## **Original Research Article**

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# Intraoperative transit time flow measurement to predict clinical outcomes in patient undergoing on pump coronary artery bypass graft

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## **ABSTRACT**

**Background:** Transit time flow measurement (TTFM) is used for intraoperative graft measurement to estimate graft failure. PI $\leq$ 3 was suggested because it shows lower incidence of early graft failure. Objective of the study was to compare myocardial function and clinical outcomes of patients who underwent coronary artery bypass graft (CABG) surgery, between PI $\leq$ 3 in all grafts (optimal group) and PI >3 in one or more grafts (suboptimal group) by Transit time flow measurement (TTFM).

**Methods:** 90 patients who underwent CABG since June 2012 to December 2014 were included. Patients were classified into 2 groups: Optimal group (n=32) and Suboptimal group (n=58). CABG with intraoperative TTFM was performed as standard. Postoperative outcomes of both groups were compared.

**Results:** Patients whose postoperative EF was increased were found in optimal group more than suboptimal group (62.1% vs 25%, p < 0.001). The patients whose postoperative EF increased equal or more than 5% was found in optimal group more than suboptimal group (73.2% vs 25%, p = 0.002). Suboptimal group found one patient with myocardial infarction but optimal group found none (3.13% and 0%). Postoperative atrial fibrillation and prolong ventilator more than 48 hours were found in suboptimal group more than optimal group (43.75% vs 37.93%, 62.50% vs 37.93%). In midterm, postoperative follow-up, all-cause mortality in suboptimal group was higher than optimal group (3.13% vs 1.72).

**Conclusions:** Optimal group had patients whose postoperative EF significantly increased more than suboptimal group. Tendency of finding postoperative complications in suboptimal group was more than in optimal group.

Keywords: Coronary artery bypass graft, Ejection fraction, Pulsatility index, Transit time flow measurement

#### INTRODUCTION

Coronary artery disease is a major cause of morbidity and mortality in Bhumibol Adulyadej hospital, Bangkok, Thailand. This disease is caused by narrowing of coronary vessels. When blood supplied to myocardium decreases, abnormal contractility of heart occurs. A poor myocardial function may not always represent irreversible myocardial necrosis. Sometimes, poor function may be reversible in hibernated myocardium. Complete revascularisation can reverse myocardial

ischemia to its normal function.<sup>1</sup> Coronary artery bypass graft (CABG) surgery would improve the myocardial function, myocardial perfusion, and functional class of the patients.<sup>2-3</sup> Patency of graft is the important indicator because it could estimate postoperative outcomes of patients.

In the past, pulse sensation was used to assess a patent graft. This method depends on surgeons' experiences. Therefore, instead of using a non-standardized pulse sensation method, transit time flow measurement (TTFM) becomes a more standardized and reliable method to measure intraoperative grafts.

Transit time flow measurement (TTFM) is used to measure flow of graft by ultrasound probe. The machine can calculate flow, resistance, percentage of flow during systolic and diastolic phase. In TTFM, two indicators used to define patency of graft are Diastolic Filling percentage (DF) and pulsatility index (PI). Diastolic filling percentage (DF) is a percentage of blood filling in diastolic phase in grafts. Pulsatility index (PI) is a graft resistance and a strong indicator to estimate intraoperative and postoperative graft failure. Patency of graft is measured as acceptable when DF>50% and PI≤5. When PI>5, it indicates some surgical technique errors such as twist or kink, which should be reassessed until the acceptable level at PI\(\leq 5\). Since Bhumibol Adulyadej Hospital was introduced to the use of TTFM, we currently accept PI≤5. However, some studies suggest using PI\le 3 because it shows lower incidence of early graft failure.4-7

Our study is to prove that PI  $\leq$ 3 in all grafts will have better postoperative outcomes than PI >3 in one or more grafts. And, if the result is different, we will apply this result to our patients.

### Research hypothesis

If pulsatility index (PI) equals or less than 3 in all grafts, myocardial function and postoperative clinical outcomes would be better than PI more than 3 in one or more grafts.

