

Diabetes- a significant contributor to complications in cardiac surgery: how and when to optimise glycaemic control

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KEY WORDS

Diabetes, cardiac surgery, glycaemic control, educational intervention

ABSTRACT

Objective

The aim is to present the literature on the association between pre-operative hyperglycaemia and post-operative complications and to review the current interventions (pre surgery, peri /intra- and post-operatively) in those with diabetes undergoing cardiac surgery.

Design

A literature review was undertaken to examine complications and interventions in those with diabetes undergoing cardiac surgery.

Setting

Acute care.

Subjects

Those with diabetes undergoing cardiac surgery.

Main outcome measures

Mortality and morbidity and improved glycaemic control.

Results

Pre-operative hyperglycaemia is associated with wound infections and prolonged length of hospital stay. Studies on intra- and post-operative medical interventions to control glycaemia in cardiac surgical patients demonstrate improved short-term medical outcomes, including decreased mortality and improved glycaemic control, reduction in infection rates and reduced length of stay. Some studies examined the roles of pre-operative glucose management (using glycosylated haemoglobin, HbA1c) prior to surgery and demonstrated that HbA1c can be decreased in short term post-educational interventions. Improvements in physical functioning and quality of life post-educational interventions have been reported. Although the primary outcome is often HbA1c, patient focused outcomes (such as empowerment and education) are equally as important in this chronic condition.

Conclusion

Diabetes is a chronic condition and patients need to be educated about the association between coronary artery disease and diabetes and the importance of glycaemic control. Interventions can improve glycaemic control in the short-term as well increasing patients' empowerment and self-mastery. There is evidence supporting the benefits of educational interventions in those with diabetes undergoing cardiac surgery.

INTRODUCTION

Diabetes is a common chronic condition associated with significant mortality and morbidity. Its worldwide prevalence is increasing from an estimated 285 million people in 2010 to 438 million by 2030 (Diabetes UK, 2009) and one study projecting that one million Australians will have diabetes by 2025 (Magliano et al 2008). Currently, the prevalence of diabetes is approximately 700,000 Australians, 2.6 million in the UK and 17.9 million in the USA. There are also a large number of undiagnosed cases (Australian Institute of Health and Welfare [AIHW] 2008; Diabetes UK 2009; Centers for Disease Control and Prevention 2008) and the majority of diagnosed cases (approximately 80-95%) are Type 2 diabetes (AIHW 2008; Diabetes UK 2009; Centers for Disease Control and Prevention 2008). Given these statistics, the burden of diabetes as a chronic condition requires significant personnel and financial input in managing and treating those with diabetes and its various complications.

As well as the potential complications of renal dysfunction/failure, peripheral neuropathy and blindness; those with diabetes (especially poorly controlled) are at an increased risk of coronary artery disease (CAD). In those with chronic hyperglycemia, an increased risk for cardiovascular disease in individuals with diabetes has been observed (Selvin et al 2004). Subsequently individuals with diabetes are at increased risk of mortality from atherosclerotic heart disease, with USA death rates from heart disease two to four times higher in those with diabetes than those without (Centers for Disease Control and Prevention, 2008). In those with less severe CAD, angioplasty and stent insertion can be performed. However, one of the problems with diabetes is the lack of symptoms (in particular angina) from CAD due to neuropathy and thus these patients present later and with more severe CAD that often requires coronary artery bypass surgery (CABS) for multi-vessel disease. Surgical revascularisation is the most commonly performed cardiac surgical procedure with approximately one third of persons undergoing CABS having diabetes (Dinh et al 2007; Ledoux and Luikart 2005; Mehta et al 2006; Robinson et al 2007). Thus optimising care in those with diabetes should be a priority and given the number of undiagnosed cases, any patient who presents with hyperglycaemia and a suspected coronary event should undergo diagnostic tests for diabetes (Kuhn and Lee 2011).

