Predictive value of graft patency and major adverse cardiac and cerebrovascular events (MACCEs) in coronary artery bypass grafting (CABG) based on Fourier transform (FFT)

Yanxiong Jia[1,2], Hongyi Xu[3], Pixiong Su[2], Jie Gao[2], Song Gu[2], Yan Liu[2], Xiangguang An[2], Jun Yan[2], Xitao Zhang[2]

[1]Capital Medical University, Beijing, China; [2]Department of Cardiovascular Surgery, Beijing Chao-yang Hospital, Capital Medical University, Beijing, China; [3]Beijing Institute of Electronic System Engineering, Beijing, China

Contributions: (I) Conception and design: Y Jia, H Xu; (II) Administrative support: Y Liu, P Su; (III) Provision of study materials or patients: Y Jia, J Gao, S Gu, X An, J Yan, X Zhang, P Su; (IV) Collection and assembly of data: Y Jia; (V) Data analysis and interpretation: Y Jia, H Xu, J Gao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Pixiong Su, MD. Department of Cardiovascular Surgery, Beijing Chao-Yang Hospital, 8 Gong Ti South Road, Chaoyang District, Beijing 100020, China. Email: supixiong1130@163.com.

Background: Transit time flow measurement (TTFM) is widely used in coronary artery bypass grafting (CABG); however, its predictive value is unclear. We aimed to identify new factors to evaluate graft quality using fast Fourier transform (FFT).

Methods: Intraoperative and postoperative 2-year follow-up data of 114 patients undergoing CABG from January 2017 to December 2018 were collected. The TTFM waveform was transformed by FFT. Mean graft flow (MGF), pulse index, the amplitude of the main wave in FFT (H_0), the amplitude of the first harmonic (H_1), H_0/H_1, and the frequency of the first harmonic (P) were analyzed as predictors using logistic regression and receiver operating characteristic (ROC) curves.

Results: The overall graft patency rate was 80.3%, and the incidence of major adverse cardiac and cerebrovascular events (MACCEs) was 14.9%. The results demonstrate that compared with the graft failure group, MGF, H_0, and H_1 were higher, but H_1 and P were lower in the patent group. With univariate and multivariate logistic regression analyses, the decrease in H_0 and H_1 and the increase in P were independent risk factors for graft failure, while the decrease in MGF and the increase in H_0/H_1 were only statistically significant with a univariate analysis. In the cardiovascular events group, the increase in P was an independent risk factor. With a ROC curve analysis, MGF, H_0, H_1, H_0/H_1, and P predicted graft failure, while only P predicted cardiovascular events. None of the indicators showed predictive value for MACCEs.

Conclusions: TTFM waveforms after FFT can be used to evaluate graft quality and cardiovascular events, but have no predictive value for MACCEs.

Keywords: Coronary artery bypass; waveform analysis; fast Fourier transform (FFT); graft patency rate; major adverse cardiac and cerebrovascular events (MACCEs)

Introduction

Coronary artery bypass grafting (CABG) plays a vital role in treating coronary heart disease (1-3). The long-term prognosis of patients who have undergone surgery is the focal point of cardiac surgeons. We regularly use the graft patency rate and major adverse cardiac and cerebrovascular events (MACCEs) to evaluate CABG quality. Transit time flow measurement (TTFM) is a method used to evaluate anastomosis quality (4,5). As it requires very few hardware
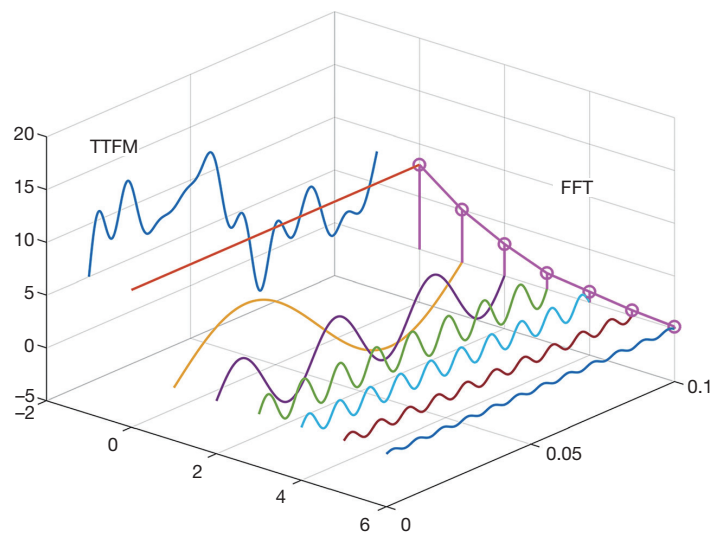
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Figure 1 The principle of the fast Fourier transform. TTFM, Transit time flow measurement; FFT, fast Fourier transform.

