

# HEMODILUTION DURING OFF-PUMP CABG: CAN WE IMPROVE FLOW AND REDUCE HYPERCOAGUBILITY?

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*The aim of this study was to compare intraoperative coronary graft flows performed on and off-pump and to evaluate the effects of hemodilution on coronary graft flows in off-pump coronary bypass grafting patients by using transit time flow measurement.*

*During a period of two years, 300 patients undergoing only a coronary bypass grafting procedure were enrolled in a prospective randomised manner. Group 1 consisted of 100 patients operated with standard cardiopulmonary bypass techniques. Group 2 consisted of 100 cases who were planned to undergo revascularisation using off-pump techniques. Group 3 consisted of 100 patients operated with off-pump techniques under controlled hemodilution.(Htc levels were kept between a range of 25-28%.) Transit time flow measurement were performed using the CTS Coronary Flometer™ System (Cardiothoracic Systems, USA). Mean flows, pulsatile index and flow patterns were evaluated. 25 patients in each group were randomly assigned for control angiography 6 days postoperatively.*

*The mean number of anastomoses were higher in Group 1 when compared to Group 2 and 3 ( $p<0.05$ ). Mean Arterial Pressure, heart rate were similar between groups during measurements. Hematocrit values in Group 2 were higher than Group 1 and Group 3 ( $p<0.05$ ).*

*Mean flows for LAD and RCA territories were significantly lower in Group 2 patients ( $p<0.05$ ). For the circumflex artery territory despite lower flows again in Group 2, this did not reach significant levels. The pulsatile index were similar in all three groups for all three coronary territories. Postoperative coronary angiography revealed similar graft patencies among three groups ( $p=ns$ ).*

*Off-pump CABG patients with hemodilution had significantly higher graft flows compared to off-pump CABG patients without hemodilution. It can be hypothesized that hemodilution may help to improve graft patency during the early postoperative period in off-pump CABG patients.*

**Key Words:** Hemodilution, Transit time flowmeter, Off-pump CABG

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**E**nsuring quality of the anastomosis during coronary artery surgery has been an important concern among cardiac surgeons, especially with the increasing popularity of off-pump coronary artery bypass revascularisation (CABG). Transit time flow measurement (TTFM) is a non-invasive method based on advanced doppler technology that can measure intraoperative coronary bypass graft flows (1). Although the efficacy of TTFM has been shown by many groups, studies comparing graft flows performed on and off-pump have been limited so far. Factors like vessel diameter, distal vessel bed, spasm and viscosity are known to affect the coronary graft flows, however the influence of these factors during off-pump CABG has not been thoroughly established. The aim of this study was:

- 1.To compare intraoperative coronary graft flows performed using on and off-pump CABG methods
- 2.To evaluate the effects of hemodilution on coronary graft flows during off-pump CABG surgery.

## MATERIAL AND METHODS

During a period of two years, 300 patients undergoing only a CABG procedure were enrolled in a prospective randomised manner. Reoperations, combined cases and emergency operations were not included. Patients requiring high doses of vasoactive drugs during the operation and patients with coronary artery diameter less than 1.25 mm. were also excluded for the benefit of a controlled vascular resistance and bed. A hundred patients were planned to undergo CABG using cardiopulmonary bypass (CPB) (Group1). These patients were operated under moderate hypothermia and standard CPB techniques. Tepid blood cardioplegia was administered in a simultaneous fashion both antegrade and retrograde for myocardial protection. Distal and proximal anastomosis were completed under a single cross-clamp period.

Group 2 consisted of 100 patients planned to be revascularised using off-pump techniques. Four patients in this group had to be

converted to CPB; two for hemodynamic instability, one for unsuitable coronary anatomy and one for mitral regurgitation needing correction. Octopus 3 Suction Stabilisation (Medtronic Inc, Minn.USA) was used for coronary stabilisation. The target vessel was occluded using silastic loops (Ethicon™ Johnson and Johnson Intl.) proximally and a blower was used to have a dry operative field. Proximal anastomosis were performed during a single side clamp and before the distal anastomoses when necessary, especially during the right coronary artery anastomosis.

