Acute Renal Failure Post Coronary Artery Bypass Grafting at The University Hospital of The West Indies

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ABSTRACT

Objectives: *The purpose of the study was to determine the period prevalence of acute renal failure (ARF) after coronary bypass surgery (CABG) at the University Hospital of the West Iindies and to identify risk factors.*

Method: *A retrospective analysis of patients who underwent CABG during the period 1994-2004 was done. Data collected included; age, gender, weight, the presence of hypertension (HTN), diabetes mellitus (DM), hypercholesterolaemia, previous myocardial infarction (MI), blood pressure on admission, urea and creatinine one year prior to surgery, on admission for surgery and post-surgery, duration of intra-operative hypotension, duration of cardiopulmonary bypass, perfusion pressure and the perioperative medications.*

Results: *The case notes of 62 patients (68.9%) were obtained for analysis. There were 47 (75.8%) males and 15 females (24.2%) – a 3:1 ratio. The prevalence of HTN and DM in the study sample was 78% and 72% respectively, hypercholesterolaemia was 31% and a previous MI was 29%. There were no differences based on gender. Post CABG complications were: persistent postoperative hypotension (6.8%), congestive cardiac failure (CCF) (6.8%), arrhythmia (6.8%), sepsis (6.8%), lower respiratory tract infection (LRTI) and pleural effusion (5.1%), heart block (3.4%), pulmonary embolism (1.7%), cellulitis and haematoma formation were 1.7% . Three patients had increases in postoperative creatinine values > 89 µmol/L over the postoperative value resulting in a prevalence of ARF of 5%. One of the three patients died and none received dialysis. There were no statistical difference in pre-operative clinical and biochemical characteristics based on the presence or absence of ARF. The presence of diabetes and increased length of stay were significant predictors of increasing postoperative creatinine values adjusting for pre-operative creatinine values. In addition, the presence of diabetes mellitus and male gender were significant predictors of increasing postoperative urea values.*

Conclusion: *DM is a significant risk factor for the development of ARF post CABG.*

Fallo Renal Agudo Tras Injerto Bypass de la Arteria Coronaria en el Hospital Universitario de West Indies

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RESUMEN

Objetivos: *El propósito del estudio fue determinar el período de prevalencia del fallo renal agudo (FRA) tras una cirugía mediante bypass de la arteria coronaria (CBAC) en el Hospital Universitario de West Indies e identificar los factores de riesgo.*

Método*: Se realizó un análisis retrospectivo de pacientes que fueron sometidos a CABG durante el período 1994-2004. Los datos recopilados incluyeron: edad; género; peso; presencia de hipertensión*

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(HTN); diabetes mellitus (DM); hipercolesterolemia; previo infarto del miocardio (IM); presión arterial en el momento del ingreso; urea y creatinina un año antes de la cirugía, a la hora de ingresar para la cirugía, y posterior a la cirugía; duración de la hipotensión intraoperatoria; duración del bypass cardiopulmonar; presión de perfusión; y medicación perioperatoria.

Resultados: *Se obtuvieron las notas de caso de 62 pacientes (68.9%) para análisis. Hubo 47 (75.8%) varones y 15 hembras (24.2%) – una proporción de 3:1. La prevalencia de HTN y DM en la muestra de estudio fue de 78% y 72% respectivamente, la hipercolesterolemia fue 31% , y la ocurrencia de un IM previo fue 29%. No hubo diferencias sobre la base del género. Las complicaciones post CABG fueron: hipotensión postoperatoria persistente (6.8%); fallo cardíaco congestivo (FCC) (6.8%), arri-tmia (6.8%), sepsis (6.8%), infección del tracto respiratorio inferior (ITRI) y efusión pleural (5.1%), bloqueo del corazón (3.4%), embolismo pulmonar (1.7%), celulitis y formación de hematomas fueron (1.7 %). Tres pacientes tuvieron incrementos en los valores post-operatorios de creatinina (> 89 µmol/L), lo que significó una prevalencia de FRA de 5%. Uno de estos tres pacientes murió y ninguno recibió diálisis. No hubo diferencias estadísticas en las características clínicas preoperatorios y bio-químicas de acuerdo con el estatus de FRA. La presencia de diabetes y el incremento en el tiempo de estadía, fueron predictores significativos de los valores de creatinina postoperatoria cada vez mayores, ajustándose a los valores de la creatinina preoperatoria.*

