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The blood saving potential of vortex versus roller pump with and without aprotinin

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To evaluate the potential of centrifugal blood pumps for saving blood, 120 patients scheduled for elective coronary artery bypass grafting were entered into a prospective randomized trial. A standard roller pump (group I) was compared with a centrifugal blood pump (group II) and roller pump plus aprotinin (group III). There was no significant difference between groups I and II with respect to free haemoglobin, lactic dehydrogenase, serum bilirubin, platelet surface glycoprotein IIb–IIIa and granule membrane protein 140, chest-tube drainage, use of blood products, length of stay in intensive care, time on ventilator and postoperative mortality. Aprotinin reduced chest-tube drainage and use of blood products significantly. Three cases of graft occlusions were noted in group III. Centrifugal blood pumps offer no advantage in routine heart surgery over conventional roller pumps. Aprotinin reduces blood loss, but does not influence GP IIb–IIIa and GMP 140 expression on blood platelets.

Introduction

The conventional roller pump (RP) has been the most widely used arterial blood pump for cardiopulmonary bypass (CPB) for many years. In 1975, a centrifugal blood pump (CP) was first used clinically.[1] On theoretical grounds, the centrifugal pump should cause less damage to corpuscular and soluble components of the blood. Previous clinical studies showed that centrifugal blood pumps shorten hospital stay and reduce hospital costs in routine coronary bypass surgery.[2] Moreover, it has been stated that a CP reduces erythrocyte damage,[3] preserves platelet function,[3] and improves haemostasis.[4]

In a prospective randomized trial, we compared the effect of an RP with and without aprotinin and a CP on postoperative blood loss, platelet function, length of stay in intensive care, time on ventilator and postoperative mortality.

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Methods

The study was approved by the institutional review board. Informed consent was obtained from all patients. The trial comprised 120 consecutive adult patients referred for elective coronary artery bypass grafting. Patients on platelet-active medication less than 10 days before the operation and patients on intravenous heparin were excluded from the study. None of the patients investigated had a history suggestive of a haemostatic disorder. Patients were randomly allocated to one of three groups. Routine clotting tests (platelet count, partial thromboplastin time, prothrombin time, thrombin time, bleeding time) were performed preoperatively and found unremarkable in all patients. In group I, a conventional standard roller pump (Stöckert Instrumente, Munich, Germany) was used. This group served as a control. In group II, CPB was conducted with a centrifugal blood pump with a BP 80 pump head (Biomedicus, Medtronik, Bad Homburg, Germany). Group III individuals were placed on CPB using a roller pump (Stöckert) and aprotinin (Trasylol, Bayer AG, Leverkusen, Germany) was given: 2×10^6 I.E. with induction of anaesthesia, 2×10^6 I.E. were added to the pump prime, and 5×10^5 I.E. per hour were infused continuously during CPB. The conduction of CPB was otherwise identical in all groups.

Details of operation

All patients had anaesthesia induced with fentanyl, etomidate and pancuronium, maintained with oxygen, isoflurane and fentanyl. An arterial line was placed into the femoral or radial artery. A central venous line and a Swan–Ganz catheter (Baxter Deutschland, Unterschleißheim, Germany) were placed into the internal jugular vein. Heparin (Liquemin N, Hoffman La Roche, Germany, 375 IU/kg) was used for anticoagulation before cannulation. The kaolin activated clotting time (ACT) was maintained over 400 seconds during CPB by supplemental heparin. A standard 8.0 mm arterial cannula (Stöckert) and a two-stage venous cannula (Stöckert) were used to institute CPB in all patients. Moderate hypothermic CPB was performed with nonpulsatile flow of 2.4 l/min/m². The extracorporeal circuit (ECC) was primed with 1500 ml of Ringer's solution

and 100 ml of mannitol 10%, and 7500 IU heparin were added to the pump prime. A membrane oxygenator (Maxima II, Medtronik, Bad Homburg, Germany) and a 40 μm arterial line filter (Jostra Medizintechnik, Hirrlingen, Germany) were used in all cases. Heparin was completely neutralized after discontinuation of CPB with protamin sulphate (Protamin, Hoffman La Roche, Germany) (1 ml protamin sulphate solution for each 1000 IU heparin given). In the postoperative period, shed mediastinal blood was collected in the cardiotomy reservoir (Dideco, SpA, Mirandola, Mod, Italy). The total amount of drainage was determined after the chest-tubes were removed (usually on the morning following the operation). No reinfusion of shed blood was performed during this study.

