Clinical research

Transit time flow measurement as a predictor of graft failure and major adverse cardiac events following coronary artery bypass grafting surgery

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Abstract

Introduction: Our aims were to characterize the differences in transit time flow measurement (TTFM) between failed and normal grafts, and to determine the association between TTFM and related clinical factors and the likelihood of graft failure and major adverse cardiac events (MACE) following coronary artery bypass grafting.

Material and methods: A retrospective observational analysis was performed on 279 patients admitted between 2017 and 2019, to compare the differences in TTFM between failed and normal grafts, and the association between TTFM and major adverse cardiac events (MACE) – specifically angina, myocardial infarction, and death.

Results: There were no differences in TTFM between failed and normal grafts. There was a greater number of failed grafts with pulsatility index (PI) > 5 compared to PI ≤ 5 (χ^2 = 4.021, p = 0.045). Multivariate analysis showed no significant association between TTFM and MACE. Increased risk of graft failure is associated with the female gender (p = 0.031), history of congestive heart failure (p = 0.025), and poor renal function (p = 0.034). Increased risk of MACE is associated with a history of coronary intervention (p = 0.041), left coronary dominance (p = 0.018), and renal function (p = 0.009).

Conclusions: Patency of graft is influenced by gender, congestive heart failure, and renal function, while MACE is influenced by history of coronary intervention and renal function.

Key words: transit time flow measurement, graft failure, major adverse cardiac events, coronary artery bypass grafting surgery.

Introduction

Coronary artery bypass grafting (CABG) surgery has remained an optimal technique for restoring blood flow to obstructed coronary arteries [1–4]. Post-CABG, success of the procedure depends on the likelihood of the graft remaining unobstructed in the long run, because significant stenosis or occlusion is a major contributor to adverse outcomes, such as mortality, myocardial infarction, and angina [5–7].

Coronary angiography (CAG) remains the gold standard for accurate graft assessment for the presence of occlusion or stenosis in blood vessels after CABG surgery. The use of post-operative CAG in assessing graft patency is dependent on the protocol of each institution. It is common practice in some centres for post-operative angiograms to be performed to confirm graft patency, even if patients do not show post-operative signs of myocardial ischaemia [8], while in others, including our own, CAGs are only conducted if patients show ischaemic signs, such as angina and abnormal electrocardiogram changes [9, 10].

In addition to CAG, in its role to assess the quality of the graft, transit time flow measurement (TTFM), which is a technique used to measure parameters related to graft flow, such as mean graft flow (Q_{mean}), pulsatility index (PI), and diastolic filling (DF%), has been used to characterize the grafts [11–13]. This method has been validated by several authors comparing TTFM with intra-operative or post-operative angiography [14, 15]. In our institution, TTFM has yet to be utilized routinely to assess graft patency despite the availability of the technique. Moreover, despite CABG surgery being widely undertaken in Brunei Darussalam to treat severe coronary artery disease, there have been no published data on the numbers and types of grafts utilized.

This study aims to provide an overview of the graft types and TTFM profiles from the CABG surgery performed in Brunei Darussalam. In addition, this study aims to characterize the differences in TTFM parameters between failed and normal grafts, as well as determining the association of these parameters and related clinical factors to the likelihood of post-surgical graft failure and adverse cardiac outcomes.

Material and methods

From 1 January 2017 to 31 December 2019, adults undergoing isolated CABG at Gleneagles Jerudong Park Medical Centre, Brunei Darussalam, were included in a retrospective observational study. Patients who underwent other cardiac surgeries (such as valve replacements) with or without CABG were excluded. Patients within the study population who underwent post-operative CAG were identified and followed up for adverse outcomes. This study was approved by our institution's Ethics Committee.

In our institution, graft patency was categorized based on the modified Fitzgibbon classification into 2 categories correlating with percentage stenosis [13]. Graft patency is categorized into (1) normal grafts – grafts which are widely patent and which have normal lumen with non-significant stenosis of less than 50%, and (2) failed grafts – grafts with abnormal patency or which are occluded and which have significant stenosis of 50% or more [8, 13].

The 3 parameters of TTFM that are utilized in this study to characterize graft condition are mean graft flow (Q_{mean}), pulsatility index (PI), and diastolic filling (DF%) measured using Medistim Flow Probes (Medistim ASA, Oslo, Norway). A graft is considered functional when blood flow is sufficiently fast flowing, with low resistance, and in high volume, which are indicated by Q_{mean} > 20 ml/min, PI < 5, and DF% > 50% [8, 12, 16]. In this study, the major adverse cardiac events (MACE) are post-operative complications of the isolated CABG surgery, which includes cardiac-related death, recurrent angina, and myocardial infarction.

