

Hemodilution during Off-Pump Coronary Artery Bypass Grafting: Can We Improve Flow and Reduce Hypercoagulability?

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ABSTRACT

Background: The aim of this study was to compare intraoperative coronary graft flows performed on pump and off pump and to evaluate the effects of hemodilution on coronary graft flows in off-pump coronary artery bypass grafting (CABG) patients by using transit time flow measurements (TTFM).

Methods: Three hundred patients undergoing only CABG procedures were enrolled in a prospective randomized manner into 3 groups. Group 1 consisted of 100 patients undergoing operations with standard cardiopulmonary bypass techniques. Group 2 consisted of 100 patients scheduled for revascularizations using off-pump techniques. Group 3 consisted of 100 patients who underwent operations with off-pump techniques under controlled hemodilution (hematocrit levels kept between 25% and 28%). TTFM were performed with the coronary Flometer system. Mean flows, pulsatility indices, and flow patterns were evaluated. Twenty-five patients in each group were randomly assigned for control angiography 6 days postoperatively. Thromboelastographic (TEG) measurements were performed for each patient before and after surgery to evaluate the patient's coagulation status.

Results: The mean number of anastomoses was higher in group 1 than in groups 2 and 3 ($P < .05$). Mean arterial pressures and heart rates were similar between groups during measurements. Hematocrit values were higher in group 2 than in groups 1 and 3 ($P < .05$). Mean flows for left anterior descending coronary artery and right coronary artery territories were significantly lower in group 2 patients ($P < .05$). For the circumflex artery territory, mean flows did not reach statistically significant levels despite lower flows again in group 2. The pulsatility indices were similar in all 3 groups for all 3 coronary territories. Postoperative coronary angiographic results revealed similar graft patencies among the 3 groups (not significantly different). Postoperative TEG patterns failed to show a hypercoagulable state in off-pump patients.

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Conclusion: Off-pump CABG patients with hemodilution had significantly higher graft flows than off-pump CABG patients without hemodilution. Although we failed to show the existence of a hypercoagulable state for patients in the off-pump group, an examination of the TTFM findings suggests that hemodilution may help to improve graft patency in off-pump CABG patients during the early postoperative period.

INTRODUCTION

Ensuring the 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 revascularization (CABG). Transit time flow measurement (TTFM) is a noninvasive method based on advanced Doppler technology that can measure intraoperative coronary bypass graft flows [Laustsen 1996]. Although the efficacy of TTFM has been shown by many groups, studies comparing graft flows performed on pump and off pump have been limited so far. Factors such as vessel diameter, distal vessel bed, spasm, and viscosity are known to affect coronary graft flows; however, the influence of these factors during off-pump CABG has not been thoroughly established. The aims of this study were (1) to compare intraoperative coronary graft flows performed with on-pump and off-pump CABG methods and (2) to evaluate the effects of hemodilution on coronary graft flows during off-pump CABG surgery.

MATERIALS AND METHODS

Three hundred patients undergoing only CABG procedures were enrolled in a prospective randomized 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 diameters of less than 1.25 mm were also excluded for the benefit of controlling vascular resistance and bed. One hundred patients were enrolled to undergo CABG using cardiopulmonary bypass (CPB) (group 1). These patients underwent operations under moderate hypothermia and with standard CPB techniques. Tepid blood cardioplegia was administered in a simultaneously antegrade and retrograde fashion to attain myocardial protection. Distal and proximal anastomoses were completed in a single cross-clamp period.

Analysis of Flow Characteristics*

| | Group 1 | Group 2 | Group 3 | P |
|--------------------------|-----------|-----------|-----------|-----------------------|
| Anastomoses, n | 3.3 ± 0.3 | 2.8 ± 0.2 | 2.5 ± 0.6 | <.05 (Groups 3-2 < 1) |
| Arterial pressure, mm Hg | 72 ± 9 | 78 ± 11 | 68 ± 10 | NS |
| Heart rate, /min | 80 ± 3 | 84 ± 5 | 90 ± 11 | NS |
| Hematocrit, % | 28 ± 4 | 36 ± 8 | 25 ± 3 | <.05 (Groups 2-3) |
| Flow values | | | | |
| LAD | | | | |
| Qmed, mL/min | 22.9 ± 13 | 22 ± 4 | 31 ± 11 | <.05 |
| Pulsatility index | 2.2 ± 1.8 | 2 ± 1.5 | 1.9 ± 0.5 | NS |
| OM | | | | |
| Qmed, mL/min | 37 ± 8 | 29 ± 5 | 42 ± 14 | NS |
| Pulsatility index | 2.0 ± 1.8 | 2.6 ± 1.4 | 2.5 ± 1 | NS |
| RCA | | | | |
| Qmed, mL/min | 47 ± 12 | 30 ± 12 | 49 ± 11 | <.05 |
| Pulsatility index | 1.8 ± 1 | 1.8 ± 1.6 | 2 ± 13 | NS |

*Data are presented as the mean ± SD. LAD indicates left anterior descending coronary artery; Qmed, mean flow; OM, obtuse marginal branch of the circumflex coronary artery; RCA, right coronary artery.