facilities and little personal ability, it is convenient for intraoperative application. Guidelines (2) recommend a mean graft flow (MGF) of >20 mL/h and a pulse index (PI) of <5 as good indicators for evaluating graft anastomosis. Amin *et al.* (6) proposed that TTFM is an accurate indicator of graft flow in CABG. Di Giammarco *et al.* (7) found that the MGF rate, the PI, and systolic reverse flow (SRF) predict graft failure.

However, while many studies have confirmed the validity of TTFM, some doubts remain. For example, Thuijs *et al.* (8) conducted a meta-analysis that showed that only 25% of problem grafts recognized by TTFM actually underwent revascularization. Desai *et al.* (9) found that TTFM had only 25% sensitivity and 98% specificity for grafts with >50% stenosis or occlusion. Singh *et al.* (10) found no significant difference in graft patency rate between TTFM and non-TTFM groups. Quin *et al.* (11) found that the association between TTFM use and clinical outcomes is uncertain.

Some studies have used methods, such as the analysis of TTFM waveforms, to improve the predictive value of TTFM. Takami *et al.* (5) introduced a method to transform TTFM waveforms using fast Fourier transform (FFT). They found that FFT waveforms had a good predictive value of graft patency. The greatest value of FFT is that it quantifies TTFM waveforms. The shape of blood flow waveforms differs in the time domain, but FFT can transform these waveforms into the frequency domain. As waveforms can be represented as the number of wave peaks with different frequencies in the frequency domain, they are

easy to analyze (*Figure 1*). In Takami's (5) study, only F_0/H_1 (the ratio of the first 2 harmonics) was used as a predictor for graft failure, but many other FFT waveform parameters may also have predictive value. In this study, we sought to explore the predictive value of these factors for graft prognosis and to verify whether FFT can feasibly be used to evaluate graft quality.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi. org/10.21037/jtd-21-178).

Methods

Study population

A total of 114 patients who underwent CABG at Beijing Chao-Yang Hospital from January 2017 to December 2018 were enrolled in this study and followed up with for 2 years. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by local research ethics board of Chaoyang Hospital (No. 2018-k-308) and individual consent for this retrospective analysis was waived. Notably, 6 patients did not wish to complete the follow-up examinations; thus, there was a follow-up loss rate of 5%. Patients were included in this study if they underwent a left internal mammary artery (LIMA) or a saphenous vein graft (SVG) surgery, and were excluded if they underwent a concomitant valvular or other surgery, or those with hemodynamic instability, or those undergoing emergency operations.

Of the 114 patients, 85 were male, and 29 were female. Patients had an average age of 61.82±8.53 years. The average follow-up time was 24.89±6.91 months, and the average graft number was 2.83±0.69. Of the patients, 65 were smokers, 46 had diabetes mellitus, 74 had hypertension, 81 had hyperlipidemia, 2 had chronic renal insufficiency, 5 had peripheral vascular disease, 13 had previous cerebrovascular accidents, 30 had a previous myocardial infarction and 19 had undergone previous percutaneous coronary intervention.

Surgical technique

The same team of surgeons performed all surgeries. Each target vessel for CABG had more than 70% stenosis, which was confirmed by coronary angiography. All the patients provided written informed consent before surgery. All patients underwent elective CABG. The LIMA was obtained directly, and the great saphenous vein was obtained endoscopically. The LIMA was anastomosed to the left anterior descending (LAD) branch. The distal great SVG was anastomosed to the non-LAD artery or to the LAD artery when necessary, and the proximal SVG was anastomosed to the ascending aorta. TTFM was measured after anastomosis, and the MGF rate and the PI were obtained. Measurements were taken when patients had stable circulation, and the average arterial pressure was kept close to the physiological level. An appropriate TTFM probe was selected to fit the graft without squeezing. Papaverine was used when the LIMA was measured. The patients were heparinized during collection and were re-tested after protamine neutralization. The MATrix LABoratory (MATLAB, 2017a) was used to perform the FFT processing of the TTFM waveforms, obtain FFT image, and measure the amplitude of the main wave (H_0), the amplitude of the first harmonic (H_1), the frequency of the first harmonic (P), and H_0/H_1.