Data on patient demographics, history of coronary artery disease, TTFM, and post-CABG complications were retrieved from the patient's hospital electronic database. The following data were collected: (1) age, body mass index, gender, race, smoking status, and diabetic status; (2) presence of coronary artery disease risk factors – hyperlipidaemia, hypertension, and peripheral vascular disease; (3) history of cardiovascular events – myocardial infarction, stable angina, congestive heart failure, percutaneous coronary intervention (PCI) or stent inserted, pre-operative intra-aortic balloon pump (IABP), unstable angina, transient ischaemic attack/stroke, cardiac arrest and pre-operative cardiogenic shock; (4) renal function – chronic renal disease/renal insufficiency and on dialysis; (5) pre-operative cardiac function – pre-operative left ventricular ejection fraction; (6) intra-operative perfusion data – on-pump arrested heart CABG, on-pump beating heart CABG, and off-pump CABG; (7) status of coronary flow dominance – left or right dominant; (8) presence of post-CABG adverse outcomes – arrhythmia, cardiac arrest, post-operative IABP, congestive heart failure, cardiogenic shock, post-operative extracorporeal membrane oxygenation (ECMO) and transient ischaemic attack/stroke; (9) presence of post-CABG impaired renal function – acute kidney injury and on post-operative dialysis; (10) presence of MACE – myocardial infarction, recurrent angina, and death; (11) TTFM values – mean graft flow (Q_{mean}), pulsatility index (PI), and diastolic filling (DF%).

Ethical approval

This study was approved by the Joint Research Ethics Committee of the Institute of Health Sciences (IHSREC), Universiti Brunei Darussalam and Ministry of Health (MHREC) (reference: UBD/PAPRSBIHSREC/2020/80, dated 13 October 2020).

Statistical analysis

All statistical analyses were performed in Macintosh Application Environment 3.0 (Apple Computer, Inc.). Univariate analyses were done on RStudio version 1.4.1106 (Posit Software, PBC), while all other analyses were done using GraphPad Prism version 9.1.0 (Graphstats Technologies). For univariate analyses, the chi-square test was used to compare the categorical variables, for which those with *p*-values of less than 0.05 were taken as significant and included in logistic regression multivariate analyses. For analyses towards characterizing differences in TTFM parameters between failed and normal grafts, the independent *t*-test and χ^2 test were used. For associative studies, patient demographics, history of coronary artery disease, TTFM, and post-CABG complications were collected as predictor variables for univariate and multivariate analyses.

Results

Patient demographics and CABG data

During the study period, a total of 279 patients underwent isolated CABG surgery. The mean age of the patients was 61.1 ±10.3 years, with the majority of patients of Malay ethnicity (90.7%) and of male gender (83.9%). Smokers made up of 52.3% of the patients, and 72.4% were diabetic (Table I).

Almost all patients presented with hypertension (98.6%) and hyperlipidaemia (97.9%), which are significant risk factors for coronary artery disease (CAD), while only 7.5% of the patients had peripheral vascular disease. The most prevalent cardiovascular events the patients presented were myocardial infarction (70.3%), stable angina (63.8%), and congestive heart failure (17.2%). Chronic renal disease or renal insufficiency was present in 30.8% of the patients, of whom 24.4% (*n* = 21) had severe renal disease leading to the need for dialysis. The majority of CABG procedures were done on the cardiopulmonary bypass machine and arrested heart (97.1%), while the remaining procedures were done on a beating heart without aortic clamp (2.9%). For all procedures, the mean cardiopulmonary bypass time was 118.9 ±35.5 min, while the mean aortic clamp time for on-pump arrested heart procedures was 73.9 ±22.1 min. Other demographics and details of CABG surgery are shown in Table I.