Group 2 consisted of 100 patients scheduled to undergo revascularization with off-pump techniques. Four patients in this group had to be converted to CPB, 2 for hemodynamic instability, 1 for unsuitable coronary anatomy, and 1 for mitral regurgitation needing correction. Octopus 3 suction stabilization (Medtronic, Minneapolis, MN, USA) was used for coronary stabilization. The target vessel was occluded proximally with polymeric silicone (Silastic) loops (Ethicon, Somerville, NJ, USA), and a blower was used to achieve a dry operative field. Proximal anastomoses 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, 1 unit of blood was withdrawn from the patient and collected in a bag to be retransfused after the operation, if necessary. One to 2 units of colloid solutions were transfused during the procedure to prevent hypovolemia and to keep the blood hematocrit levels between 25% and 28%. Three patients in this group had to be excluded from the study because they had to undergo conversion to CPB. The rest of the patients underwent off-pump CABG with the same methods described for the patients in group 2.

In group 1, measurements were performed in 10 minutes after weaning the patient from CPB. In groups 2 and 3, measurements were done 10 minutes after all the anastomoses were completed. Three consecutive measurements were performed for each anastomosis, and the mean value was considered the final result. To avoid spasm or damage to the vessel, we performed all measurements without using proximal snares.

Patients received a perfusion of up to 2 µg/kg per minute nitroglycerin and 0.03 µg/kg per minute adrenaline during measurements. Any patient who needed higher doses of vasoactive drugs was excluded from the study to enable the control of vascular resistance. Within these criteria, 95 patients in group 1, 96 patients in group 2, and 96 patients in group 3 constituted the study population.

The coronary Flometer system (CFM 100; Transonic Systems, Ithaca, NY, USA) TTFM device was used for flow measurements.

A 2-mm probe was used for measurements of internal thoracic artery flow, and measurements for venous grafts were performed with 3-mm and 4-mm probes. Systolic, diastolic, and mean flows (Qmed) were measured for each anastomosis. Qmed is the primary determinant of the quality of grafts. A high average flow rate always indicates a viable graft, and a near-zero flow rate always indicates a graft in trouble. Qmed can vary over a wide range. It is influenced by and should be evaluated with respect to the size and quality of the graft, the size and quality of the recipient vessel, the mean arterial pressure, and the runoff quality of the coronary bed. The pulsatility index (PI) was calculated as follows: PI = (Systolic Flow – Diastolic Flow)/Mean Flow. The PI has been accepted by many authors as a valuable indicator of the quality of an anastomosis. D'Ancona et al have suggested that values of PI between 1 and 5 are acceptable [D'Ancona 2000]. Thromboelastographic (TEG) measurements (ROTEG; Pentapharm, Munich, Germany) were performed for each patient after the induction of anesthesia and after the operation when the patient arrived in the intensive care unit.

Statistical Analysis

All values are expressed as the mean ± SD. The Kruskal-Wallis *H* test was used for the comparison of parameters among the 3 groups. The Dunn multiple comparisons test was used for subgroup analysis. A *P* value <.05 was considered to be statistically significant (SPSS version 10; SPSS, Chicago, IL, USA).

RESULTS

The Table shows a detailed analysis of the results for the 3 groups. None of the patients in the 3 groups experienced from any neurologic, renal, or cardiac complications. One patient in group 1 underwent a reoperation for bleeding.

In summary, the mean number of anastomoses was higher in group 1 than in groups 2 and 3 ($P < .05$). There were no differences in mean arterial pressures and heart rates during flow measurements. Hematocrit levels were higher in group 2 patients ($P < .05$).

Qmed values were compared for left anterior descending, circumflex, and right coronary artery territories, and 3 findings were notable:

1. Qmed values for groups 1 and 3 for all 3 coronary artery territories were similar.
2. The Qmed values for group 2 were lower than those of groups 1 and 3 for left anterior descending and right coronary artery territories ($P < .05$). Group 2 Qmed values for the circumflex artery area were lower than those of groups 1 and 3 for the same territory, and the differences did not reach statistical significance.
3. Despite the differences in Qmed values, the pulsatility indices of the 3 groups were similar for all territories.

Graft Revisions

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

Angiographic Results

In group 1, the overall graft patency was 97%, and the patency of the left internal thoracic artery (LITA) was 100%. In group 2, the overall graft patency was 95%, and the LITA patency was 100%. In group 3, the overall graft patency was 96%, and the LITA patency was 100%.

TEG Values

The evaluation of TEG patterns among the 3 groups of patients did not reveal any significant differences between preoperative values.

TEG values such as clotting time, clot formation time, and maximum clot firmness values were similar among the 3 groups during postoperative measurements. Some of the group 3 patients showed a decrease in the alpha angle, which is one of the parameters of clot firmness, but this finding alone was not of significance.