Follow-up

In our study, the follow-up examination mainly focused on patients' symptoms, medication, and imaging. Patients' symptoms were monitored, and their computed tomography coronary angiography (CTCA) results were obtained up to 2 years after surgery, and MACCEs and graft lesions were recorded. 2 cardiac surgeons and 2 radiologists evaluated the CTCA results according to the Fitzgibbon criteria (12). Grafts with no stenosis or <50% stenosis were defined as

the patency group, and the rest were defined as the graft failure group. The predictive value of the above parameters for graft failure and MACCEs was also analyzed.

Statistical analysis

In the statistical analysis of graft failure, an individual graft was defined as a unit of analysis. For MACCEs, grafts were used as the unit to analyze FFT and TTFM parameters, while patients were used as the unit in other analyses. SPSS 26.0 was used to perform t-tests, non-parametric tests, binary logistic regression analysis, and receiver operating characteristic (ROC) curve analysis. A P value of <0.05 was considered statistically significant.

Results

Table 1 shows patients' baseline characteristics. A total of 320 grafts were used in 114 patients with a patency rate of 80.3% (257/320). The LIMA and SVG graft patency rates were 89.4% (101/113) and 75.4% (156/207), respectively. Based on a standard that required an MGF >20 mL/min and a PI <5, only 7.18% (23/320) of the grafts and 16.67% (19/114) of the patients were required to undergo revision. All the LIMAs were anastomosed to the LAD artery. The SVG grafted patency rate to a different target coronary artery was not significantly different (χ^2=7.735, P=0.357). There were 15 cases of repeat revascularization, 8 cases of myocardial infarction, 2 cases of stroke, and no cases of all-cause death. A total of 17 MACCEs occurred, with a rate of 14.9%.

Table 2 shows the TTFM and FFT data of different outcomes, and *Figure 2* compares the patency and graft failure groups with FFT. When defining graft failure as a grouping variable, MGF (P=0.020), H_0 (P<0.001), H_1 (P<0.001), H_0/H_1 (P<0.001), and P (P<0.001) were significantly different between the patency and graft failure groups, but the PI (P=0.056) was not. When MACCEs was defined as a grouping variable, there was no significant difference in any of the two groups' parameters between the 2 groups.

The results of the binary logistic regression analysis of graft failure and MACCEs as dependent variables are shown in *Table 3*. Univariate and multivariate regression models were built. In relation to the univariate regression analysis, a decrease in MGF [odds ratio (OR) 0.98, 95% confidence interval (CI): 0.96–1.00, P=0.021], H_0 (OR 0.92, 95% CI: 0.90–0.95, P<0.001), H_1 (OR 0.45, 95% CI: 0.36–0.56,

Table 1 baseline characteristics

Variables	Study population	No graft failure	Graft failure	P
Female (n, %)	29 (25.44)	11 (23.40)	18 (26.87)	0.676
Age (years)	61.82±8.53	63.60±9.12	60.58±7.92	0.063
Smoking (n, %)	65 (57.02)	26 (55.32)	39 (58.21)	0.759
Diabetes (n, %)	46 (40.35)	19 (40.43)	27 (40.30)	0.989
Hypertension (n, %)	74 (64.91)	32 (68.09)	42 (62.69)	0.552
Hyperlipemia (n, %)	81 (71.05)	32 (68.09)	49 (73.13)	0.558
Chronic renal insufficiency (n, %)	2 (1.75)	2 (4.26)	0 (0)	0.328
PVD (n, %)	5 (4.39)	1 (2.13)	4 (5.97)	0.602
Previous cerebrovascular accidents (n, %)	13 (11.40)	7 (14.89)	6 (8.96)	0.326
Previous MI (n, %)	30 (26.32)	14 (29.79)	16 (23.88)	0.481
Previous PCI (n, %)	19 (16.67)	7 (14.89)	12 (17.91)	0.671
Number of grafts	2.83±0.69	2.77±0.87	2.88±0.54	0.472
Follow time (month)	24.89±6.91	25.45±7.25	27.91±8.42	0.385

*, continuous variables with normal distribution are presented as mean ± SD unless otherwise noted. PVD, peripheral vascular disease; MI, myocardial infarction; PCI, percutaneous coronary intervention