Group 3 consisted of 100 patients undergoing off-pump CABG under a hemodilution protocol. After the induction of anesthesia, one unit of blood was withdrawn from the patients and collected in a bag to be retransfused after the operation if necessary. One to two units of colloid solutions were transfused during the procedure; to prevent hypovolemia and to keep the blood hematocrit levels between 25-28%. Three patients in this group had to be excluded from the study because they had to be converted to CPB. The rest of the patients underwent off-pump CABG using the same methods as described in patients in Group 2.

Measurements were performed 10 minutes after weaning from CPB in Group 1. In Group 2 and Group 3 measurements were done 10 minutes after all the anastomoses were completed. Three consecutive measurements were performed for each anastomoses and the mean value was taken into consideration as the final result. All measurements were performed without using proximal snares to avoid spasm or damage to the vessel.

Patients received up to 2 mcg/kg/min nitroglycerine and 0.03 mcg/kg/min adrenaline perfusion during measurements. Any patient who needed higher doses of vasoactive drugs were excluded for the aim of a controlled vascular resistance. Within these criteria, 95 patients in Group 1, 96 patients in Group 2 and 96 patients in Group 3 concluded the study.

A CTS Coronary Flometer TM System (Cardiothoracic Systems, USA) TTFM device was used for flow measurements.

A 2 mm probe was used for internal thoracic artery (ITA) flow measurements, while

measurements for venous grafts were performed using 3 and 4 mm probes. Systolic, diastolic and mean flows (Qmed) were measured for each anastomosis and the pulsatile index (PI) was calculated.

The pulsatile index (PI) =

$$\frac{\text{Systolic flow} - \text{diastolic flow}}{\text{Mean Flow}} \quad \text{has been accepted}$$

As a valuable indicator of the quality of the anastomosis by many authors. Values of PI between 1 and 5 have been accepted within the limits as suggested by D'Ancona et al (2).  
 Statistical Analysis: All values are expressed as mean + SD. Kruskal-Wallis H test was used for comparison of parameters between three groups. Dunn's Multiple Comparison Test was used for sub-group analysis. P<0.05 was considered significant. (SPSS Version 10 (Chicago ILL)).

## RESULTS

Table 1 shows a detailed analyses of the results among the three groups. None of the

**Table 2.** Analysis of flow characters

	Group 1	Group 2	Group 3	p
M.N.A	3.2+0.4	2.6+0.2	2.4+0.6	p<0.05 (Group 3-2<1)
M.A.P(mmHg)	70+10	75+12	65+10	ns
HR	78+5	82+4	87+12	ns
Htc	28+4	36+8	25+3	p<0.05 (Group 2-3)
<b>Flow Values</b>				
<b>LAD</b>				
Q med (ml/min.)	28+11	20+7	30+12	p<0.05
PI	2.2+1.8	2+1.5	1.9+0.5	ns
<b>OM</b>				
Q med (ml/min.)	36+10	28+5	40+15	ns
PI	2+1.8	2.6+1.4	2.5+1	ns
<b>RCA</b>				
Q med (ml/min.)	49+14	30+10	50+12	p<0.05
PI	1.8+1	1.8+1.6	2+1.3	ns

HR:heart rate, Htc: hematocrit  
 LAD:left anterior descending coronary artery  
 MNA:mean number of anastomosis  
 MAP:mean arterial pressure  
 OM:obtuse marginal branch of circumflex coronary artery, PI:pulsatile index, RCA:right coronary artery  
 Qmed:mean flow

patients in 3 groups suffered any neurological, renal or cardiac complications. One patient in group 1 underwent a reoperation for bleeding. In summary, the mean number of anastomosis was higher in Group 1 in comparison to Groups 2 and 3 (p<0.05). There were no differences between mean arterial pressures (MAP) and heart rates (HR) during flow measurements. Hematocrit levels were higher in Group 2 patients (p<0.05).

When the mean flows(Qmed) were compared for LAD, CX and RCA territories;

1.Qmed values were similar between Groups 1 and 3 for all three coronary territories.

2.Q med in Group 2 was lower than Q med in Group 1 and 3 in LAD and RCA territories (p<0.05). Qmed values for the CX area in Group 2 were lower than Qmed values for Group 1 and Group 3 patients for the same territory without reaching statistical significance.

3.Despite the differences in Qmed values, the pulsatile indexes were similar between the three groups for all territories.

