>1c</sub> differentiates these conditions as levels are normal in stress hyperglycemia. The exact reasons for adverse outcomes with perioperative hyperglycemia remain unclear but putative mechanisms include free radical generation and injury from glycated haemoglobin and other proteins.

The NIHR commissioned initial DARE (Database of Abstracts of Reviews of Effects) review from 7 randomized control trials found that tight glycaemic control significantly reduced the incidence of early mortality following cardiac surgery (OR 0.52, 95% CI 0.30 to 0.91; three RCTs), post-surgical atrial fibrillation (OR 0.76, 95% CI 0.58 to 0.99; five RCTs), length of stay in the intensive care unit (MD -0.57 days, 95% CI -0.60 to -0.55; three RCTs), duration of mechanical ventilation (MD -3.69, 95% CI -3.85 to -3.54; four RCTs) and use of epicardial pacing (OR 0.28, 95% CI 0.15 to 0.54; three RCTs)[13]. There was significant statistical heterogeneity for early mortality ( $I^2=71\%$ ), duration of mechanical ventilation ( $I^2=94\%$ ), and time spent in the intensive care unit ( $I^2=99\%$ )[14]. Perioperative dysglycemia (both hyper and hypoglycaemia are deleterious [14]). Glycemic variability rather than glucose levels

were a predictor of length of ICU stay, rise in creatinine and acute kidney injury after cardiac surgery [15,16].

In a single center retrospective analysis of 3555 patients, an elevated HbA<sub>1c</sub> level predicted in-hospital mortality after coronary artery bypass grafting (odds ratio 1.40 per unit increase, P = .019). HbA<sub>1c</sub> > 8.6% was associated with a 4-fold increase in mortality [16]. For each unit increase, there was a significantly increased risk of myocardial infarction and deep sternal wound infection. By using receiver operating characteristic value thresholds, renal failure (threshold 6.7, odds ratio 2.1), cerebrovascular accident (threshold 7.6, odds ratio 2.24), and deep sternal wound infection (threshold 7.8, odds ratio 5.29) occurred more commonly in patients with elevated hemoglobin A1c. Alserius et al., also demonstrated significantly reduced 3-year survival, and elevated rates of early superficial wound infection to be associated with HbA<sub>1c</sub> ≥6.0% [42 mmol/l] following CABG [18].

A summary of the recent studies in diabetes is provided in Table 2 [19–25].

**Table 2.** Table of studies:.

Study details (reference)	Study design	Population n	Main findings	Conclusion
Cooke, 2023 [17]	Retrospective cohort study	N= 2560	High HbA <sub>1c</sub> for ONCABG: <ul style="list-style-type: none"> <li>- new post-operative dialysis (p=0.01),</li> <li>- rates of readmission (p=0.003),</li> <li>- greater lengths of stay (p=0.002).</li> </ul> High HbA <sub>1c</sub> for OPCABG: <ul style="list-style-type: none"> <li>- rates of operative mortality (p=0.04),</li> <li>- post-operative renal failure (p=0.0001),</li> <li>- new post-operative dialysis (p=0.0001),</li> <li>- sternal wound infection (p=0.01),</li> <li>- greater lengths of stay (p=0.03).</li> </ul>	Increasing HbA <sub>1c</sub> correlated with numerous adverse patient outcomes in both ONCABG and OPCABG. Differences were noted in which outcomes were most impacted between the two techniques. Pre-operative medical optimization from a diabetes standpoint is paramount to improve CABG outcomes in both onpump or off-pump techniques.
Corazzari, 2022 [18]	Systematic review and Meta-analysis	N= 34,650	Early mortality: reduced in each threshold comparison; highest reductions when glycosylated hemoglobin levels less than 5.5% versus greater than 5.5 % (risk ratio, 0.39; 95% confidence interval, 0.18-0.84; P ¼ .02). Late mortality: reduced with lower levels of glycosylated hemoglobin. Low preoperative glycosylated hemoglobin: <ul style="list-style-type: none"> <li>- lowest risk of sternal wound infections (risk</li> </ul>	Lower levels of glycosylated hemoglobin in patients undergoing cardiac surgery are associated with a lower risk of early and late mortality, as well as in the incidence of postoperative acute kidney injury, neurologic complications, and wound infection, compared with higher levels.