Table 2 TTFM and FFT data of graft failure and MACCEs

Parameters*	Patency (N=257)	Graft failure (N=63)	P	MACCEs	NO MACCEs	P
PI	2.85±1.49	4.11±9.29	0.056	3.36±6.77	3.15±1.93	0.759
MGF	22.99±12.91	19.60±11.32	0.020	22.58±12.67	20.16±11.91	0.103
H_0	43.00±13.67	33.06±8.05	<0.001	40.09±13.41	38.24±11.70	0.230
H_1	3.45±1.34	2.17±1.20	<0.001	3.02±1.42	2.95±1.46	0.673
H_0/H_1	16.45±16.00	33.37±75.75	<0.001	23.53±17.81	20.15±22.24	0.311
P	2.46±0.94	3.14±0.81	<0.001	2.66±0.94	2.78±0.98	0.290

*, continuous variables with normal distribution are presented as mean ± SD unless otherwise noted. PI, pulse index; MGF, mean graft flow; H_0, the amplitude of the main wave; H_1, the amplitude of the first harmonic; P, the frequency of the first harmonic; MACCEs, major adverse cardiac and cerebrovascular events.

P<0.001), and an increase in H_0/H_1 (OR 1.02, 95% CI: 1.01–1.03, P<0.001) and P (OR 2.43, 95% CI: 1.78–3.33, P<0.001) were identified as independent risk factors affecting graft failure, but the PI was not. In relation to the multivariate regression analysis, a decrease in H_0 (OR 0.92, 95% CI: 0.89–0.95, P<0.001) and H_1 (OR 0.43, 95% CI: 0.32–0.58, P<0.001) and an increase in P (OR 2.28, 95% CI: 1.62–3.20, P<0.001) were identified as independent risk factors. These factors were not risk factors for MACCEs. *Table 4* sets out the multivariate binary logistic regression analysis results for the clinical factors of graft failure

and MACCEs. The postoperative clopidogrel was an independent risk factor for graft failure (OR 2.43, 95% CI: 1.07–5.51, P=0.033). The proportion of graft failure (OR 1.03, 95% CI: 1.01–1.05, P=0.002) was an independent risk factor for MACCEs.

To explore the predictive value of these indicators for cardiovascular events, we performed a logistic regression and ROC curve analyses in which repeat revascularization and myocardial infarction were the dependent variables. In relation to the logistic regression, only an increase in P was an independent risk factor for repeat revascularization
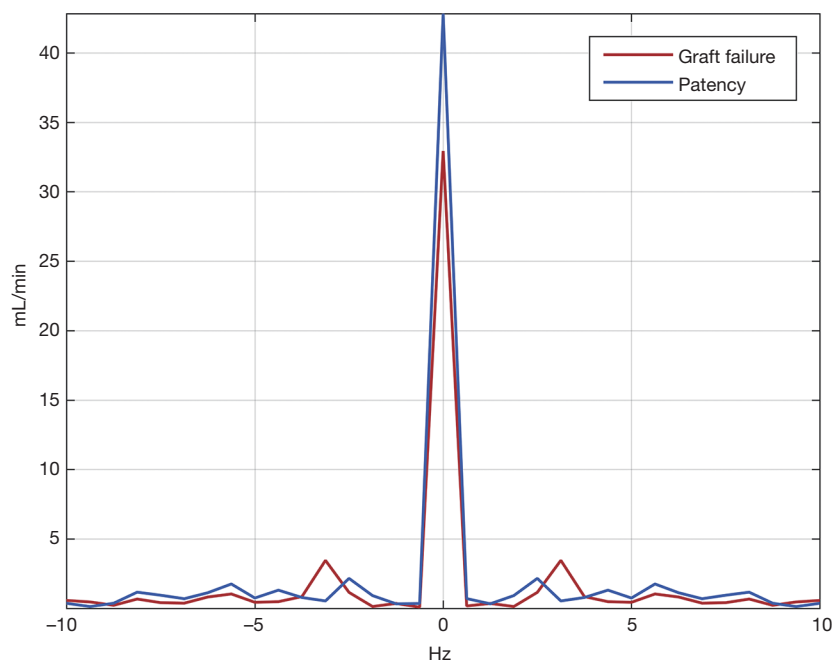
Figure 2 The comparison between the patency and graft failure groups with FFT. The figure shows the FFT curve of the graft failure group (red line) and the patency group (blue line). FFT, fast Fourier transform.