Conclusión: *La DM es un factor de riesgo significativo para el desarrollo del FRA post CABG.*

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INTRODUCTION

The incidence of acute renal failure (ARF) post coronary artery bypass grafting (CABG) is one to five per cent and is therefore regarded as an uncommon complication (1). However, patients who develop this complication suffer increased morbidity and mortality (2–3). It has been reported that positive risk factors for ARF include: duration of cardiopulmonary bypass (CPB), bypass perfusion pressure, age, elevated preoperative urea and creatinine, and comorbid diseases such as chronic renal failure (CRF) and diabetes mellitus (DM) (3–4). The aetiology of ARF following CABG is multifactorial. Ischaemic and drug induced tubular injury are the most likely causes. Aminoglycoside antibiotics and the nonsteroidal anti-inflammatory drugs are known nephrotoxic agents. However, the duration of CPB and the bypass perfusion pressure are regarded as major factors contributing to ARF (5). Longer periods of CPB and perfusion pressures below 60 mmHg are associated with increase incidence of postoperative renal failure (5). A retrospective study was therefore undertaken to determine the incidence of ARF post CABG at the University Hospital of the West Indies (UHWI), Jamaica, and to determine the major risk factors associated with this condition.

SUBJECTS AND METHODS

All patients who underwent CABG at the UHWI between 1994 and 2004 were eligible for enrolment. The data collected included, age, gender, weight, the presence of hypertension (HTN), DM, hypercholesterolaemia, previous myocardial infarction (MI), blood pressure on admission, urea and creatinine one year prior to surgery, on admission for surgery and 12–24 hours post-surgery. Intra-operative hypotension was determined as recorded in the anaesthetist's notes for the patients. Intra-operative hypotension was defined as a mean arterial pressure below 60 mmHg. Peri-operative medications were also recorded and added to the database, looking specifically at drugs such as angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), digoxin, nonsteroidal anti-inflammatory drugs (NSAIDS) including low dose aspirin therapy, aminoglycosides, cephalosporins, macrolides, diuretics and calcium channel blockers. For this study, ARF was defined as an increase in serum creatinine of 89 micromols per litre (over the pre-operative value) in the first 24 hours after surgery. All data collected were analyzed using the Stata Statistical software verson 8 (College Station, 77845, USA). As the number of subjects with ARF was low, multiple regression analysis was performed to determine predictors of postoperative creatinine controlling for pre-operative creatinine and postoperative urea concentrations.

RESULTS

Ninety patients underwent CABG during the study period but only 62 case notes were obtained. During the study period the death rate was recorded as 22% or approximately 20 patients. The records of the patients who died were not obtained. The mean age (sd) of patients were 61.2 (10.7) years with range of 40 to 85 years. There were 47 (75.8%) males and 15 females (24.2%) – a 3:1 ratio. The prevalence of HTN and DM in the study sample were 59.7% and 54.8% respectively, hypercholesterolaemia was 24.2% and a previous MI was 22.6% (Table 1). There were no differences in clinical and biochemical characteristics by gender (Table 2).

Peri-operative medications administered included: low dose aspirin therapy in 72.4%, beta blockers in 63.8%, furosemide in 60.3%, amikacin in 50.0%, an ACEI in 48.3%,

Table 1: Clinical characteristics of sample

Variable	n	%		
Male: female	47:15	(76:24)		
Pre-operative Co-morbid diseases				
Hypertension	37	(59.7%)		
Diabetes mellitus	34	(54.8%)		
Hypercholesterolaemia	15	(24.2%)		
MI	14	(22.6%)		
Smoking	4	(6.5%)		
Alchohol	1	(1.6%)		
	n	**Mean (sd)**	**Minimum**	**Maximum**
Pre-operative serum creatinine concentration	62	101.7 (31.7)	38	209
Pre-operative serum urea concentration	62	5.7 (2)	2.1	12.3
# Serum creatinine concentration difference µmol/L	62	11.4 (38.2)	-86	140
# Serum urea concentration difference µmol/L	62	1.4 (3.4)	-5.2	13.5
MDRD GFR	54	91.9 (39.0)	37.4	260.9
Age (years)	62	61.2 (10.7)	40	85
Systolic BP (mmHg)	61	132.3 (16.5)	110	179
Diastolic BP (mmHg)	61	80.1 (11.2)	50	100
Period of hypotension (minutes)	62	115.9 (145.2)	0	490
Bypass time (minutes)	61	165.5 (66.3)	38	432
Length of stay (days)	59	15.3 (10.3)	2	48

Abbreviations: MDRD = Modification of diet in renal disease equation; n = frequency; sd = standard deviation; ARF = postoperative acute renal failure; MI = myocardial infraction; # = post-surgery serum creatinine – pre-surgery serum creatinine and post-surgery serum urea concentrations – pre-surgery serum urea concentrations.