			ratio, 0.50; 95% confidence interval, 0.32-0.80; P = .003 and risk ratio, 0.53; 95% confidence interval, 0.39-0.70; P < .0001), lower risk of acute kidney injury (risk ratio, 0.65; 95% confidence interval, 0.54-0.79; P < .0001).	
Ozturk, 2021 [19]	meta-analysis	N= 3500	High preoperative hemoglobin A1c levels increases risk of: - mediastinitis (OR: 1.08, 95% CI: 0.88-1.28 and p<0.001), - stroke (OR: 0.42, 95% CI: 0.14-0.71 and p=0.004), - pneumonia (OR: 0.45, 95% CI: 0.14-0.75 and p=0.004), - sepsis (OR: 0.57, 95% CI: 0.02-1.11 and p=0.04), - renal failure (OR: 0.49, 95% CI: 0.40-0.58 and p<0.001) mortality (OR: 0.289, 95% CI: 0.088-0.490 and p=0.005).	There was a relationship between preoperative HbA1c high levels and mediastinitis, stroke, pneumonia, sepsis, renal failure and mortality after cardiac surgery.
Wong, 2020 [20]	Meta-analysis	N= 25,036	High HbA1c: - greater risk of anastomotic leaks (odds ratio [OR]: 2.80, 95% CI [1.63, 4.83], P < 0.001); - wound infections (OR: 1.21, 95% CI [1.08, 1.36], P = 0.001); - major complications (OR: 2.16, 95% CI [1.54, 3.01], P < 0.001); overall complications (OR: 2.12, 95% CI [1.48, 3.04], P < 0.001).	An HbA1c between 6% and 7% is associated with higher risks of postoperative complications. Currently, only the US guidelines recommend a target HbA1c of 7%, while the Great Britain and Australian guidelines recommend a target HbA1c of 8.5% and 9%, respectively. Therefore, guidelines with an HbA1c threshold > 7% may be putting elective pre-optimized patients at risk of not have the best chance of being complication-free postoperatively
Wang, 2020 [21]	Systematic review and Meta-analysis		Low HbA1c in diabetic patients after CABG: - reduced incidence of surgical site infections (OR = 2.94, 95% CI 2.18-3.98),	Higher preoperative HbA1c levels may potentially increase the risk of surgical site infections, renal failure, and myocardial infarction

			<ul style="list-style-type: none"> <li>- reduced renal failure events (OR = 1:63, 95% CI 1.13-2.33),</li> <li>- reduced myocardial infarction events (OR = 1:69, 95% CI 1.16-2.47),</li> <li>- shortened hospital stay (MD = 1:08 , 95% CI 0.46-1.71</li> </ul> <p>For nondiabetic patients with higher preoperative HbA1c level:</p> <ul style="list-style-type: none"> <li>- increase incidence of mortality (OR = 2:23, 95% CI 1.01-4.90)</li> <li>- increase renal failure (OR = 2:33, 95% CI 1.32-4.12).</li> </ul>	<p>and increase the length of hospital stay in diabetic subjects after coronary artery disease and increase the risk of mortality and renal failure in nondiabetic patients. However, there was great inconsistency in defining higher preoperative HbA1c levels in the studies included;</p>
Natarajan, 2019 [22]	prospective observational study.	N= 1080	<ul style="list-style-type: none"> <li>- 71.4% of patients with diabetes mellitus: HbA1c &gt;7%.</li> <li>- In-hospital mortality 6.3% (68/1080): 46 diabetic patients.</li> <li>- 70% of 46 diabetic patients: HbA1c levels &gt;7%. Diabetic group with HbA1c &gt;7%:</li> <li>- longer ICU stay (4.19±2.91 Vs 1.25±3.37, p&lt;0.001),</li> <li>- longer hospital stay (10.62±3.74 Vs 9.71±4.78)</li> <li>- increased duration of mechanical ventilation (0.11±0.31 Vs 1.15±1.67 p &lt;0.001).</li> <li>- Mortality OR 1.057 (0.85-1.31) CI 95% p 0.62) and Renal failure OR 0.99 (0.99-1.00) CI 95% p 0.47)</li> </ul>	<p>Increased HbA1c is associated with increased morbidity and mortality in patients undergoing cardiac surgery using cardiopulmonary bypass. Optimal preoperative HbA1c may improve the outcome following cardiac surgery.</p>
Duncan, 2018 [23]	dual-center, parallel group, randomized trial	N= 1,439	<p>Significant statistical heterogeneity for:</p> <ul style="list-style-type: none"> <li>- early mortality (I<sup>2</sup>=71%),</li> <li>- duration of mechanical ventilation (I<sup>2</sup>=94%),</li> <li>- time spent in the intensive care unit (I<sup>2</sup>=99).</li> </ul>	<p>Intraoperative hyperinsulinemic normoglycemia reduced mortality and morbidity after cardiac surgery and, providing exogenous glucose while targeting normoglycemia, may be preferable to simply normalizing glucose concentrations.</p>