Objectives of the study were to compare myocardial function of patients, who underwent CABG surgery, between PI≤3 in all grafts, and PI>3 in one or more grafts, to study of postoperative outcomes during hospital stay: Major adverse cardiac events (MACE) such as atrial fibrillation (AF), and myocardial infarction (MI), prolong ventilator, and duration of hospital stay, to study of postoperative outcomes during follow-up terms: all-cause mortality and incidence of readmission for cardiac events

## Expected outcomes

Primary expected outcomes

Patients whose PI≤3 in all grafts would have better myocardial function than whose PI>3 in one or more grafts.

Secondary expected outcomes

Patients whose PI $\leq$ 3 in all grafts would have lower, lower rate of prolong ventilator, and shorter duration of hospital stay than patients whose PI>3 in one or more grafts. Patients whose PI  $\leq$  3 in all grafts would have lower all-cause mortality and incidence of readmission for cardiac events than patients whose PI > 3 in one or more grafts.

#### **METHODS**

All consecutive 151 patients of Bhumibol Adulyadej Hospital who underwent CABG surgery with graft flow measurements since June 2012 to December 2014 were a population of the research. However, 61 patients were excluded because 53 patients had loss follow-up, 1 patient had been off pump CABG surgery, and 7 patients were operated CABG with valve replacement. So, only 90 patients were qualified as our sample.

Ninety patients were classified into 2 groups: Optimal group and Suboptimal group. Optimal group was a group of patients with PI≤3 in all grafts (58 patients). Suboptimal group was a group of patients with PI>3 of one or more grafts (32 patients).

Pilot study was used to find a least acceptable sample size by randomize 12 patients in the follow-up program during June to August of 2014 from optimal group (6 patients) and Suboptimal group (6 patients).

The result of study showed 66.67% (4/6) of patients in optimal group had postoperative EF increased. Whereas, 33.33% (2/6) of patients in suboptimal group had postoperative EF increased.

Sample size was calculated from this formula as shown below.

$$n = \frac{2[(Z_{\alpha} + Z_{\beta})^{2} p(1-p)]}{(P_{1} - P_{2})^{2}}$$

When  $\alpha$  equals to 0.05,  $\beta$  equals to 0.2, and Power equals to 0.8.  $P_1$  equals to ratio of patients who had increased postoperative EF in Optimal group (4/6).  $P_2$  equals to ratio of patients who had increased postoperative EF in Suboptimal group (2/6).  $Z_{\alpha}$  (one-sided) equals to 1.645.  $Z_{\beta}$  (one-sided) equals to 0.842. p equals to  $(P_1 + P_2)/2$ .

The calculation gave 29 patients per group was a least acceptable sample size. So, our sample size of 32 patients in Optimal group and 58 patients in Suboptimal group were appropriate.

The MediStim Butterfly Model BF 2004 transit time flow meter (MediStim AS, Oslo, Norway) was used in this study. The basic principle of this machine was based on D'Ancona et al. The device is available with 2 to 32 mm flow probes. The flow probe consists of two small piezoelectric crystals one upstream and one downstream mounted on the same side of vessel. Opposite to the crystals, there is a small metallic reflector. Each crystal produces a wide pulsed ultrasound beam covering the entire vessel width. The area of the transducers and the distance the beam has to travel between the two transducers are known. The necessary time for an ultrasound beam, emitted from the up-stream crystal, to arrive at the downstream crystal after being reflected, and for a signal from the downstream crystal to reach the

upstream crystal, is measured. Since ultrasound travels faster if transmitted in the same direction as flow, a small-time difference between the two beams is calculated as the transit time of flow. Measurements are also independent of the hematocrit level, heart rate, and thickness of the vessel wall.<sup>8</sup>

PI was chosen as the principal measure of graft patency. Patent bypass graft means a graft with stenosis below 50% at the anastomosis site. PI should be less than 5. DF should be more than 50%.

## Methodology

## Preoperative evaluation

Coronary angiography (CAG) was used by cardiologists for preoperative evaluation and mapping of coronary artery (territory and percentage of stenosis) and for evaluation of left ventricle ejection fraction (LVEF). Preoperative echocardiography (modified Simpson's method) was performed in all patients. The goal in all cases was complete revascularisation.

## Surgical procedure

A median sternotomy was done in all patients. A bypass graft (saphenous vein grafts (SVG) or left internal mammary artery (LIMA)) was harvested. Surgeons can design the choice of conduits as prefer. On pump CABG surgery performed as standard. After the cross-clamp was removed and protamine was administrated to reverse heparin, a patient was maintained the systolic blood pressure at 90-100 mmHg, then TTFM was measured. If the PI>5, the graft was reassessed for surgical technique error, such as kinking, twisting, spasm or dissection. If the error was identified, then the graft was revised.