Outcomes among CABG patients with post-operative CAG

Among the 279 patients, 26 (2.7%) had CAG after the CABG surgery, to assess graft failure due

Table I. Demographics of coronary artery bypass grafting patients (*n* =279)

Variables	Value
Age, mean (SD)	61.1 (10.3)
Body mass index, mean (SD)	27.3 (4.7)
Socio-demographic:	*n* (%)
Gender:	
Male	234 (83.9)
Female	45 (16.1)
Race:	
Malay	253 (90.7)
Chinese	17 (6.1)
Others	9 (3.2)
Smoking status:	
Non-smoker	100 (35.8)
Smoker	146 (52.3)
Ex-smoker	33 (11.8)
Diabetic status:	
Type I diabetes mellitus	30 (10.8)
Type II diabetes mellitus	172 (61.6)
Coronary artery disease risk factors:	*n* (%)
Hyperlipidaemia	275 (98.6)
Hypertension	273 (97.9)
Peripheral vascular disease	21 (7.5)
Medical history of cardiovascular events:	*n* (%)
Myocardial infarction	196 (70.3)
Stable angina	178 (63.80)
Congestive heart failure	48 (17.2)
Percutaneous coronary intervention (PCI) / stent insertion	33 (11.8)
Pre-operative intra-aortic balloon pump (IABP)	33 (11.8)
Unstable angina	22 (7.89)
Transient ischaemic attack/Stroke	17 (6.1)
Cardiac arrest	4 (1.4)
Pre-operative cardiogenic shock	4 (1.4)
Dominance of coronary flow:	*n* (%); total *n* = 26
Left	6 (23.1)
Right	20 (76.9)
Renal function:	*n* (%)
Chronic renal disease/ renal insufficiency	86 (30.8)
On dialysis	21 (7.5)
Intra-operative CABG surgery data:	*n* (%), *n* = 278
On-pump arrested heart CABG	270 (97.1)
On-pump beating heart CABG	8 (2.9)
Off-pump CABG	0 (0.00)
Intra-operative CABG surgery data (continued):	Mean (SD)
Cardiopulmonary bypass time [min]	118.9 (35.5)
Aortic clamp time [min]	73.9 (22.1)

Means are expressed with standard deviation (SD) in parenthesis, while numbers are expressed alongside percentages in parenthesis.

Table II. Clinical outcomes among coronary artery bypass grafting surgery patients with post-operative coronary angiogram (CAG) (*n* = 26)

Variable	Value
Post-CABG adverse cardiac-related outcomes:	*N* = 26 (%)
Arrhythmia	10 (38.5)
Cardiac arrest	8 (30.8)
Post-operative intra-aortic balloon pump (IABP)	7 (26.9)
Congestive heart failure	5 (19.2)
Cardiogenic shock	4 (15.4)
Post-operative extracorporeal membrane oxygenation (ECMO)	4 (15.38)
Transient ischaemic attack/stroke	0 (0)
Major adverse cardiac events (MACE):	
Myocardial infarction	14 (53.9)
Recurrent angina	10 (38.5)
Death	5 (19.2)
Post-CABG impaired renal function:	
Acute kidney injury	21 (80.8)
On dialysis	9 (38.5)
Graft failure:	
30-day graft failure	6 (23.1)
1-year graft failure (excludes first 30 days)	7 (26.9)
4-year graft failure (2017 to January 2021; excludes first year)	6 (23.1)
Overall graft failure	19 (73.1)

Numbers are expressed alongside percentages in parentheses.

to the presentation of clinical signs of cardiac-related symptoms (such as arrhythmia) and MACE (for example, angina), which could indicate graft failure. The majority of these 26 patients were identified to have a right-dominant coronary artery system (76.9%). 73.1% of these patients had a failed graft identified during CAG. Follow-up on the prevalence of MACE showed that more than half of the 26 patients presented with myocardial infarction (53.9%), with more than one-third of the patients having recurrent angina (38.5%) (Table II). Five patients died from cardiac-related causes such as cardiac arrest, heart failure, and ventricular arrhythmia. Other post-operative outcomes are shown in Table II. The most prevalent adverse post-surgical outcomes were arrhythmias (38.5%), cardiac arrest (30.8%), and insertion of post-operative intra-aortic balloon pump (26.9%). Almost all patients presented with acute kidney injury (80.8%), with 9 out of 26 patients on dialysis.

All the 26 patients with post-operative CAG had significant native vessel stenosis, which is defined by any stenosis 50% or greater in the left main coronary artery, 70% or greater in any other coronary artery, or both [17]. In addition, the majority of the patients with post-operative CAG experienced a failed graft (73.1%), with 23.1% of failed cases occurring within 30 days and another 26.9% occurring within 1 year (Table II).