Laboratory procedures

The data collected included chest-tube drainage, requirements for blood products, duration of mechanical ventilation, stay in intensive care unit, serum levels of creatinine, free haemoglobin, full blood count, total protein, lactic dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) during and after the operation. In a subset of 10 individuals per group, further blood samples were taken for investigation of thrombocyte function just prior to heparinization (A), before cannulation (B), at one hour of CPB (C) and one hour after discontinuation of CPB (D). Platelet function was tested by flowcytometric assay of the surface expression of the antigens flycoprotein (GP) IIb–IIIa and granule membrane protein (GMP) 140 in platelet-rich plasma. The GP IIb–IIIa complex represents the fibrinogen receptor on the platelet surface responsible for platelet aggregation.[5] GMP 140 (P-selectin), a component of the alpha-granule membrane, and GP 53, a lysosome-like granule protein, are markers of platelet activation.[5] Platelet-rich plasma was prepared by centrifugation at $150 \times g$ for 15 minutes. The supernatant was withdrawn and resuspended in phosphate buffered saline (Biochrom, Berlin, Germany) containing 1 mg/ml bovine serum albumin (PBS/BSA) and adjusted to 20 000 platelets/μl. The dilution is necessary to ensure analysis of individual platelets. All samples were incubated for five minutes with the following FITC-labelled monoclonal antibodies: anti-GPIIb/IIIa (CD41a,

P2), anti-GMP 140 (CD 62, CLB-Thromb/6) (all antibodies supplied by Immunotech, Marseille, France). Samples were diluted with 300 μl of PBS/BSA and analysed in a Becton Dickinson FACScan flow cytometer (Becton Dickinson, San José, CA, USA). A Lysis II software was used for measurements. A total of 10 000 platelets were acquired in list mode at a flow rate of 12 μl/minute, 500–1000 particles/second.

Statistics

SPSS software for windows was used for statistics. The Student's *t*-test was used for normally distributed variables. The U test according to Wilcoxon, Mann and Whitney was used as nonparametric test.

Results

Data of patients and operations

Relevant data on patients and operative procedure are summarized in Table 1. There were significant differences between groups for preoperative ejection fraction and the use of internal thoracic artery (ITA) grafts. ITA grafts were used significantly more often in groups II and III ($p < 0.05$). There were no perioperative deaths in group I and II, but two patients died in the aprotinin group. The perioperative mortality for the total study population was 1.7%.

Blood loss and use of blood products

There was no significant difference in chest-tube drainage and use of blood products between group I and group II (Table 2). Two subgroups were formed from all patients of group I and II, with and without internal thoracic artery grafting. There was no significant difference in blood loss between groups I and II for either subgroup. In contrast, blood loss and the use of blood products was significantly reduced in group III compared with groups I and II. Only one patient of group I required reoperation for bleeding.

Postoperative course and laboratory data

There was no significant difference between any of the groups with respect to duration of mechanical ventilation, stay in intensive care unit (ICU) and laboratory data before, during and following surgery, as shown in Table 1. In

particular, there was no significant difference in free haemoglobin (Figure 1), and LDH (Figure 2) between groups I and II.

Thrombocyte function was assessed at four time points during the operation. The platelet surface expression of GP IIb–IIIa and GMP 140 is shown in Figures 3 and 4. There was no significant difference between any of the groups for either surface antigen. Platelet count did not reveal significant differences between groups (Figure 5).

Discussion

Centrifugal blood pumps, also called constrained vortex pumps, have been shown to reduce trauma to the blood components in a number of studies performed *in vitro* and clinically.[3,6,7] Although the advantages of CP in long-term extracorporeal circulation are well established, the role of this pump in routine cardiac surgery is controversial.[2,6,8–11] In particular, it has been stated that the use of a centrifugal blood pump may improve haemostasis and, thus, reduce postoperative chest-tube drainage.[11] Others have been unable to confirm these findings.[10] Our study is the first to compare different blood pumps with aprotinin with regard to blood loss and other variables in a prospective randomized trial. The centrifugal pump was compared with aprotinin because of the well-established beneficial effects on chest-tube drainage and the use of blood products of aprotinin in cardiac surgery.[12]

Since centrifugal pumps were reported to preserve platelets better than conventional pumps,[4,10] we examined platelet count and platelet function using a flow cytometric assay of surface antigen expression on platelets. This method has been used previously to describe the platelet function defect following cardiopulmonary bypass.[13]

Patients were randomly allocated to the study groups. There was no difference in any variable with the exception of preoperative ejection fraction and use of the internal thoracic artery which were significantly less in both study groups compared with control. Since additional surgical dissection is needed when the ITA is used, postoperative chest-tube drainage may possibly be increased. This would cause a bias towards the centrifugal pump and any haemostatic effect

of the centrifugal pump should, therefore, be reinforced. However, we were unable to find a significant difference between both blood pumps. To exclude any potential bias of ITA use, we divided the study population into two subgroups, with and without ITA use. Again no significant difference was noted in any of the subgroups between groups I and II. A dramatic decrease in chest-tube drainage was noted in group III. The decrease is within the range reported by other groups.[12] Moreover, the use of blood products was reduced significantly in the aprotinin group. Thirty-five patients in group III did not require any blood products in comparison to only 16 in group I and 18 in group II. In contrast to the findings of Lynch *et al.*, the use of a centrifugal pump had no influence on postoperative blood loss in our patients.[11] This is in accordance with data published by others.[14,15] Similarly, the centrifugal pump had little influence on laboratory data that would indicate significant blood trauma. LDH and free haemoglobin were reduced insignificantly in the centrifugal pump group and the effect was only short-lived and not marked in absolute terms. In routine bypass surgery, most cited authors found equally little influence of a centrifugal pump on LDH and free haemoglobin.[10,15,16]