All patients were admitted at a cardiovascular intensive care unit (CVICU) and continuously monitored for at least 96 hours. Patient discharged from the CVICU were transferred to a general ward.

## Measured outcomes

The MediStim Butterfly Model BF 2004 transit time flow meter (MediStim AS, Oslo, Norway) was used to measure intraoperative flows of all bypass grafts. The data collection involved mean flow, DF, and PI. The data was then analysed by comparing optimal group and suboptimal group. After discharge, a patient would have to follow up every 3 months. At 1 year, Echocardiography was performed by modified Simpson's method to evaluate for postoperative EF.

All analyses were performed with the PASW statistics data editor. In the statistics, there were 2 types of variables which were continuous variables and categorical variables. Continuous variables were age,

time to echocardiography, preoperative EF, mean flow, DF, clamp time, bypass time, and duration of hospital stay. Categorical variables were gender, coronary lesions, patient characteristic such as patient status and underlying diseases, postoperative EF changed (increased or decreased) and in-hospital outcomes such as myocardial infarction, atrial fibrillation, prolong ventilator, all-cause mortality, and incidence of readmission for cardiac events.

For continuous variables, the unpaired Student's t test or Wilcoxon rank sum test was used to analyse the data. For categorical variables, chi-square test or Fisher's exact test was used to analyse the data. A p value of <0.05 was considered to be statistically significant.

#### RESULTS

The data collection from overall 90 patients (N=90) in aspects of gender, age, EF evaluation, coronary lesions, and underlying disease were as follows. From overall 90 patients, 71 patients were men and 19 were women. The overall mean age was 66.16±9. 21-year-old (ranged from 40 to 85-year-old). The overall mean EF was 55.9±16.5%. The time to echocardiography was 15.5±5.8 months. For coronary lesions, 68 patients (75.56%) had triple vessels disease (TVD), 20 patients (22.22%) had double vessels disease (DVD), and 2 patients (2.22%) had single vessel disease (SVD).

For underlying disease, 71 patients (78.89%) had hypertension (HT), 38 patients (42.22%) had diabetes mellitus (DM), and 67 patients (74.44%) had dyslipidemia (DLP). The data was shown in Table 1. After CABG surgery, changes between pre-operative and postoperative EF in patients were analysed. From overall 90 patients, 44 patients (48.89%) had increased EF after surgery while 46 patients (51.11%) had decreased EF. For Optimal group of 58 patients, 36 patients (62.07%) had increased EF after surgery while 22 patients (37.93%) had decreased EF. For suboptimal group of 32 patients, 8 patients (25%) had increased EF after surgery while 24 patients (75%) had decreased EF.

American Society of Echocardiography concluded that reproducibility of EF on Echocardiography can be as good as about  $\pm 7\%$ , and test-retest reliability is  $\pm 5\%$ . Accordingly, our study assumed the patients who had difference of EF below 5% was not significant difference. Only patients whose EF changed equal or more than 5% after surgery were analysed.

When analysing only patients whose postoperative EF changed equal or more than 5%, the numbers of patients were narrowed down to 53 patients overall.

From overall 53 patients who had significant changes in postoperative EF, 41 patients were in optimal group and 12 patients were in suboptimal group. As the results, patients whose postoperative EF increased significantly

was found in Optimal group more than suboptimal group (73.2% and 25.0%, respectively), with statistical

significant (p-value=0.002). The postoperative EF data was shown in Table 2.

Table 1: Population demographic data.

Parameter	Overall N=90	Optimal gr. N=58	Suboptimal gr. N=32	P value
Gender (M/F)	71/19	42/16	29/3	0.046
Age (years)				
Mean±SD	66.2±9.2	66.7±8.2	65.2±10.8	0.24
range	40-85	49-85	40-84	
EF evaluation				
Preoperative ejection fraction	55.9±16.5	54.4±16.7	58.6±16.0	0.13
Time to echocardiography (months)	15.3±5.5	14.8±5.8	16.3±5	0.12
Coronary lesions				
Triple vessels disease	75.56% (68/90)	72.41% (42/58)	81.25% (26/32)	0.35
Double vessels disease	22.22% (20/90)	24.14% (14/58)	18.75% (6/32)	0.56
Single vessels disease	2.22% (2/90)	3.45% (2/58)	0% (0/32)	0.29
Patient characteristic				
Hypertension	78.89% (71/90)	79.31% (46/58)	78.13% (25/32)	0.90
Diabetes mellitus	42.22% (38/90)	48.28% (28/58)	31.25% (10/32)	0.12
Dyslipidemia	74.44% (67/90)	74.14% (43/58)	75% (24/32)	0.93

Table 2: Postoperative ejection fraction data.