Table 2: Clinical and biochemical characteristics by gender

Variables	Females		Males	
	n	Mean (± sd)	n	Mean (sd)
# Serum creatinine concentration difference	15.0	3.7 (23.1)	47.0	13.9 (41.8)
# Serum urea concentration difference	15.0	0.6 (1.9)	47.0	1.7 (3.7)
MDRD (GFR) ml/min	14.0	87.2 (35.1)	40.0	93.6 (40.6)
Age (years)	15.0	60.6 (12.9)	47.0	61.4 (10.1)
Systolic BP (mmHg)	15.0	139.1 (20.8)	46.0	130.0 (14.5)
Diastolic BP (mmHg)	15.0	80.4 (10.6)	46.0	80.0 (11.4)
Period of hypotension (minutes)	15.0	114.5 (161.9)	47.0	116.3 (141.4)
Bypass time (minutes)	15.0	160.6 (52.8)	46.0	167.1 (70.5)
Length of stay (days)	14.0	16.5 (16.5)	45.0	15.0 (10.1)

Abbreviations: MDRD = Modification of diet in renal disease equation; # post-surgery serum creatinine – pre-surgery serum creatinine and post-surgery serum urea concentrations – pre-surgery serum urea concentrations

NSAIDs in 37.0%, cephalosporin in 32.8%, calcium channel blockers in 27.6%, digoxin in 22.4% and gentamicin in 19.0% of patients.

Post CABG complications in the sample such as persistent postoperative hypotension, congestive cardiac failure (CCF), arrhythmia and septicaemia were 6.8%, lower respiratory tract infection (LRTI) and pleural effusion 5.1%, heart block 3.4%, pulmonary embolism 1.7%; cellulitis and haematoma formation were 1.7%.

Three patients had increases in postoperative creatinine values > 89 µmol/L resulting in a prevalence of ARF of 5% (Table 3). One of the three patients died and none received dialysis. There was no statistical difference in pre-operative clinical and biochemical characteristics based on the presence or absence of ARF. The prevalence of ARF in this sample was low which would have resulted in unstable estimates of the risks associated with ARF and putative predictors. Consequently a multiple regression approach was used to determine the factors that were associated with increased

Table 3: Clinical and biochemical characteristics by ARF status

Variable	No ARF n = 59	ARF n = 3
Male:female[1]	44:15	3:0
Preoperative conditions		
Hypertension[1]	34	3
Diabetes[1]	31	3
Hypercholesterolemia[1]	14	1
MI[1]	14	0
Smoking[1]	4	0
Alchohol[1]	1	0
Postoperative complications		
Sepsis[1]	4	1
LRTI[1]	3	0
Arrhythmia[1]	3	0
Death[1]	1	1
Hepatitis[1]	1	1
Dialysis[1]	1	0
Preoperative serum creatinine concentration[2]	102.2 ± 32	91.7 ± 28.7
Preoperative serum urea concentration[2]	91.7 ± 28.7	8.6 ± 1.7
# Serum Creatinine concentration difference µmol/L[2]	5.7 ± 28.9	122.7 ± 27.5
# Serum Urea concentration difference µmol/L[2]	1.4 ± 3.4	2.2 ± 3.7
MDRD GFR[2]	90.9 ± 38.9	119 ± 47.3
Age (years)[2]	61.3 ± 10.9	59.3 ± 8.1
Systolic BP (mmHg)[2]	132.4 ± 16.6	130 ± 17.3
Diastolic BP (mmHg)[2]	79.9 ± 10.7	83.3 ± 20.8
Period of Hypotension (minutes)[2]	115 ± 142.6	133 ± 230.4
Bypass time (minutes)[2]	163.6 ± 67.4	201.3 ± 17.2
Length of stay (days)[2]	15.1 ± 10.5	20.5 ± 0.7

[1]Values are counts. [2] Values are mean ± sd. Abbreviations: LRTI = Lower Respiratory Tract Infection; MI = Myocardial Infarction. n = frequency; ARF = postoperative acute renal failure. MDRD = Modification of diet in renal disease equation; # post-surgery serum creatinine – pre-surgery serum creatinine and post-surgery serum urea concentrations – pre-surgery serum urea concentrations.

postoperative serum creatinine adjusting for pre-operative values. The results of this analysis suggests that the presence of diabetes mellitus and increased length of stay were significant predictors of increased postoperative creatinine values adjusting for pre-operative creatinine values. In addition, the presence of diabetes and male gender were significant predictors of increased postoperative urea values.