Although once formally diagnosed, those with diabetes are usually under the care of the diabetes team who educate them regarding their diet, their medication and how to manage their blood glucose levels; regular blood tests for glycosylated haemoglobin (HbA1c) should also be undertaken. This can easily be performed within the primary care setting. It is a commonly used accurate measurement of glycaemic control reflecting HbA1c for the previous two to three months (Guyen et al 2005). Optimal HbA1c levels are defined as those less than 7% [53 mmol/mol] and ideally below 6.5% (48 mmol/mol) and levels higher than 7% indicate poorly controlled diabetes. These individuals require additional medication (potentially insulin) and/or review by their General Practitioner and diabetes healthcare professionals (Diabetes Australia 2009; International Diabetes Federation [IDF] Clinical Guidelines Taskforce 2005). A new measurement was recently introduced using the International Federation of Clinical Chemistry units however the literature presented here uses the HbA1c nomenclature.

The aim of this paper is i) to present the association between hyperglycaemia and post-operative complications and ii) to review the current interventions (pre surgery, peri /intra-and post-operatively) that have been undertaken in those in diabetes undergoing cardiac surgery.

Several studies from cardiac surgical populations have identified diabetes and pre-operative hyperglycaemia as independent risk factors for the development of post-operative complications as presented in table 1.

Complications include infection (Robinson et al 2007; Harrington et al 2004; Golden et al 1999; Guvener et al 2002; Carson et al 2002), renal dialysis (Mehta et al 2006) and increased length of hospital stay and costs (Bucarius et al 2003; Carson et al 2002; Estrada et al 2003; Ngaage et al 2009). However while there is general agreement in the literature regarding the association between diabetes, hyperglycaemia and poorer post-operative complications, some studies have found conflicting results, such as in rates of post-operative mortality, non-infective morbidity and infection (Estrada et al 2003; Hakala et al 2005; Ngaage et al 2009). As can be seen in table 1, there is substantial high level of evidence to demonstrate the relationship between pre-operative hyperglycaemia and post-operative complications in those with diabetes undergoing CABS. The next question is to determine whether undertaking interventions to control glycaemia prior to cardiac surgery is beneficial and secondly what type of interventions are beneficial?

Table 1: Selected results of studies investigating the association between pre-operative hyperglycaemia, diabetes and post-operative complications following cardiac surgery

Study	Type of study	Sample No.	Key Findings
Bucarius et al 2003	Prospective analysis, CABGS and heart valve surgery, Germany	16,184	Diabetes an independent predictor of various complications, including increased length of intensive care unit (ICU) stay, sternal instability/infection and peri-operative stroke ($p < 0.05$).
Carson et al 2002	Retrospective cohort study, CABGS in 434 hospitals in North America	146,786	Increased 30-day mortality in patients with diabetes than those without (3.74% and 2.70% respectively) (Unadjusted odds ratio [OR] 1.40, 95% confidence interval [CI95] 1.31-1.49. Adjusted OR for baseline risk factors 1.23 CI95 1.15-1.32). Increased incidence of infections and morbidity in patients with diabetes than non-diabetes (Adjusted OR ~35% greater in diabetic population). Higher median hospital length of stay in patients with diabetes than those without (8.0 and 7.0 days respectively) ($p < 0.001$).
Estrada et al 2003	Historic cohort study, CABGS, single centre, USA	1,574	Increases in BGL of 50mg/dL associated with: Longer post-operative days (0.76 days) (CI95 0.36-1.17 days, $p < 0.001$). Greater hospitalisation charges (2824 dollars) (CI95 1599-4049 dollars, $p < 0.001$). Greater hospitalisation costs (1769 dollars) (CI95 928-2610 dollars, $p < 0.001$). Increased infection incidence in diabetic group than non-diabetic (6.6% and 4.1% respectively) ($p = 0.03$). Increases in BGL of 50mg/dL not associated with: Increased mortality (OR 1.37, [CI95 0.98-1.92], $p = 0.07$). Increased infection rate (OR 1.23, [CI95 0.94-1.60], $p = 0.14$).
Golden et al, 1999	Prospective cohort study, CABGS, single centre USA	411	Increased risk of post-operative infection with higher average glucose peri-operatively, when data adjusted for patient sex, age, race, Charlson Comorbidity Index, APACHE III score, surgical ICU length of stay ($p = 0.05$).