DISCUSSION

An objective method for determining intraoperative graft flow patency is an essential part of the minimally invasive direct coronary artery bypass, especially considering the 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 revealing technical errors. Among the other technologies used for this purpose, TTFM offers stable and reproducible measurements

that represent the real flow within the constructed graft with a high degree of sensitivity and specificity [Laustsen 1996, D'Ancona 1999, D'Ancona 2000]. The agreement between the transit time blood flow volumes and directly measured blood flows [Laustsen 1996] and the noninvasive nature of the method has made it our method of choice for the measurement of blood flow volume in venous and arterial grafts. Despite these assets, the method is not without flaws. Qmed per se is not a good indicator of the quality of the anastomosis [D'Ancona 1999]. One has to consider the Qmed, PI, and flow patterns together while analyzing the results. Vessel diameter, distal vessel bed, and high vascular resistance are some of the factors that can influence TTFM and have to be taken into account [D'Ancona 1999, D'Ancona 2000]. A low Qmed value for an anastomosis of a very small vessel can be accepted if the flow pattern is mainly diastolic and the PI is within the acceptable limits. Conversely, very low flow in a large vessel is not acceptable. These considerations suggest that some experience and clinical sense are needed to evaluate the results obtained during TTFM.

Our experience with TTFM suggested that coronary graft flows are consistently higher in on-pump CABG patients than in off-pump CABG patients. This observation was the main reason that led us to undertake this study. One interesting finding was that despite the low flow rates in off-pump CABG patients, the PI and flow patterns, both indicators of anastomosis quality, were similar. Initially, we had planned to evaluate graft flows in 2 groups (on pump and off pump) of patients. As the study advanced and the difference between on-pump and off-pump patients in graft flows became more apparent, we tried to find an explanation for this phenomenon. Graft flows might have been affected by factors such as vessel diameter, distal vessel bed, spasm, and high vascular resistance. However, the patients were randomly assigned to the groups, 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 group 1, 9 in group 2, and 13 in group 3. However, we emphasize that this study is ongoing, and with larger numbers of patients in each group, these differences should be even smaller. Coronary vessel diameters ranged between 1.25 mm and 2.5 mm in all 3 groups, and there was no indication that vessel sizes were different among the 3 groups. We know from evidence, both in the literature and from our own published work, that angiographically detected graft patency rates are similar for on-pump and off-pump CABG patients [Akpınar 2000, Arom 2000]. In addition, early angiographic evaluation of 75 patients in this study also revealed similar incidences of graft patency, suggesting similar qualities of the anastomoses.

One factor that came to our attention was the high hematocrits in off-pump patients during flow measurements. The mean hematocrit value was 36% for these patients (group 2) during flow measurements versus hematocrit values of 28% for on-pump patients (group 1). After obtaining 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 Qmed values in off-pump CABG patients with hemodilution than in their counterparts without hemodilution ($P < .05$).

Hemodilution has been one of the major improvements in CPB technology. A reduction in viscosity, an increase in flow to organs, a reduction in mean arterial pressure, and a dilution of coagulation factors are some of the effects of hemodilution [Bojar 1992, Doss 1995]. Besides, the safety of hematocrit values between 24% and 28% have been established in the literature [Bojar 1992], and we did not observe any adverse effects due to hemodilution in group 3 patients. The rates of bleeding complications and transfusions were similar in 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 [Mariani 1999]. Silvay et al have elegantly shown this hypercoagulable state with TEG in off-pump patients during the early postoperative period, which was not observed in postoperative CPB patients [Silvay 2000]. During CPB, there is a 30% to 50% decrease in platelet numbers due to consumption and hemodilution. Another important consequence of CPB is fibrinolysis, which is absent in off-pump patients. The studies of both Mariani et al and Silva suggested that lack of fibrinolysis after surgery in 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 these workers advised the use of clopidogrel bisulfate (Plavix) during this period [Gu 1998, Mariani 1999, Silvay 2000]. However, we found no major difference in TEG patterns among the 3 groups of patients in our series. This discrepancy in results may be due to different anticoagulation protocols used between centers.

The mechanism of an acute normovolemic hemodilution (ANHD)-induced fall in systemic vascular tone has not been fully elucidated. However, the mediation of local endothelium-based (nitrous oxide) mechanisms has been implicated in the vasodilatory responses to hemodilution [Doss 1995]. 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 so-called hypercoagulable state that off-pump patients may be going through. Mechanisms such as reduction in viscosity, dilution of coagulation factors, and nitrous oxide up-regulation that contribute to vasodilatation after ANHD may help in the

design of novel therapeutic strategies [Doss 1995, Silvay 2000]. We realize that larger prospective randomized trials are needed to support these hypotheses. Within the limitation of this study, however, we conclude that (1) flow rates were lower in off-pump CABG patients than in on-pump CABG patients ($P < .05$); (2) off-pump patients with hemodilution had flows comparable with on-pump CABG patients; (3) hemodilution did not cause any adverse effects in the early postoperative period; and (4) hemodilution may help to improve graft patency in off-pump patients during the early postoperative period. Trials with larger numbers of patients are needed to further support this hypothesis.

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