Overview of graft types from CABG surgery

In the 279 patients who underwent CABG surgery, a total of 953 grafts were identified. The

Table III. Numbers and types of coronary artery bypass grafts coupled with target vessels and their failure rates

Graft type	(Abnormal, occluded)	Percentage of failed grafts (within respective graft type group)
SVG-LAD (*n* = 8)	(0,1)	12.5% (*p* = 0.1154)
RAD-LCx (*n* = 26)	(2,0)	7.7% (*p* = 0.1652)
SVG-Diag (*n* = 122)	(0,6)	4.9% (*p* = 0.2394)
SVG-LCx (*n* = 223)	(2,8)	4.5% (*p* = 0.2398)
SVG-RAM. INT. (*n* = 33)	(1,0)	3.0% (*p* = 0.9754)
SVG-RCA (*n* = 245)	(2,3)	2.0% (*p* = 0.7654)
LIMA-LAD (*n* = 269)	(2,1)	1.1% (*p* = 0.0931)
RAD-Diag (*n* = 18)	(0,0)	0.0%
LIMA-Diag (*n* = 4)	(0,0)	0.0%
RAD-RAM.INT (*n* = 2)	(0,0)	0.0%
RAD-RCA (*n* = 2)	(0,0)	0.0%
RAD-LAD (*n* = 1)	(0,0)	0.0%
Total grafts (*n* = 953)	Total failed (*n* = 28)	2.9%

Diag – diagonal artery, LAD – left anterior descending artery, LCx – left circumflex artery, LIMA – left internal mammary artery, RAD – radial artery, RAM. INT. – ramus intermedius artery, RCA – right coronary artery, SVG – saphenous vein graft.

majority of the grafts used were saphenous venous grafts (SVG) (n = 631/953, 66.2%), while the least utilized was the radial artery (RAD) graft (n = 49/953, 5.1%). However, in terms of graft to target vessel pairing combination, the artery graft was most used (left internal mammary artery, LIMA-left anterior descending, LAD, n = 269/953, 28.3%), followed by SVG-right coronary artery, RCA (n = 245/953, 25.7%). The total number of failed grafts and the types that failed are shown in Table III. Among them, the SVG-LAD combination had the highest likelihood of graft failure among the population (12.5%; p = 0.1154).

Comparison of TTFM between different graft subtypes from CABG surgery

For all 953 grafts identified in this study, all 3 parameters of the TTFM and their median (IQR) values were as follows: Q_{mean} (ml/min) = 27.0 (24.0); PI = 2.8 (1.7); and DF% = 65.0 (15.0). All the parameter values were above the cut-offs (Q_{mean} > 20 ml/min, PI < 5, DF% > 50%), indicating satisfactory and sufficient blood flow in the grafts of the CABG surgeries performed. There were no significant differences between the medians of Q_{mean} of different graft combinations (Table IV).

When comparing the different types of graft, arterial grafts have significantly lower PI (2.6) and higher DF% (72%) than venous grafts (PI = 2.9; DF% = 63%). When the arterial grafts were subtyped into LIMA-only grafts, which is the dominant arterial graft, they have significantly lower PI (2.7) and higher DF% (72%) than SVG (PI = 2.9; DF% = 63%). Such arterial versus venous graft trends for PI and DF% were also observed when the comparison was made between graft to target vessel combinations, for example LIMA-LAD (Table IV). When comparing left-sided to right-sided grafts, only the DF% parameter showed a significant difference, with left-sided grafts having greater DF% values (67%) than right-sided grafts (DF% = 62.5%). When comparisons were made between the TTFM parameters based on functional status of normal and failed grafts, there were no significant differences in the medians of Q_{mean}, PI, and DF% between normal and failed grafts; however, the normal grafts reported a higher median PI than the failed grafts.

Likelihood of normal and failed grafts based on TTFM parameter cut-offs

Functional grafts are indicated by a blood flow that is sufficiently fast, with low resistance,

Table IV. Comparisons of transit time flow measurements (TTFM) between graft types