Parameter	Overall N=90	Optimal gr. N=58	Suboptimal gr. N=32	P value
Number of patient with ejection fraction changes after surgery				
Increase	48.89% (44/90)	62.07% (36/58)	25% (8/32)	< 0.001
Decrease	51.11% (46/90)	37.93% (22/58)	75% (24/32)	< 0.001
Number of patient whose postoperative EF changed $\geq 5\%$				
Increase	62.3% (33/53)	73.2% (30/41)	25.0% (3/12)	0.002
Decrease	37.7% (20/53)	26.8% (11/41)	75.0% (9/12)	0.002

Table 3: Intraoperative data.

Parameter	Overall N=90	Optimal gr. N=58	Suboptimal gr. N=32	P value
Transit time flow measurement variables				
Mean flow (ml/min)	32.1±15.8	35.2±16.7	26.6±12.5	0.0065
Diastolic filling percentage	72.7±7.3	73.4±6.9	71.5±8.0	0.12
Graft per patient				
Mean±SD	3.33±0.912	3.28±1.022	3.44±0.669	0.18
Intraoperative time				
Clamp time (min)	120.06±38.51	123.79±43.39	113.28±26.88	0.08
Bypass time (min)	183.97±48.15	186.05±53.73	180.18±36.41	0.30

The intraoperative data collection in aspects of TTFM variables, numbers of graft per patient, and intraoperative time were analysed.

Intraoperative data expressed that optimal group had mean flow more than suboptimal group  $(35.2\pm16.7 \text{ ml/minute})$  and  $26.6\pm12.5 \text{ ml/minute}$ , respectively) with

statistical significant (p<0.05). The DF percentage in optimal group was also more than suboptimal group (73.4±6.9 and 71.5±8.0, respectively). Both optimal and suboptimal groups had average number of 3 grafts per patient (3.28±1.022 and 3.44±0.669, respectively). In terms of intraoperative time, optimal group tended to have a prolong intraoperative time more than Suboptimal group for both clamp time and bypass time

 $(123.79\pm43.39 \text{ min} \text{ and } 113.28\pm26.88 \text{ minutes clamp time; } 186.05\pm53.73 \text{ min} \text{ and } 180.18\pm36.41 \text{ minutes bypass time, respectively) but the difference was not statistical significant. Intraoperative data are shown in Table 3.$ 

The postoperative outcomes in related to clinical outcomes were analysed in both in-hospital outcomes and midterm outcomes. In-hospital outcomes showed that Optimal group was less likely to have major adverse cardiac events (MACE) than Suboptimal group. Optimal group found no patient with myocardial infarction but suboptimal group found one (0% and 3.13%, respectively). Postoperative atrial fibrillation was found

in optimal group less than optimal group (37.93% and 43.75%, respectively). Prolong ventilator more than 48 hours was found in optimal group less than suboptimal group (37.93% and 62.50%, respectively). However, optimal group had duration of hospital stay more than Suboptimal group (27.31±18.50 days and 24.25±11.25 days, respectively). In midterm, postoperative follow-up, all-cause mortality in optimal group was lower than suboptimal group (1.72% and 3.13%, respectively). On the other hand, incidence of readmission for cardiac events in optimal group was higher than suboptimal group (10.3% and 9.4%, respectively). Post-operative outcomes data are shown in Table 4.