**Graft Revisions:**

One anastomosis in Group 1, two in Group 2 and one in Group 3 were revised. In three instances, the inadequate flows were due to intimal flaps and localised dissections at the site of anastomoses and TTFM measurements improved after the correction of the anastomosis. In one case TTFM did not improve after the anastomosis was repeated, probably due to poor vessel and distal coronary bed quality. MR imaging one week after the operation suggested an occluded graft.

**Angiographic results:**

Group 1: Overall graft patency was 97%. LITA patency was 100 %.

Group 2: Overall graft patency was 95 %. LITA patency was 100 %.

Group 3: Overall graft patency was 96 %. LITA patency was 100 %.

## DISCUSSION

An objective method for determining intraoperative graft flow patency is an essential part of minimally invasive direct

coronary artery bypass, especially with concerns about graft patency and long term outcome. Intraoperative measurement of graft volume blood flow during cardiac surgery can be useful for quality control and to reveal technical errors. Among other technologies used for this purpose, TTFM offers stable and reproducible measurements representative of the real flow within the constructed graft with a high sensitivity and specificity (1,2,3). The agreement between the transit time volume blood flow values and the directly measured blood flows (1) and the non-invasive nature of the method has made this our method of choice for measurement of volume blood flow in venous and arterial grafts. Despite these assets, the method is not without flaws. Mean flow per se is not a good indicator for the quality of the anastomosis (3). One has to consider mean flow, the pulsatile index and the flow patterns all together while analysing the results. Vessel diameter, distal vessel bed, high vascular resistance are some of the factors that can influence TTFM and have to be taken into account as well (2,3). A low Q med in a very small vessel anastomosis can be accepted if the flow pattern is mainly diastolic and the PI is within the limits. Conversely, a very low flow in a large vessel should not be acceptable. These suggest that some experience and clinical sense are needed to evaluate results during TTFM.

Our experience in more than 500 patients with the TTFM has suggested that coronary graft flows were constantly higher in on-pump CABG patients in comparison to off-pump CABG patients; which was the main reason leading us to undertake this study. One interesting finding was that despite the low flows in off-pump CABG patients, the pulsatile index (PI) and the flow patterns; both indicators of the quality of the anastomoses were similar. Initially in the study, we had planned to evaluate graft flows in two groups (on and off-pump) of patients. As the study advanced and the difference in graft flows became more apparent between on and off-pump patients, we tried to find an explanation for this. Graft flows could be affected by factors such as vessel diameter, distal vessel bed, spasm and high vascular resistance. However patients were randomised

and they all received similar doses of vasoactive drugs. It is known that patients with diabetes mellitus have smaller coronary arteries and more severe distal vessel disease. In this study there were 11 patients with diabetes mellitus in group1, 9 in group 2 and 13 in group3. However, it should be emphasized that this is an ongoing study and with larger number of patients in each group, these differences should be even less. Coronary vessel diameters ranged between 1.25 mm to 2.5 mm's in all three groups and there was no indication that vessel sizes were different in three groups. We know from the evidence both in the literature and from our published work that angiographic graft patencies are similar between on and off-pump CABG patients (4,5). In addition, early angiographic evaluation of 75 patients in this study also revealed similar graft patencies; suggesting similar quality anastomoses.

One factor that came to our attention was the high levels of blood hematocrit levels in off-pump patients during flow measurements. The mean Htc value was 36 % for these patients (Group 2) during flow measurements versus Htc values of 28 % for on-pump patients (Group 1). After these findings we decided to add a third group to the study to evaluate the effects of hemodilution in off-pump patients (Group 3) and under similar hemodynamic parameters, we observed higher mean flows (Qmed) in off-pump CABG patients with hemodilution in comparison to their counterparts without hemodilution. ( $p < 0.05$ )

Hemodilution has been one of the major improvements during the advance of CPB. Reduction in viscosity, increase in organ flow, reduction in mean arterial pressure and the dilution of coagulation factors are some of the effects of hemodilution.(6,7) Besides, safety of hematocrit values between 24-28 % have been established in the literature (6) and we did not observe any adverse effects due to hemodilution in Group 3 patients. The rate of bleeding complications and transfusions were similar between Group 2 and Group 3 patients.