Parameter	Arterial grafts (n = 323)	Venous grafts (n = 631)	P-value (Mann-Whitney)
Q_{mean} [ml/min]	26.0 (23.00)	27.0 (24.00)	0.4317
PI	2.60 (1.40)	2.90 (2.00)	0.0023*
DF%	72.0 (11.00)	63.0 (14.00)	< 0.0001*
Parameter	**LIMA grafts (n = 273)**	**SVG grafts (n = 631)**	**P-value**
Q_{mean} [ml/min]	26.0 (22.0)	27.0 (24.0)	0.757
PI	2.7 (1.4)	2.9 (2.0)	0.0140*
DF%	72.0 (11.0)	63.0 (14.0)	< 0.0001*
Parameter	**LIMA-LAD grafts (n = 269)**	**SVG grafts (except SVG-LAD) (n = 622)**	**P-value**
Q_{mean} [ml/min]	26.0 (22.0)	27.0 (24.0)	0.754
PI	2.7 (1.4)	2.9 (1.9)	0.0110*
DF%	72.0 (11.0)	63.0 (14.0)	< 0.0001*
Parameter	**LIMA-LAD grafts (n = 269)**	**All other grafts (n = 684)**	**P-value**
Q_{mean} [ml/min]	26.0 (22.000)	27.0 (24.000)	0.8826
PI	2.7 (1.400)	2.8 (1.875)	0.0008*
DF%	72.0 (11.000)	63.0 (15.000)	< 0.0001*
Parameter	**Left sided grafts (n =706)**	**Right sided grafts (n = 247)**	**P-value**
Q_{mean} [ml/min]	27.0 (24.00)	27.0 (23.00)	0.4208
PI	2.80 (1.70)	2.8 (1.90)	0.9857
DF%	67.0 (15.00)	62.5 (13.00)	< 0.0001*
Parameter	**Normal grafts (n = 925)**	**Failed grafts (n = 28)**	**P-value**
Q_{mean} [ml/min]	27.00 (24.00)	25.00 (17.25)	0.0998
PI	2.80 (1.70)	2.60 (2.25)	0.8934
DF%	65.50 (15.00)	62.50 (6.75)	0.1434

Table V. Likelihood of failed grafts based on TTFM parameter cut-offs

TTFM parameter cut-offs	Number of normal grafts *n* = 925	Number of failed grafts *n* = 28
Q_{mean} [ml/min] > 20 (*n* = 648)	633	15
Q_{mean} [ml/min] ≤ 20 (*n* = 305)	292	13
PI > 5 (*n* = 71)	66	5
PI ≤ 5 (*n* = 872)	859	23
DF% > 50 (*n* = 850)	827	23
DF% ≤ 50 (*n* = 103)	98	5

and high volume (Q_{mean} > 20 ml/min, PI ≤ 5 and DF% > 50%). In our study, for each TTFM parameter cut-off, there were significantly more normal grafts than failed grafts (χ^2 $p < 0.0001$). Among the normal grafts, there were similar proportions of normal grafts in the Q_{mean}, PI, and DF% groups (*p* = 0.8390, 0.7440, and 0.8811, respectively). As for the failed grafts, there were similar proportions for Q_{mean} and DF% groups (*p* = 0.1080 and 0.2402, respectively), but there were slightly more failed grafts in the PI > 5 (6.6%) cut-off group than PI ≤ 5 (2.6%) (χ^2 = 4.021, *p* = 0.0449) (Table V).

Multivariate analysis predicting graft failure in all CABG patients

Sociodemographic factors, presence of coronary artery disease risk factors, history of cardiovascular events, preoperative cardiac function, renal function, intraoperative perfusion data, and status of coronary flow dominance were considered for multivariate analysis due to their association with graft failure in this model for all 279 CABG patients. Univariate analysis indicated that 6 variables were significant for graft failure: sociodemographic status – gender; history of cardiovascular events – congestive heart failure, cardiac arrest and cardiogenic shock; and renal function – chronic renal disease/renal insufficiency and on dialysis. Of these 6 variables, 3 were significant associative factors with graft failure as an outcome (Table VI). Female patients (OR = 2.56, *p* = 0.0310) and patients with congestive heart failure (OR = 2.70, *p* = 0.0252) were significantly associated with a higher risk of graft failure. The absence of chronic renal diseases or renal insufficiency (OR = 0.389, *p* = 0.0344) lowers the odds of graft failure by 61%.

Multivariate analysis predicting graft failure in CABG patients with post-surgical CAG

Sociodemographic factors, presence of coronary artery disease risk factors, history of cardiovascular events, pre-operative cardiac function, renal function, intra-operative perfusion data, status of coronary flow dominance, presence of post-CABG adverse outcomes, presence of post-CABG impaired renal function, and presence of MACE were considered for multivariate analysis due to their association with graft failure in this model for 26 patients with post-operative CAG. Univariate analysis of these variables indicated that the renal function (on dialysis) and presence of post-CABG adverse outcomes (specifically, congestive heart failure) were significant for graft failure (Table VII).