Duncan et al found that intraoperative hyperinsulinemic normoglycemia reduced mortality and morbidity after cardiac surgery and concluded that providing exogenous glucose while targeting normoglycemia may be preferable to simply normalizing glucose concentrations [19]. Narayan et al in their retrospective analysis of 4,678 patients found no difference in mortality rates between HbA<sub>1c</sub> < 6.5% (52.93%) and those with HbA<sub>1c</sub> > 6.5% (47.07%) (odds ratio, 1.36; 95% confidence interval [CI], 0.95 to 1.953; p = 0.08)[26]. Overall, an HbA<sub>1c</sub> of 6.5% or higher was an independent risk factor for respiratory complications (odds ratio, 1.05; 95% CI, 1.008 to 4.631; p = 0.01) and sternal dehiscence (odds ratio, 2.161; 95% CI, 1.008 to 4.63; p = 0.04).

Although associations have been clear between high HbA<sub>1c</sub> levels and wound infection rates, renal failure and perioperative ischemic events, some studies have failed to establish prolonged length of stay and increased perioperative mortality [27–31].

In a recent meta-analysis of 33 studies with 3500 patients, Ozturk et al found a significant adverse relationship between preoperative hemoglobin A1c levels and mediastinitis (OR: 1.08, 95% CI: 0.88-1.28 and p<0.001), stroke (OR: 0.42, 95% CI: 0.14-0.71 and p=0.004), pneumonia (OR: 0.45, 95% CI: 0.14-0.75 and p=0.004), sepsis (OR: 0.57, 95% CI: 0.02-1.11 and p=0.04), renal failure (OR: 0.49, 95% CI: 0.40-0.58 and p<0.001) and mortality (OR: 0.289, 95% CI: 0.088-0.490 and p=0.005). The other complications such as atrial fibrillation (OR: -0.01, 95% CI: -0.10-0.07 and p=0.77), myocardial infarction (OR: 0.57, 95% CI: -0.07-1.20 and p=0.079), cardiac tamponade (OR: 0.03, 95% CI: -0.75-0.81 and p=0.93), re-operation (OR: -0.20, 95% CI: -0.46-0.05 and p=0.12), low cardiac output syndrome (OR: 0.09, 95% CI: -0.12-0.30 and p=0.41), gastrointestinal system complications (OR: -0.004, 95% CI: -0.38-0.38 and p=0.08), and multi-organ failure (OR: 0.77, 95% CI: -1.40-2.94 and p=0.49) were not related with HbA<sub>1c</sub> levels.

This association is also better established for high HbA<sub>1c</sub> levels and late vascular and microvascular complications (including retinopathy) and late survival. The estimated glucose disposal rate (eGDR) is calculated from HbA<sub>1c</sub> ((24.31 - (12.2 x waist to hip ratio) - 3.29 x hypertension - 0.57 x HbA<sub>1c</sub>) [32]. eGDR is a useful clinical marker for insulin resistance which has been associated with increased risk of coronary artery disease, microvascular complications and premature death. In the SWEDHEART registry, there was a significant association between eGDR and increased risk of death (adjusted hazard ratio; 1.46 (95% CI; 1.12-1.90) [33]. Similarly, Epstein et al, showed that patients with the lowest eGDR (most insulin resistant) compared with the highest (least insulin resistant) had a significantly greater risk of any diabetes complication (OR; 3.1, 95% CI; 1.2-8.1). [34]

### Guidelines for Pre-Screening and Perioperative Management

The Joint British Diabetes Societies for Inpatient Care Group (JBDS-IP) was created in 2008 to 'deliver a set of diabetes inpatient guidelines and proposed standards of care within secondary care organisations, with the overall aim of improving inpatient diabetes care through the development and use of high quality evidence based guidelines, and through better inpatient care pathways. It was created and supported by Diabetes UK, Association of British Clinical Diabetologists (ABCD) and the Diabetes Inpatient Specialist Nurse (DISN) UK group, and works with NHS England, TREND-UK and with other professional organisations. JBDS-IP has published comprehensive set of guidelines for referral, preoperative assessment, perioperative management and care after discharge of adults with diabetes undergoing surgery [35]. A summary of JBDS-IP recommendations includes