Guvener et al 2002	Retrospective cohort study, Type 2 diabetes post CABGS, Turkey	1,090	<p>Pre-operative hyperglycaemia 1 and 2 days before CABGS risk factor for post-operative infection ($p = 0.012$ and $p = 0.028$ respectively).</p> <p>Greater incidence of post-operative complications in diabetic than non-diabetic participants:</p> <p>Deep sternal wound infection ($p = 0.048$).</p> <p>Donor site infection ($p = 0.013$).</p> <p>Total infection ($p = 0.044$).</p> <p>Greater early mortality in diabetic than non-diabetic group ($p = 0.048$).</p>
Hakala et al 2005	Case control prospective study, CABGS, matching patients of Type 1 and 2 diabetes, Finland	1,732	<p>Increased mortality at follow-up (69 +/- 37 months) in diabetic patients (14.4%) than non-diabetic patients (8.2%) ($p = 0.00002$).</p> <p>Cumulative 5 and 10 year survival decreased in diabetic group (96% and 88% respectively) than non-diabetic group (97% and 91% respectively) ($p = 0.02$).</p> <p>Nil significant differences in:</p> <p>30-day mortality in diabetic patients (2.0%) and non-diabetic (1.0%) ($p = 0.15$).</p> <p>Deep sternal wound infection (0.7% and 0.2% respectively) ($p = 0.29$).</p> <p>Length of ICU stay ($p = 0.65$).</p> <p>Length of hospital stay ($p = 0.47$).</p>
Harrington et al 2004	Prospective study, CABGS, Victoria Australia	4,474	<p>Diabetes independent predictor of surgical site infection (OR 1.6, [CI95 1.4-2.3], $p < 0.001$).</p> <p>Diabetes independent predictor of deep-incision sternal surgical site infection (OR 2.16, [CI95 1.2-3.9], $p = 0.01$).</p>
Mehta et al 2006	Evaluation of data from CABGS and/or heart valve surgery in >600 hospitals in Canada and USA	449,524	<p>Diabetes associated with patients requiring post-operative renal dialysis ($p < 0.0001$).</p>
Ngaage et al 2009	Retrospective analysis of CABGS and heart valve surgery	6,679	<p>Increased cardiovascular risk factors in diabetic patients when present for surgery.</p> <p>Increased risk of non-infective outcomes: cerebrovascular accident ($p=0.04$), renal dialysis ($p<0.0001$).</p> <p>Increased postoperative stay (9.7 +/- 10.5 days Vs 8.4 +/- 6.7 days), ($p<0.0001$).</p> <p>But diabetes not directly associated with non-infective morbidity postoperatively.</p>
Robinson et al 2007	Multiple logistic regression analysis, cardiac surgery, Victoria Australia	11,848	<p>Diabetes a pre-operative risk factor for deep sternal wound infections (OR 2.5, [CI95 1.79-3.47], $p = 0.000$).</p>

Note: Statistical significance at $p < 0.05$

The primary diabetes outcome measure in the literature is HbA1c and the association between higher levels of HbA1c and morbidity and mortality have been reported. Pre-operative levels of elevated HbA1c were associated with greater incidence of in-hospital morbidity, including myocardial infarction (OR 1.55, 95% CI 1.00 – 2.41, $p=0.05$) and deep sternal wound infection (OR 1.38, 95% CI 1.03-1.84, $p=0.029$) (Halkos et al 2008). In-hospital mortality (OR 1.40, 95% CI 1.06-1.86, $p=0.019$) and unadjusted five year survival post-CABS ($p=0.001$) have also been associated with elevated HbA1c (Halkos et al 2008). In patients with and without diabetes undergoing CABS or vascular surgical procedures, elevated HbA1c has also been associated with six-month post-operative cognitive impairment ($p = 0.047$) (Kadoi et al 2005) and a predictor of prolonged length of stay (Medhi et al 2001), as well as increased risk of post-operative 30-day mortality ($p < 0.001$), myocardial ischaemia (OR 2.8, 95% CI: 1.3-6.0) and 30-day cardiac events (OR 5.3, 95% CI: 1.7-16.6) (Feringa et al 2008). These findings support the importance of optimising HbA1c levels before CABS with the aim of improving outcomes.