(univariate: OR 1.66, 95% CI: 1.16–2.39, P=0.006; multivariate: OR 1.64, 95% CI: 1.13–2.36, P=0.008) and myocardial infarction (univariate: OR 1.90, 95% CI: 1.21–2.97, P=0.005; multivariate: OR 1.86, 95% CI: 1.18–2.93, P=0.008).

Table 5 and *Figure 3* show the results of the ROC curve analysis. The cut-off values for predicting graft failure were as follows: MGF, >23.90 mL/min (P=0.026), H_0, >39.31 mL/min (P<0.001), H_1, >3.20 mL/min (P<0.001), H_0/H_1, <17.41 (P<0.001), and P<2.99 Hz (P<0.001). However, the PI was not a significant predictor of graft failure (P=0.259). In the MACCEs group, none of the parameters had predictive value (P>0.050). In the repeat revascularization and myocardial infarction groups, only P had predictive value with cut-off values of 3.24 Hz (P=0.008) and 3.10 Hz (P=0.037), respectively.

Discussion

TTFM is an important method to assess intraoperative graft quality in CABG. The main indicators of TTFM include MGF, the PI, the diastolic filling index, and SRF. These parameters are calculated using a formula on the TTFM blood flow waveform to reflect blood flow characteristics in grafts. Among these parameters, MGF and the PI are the most important in a clinical setting. In a retrospective analysis of the ROOBY study, Quin *et al.* (13) found that the re-graft rate was significantly higher in the low MGF group (<20 mL/min) than the high MGF group (>20 mL/min). Lehnert *et al.* (14) conducted a 1-year follow-up study of grafts and found a significant correlation between MGF and graft failure. Concerning the PI, Jokinen *et al.* (15) and Di Giammarco *et al.* (16) reported that a PI of >3 could be used as a predictor of graft failure, while Tokuda *et al.* (17) reported that a PI of >5 could be used as a cut-off. In the present study, grafts in the patency group had a higher MGF rate (P=0.020) than those of the graft failure group, but the difference in the PI was not significant (P=0.056) between the two groups. The logistic regression and ROC curve analyses showed that the PI was also not related to graft failure. Indeed, the formula for PI shows that it is inversely proportional to MGF. Except for the MGF rate, the PI's factor is the difference between the maximum and minimum blood flow. High sharp waves and negative blood flow can increase this difference. These features are more alarming to surgeons than MGF. Quin *et al.* (13) also confirmed that the re-anastomosis rate increased with an increase in the PI. No significant difference in the PI was found between the two groups; however, the average PI in the patency group was lower than that of the graft failure

Table 3 The results of the binary logistic regression analysis of graft failure and MACCEs

Dependent	Covariant	Univariate				Multivariate			
		P	OR	95% CI		P	OR	95% CI	
				Lower	Upper			Lower	Upper
Graft failure	PI	0.071	1.12	0.99	1.27	0.270	1.11	0.92	1.35
	MGF	0.021	0.98	0.96	1.00	0.384	0.99	0.96	1.01
	H_0	<0.001	0.92	0.90	0.95	<0.001	0.92	0.89	0.95
	H_1	<0.001	0.45	0.36	0.56	<0.001	0.43	0.32	0.58
	H_0/H_1	0.001	1.02	1.01	1.03	0.823	1.00	0.99	1.01
	P	<0.001	2.43	1.78	3.33	<0.001	2.28	1.62	3.20
MACCEs	PI	0.762	0.99	0.95	1.04	0.513	0.98	0.93	1.04
	MGF	0.105	0.98	0.96	1.00	0.116	0.98	0.96	1.00
	H_0	0.230	0.99	0.97	1.01	0.502	0.99	0.97	1.01
	H_1	0.672	0.97	0.82	1.14	0.658	0.96	0.79	1.16
	H_0/H_1	0.564	1.00	0.99	1.00	0.503	1.00	0.99	1.01
	P	0.290	1.14	0.89	1.46	0.336	1.13	0.88	1.45
Repeat revascularization	PI	0.896	1.00	0.95	1.06	0.782	0.99	0.94	1.05
	MGF	0.239	0.98	0.95	1.01	0.281	0.98	0.95	1.01
	H_0	0.138	0.98	0.95	1.01	0.613	0.99	0.96	1.02
	H_1	0.879	1.02	0.81	1.28	0.666	0.93	0.66	1.31
	H_0/H_1	0.239	0.99	0.96	1.01	0.288	0.98	0.95	1.01
	P	0.006	1.66	1.16	2.39	0.008	1.64	1.13	2.36
MI	PI	0.788	0.98	0.84	1.14	0.785	0.98	0.86	1.12
	MGF	0.592	1.01	0.98	1.04	0.591	1.01	0.98	1.04
	H_0	0.312	0.98	0.95	1.02	0.792	1.00	0.96	1.04
	H_1	0.765	0.96	0.71	1.29	0.486	0.86	0.55	1.32
	H_0/H_1	0.540	0.99	0.97	1.02	0.423	0.99	0.96	1.02
	P	0.005	1.90	1.21	2.97	0.008	1.86	1.18	2.93