- (a) Referrals for surgery must provide the current HbA<sub>1c</sub>, blood pressure and weight measurements with details of relevant complications and medications in the referral letter.
- (b) Ensure that glycaemic control is optimised prior to surgery if safe to do so, aiming for an HbA<sub>1c</sub> < 69mmol/mol.
- (c) Establish an individualised diabetes management plan, agreed with the patient, for the pre-admission and peri-operative period.
- (d) Referral to the diabetes specialist team according to local policy for all patients with hypoglycaemia unawareness and HbA<sub>1c</sub> > 69mmol/mol (8.5%) where optimisation is safely achievable.

- (e) The target blood glucose in the pre-operative, anaesthetised or sedated patient should be 6-10mmol/L (up to 12mmol/L may be acceptable). Acceptable post-operative range in the awake patient on a variable rate intravenous insulin infusion is 6-12mmol/L and 4-12mmol/L without.
- (f) Safe discharge planning, patient education and communication with community teams to provide ongoing post-discharge support. HbA<sub>1c</sub> levels to be checked every 3-6 months.

JBDS-IP further sets institutional, National Patient Safety Agency (NPSA) and local audit standards to achieve these management goals.

NICE (National Institute of Health and Clinical Excellence, UK) guidance for type 2 diabetes in adults (NG28, published Dec 2015, updated Aug 2019) focuses on patient education, dietary advice, managing cardiovascular risk, managing blood glucose levels, and identifying and managing long-term complications [36]. The recommendations include pre-screening with HbA<sub>1c</sub> for all patients with a surgical referral. Known diabetics should have HbA<sub>1c</sub> repeated if a test has not been done in the last 3 months.

The Society of Thoracic Surgeons Practice Guideline Series for Blood Glucose Management During Adult Cardiac Surgery similarly recommended routine use of HbA<sub>1c</sub> for preoperative screening in cardiac surgery patients to guide perioperative glucose management (Class 1, LOE C) [37].

Adequate glycemic control is associated with an HbA<sub>1c</sub> <7% (<5.3mmol/mol and average blood glucose levels of <8.6mmol/l).

### Point of Care Testing (POCT) and Assays

Point of care testing is defined as rapid testing using portable instruments (typically with a small footprint) at the time of patient consultation. It aims to provide immediate results at the time to enable therapeutic decisions to be made at the earliest, resulting in fewer patient visits and improved glycaemic control. Point of care testing for HbA<sub>1c</sub> has improved clinical outcomes in the primary as well as secondary care settings, reduces visits, improves patient satisfaction and brings down costs in management of diabetes [38–41]. They can also be used easily in remote and poorly accessible geographical areas.

A number of kits are available for POCT which require 1-5µL freshly collected capillary blood from a finger prick or venous blood anticoagulated with heparin, ethylenediaminetetraacetic acid or fluoride oxalate [42]. Results are available within minutes after placing the blood on a test cartridge. Analysis is based on either differences in structure or charge of glycated versus non-glycated hemoglobin. Imprecision for most devices is <3%.

Four types of assays are available -

- (a) *Cation-exchange chromatography*: Haemoglobin species (HbA<sub>1c</sub> and HbA<sub>0</sub>) are separated based on the difference in isoelectric point, by employing differences in ionic interactions between the haemoglobin in the blood sample and the cation exchange groups on the column resin surface.
- (b) *Immunoassay*: The immunoassay method uses antibodies which bind to the N-terminal glycated tetrapeptide or hexapeptide group of the HbA<sub>1c</sub>, forming immunocomplexes which can be detected and measured using a turbidimeter or a nephelometer.
- (c) *Affinity chromatography*: Affinity chromatography is a separation technique based on structural differences between glycated vs non-glycated haemoglobin which utilises m-aminophenylboronic acid and its specific interactions with the glucose adduct of glycated haemoglobin.
- (d) *Enzymatic assay*: Enzymatic quantification of HbA<sub>1c</sub> is based on cleavage of the beta chain of haemoglobin by specific proteases to liberate peptides, which then further react to produce a measurable signal.