Diabetes intervention studies in a cardiac population

Many studies have been conducted on intra- and post-operative medical interventions to control glycaemia in cardiac surgical patients with or without diagnosed diabetes. These studies generally involved the use of medical interventions with medical goals, aiming to control glycaemia and limit post-operative complications in the short-term, through some form of insulin regime or protocol such as intensive insulin therapy, continuous intravenous insulin therapy or glucose-insulin-potassium solutions. Results of these studies generally demonstrated improved short-term medical outcomes, including decreased mortality and improved glycaemic control (Furnary et al 2004; Goldberg et al 2004; Kee et al 2006; Ingels et al 2006), reduction in infection rates (Furnary et al 2004) and reduced length of stay (Lazar et al 2004). Some longer-term outcomes of three and four-year survival and quality of life were not improved (Ingels et al 2006). Interestingly, a review of randomised controlled trials investigating insulin-use in critically ill adults, identified no benefit of insulin administration amongst thirteen studies in the cardiac surgery setting, but there were benefits seen in mortality in patients in the surgical ICU setting and in those with diabetes (Pittas et al 2006). Given the number of studies demonstrating the benefits of glycaemic control, there is a paucity of studies attempting intervention and improvement of glycaemic control pre-operatively.

Pre-operative intervention studies

Few studies were found that examined the roles of pre-operative glucose management in lowering HbA1c prior to surgery. Lowering of HbA1c/diabetes risk factors prior to surgery may improve post-operative outcomes, such as those identified by Halkos et al (2008). A recent study of 317 Type 2 patients undergoing CABS concluded patients may benefit from better CAD and diabetes management both before and after surgery, as less than half of the total sample met pre-operative treatment goals for HbA1c, systolic blood pressure, high-density lipoproteins and body mass index. Insulin-treated patients were highlighted due to their higher risk of poor post-operative outcomes (Deaton and Thourani 2009). Preliminary results of a peri-operative multidisciplinary medical intervention in Israel involving patients with diabetes undergoing elective CABS ($n = 147$) indicate medical management may improve glycaemic control between hospital admission and the post-operative period (Cohen et al 2003). However this is only a preliminary study and further conclusions could not be made due to too few post-operative complications in the study group (Cohen et al 2003).

The use of patient education in the pre-operative, cardiac setting to improve glycaemic control has not been investigated in the literature, but may provide an adjunct to peri-operative medical therapies, also improving psychological factors such as diabetes knowledge and personal empowerment not normally considered. Patient education has been largely used in the primary care setting, with interventions in outpatient and

occasionally inpatient units also being reported. Interventions vary in their approach, manner of delivery and theoretical basis. Recent attention has been given to empowerment-based interventions, which it is argued, enable patients and allow them to be more responsible for their self-management and care decisions, thus managing their care more effectively (Meetoo and Gopaul 2005).

Table 2: Previously attempted peri-operative interventions to improve blood glucose control and post-operative outcomes (selected) in patients with diabetes / hyperglycaemia