Table 4: Postoperative of	outcomes	data.
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Parameter	Overall N = 90	Optimal gr. N = 58	Suboptimal gr. N = 32	P value
In-hospital outcomes				
Postoperative myocardial infraction	1.11% (1/90)	0% (0/58)	3.13% (1/32)	0.18
Postoperative atrial fibrillation	40% (36/90)	37.93% (22/58)	43.75% (14/32)	0.59
Prolong ventilator	44.44% (4/90)	34.48% (2/58)	62.50% (2/32)	0.54
Duration of ICU (days)	8.51±6.25	8.62±6.08	8.31±6.65	0.41
Duration of stay (days)	26.22±16.29	27.31±18.50	24.25±11.25	0.20
Midterm outcomes				
All-cause mortality	2.22% (2/90)	1.72% (1/58)	3.13% (1/32)	0.67
Incidence of readmission for cardiac events	10% (9/90)	10.3% (6/58)	9.4% (3/32)	0.88

#### **DISCUSSION**

Transit-time flow measurement (TTFM) recommended standard for evaluation of intraoperative patency degree of coronary artery graft. Patency of graft is measured as acceptable when DF>50% and PI≤5. T.M. Keiser et al. studied in a series of 1000 consecutive arterial grafts and reported that patients with high PI values, PI>5, in at least one graft should serve as an indicator that graft should be re-assessd and that revision maybe appropriate. <sup>5</sup> Tokuda et al. studied in 104 coronary artery grafts, compared post-operative between a new occluded graft within 1 to 4 years and patent graft. This study reported that a graft with intraoperative lower mean flow, and especially with a higher percentage of backward flow, should be carefully monitored, even if it was initially anatomical patent. They also suggested that mean flow of around 15 or less, a PI of about 3 or higher, and a %BF of approximately 3 or higher were previously proposed as the cut-off criteria to predict a higher incidence of early graft failure, for both arterial and venous conduits.7

In our study, population demographic results revealed that characteristics of both optimal and suboptimal groups of patient were similar to each other in terms of mean age, preoperative EF, underlying diseases such as diabetes mellitus, hypertension, and hyperlipidemia. However, gender was the only factor that we found difference. Both groups had male patients more than female patients with statistical significant.

Intraoperative TTFM results convinced that DF in both groups was not significantly different. However, mean flow in optimal group was higher than suboptimal group, with statistical significant. In fact, mean flow could depend on many factors such as percentage of stenosis, flexibility, or diameter of graft. In diastolic phase, DF in both groups were similar as above 70%, but mean flow in optimal group was higher than suboptimal group. as the results, it indicated that patients in optimal group had lower resistance of vessels run off than in suboptimal group. Low resistance of vessel run off could be low percentage of stenosis, higher flexibility, or large diameter of graft.

After follow-up for 1 year, echocardiography was performed. We found that optimal group had patients whose postoperative EF significantly increased more than suboptimal group. This result indicated that myocardial function in optimal group was better than suboptimal group. Optimal group had lower resistance of bypass

grafts and higher blood supply to ischemia myocardium that can be reversible than in suboptimal group. Patients in optimal group whose postoperative EF was significant decreased probably caused by natural history of disease and underlying diseases progressed. When compared to postoperative outcomes, we found that complications, included myocardial infarction (MI), atrial fibrillation (AF), prolong ventilator, and all-cause mortality in Suboptimal group were higher than optimal group. However, duration of hospital stay and incidence of readmission for cardiac events in optimal group were higher than suboptimal group. For duration of hospital stay, there was bias because some patients were admitted for wound care even they can be treated as OPD case. It was believed that optimal group had patent and good quality of graft and could estimate better outcomes after surgery. For suboptimal group, closed follow-up, tight life style modification such as regular light exercise, smoking cessation, consume fibers diet were important roles to prevent cardiovascular events. We would reassure patient in this group to recognize and beware of cardiovascular events.

#### Limitations

Firstly, this study decided to evaluate myocardial function in indirect way. We decided to evaluate myocardial function by using EF for an indicator and compared preoperative and postoperative outcomes. However, echocardiography was an operator-dependent procedure. The little difference in percentage of postoperative EF can indicate that it was not significant changed. Secondly, this study had a small sample size because many patients had lost follow-up program with us as they preferred to follow-up at hospitals nearby their areas. Thirdly, duration of follow-up and performed Echocardiography was varied from 6 to 24 months. That was because, in our hospital, follow-up with Echocardiography was varied.

#### **CONCLUSION**

The results proved the hypothesis was true. Optimal group had patients whose postoperative EF significantly increased more than suboptimal group, with statistical significant. This concluded that postoperative myocardial function was improved in optimal group more than in suboptimal group. Tendency of finding postoperative complications in suboptimal group was more than in optimal group.

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