POCT devices must meet criteria for quality and standardization which are set by national agencies and are targeted to the IFCC Reference Measurement Procedure (RMP). External quality assessment (EQA) data with a 'real world' perspective on method performance has been used and more recently sigma metrics have been applied alongside CLSI guidance [43].

## Problems in Pre-Screening and Limitations in Cardiac Surgery

The utility of HbA<sub>1c</sub> in cardiac surgery is limited to pre-screening and monitoring of preoperative intervention only. It is also not a reliable indicator of glycemic therapy after cardiopulmonary bypass that is associated with Hageman factor activation, cell clumping and red cell destruction. Since the levels are based on the average life span of red blood cells, HbA<sub>1c</sub> may not be a reliable indicator of glycemic control in anaemic patients, after blood loss, blood transfusions, valve related hemolysis and those with renal and liver disease. Patients with renal disease have higher HbA<sub>1c</sub> levels as measured by ion exchange chromatography but normal levels with specific glycation tests. Dietary modifications with multiple strains of probiotics significantly reduce levels. Patients with sickle cell disease and hemoglobinopathies also have abnormal results.

HbA<sub>1c</sub> levels reflect the glycemic exposure over a 3 month period. It shows any significant change only after about 3 weeks from the start or intensification of glucose-lowering treatment [44]. Therefore the utility is limited to elective surgery patients only on the waiting list and there is limited role of disease modification for risk amelioration in urgent and emergency cases. The levels have prognostic value and are predictive of postoperative outcomes. Referral patterns have changed with greater emphasis on urgent rather than elective surgery. The SCTS 2019-20 taskforce report, showed a 50% decline in the elective CABG referrals and a 33% increase in urgent CABG referrals over the last decade. Further, most patients with chest pain, acute ischemic events and shortness of breath cannot wait for months even on elective cardiac waiting lists for optimization of cardiac risk factors including diabetes based on pre-screening results of HbA<sub>1c</sub>. Our own analysis of the pre-trial feasibility survey of the OCTOPUS trial for preoperative optimization of diabetes (based on HbA<sub>1c</sub> pre-screening, review of medications and advice on diet and exercise) among cardiac surgeons confirmed a lack of concern and engagement with diabetic teams despite perceived and acknowledged risks of adverse outcomes in poorly controlled diabetic patients [45]. Despite guidelines and recommendations, less than 50% of the units routinely pre-screened their patients for HbA<sub>1c</sub> even among diabetics in the United Kingdom.

## Other Glycated Proteins

Other sugars in the blood like fructose and galactose bind to haemoglobin and other proteins in the blood in an irreversible non-enzymatic reaction, similar to glucose. The avidity for haemoglobin and other blood proteins for fructose is much higher than glucose. The assays are however more difficult for other protein-carbohydrate complexes.

Glucose can also bind non-enzymatically to albumin (glycated albumin) which has been used a glycemic biomarker [46,47]. Because of half-life of albumin of 10 days, glycated albumin reflects glycemic status and control more rapidly than HbA<sub>1c</sub> over a much shorter 2-3 week. It is not influenced by albumin levels as it is the ratio of glycated to non-glycated fraction. It is a more sensitive marker in renal impairment and those on dialysis [48-50]. Unlike HbA<sub>1c</sub>, it is not affected by cardiopulmonary bypass, blood loss and transfusions in the perioperative period or renal impairment. Unlike HbA<sub>1c</sub>, glycated albumin does not show variations for same levels of glycemia in patients of different ethnicities. It has the potential to be of greater utility in elective and urgent cardiac surgery patients than HbA<sub>1c</sub>. Its use has however not been substantiated in cardiac surgery patients for preoperative optimization and will need further trials. Glycated albumin also has a rapid POCT for pre-screening.

Other potential glycemic biomarkers include fructosamine, and 1,5-anhydroglucitol (1,5-AG). Their correlation with average glucose levels and their prognostic significance are not as clear and point of care tests are not available.

## Summary

HbA<sub>1c</sub> remains an important pre-screening tool and reflects immediate postoperative and long term prognosis in cardiac surgery. It reflects glycemic exposure over a 3 month period. Its utility may however be limited to elective cardiac surgery patients due to changing referral practices and

caseload patterns in cardiac surgery units with greater emphasis on urgent cases and expedited patient care pathways.

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