Study	Type of study	Intervention	Sample No.	Study findings
Furnary et al 2004	Non-randomized prospective interventional study, cardiac surgery, USA	Continuous intravenous insulin therapy (peri-operative)	4,864	Decreased risk of post-operative mortality by 57% ($p < 0.0001$). Decreased risk of deep sternal wound infections by 66% ($p < 0.0001$).
Goldberg et al 2004	Prospective cohort study, ICU, USA	Intensive insulin infusion protocol (nurse driven) (post-operative)	118	When blood glucose of <140 mg/dL reached, 58% of subsequent hourly BGLs within target range (100-139 mg/dL), 73% within desirable range (80-139 mg/dL), 94% within acceptable range (80-199 mg/dL), 0.2% less than 60 mg/dL.
Ingels et al 2006	RCT, cardiac surgery, ICU, Belgium	Intensive insulin therapy (post-operative)	970	Decreased mortality during ICU stay (2.1% versus 5.1%, $p = 0.01$) and two-years post surgery (6.9% versus 11.7%, $p = 0.01$) in intervention group compared to control respectively. Nil significant difference in mortality three years (10.8% versus 13.8%, $p = 0.1$) or four years (15.7% versus 18.7%, $p = 0.2$) post surgery between intervention and control groups respectively. Nil significant difference in quality of life four years after surgery between intervention and control groups ($p > 0.05$).
Kee et al 2006	Cohort study, cardiac surgery, ICU, USA	Insulin nomogram (post-operative)	103	Improved blood glucose control within target limits (6.1-10.0 mmol/L) (by 20%) following implementation of intervention ($p < 0.001$). Decreased mean BGLs following intervention ($p < 0.001$).
Lazar et al 2004	Prospective randomized trial, CABGS, USA	Tight glycaemic control with a glucose-insulin-potassium solution (intra- and post-operative)	141	Decreased post-operative length of stay in intervention group (6.5 \pm 0.1 days) than control (9.2 \pm 0.3 days) ($p = 0.003$). Increased two-year survival post-surgery in intervention group than control ($p = 0.04$). Decreased incidence of recurrent wound infections in intervention group (1%) than control (10%) ($p = 0.03$). Nil difference in 30-day mortality between either group ($p = 0.99$).

Note: Statistical significance at $p < 0.05$

Studies of educational interventions generally only investigate short-term outcomes, with HbA1c the common outcome measure (Albano et al 2008). Reviews of published studies have found that HbA1c can be decreased in the short term post-educational interventions (Clark 2008; Ellis et al 2004; Norris et al 2002; Sigurdardottir et al 2007), with a greater decrease of up to 2.5% in patients with initial HbA1c greater than 8% (63.9 mmol/mol) (Sigurdardottir et al 2007). An increasing number of studies are assessing their interventions on psychosocial outcomes with reviews identifying improved physical functioning, mental health and quality of

life, and decreased bodily pain post-educational interventions (Zhang et al 2007; Steed et al 2003). Further research into long-term outcomes is required (Clark 2008), however some recent studies with lengthened follow-up periods of between 14 months and five years demonstrated promising long-term results, with improvements in HbA1c (Deakin et al 2006; Hornsten et al 2008; Ko et al 2007; Sarkadi and Rosenqvist 2004), empowerment (Deakin et al 2006) and treatment satisfaction (Deakin et al 2006) identified at final follow-up. These studies suggest that although the primary outcome was often HbA1c, patient focused outcomes (such as empowerment and education) are equally as important in this chronic condition.

CONCLUSION

Current management of patients with Type 2 diabetes undergoing cardiac surgery, namely CABS, focuses upon medical management during the intra- and post-operative periods. Few studies investigate the use of preoperative glycaemic control, in particular using HbA1c. It appears that glycaemic control is an important aspect but with no longer-term benefits reported. It would seem pertinent to undertake glycaemic control pre-operatively but to add educational components to improve patients' understanding of their diabetes and allow greater empowerment and self-mastery. This approach would be a multi-disciplinary approach including physicians, diabetes educators, and dieticians, nursing staff and psychologists for example. Diabetes is a chronic condition and patients need to be educated about the association between CHD and diabetes and the importance of glycaemic control. Nursing staff also need to be cognisant of the impact of diabetes on cardiac patients and to involve the diabetes team as early as possible in the patients' care.

There is now some evidence to support patient education in the preoperative setting with the aim of improving and/or optimising glycaemia prior to admission for surgery. Education may also improve psychological factors such as empowerment and self-management, which may continue beyond discharge from hospital; an important consideration in any chronic condition.

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