MACCEs, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; OR, odds ratio; CI, confidence interval. PI, pulse index; MGF, mean graft flow; H_0, the amplitude of the main wave; H_1, the amplitude of the first harmonic; P, the frequency of the first harmonic.

group. Thus, we believe that a higher MGF rate predicts better graft quality, and while there was no significant difference, a lower PI tends to lead to a better prognosis.

In the present study, we used FFT as a transfer method for TTFM waveforms. *Figure 1* shows that the time domain's blood flow waveform was transformed into the FFT waveform in the frequency domain. The waveform of FFT comprised the main crest (H_0) and many harmonics

(H_1–H_n). In our study, the main crest was equivalent to MGF, but this was a trend, not an equal number. The harmonics reflected the complexity of the TTFM waveform. For example, the sine wave has only 1 harmonic, and the more harmonics, the more complex the wave. The frequency of harmonics also reflected waveform complexity; the higher the frequency, the shorter the period of change, and the lesser the similarity between the waveform and the

Table 4 The results of the binary logistic regression analysis for clinical factors

Variables	Graft failure				MACCEs			
	P	OR	95% CI		P	OR	95% CI	
			Lower	Upper			Lower	Upper
Population data								
Male	0.076	2.47	0.91	6.70	0.996	1.00	0.16	6.07
Age	0.659	0.99	0.96	1.03	0.889	1.00	0.93	1.07
Height	0.135	0.77	0.54	1.09	0.738	1.11	0.59	2.09
Weight	0.181	1.32	0.88	1.99	0.661	0.85	0.41	1.76
Risk factors								
BMI	0.151	0.43	0.14	1.36	0.640	1.61	0.22	11.75
Previous or present smoking	0.638	0.85	0.44	1.66	0.342	0.54	0.15	1.92
Diabetes mellitus	0.738	0.91	0.52	1.59	0.390	1.60	0.55	4.69
Hypertension	0.535	1.22	0.66	2.25	0.197	2.28	0.65	7.95
Hyperlipidemia	0.303	1.38	0.75	2.56	0.925	1.06	0.35	3.19
Chronic renal insufficiency	0.999	0.00	0.00	0.00	0.303	5.69	0.21	155.85
Peripheral vascular disease	0.248	2.25	0.57	8.88	0.370	3.99	0.19	82.60
Previous stroke	0.444	0.72	0.31	1.67	0.187	0.24	0.03	2.02
Previous MI	0.136	0.57	0.27	1.19	0.531	0.62	0.14	2.76
Previous PCI	0.451	1.40	0.59	3.31	0.938	1.07	0.18	6.46
Perioperative data								
Target vessel lesion	0.254	0.96	0.90	1.03	0.531	0.99	0.95	1.03
Target vessel diameter	0.122	0.48	0.19	1.22	0.557	0.73	0.26	2.06
Perioperative myocardial infarction	0.191	0.43	0.12	1.53	0.177	4.93	0.49	50.04
Postoperative atrial fibrillation	0.052	2.66	0.99	7.12	0.718	1.43	0.21	9.86
Follow-up data								
Graft failure of LIMA-LAD					0.295	0.47	0.12	1.93
Proportion of graft failure					0.002	1.03	1.01	1.05
Medication before surgery								
Intravenous nitrates	0.989	1.01	0.51	1.99	0.404	0.58	0.16	2.09
Beta blockers	0.288	1.44	0.74	2.81	0.726	0.80	0.22	2.83
ACEI/ARB	0.517	0.81	0.44	1.52	0.165	0.42	0.12	1.43
Statins	0.869	0.91	0.31	2.71	0.551	1.92	0.22	16.48
Medication after surgery								
Beta blockers	0.590	1.71	0.24	11.97	0.437	0.30	0.01	6.24
ACEI/ARB	0.786	0.91	0.45	1.83	0.979	0.98	0.23	4.27
Statins	0.119	3.00	0.76	11.89	0.625	0.51	0.04	7.52
Aspirin	1.000	1.23	0.00	0.00	1.000	5.35	0.00	0.00
Clopidogrel	0.033	2.43	1.07	5.51	0.556	0.63	0.14	2.94