Table 4: Predictors of postoperative creatinine controlling for pre-operative creatinine

Independent Variables	β	p value	Lower 95% CI	Upper 95% CI
Pre-op serum creatinine µmol/L	0.57	0.001	0.24	0.90
Male 21.50	0.065	-1.39	44.40	
Age (years)	0.63	0.173	-0.28	1.54
Presence of diabetes	19.57	0.047	0.29	38.85
Diastolic blood pressure (mmHg)	0.57	0.196	-0.31	1.45
Log (length of stay)	15.70	0.049	0.09	31.30
Constant	-96.45	0.069	-200.54	7.63

Abbreviations – β = regression coefficient, CI = confidence interval

Table 5: Predictors of postoperative urea controlling for pre-operative urea

Independent Variables	β	p value	Lower 95% CI	Upper 95% CI
Pre-op serum urea	0.10	0.600	-0.29	0.49
Male	2.26	0.017	0.42	4.09
Age (years)	0.05	0.155	-0.02	0.13
Period of hypotension	0.00	0.159	0.00	0.01
Presence of diabetes	1.99	0.014	0.42	3.56
Constant	0.18	0.946	-4.97	5.32

Abbreviations – β = regression coefficient, CI = confidence interval

DISCUSSION

The results of this retrospective study suggested that the diabetic patients had significantly decreased renal function after CABG when this was compared to other descriptive variables. This is evidenced by increased levels of creatinine and urea postoperatively. Diabetic patients are at increased risk of pre-renal azotemia and parenchymal renal damage secondary to haemodynamic factors related to endothelial dysfunction in long standing DM (6). If such mechanisms hold in this patient population, the lack of a significant correlation between the postoperative urea and intra-operative hypotension could possibly be explained by very good intravascular volume control during surgery, although the mean period of intra-operative hypotension was 116.3 minutes (Table 2). If all episodes were corrected quickly, then total intra-operative hypotension as measured in this study, may not be a reliable indicator of hypotension sufficient to cause renal injury, despite a mean length of hypotension of 111 minutes. The study was limited by the unavailability of some records. Being retrospective in nature, the study is easily prone to bias at the level of record selection, as those patients who died were filed separately and such records were more difficult to retrieve. Also, those patients may have had significant pre and postoperative factors which contributed to the increase in morbidity and mortality as evident by the high New York Heart Association Score (NYHA) given to most of them. The lack of detailed documentation related to the follow-up of patients beyond two to three postoperative days (which is usually the period of admission in ICU) was a possible confounding factor when using a change in serum creatinine as a marker of renal injury. Elevation in levels of this metabolite is well known to lag behind decreases in the glomerular filtration rate (GFR) by up to three days. Despite confounding factors related to the design of the study, diabetics clearly were at increased risk of ARF as evident by an increase in serum creatinine (due to a decline in the glomerular filtration rate) despite proper intra-operative fluid management. Although this increase in serum creatinine was small, it should be noted that an increase in serum creatinine by as little as 44 µmol/L in the case of patients who developed ARF secondary to contrast nephropathy produced a 5.5 fold increase risk of mortality (7). This risk is likely to represent a continuum instead of a threshold or a one-off effect. Therefore given a mean increase of serum creatinine of 122.7 ± 27.5 µmol/L in the patients who developed acute renal failure in this study, one may conclude that they were at significantly increased risk of death when compared to patients that had no elevations in creatinine. However a properly conducted prospective trial looking at the outcome of these patients at 1 year post CABG would be needed in order to make such a determination.

CONCLUSION

Diabetic patients who underwent CABG at the UHWI had increased serum creatinine postoperatively. It is likely that this placed them at an increased risk of mortality as compared to the non-diabetic and hypertensive patients. This hypothesis has been postulated from other studies. The magnitude of the risk of ARF and the degree of elevation of creatinine associated with it remains unknown. This could be determined by an appropriately powered prospective study to detect the minimum increase in creatinine associated with increased mobidity (*eg* requiring renal dialysis) and the risk of death before five years.

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