Multivariate analysis predicting MACE

Recurrent angina, death, and myocardial infarction are examples of MACE that can be a result of

Table VI. Multivariate logistic regression models predicting failed graft as an outcome for all grafts in all CABG patients (*n* = 279)

Variables	Regression (SE)	Odds ratio (95% CI)	*P*-value
Sociodemographic variables:			
Female	0.9413 (0.4363)	2.563 (1.043, 5.889)	0.0310*
Medical history of cardiovascular events:			
Congestive heart failure	0.9916 (0.4431)	2.696 (1.093, 6.340)	0.0252*
Cardiac arrest	1.541 (1.162)	4.668 (0.4361, 39.46)	0.1849
Cardiogenic shock	1.415 (1.142)	4.118 (0.3856, 31.44)	0.2150
Renal function:			
Renal insufficiency/chronic renal disease	–0.9432 (0.4457)	0.389 (0.1620, 0.9516)	0.0344*
On dialysis	0.1688 (0.7087)	1.184 (0.2558, 4.363)	0.8117

Table VII. Multivariate logistic regression models predicting failed graft as an outcome for all grafts in 26 patients with post-operative CAG

Variable	Regression (SE)	Odds ratio (95% CI)	*P*-value
Demographics:			
On dialysis	0.9950 (0.7887)	2.705 (0.5765 to 13.68)	0.2071
Post-operative outcomes:			
Congestive heart failure	–1.033 (0.6362)	0.3559 (0.09184 to 1.160)	0.1044

graft failure. In this study, they were considered as outcome variables. Sociodemographic factors, presence of coronary artery disease risk factors, history of cardiovascular events, pre-operative cardiac function, renal function, intra-operative perfusion data, status of coronary flow dominance, presence of post-CABG adverse outcomes, presence of post-CABG impaired renal function, presence of MACE, and TTFM values were considered in the multivariate analysis (Table VIII).

There were 4 significant associative factors with recurrent angina as an outcome. Patients with a history of percutaneous coronary intervention or stent insertion (OR = 23.10, p = 0.0410), higher

Table VIII. Logistic regression predicting MACE as an outcome for CABG patients with relook CAG

Predictor variables	Outcomes		
	Recurrent angina	Death	Myocardial infarction
Sociodemographic variables:			
Age	n/s (0.4801; 0.9544)	n/s (0.5263; 1.045)	n/s in Univariate
Body mass index	n/s (0.0793; 0.8216)	n/s in Univariate	n/s in Univariate
Gender (female)	n/s in Univariate	* in Univariate; N/A in Multivariate	n/s in Univariate
Smoking status	n/s in Univariate	n/s in Univariate	n/s in Univariate
Diabetes mellitus	n/s (0.0603; 0.0453)	n/s (0.8857; 0.8071)	n/s in Univariate
Coronary artery disease risk factors:			
Hyperlipidaemia	N/A	N/A	N/A
Hypertension	N/A	N/A	N/A
Peripheral vascular disease	n/s in Univariate	n/s in Univariate	N/A
Medical history of cardiovascular events:			
Myocardial infarction	N/A	N/A	N/A
Stable angina	n/s in Univariate	n/s in Univariate	n/s in Univariate
Congestive heart failure	n/s (0.5187; 0.5296)	n/s (0.0716; 6.513)	n/s in Univariate
Percutaneous coronary intervention (PCI) or stents inserted	* (0.0410; 23.10)	n/s in Univariate	* (0.0262; 5.542)
Pre-operative intra-aortic balloon pump (IABP) inserted	n/s in Univariate	n/s in Univariate	n/s in Univariate
Unstable angina	n/s (0.0919; 12.40)	n/s in Univariate	N/A
Transient ischaemic attack/stroke	n/s in Univariate	n/s in Univariate	N/A
Cardiac arrest	N/A	N/A	N/A
Pre-operative cardiogenic shock	N/A	N/A	N/A
Preoperative cardiac function:			
Pre-operative left ventricular ejection fraction (%)	* (0.0215; 1.083)	n/s (0.4523, 0.9324)	n/s in Univariate
Status of coronary flow dominance:			
Left coronary dominance	* (0.0181, 11.04)	n/s in Univariate	n/s in Univariate
Renal function:			
Chronic renal disease/ renal insufficiency	n/s in Univariate	n/s in Univariate	* (0.0094; 0.2713)
On dialysis	n/s in Univariate	n/s in Univariate	N/A

Table VIII. Cont.