MACCEs, major adverse cardiac and cerebrovascular events; BMI, body mass index; MI, myocardial infarction; PCI, percutaneous coronary intervention; LIMA, left internal mammary artery; LAD, left anterior descending branch; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; OR, odds ratio; CI, confidence interval.

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Table 5 The results of the ROC curve analysis

Test variable	State variable	AUC	SE	P	95% CI	
					Lower	Upper
Graft failure	PI	0.462	0.034	0.259	0.395	0.529
	MGF	0.575	0.034	0.026	0.509	0.641
	H_0	0.720	0.028	<0.001	0.666	0.775
	H_1	0.766	0.027	<0.001	0.713	0.820
	H_0/H_1	0.625	0.033	<0.001	0.561	0.690
	P	0.707	0.029	<0.001	0.650	0.763
MACCE	PI	0.475	0.035	0.466	0.406	0.543
	MGF	0.562	0.035	0.074	0.494	0.630
	H_0	0.542	0.033	0.220	0.477	0.608
	H_1	0.516	0.035	0.633	0.448	0.585
	H_0/H_1	0.500	0.035	0.994	0.431	0.568
	P	0.474	0.034	0.444	0.406	0.541
Repeat revascularization	PI	0.556	0.049	0.254	0.460	0.652
	MGF	0.571	0.049	0.146	0.474	0.668
	H_0	0.563	0.047	0.196	0.471	0.656
	H_1	0.508	0.046	0.864	0.419	0.598
	H_0/H_1	0.450	0.048	0.302	0.356	0.543
	P	0.630	0.048	0.008	0.537	0.724
MI	PI	0.525	0.065	0.691	0.398	0.652
	MGF	0.520	0.064	0.754	0.394	0.645
	H_0	0.573	0.066	0.241	0.443	0.704
	H_1	0.520	0.060	0.752	0.402	0.638
	H_0/H_1	0.524	0.062	0.706	0.402	0.645
	P	0.631	0.062	0.037	0.509	0.752

MACCEs, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; AUC, area under the curve; SE, standard error; CI, confidence interval. PI, pulse index; MGF, mean graft flow; H_0, the amplitude of the main wave; H_1, the amplitude of the first harmonic; P, the frequency of the first harmonic.

sine wave. As the description of waveform shape has strong subjectivity, there are few studies in this field. We used FFT to transform the shape of the waveform into data that could be analyzed, which was our initial aim.

