

# Platelet Function after Off Pump Coronary Surgery

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## ABSTRACT

**Background:** Little is known about the impact of off pump coronary artery bypass (OPCAB) on platelet function. Although improved platelet function may decrease bleeding and reduce cerebral and pulmonary damage, there is a concern that changes in platelet function may also accentuate bypass graft occlusion or other thrombotic processes. In this pilot study we used a point-of-care test—Hemostatus (Medtronic, Minneapolis, MN, USA)—to assess changes in platelet function after OPCAB.

**Methods:** We analyzed data from 11 adult patients undergoing CAB surgery whose platelet function was assessed before and after OPCAB. A Hemostatus test was conducted prior to heparin administration and after protamine reversal.

**Results:** There was a significant improvement in platelet function as measured in both channels 5 and 6 of the Hemostatus test. Blood loss was  $598 \pm 244$  mL in the first 24 hours. One patient received blood products.

**Conclusion:** This pilot study suggests that platelet function is not diminished but instead is improved after OPCAB. This improvement may be due to the release of newer, larger platelets from the bone marrow into the circulation. This finding has important implications for the use of antiplatelet agents perioperatively. Furthermore, more detailed studies in this field are needed.

## INTRODUCTION

Off pump coronary artery bypass (OPCAB) offers many potential advantages along with the avoidance of cardiopulmonary bypass (CPB). The reported decreased incidence of stroke and bleeding may be due in part to diminution of the inflammatory response [Ascione 2001]. There is a paucity of information regarding changes in platelet function after OPCAB. Preserved platelet function may reduce bleeding but conversely may result in increased rates of graft occlusion and other arterial thrombotic complications in the absence of the effects of CPB.

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The contribution of platelets to graft patency has been recognized since the seminal work of Chesebro and Fuster [Chesebro 1982], and the use of antiplatelet agents to frustrate normal function is now entrenched in cardiac surgical practice.

Platelet function can be assessed by several means. These include aggregometry and flow cytometry, clinically with a template bleeding time and as part of the overall coagulation process by thrombelastography (Haemoscope, Niles, IL, USA) or Sonoclot (Sienco, Wheat Ridge, CO, USA) [Tuman 1989]. The Hemostatus test (Medtronic, Minneapolis, MN, USA) uses an existing technology for endpoint detection and a single agonist, platelet activating factor (PAF), at several concentrations dispensed in an automated unit. As a point-of-care test it is suitable for use in the operating suite [Despotis 1996]. Our service has used Hemostatus for some time to assess platelet function perioperatively. In this study we used collected Hemostatus data to determine the effect of OPCAB on platelet function as measured by Hemostatus.

## METHODS

Adult patients undergoing coronary bypass without CPB had a Hemostatus test prior to administration of heparin, 200 IU/kg body weight for OPCAB patients. An activated clotting time (ACT) of  $>300$  seconds was effected in OPCAB patients, with administration of further heparin as necessary. Following completion of all anastomoses and checking for hemostasis, we administered protamine sulfate (0.7 mg/100 IU heparin given). The ACT was returned to within 20% of the preoperative value. A postsurgical Hemostatus test was then performed. Following chest closure, the patient was transferred to the cardiac intensive care unit, ventilated for a short while, and extubated at an appropriate time. Blood loss, use of blood products, and hematological parameters were recorded. All patients gave written informed consent for the procedure.

## PLATELET FUNCTION ANALYSIS

The Hemostatus cartridge uses an existing dispensing and recording device (HepCon HMS, Medtronic). The first generation test used a 6-channel cartridge with increasing doses of PAF as a platelet agonist. Two channels had no agonist and acted as a baseline. Doses of PAF were 1.25, 6.25, 12.5, and 150 nM. An ACT value was obtained from each channel in the Hepcon. A measure of function, the clot ratio (CR), was calculated using the formula  $CR = 1 - (ACT/control\ ACT)$ . This value was also expressed as a maximum percentage based on a normal population [Despotis 1996].