Predictor variables	Outcomes		
	Recurrent angina	Death	Myocardial infarction
Intraoperative CABG surgery data:			
Off-pump surgery (N)	n/s in Univariate	n/s in Univariate	n/s in Univariate
On-pump arrested heart surgery	n/s in Univariate	n/s in Univariate	n/s in Univariate
On-pump beating heart surgery	n/s in Univariate	n/s in Univariate	n/s in Univariate
Post-CABG adverse cardiac-related outcomes:			
Arrhythmia	n/s in Univariate	n/s (0.8506; 0.7663)	n/s in Univariate
Cardiac arrest	N/A	n/s (0.1024; 10.570)	n/s in Univariate
Post-operative intra-aortic balloon pump (IABP)	*(0.0247; 0.002896)	n/s (0.4512; 2.967)	n/s in Univariate
Congestive heart failure	n/s in Univariate	n/s in Univariate	n/s in Univariate
Cardiogenic shock	n/s in Univariate	n/s (0.4557; 3.191)	n/s in Univariate
Post-operative extracorporeal membrane oxygenation (ECMO)	N/A	* in univariate; N/A in multivariate	n/s in Univariate
Transient ischaemic attack/stroke	n/s in Univariate	n/s in Univariate	n/s in Univariate
Post-CABG impaired renal function:			
Acute kidney injury (N)	n/s in Univariate	n/s in Univariate	N/A
On post-op dialysis (Y)	n/s in Univariate	n/s in Univariate	n/s in Univariate
Transit time flow measurement (TTFM) parameters:			
Q_{mean} [ml/min]	n/s in Univariate	n/s in Univariate	* (0.0057; 0.9565)
PI	n/s in Univariate	n/s in Univariate	n/s in Univariate
DF%	n/s in Univariate	n/s in Univariate	n/s in Univariate

**Significance in the multivariate model. The first number in the parentheses indicates the p-value for significance of the variable, while the second number indicates the odds ratio. N/A – data are not available due to perfect separation or they are linearly dependent.*

preoperative left ventricular ejection fraction (%) (OR = 1.083, p = 0.0215), and left coronary dominance (OR = 11.04, p = 0.0181) were significantly associated with a higher risk of angina. Alternatively, having a post-operative IABP (OR = 0.0029, p = 0.0247) was associated with a lower risk of angina. With myocardial infarction as an outcome, a history of percutaneous coronary intervention or inserted stent (OR = 5.542, p = 0.0262) was associated with an increased risk. On the other hand, the absence of renal disease and renal insufficiency (OR = 0.2713, p = 0.0094) reduced the risk of myocardial infarction. Q_{mean} was also a significant predictor, with a 5% increase in risk of death for every unit increase in Q_{mean} (ml/min). With death as an outcome, there were no significant predictors in the multivariate model.

Discussion

In this study, LIMA-LAD was the most widely used graft to target vessel combination (28.2%) in all the identified grafts. LIMA has been established as the cornerstone for bypassing lesions of the LAD, due to the advantages in its anatomical location, which allows better blood flow and resistance to atherosclerosis in comparison to other grafts [17, 18]. Better blood flow in arterial grafts, especially LIMA, is reported in this study, in which arterial grafts have significantly lower PI and higher DF% than venous grafts. Our study also showed that right-sided grafts had lesser blood filling as indicated by lower DF%, and these were grafts inserted into the RCA, and almost all were sourced from venous grafts (n = 245/247; 99.2%). Nonetheless, a venous graft was the most commonly used graft (66.2%) due to its relative ease in harvesting and lower risk of iatrogenic injury during harvesting [19]. Despite LIMA being perceived as superior to a venous graft, the current graft to target vessel combination is in line with best international practices, which contributed to increased patency and improved survival rates over time [18, 20], which is consistent with the findings in our study of low prevalence of graft failure (n = 28/953; 2.9%).