Mariani et al described a hypercoagulable state that is observed in off-pump CABG patients on the second and third postoperative days (8). Silvay et al have elegantly shown

this hypercoagulable state in off-pump patients during the early postoperative period using thromboelastograms (TEG); which was not observed in postoperative CPB patients.(9) During CPB there is a 30-50 % decrease in platelet numbers due to consumption and hemodilution. Another important consequence of CPB is fibrinolysis which is absent in off-pump patients. Both Mariani and Silva suggested that lack of fibrinolysis after off-pump cases could be the main reason for the hypercoagulable state seen in these patients which could lead to early graft thrombosis or other end organ complications and advised the use of Plavix (Clopidogrel) during this period (8,9,10). However, between three groups we could not show any major difference in TEG patterns.

The mechanism of an acute normovolemic hemodilution (ANHD) induced fall in systemic vascular tone has not been fully elucidated. However, local endothelium-based (nitrous oxide) mediated mechanisms have been implicated in the vasodilatory responses to hemodilution (7). Although a technically perfect anastomosis is the gold standard for graft patency, hemodilution may be another helpful tool to improve graft flow and perhaps patency during this critical hypercoagulable state that off-pump patients are going through. Mechanisms such as reduction in viscosity, dilution of coagulation factors and nitrous oxide upregulation that contribute to vasodilatation after ANHD may help in the design of novel therapeutic strategies (7,9). The authors realise that higher volume prospective randomised trials are needed to support these hypotheses. However, within the limitation of this study, we conclude that;

- 1.Flow rates were lower in off-pump CABG patients when compared to on-pump CABG patients.( $p < 0.05$ )
- 2.Off-pump patients with hemodilution had comparable flows with on-pump CABG patients.
- 3.Hemodilution did not cause any adverse effects in the early postoperative period.
- 4.It can be hypothesized that hemodilution may help to improve graft patency during the early postoperative period in off-pump patients. Higher volume trials are needed to further support this hypothesis.

## REFERENCES

1. Laustsen J, Pedersen EM, Terp K et al. Validation of a new transit time ultrasound flow meter in man. *Eur J Vasc Endovasc Surg.* 1996 Jul;12 (1):91-6.
2. D'Ancona G, Karamanoukian HL, Ricci M et al. Intraoperative graft patency verification: should you trust your fingertips? *Heart Surg Forum.* 2000;3(2):99-102.
3. D'Ancona G, Karamanoukian HL, Salerno TA, Schmid S, Bergsland J. Flow measurement in coronary surgery. *Heart Surg Forum.* 1999;2(2):121-4.
4. Akpınar B, Güden M, Sağbaş E, Sanisoğlu İ, Aytakin V, Bayındır O. Off-pump coronary bypass grafting with the use of the octopus 2 stabilization system. *Heart Surg Forum.* 2000;3(4):282-6.
5. Arom KV, Flavin TF, Emery RW, Kshetry VR, Janey PA, Peterson RJ. Safety and efficacy of off-pump coronary artery bypass grafting. *Ann Thorac Surg.* 2000 Mar;69(3):704-10.
6. Bojar R M. *Cardiopulmonary Bypass.* In *Adult Cardiac Surgery.* Blackwell Scientific Publications 1992:4-27.
7. Doss DN, Estafanous FG, Ferrario CM, Brum JM, Murray PA. Mechanism of systemic vasodilation during normovolemic hemodilution. *Anesth Analg.* 1995 Jul;81(1):30-4.
8. Mariani MA, Gu YJ, Boonstra PW, Grandjean JG, Oeveren W, Ebels T. Procoagulant activity after off-pump coronary operation: is the current anticoagulation adequate? *Ann Thorac Surg.* 1999 May;67(5):1370-5.
9. Silvay G. Risk management in major surgery III: Myocardial injury after cardiac surgery. *J Cardiothorac and Vasc Anesth.* 2000 Jun;14(3 Suppl 1):1
10. Gu YJ, Mariani MA, Van Oeveren W, Grandjean Jg, Boonstra PW. Reduction of the inflammatory response in patients undergoing minimally invasive coronary artery bypass grafting. *Ann Thorac Surg.* 1998 Feb;65(2):420-4