According to our results, patent grafts tended to have higher H_0 and H_1 values and lower P values. As stated above, H_0 reflected MGF, which is consistent with most studies that state that a higher MGF indicates a better graft quality. H_1 and P reflected the characteristics of the first harmonic. We analyzed the first harmonic because it was the most obvious in the FFT waveform. The sum of harmonic amplitude values is a definite value; thus, a higher H_1 equates to a lower amplitude for the other harmonics. High-frequency harmonics represent more complex TTFM waveforms, such as high sharp waves or tremor waves caused by vasospasm. Concerning amplitude, these harmonics are positively correlated with abnormal waveforms. Thus, in an ideal TTFM waveform, each harmonic
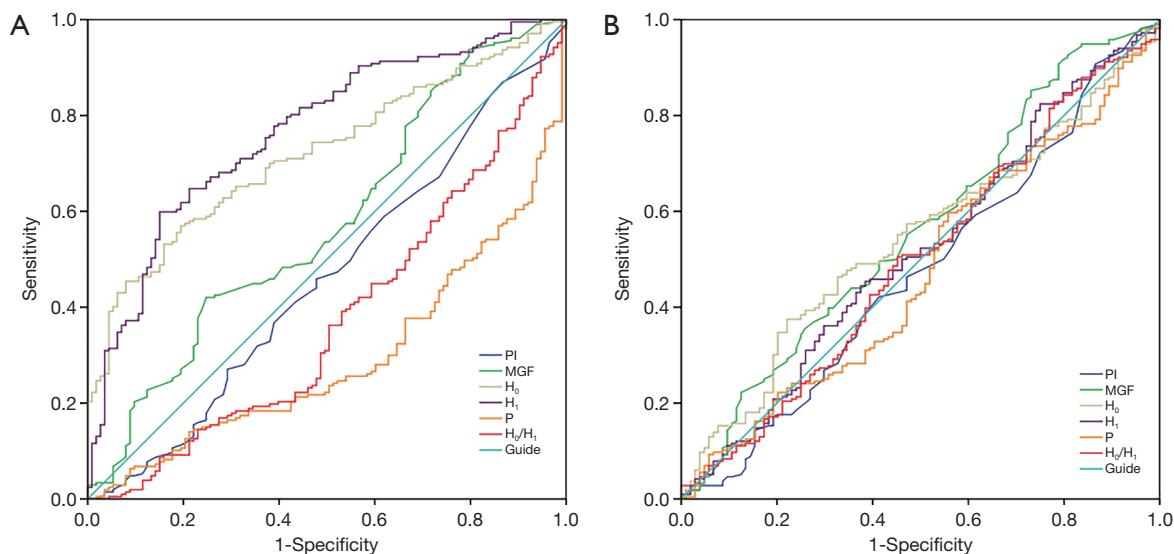
Figure 3 The ROC curve of outcomes after surgery. The ROC curve of graft failure (A) and MACCEs (B). MGF, PI, H_0, H_1, H_0/H_1, and P are using as predictors for analysis. ROC, receiver operating characteristic; MACCEs, major adverse cardiac and cerebrovascular events; PI, pulse index; MGF, mean graft flow; H_0, the amplitude of the main wave; H_1, the amplitude of the first harmonic; P, the frequency of the first harmonic.

frequency and the amplitude beyond the first harmonic should be as low as possible. These characteristics are consistent with the results obtained in our research. H_0/H_1 had predictive value in graft evaluation; however, its accuracy was lower than that of other parameters, and thus its use is not recommended.

In the analysis of MACCEs, none of the indicators showed predictive value. A number of points should be noted. First, it might be because TTFM only reflects graft quality, while MACCEs cover a wider range (11). Second, while some patients had graft failure, no cardiovascular symptoms were observed due to long-term ischemic tolerance or collateral circulation. Third, incomplete revascularization in some patients led to cardiovascular symptoms in the short term after surgery. Finally, the sample size was small; thus, it is possible that the sample was unable to reflect this trend. When we considered cardiovascular events as a dependent variable, we found that the P was a statistically significant predictor of cardiovascular events. These results suggest that graft quality correlates with postoperative cardiovascular events. However, to predict MACCEs, a more comprehensive approach is needed.

The present study had relatively low graft patency rates, which the low revision rate might have caused. Additionally, we believe that patients with symptoms were more likely

to participate in the follow-up examinations, and this bias led to a lower patency rate. Future research will find ways to eliminate any such bias to ensure more valuable data is gathered. We also found consistent with the guideline recommendations; the postoperative clopidogrel was an independent risk factor for graft failure. Thus, it is our view that after CABG, all patients should be routinely treated with dual antiplatelet therapy, except those with antiplatelet contraindications.

The present study had several limitations. First, this study was performed at a single center with a relatively small cohort of patients. Thus, the level of evidence for the conclusion is low. Second, only the LIMA and the SVG were used. Future research should include more graft types. Third, our transform process was based on a MATLAB code that we wrote ourselves. We performed FFT on each TTFM waveform and manually acquired various data in this process. However, as a consequence, the results are not universal and are difficult to replicate. We hope that TTFM instrument manufacturers will realize the value of FFT in the future.

Conclusions

TTFM waveforms that undergo FFT can be used to evaluate graft quality and cardiovascular events. H_0, H_1, and

P are predictive parameters for graft failure, but they have no predictive value for MACCEs. MGF is also a predictor of graft failure, while the PI has no predictive value. We believe that the combination of TTFM measurement and FFT will improve the evaluation accuracy of graft quality in future clinical applications.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by local research ethics board of Chaoyang Hospital (No. 2018-k-308) and individual consent for this retrospective analysis was waived.

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