In terms of TTFM characteristics with respect to function, there were no significant differences in Q_{mean}, PI, and DF% between normal and failed grafts in our study. This could be due to a limitation in this study where grafts were defined as failed only upon confirmation at follow-up CAG, while grafts from patients who did not present with post-surgical ischaemic symptoms were not subjected to confirmation CAG and were deemed as normal. This can result in normal grafts being over-reported and, conversely, asymptomatic failed grafts being under-reported. While the degree of over- or under-reporting is not known in this study, there were significantly more normal grafts than failed grafts for all TTFM parameter cut-offs. Several studies utilizing confirmation CAG as a follow-up assessment of graft patency for all patients, regardless of their asymptomatic or symptomatic status, reported that TTFM parameters are associated with graft function, whereby high Q_{mean}, low PI, and high DF% are associated with a decreased risk of graft failure [8, 21–25].

Among the 3 TTFM parameters, the likelihood of failed grafts is only associated with PI. There were significantly more failed grafts in the PI > 5 than in the PI ≤ 5 cut-off group. Therefore, PI is more indicative of grafts failing than Q_{mean} or DF%. This is in accordance with the conclusions from most studies, which reported PI as a significant marker for worse graft function and outcomes [24, 26, 27]. Kieser TM *et al.* concluded that PI when measured using TTFM is a valuable tool for assessing the adequacy of arterial grafts and in predicting post-CABG adverse events, especially operative mortality, which were significantly higher in patients with grafts with a high PI [24]. Jokinen *et al.* also found that among all the parameters measured by TTFM, PI was the most applicable tool for day-to-day clinical practice [27]. However, they recommended that the decision to revise a graft cannot be set on the basis of the TTFM result alone. They also found that TTFM predicted graft failure within 6 months after CABG but did not predict the long-term outcome [27].

Reports also highlighted that the main limitation of TTFM is the lack of standard interpretation of the TTFM parameters to establish which graft can fail in the post-operative period [25, 27]. Tokuda *et al.* reported that TTFM provided a good prognostic index, both in the immediate term and in the midterm follow-up [22]. They proposed that a graft with intra-operative lower mean flow (Q_{mean}) and especially with a high diastolic filling (DF%) should be carefully monitored, even if it was initially anatomically patent.

While more males underwent CABG surgery, being female is significantly associated with higher risk of graft failure; this is consistent with literature that reported that females are at higher risk of worse outcomes post-CABG such as mortality [28]. Our findings also found that having a medical history of congestive heart failure is also significantly associated with higher risk of graft failure, while the absence of renal insufficiency or chronic renal disease has a protective effect. Given that lifestyle has a chronic impact on cardiac and renal health, future studies should investigate lifestyle factors among males and females who have undergone CABG to determine if lifestyle has an impact on post-surgery results.

A history of percutaneous coronary intervention, stent insertion, or left coronary dominance significantly increased the risk of recurrent angina. It has been noted that recurrent angina after coronary angioplasty procedures is a common finding often reported by cardiologists [29]. On the other hand, having a post-operative IABP has a protective effect because it reduces the likelihood of angina post-surgery. This could be explained by IABP increasing myocardial oxygen perfusion and cardiac output, which in turn reduces myocardial ischaemia [30]. However, it was noted that for a unit increase in pre-operative left ventricular ejection fraction, there was an 8% increase in risk of angina, which is unexpected because a high ejection fraction suggests good left ventricular function, which equates to improved systematic blood flow as well as resulting in greater blood flow to the myocardium.

A history of percutaneous coronary intervention or stent insertion increases the risk of angina and myocardial infarction. A surprising finding in this study is the increased risk for myocardial infarction for each unit increase in Q_{mean}, because faster and greater blood-flow across a graft as indicated by a higher Q_{mean} would be expected to reduce the risk of ischaemia in the myocardium. An absence of medical history of renal insufficiency or chronic renal disease was shown to reduce the risk of myocardial infarction. This suggests that renal function plays a significant role in terms of cardiac-associated outcomes after CABG surgeries.

In conclusion, this study provides an overview of the existing profiles of graft types and TTFM from CABG surgeries in Brunei Darussalam. In summary, this study shows that patency of graft is influenced by gender, congestive heart failure, and renal function, while major adverse cardiac events are collectively influenced by history of coronary intervention and renal function. While TTFM is not indicative of failed graft upon ischaemic signs, patient comorbidities were informative. Despite this, PI as a parameter for predicting long-term post-operative graft failure appears promising. Follow-up studies should include a larger sample size of patients to assess correlation of graft failure over a 5–10-year follow-up period post-CABG.

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Conflict of interest

The authors declare no conflict of interest.

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