Table 1. Patient Characteristics

|                             |           |
|-----------------------------|-----------|
| N                           | 11        |
| Male sex                    | 11        |
| Age, y                      | 60 ± 6.9  |
| No. of grafts, mean (range) | 3.2 (1-5) |

## STATISTICAL ANALYSIS

All data were analyzed using Statistica Mac package (Statsoft, Tulsa, OK, USA). Data is described as mean and standard deviation. Comparisons were made with pre- and postoperative platelet function tests using a paired *t* test.

## RESULTS

Suitable data were obtained from 11 adult male patients undergoing elective OPCAB. These data are set out in Table 1.

Postoperative outcome data, which may be influenced by platelet function, including blood loss, platelet numbers, and use of blood products, are set out in Table 2.

Postoperative platelet function was greater than preoperative in channel 6 (150 nM PAF) 89.1% versus 77.5% ( $P = .016$ ). In channel 5 (12.5 nM PAF), platelet function rose from 56% preoperatively to 63% postoperatively ( $P = .00043$ ) (Table 2).

## DISCUSSION

CPB has long been recognized to have deleterious effects when it is used to support the circulation during open heart surgery. Of these, excessive blood loss leading to the use of blood products has been linked to disturbances of platelet function [Rinder 1991]. Other untoward effects include stroke and neuropsychological deficit and organ failure. OPCAB provides an opportunity to reduce or eliminate these complications but must also provide equivalent or better outcomes. This pilot study suggests that platelet function is not attenuated after OPCAB but may be improved.

Platelets become activated during their passage through the heart-lung machine. Surface receptors become up-regulated, allowing internal pathways to permit granule release and shape change [Rinder 1991]. Agonists such as thrombin, which circulate despite heparin, initiate this process. Other receptors become down-regulated, and at the end of a period of cardiopulmonary bypass there is a pool of exhausted platelets, some of which are “stunned,” and only a small number may be intact and able to respond to normal stimuli [Edmunds 1993]. Because of the absence of the artificial surfaces of the heart-lung machine, these platelet activation mechanisms are avoided during OPCAB, although with the trauma of surgery there is likely to be some activation. This activation is a stimulus for new platelets to be released from the marrow, a response that can be detected by examining platelet size and function and provides a possible explanation for these preliminary results.

Surgeons have expressed concern about graft occlusion during OPCAB. Reasons advanced are the inability to perform a technically adequate anastomosis while there is motion or an obscured field and the possibility of a hyperco-

Table 2. Perioperative Measurements

|                                    |                           |
|------------------------------------|---------------------------|
| Platelet number*                   |                           |
| Preoperative                       | 244 × 10 <sup>9</sup> /mL |
| Postoperative                      | 187 × 10 <sup>9</sup> /mL |
| Platelet function†                 |                           |
| Preoperative channel 6             | 77.5%                     |
| Postoperative channel 6            | 89.1%                     |
| Preoperative channel 5             | 56%                       |
| Postoperative channel 5            | 63%                       |
| Blood loss, mL                     | 598 ± 244                 |
| Patients receiving transfusions, n | 1                         |

\*Postoperative platelet number was significantly lower than preoperative ( $P = .002$ ).

†Postoperative platelet function was greater than preoperative ( $P = .016$  for channel 6;  $P = .00043$  for channel 5).

agulable state immediately postoperatively [Puskas 1999]. Many surgeons have acknowledged this phenomenon and address it by commencing antiplatelet agents prior to surgery. CAB with CPB is somewhat protected at this stage with a period of hypocoagulability immediately after surgery. Deep venous thrombosis has also been of concern after OPCAB. The lack of a marked increase in fibrinolytic activity may be a possible explanation for this.

This limited pilot study provides a stimulus for further investigations into the extent of changes in platelet function during OPCAB and the mechanisms for any change of platelet function and for further assessment of Hemostatus as a suitable screening/clinical test. The use of preoperative antiplatelet agents warrants investigation into what agents to use, when to administer them, and how much to administer.

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