In contrast, during long-term extracorporeal circulation (ECMO, ventricular assist), the centrifugal pumps yield superior results when compared with roller pumps.[6,8,9]

This is the first study, to our knowledge, to investigate the expression of platelet surface antigens and platelet count in a comparison of roller to centrifugal blood pumps. Platelet count and the expression of platelet surface antigens was not significantly different for the study groups compared with controls. The initial drop in platelet count during and after ECC in all groups is probably caused by haemodilution. These results support the findings of Driessen *et al.*,[16] but are in contrast to others.[3] Our data on platelet count are supported by the similarity of platelet surface antigen expression in all groups. GP IIb–IIIa, the fibrinogen receptor on the platelet surface, was

Table 1   Details of patients and surgical procedure (mean ± standard deviation)

	Age	EF (%)	Minimum core temp. (°C)	ECC time	Crossclamp time	Distal anastomosis (no.)	ITA grafts (%)	Stay on ICU	Ventilation (h)	Periop. deaths (no.)
Group I (n = 40)	61.7 ± 8.0	64 ± 16	31.9 ± 1.4	103 ± 28	62 ± 20	3.5 ± 1.0	60	1.1 ± 0.3	16 ± 4	0
Group II (n = 40)	63.1 ± 8.5	53 ± 21*	31.8 ± 1.4	100 ± 24	60 ± 18	3.6 ± 1.1	35*	1.3 ± 1.5	16 ± 5	0
Group III (n = 40)	63.5 ± 8.6	55 ± 16*	31.5 ± 1.6	102 ± 22	62 ± 19	3.7 ± 1.1	43*	1.6 ± 1.9	17 ± 5	2

ECC, extracorporeal circulation; ITA, internal thoracic artery; EF, ejection fraction; ICU, intensive care unit.
*$p < 0.05$

Table 2   Postoperative data and use of blood products

	CTD in ml (mean ± SD)	Rethoracotomy for bleeding (no.)	Units of FFP (mean ± SD)	Patients requiring FFP (no.)	Units of packed cells (mean ± SD)	Patients requiring packed cells (no.)
Group I (n = 40)	840 ± 335	1	1.2 ± 2.0	14	2.0 ± 2.3	24
Group II (n = 40)	820 ± 366	0	1.1 ± 2.2	10	1.5 ± 1.8	22
Group III (n = 40)	513 ± 409*	0	0.4 ± 1.0*	5*	1.0 ± 1.7*	5*

CTD, chest-tube drainage; FFP, fresh frozen plasma.
*$p < 0.05$
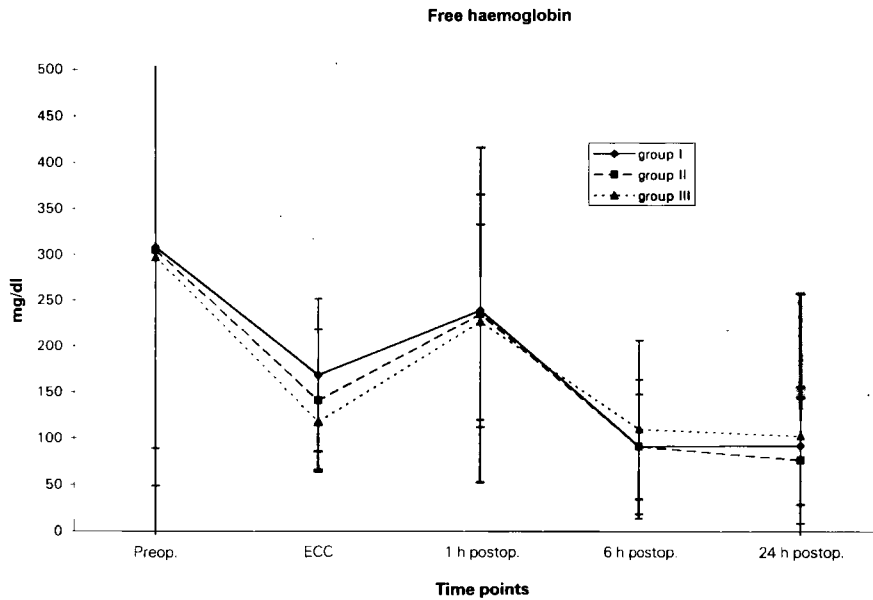
Free haemoglobin

Figure 1 Free haemoglobin in groups I, II and III
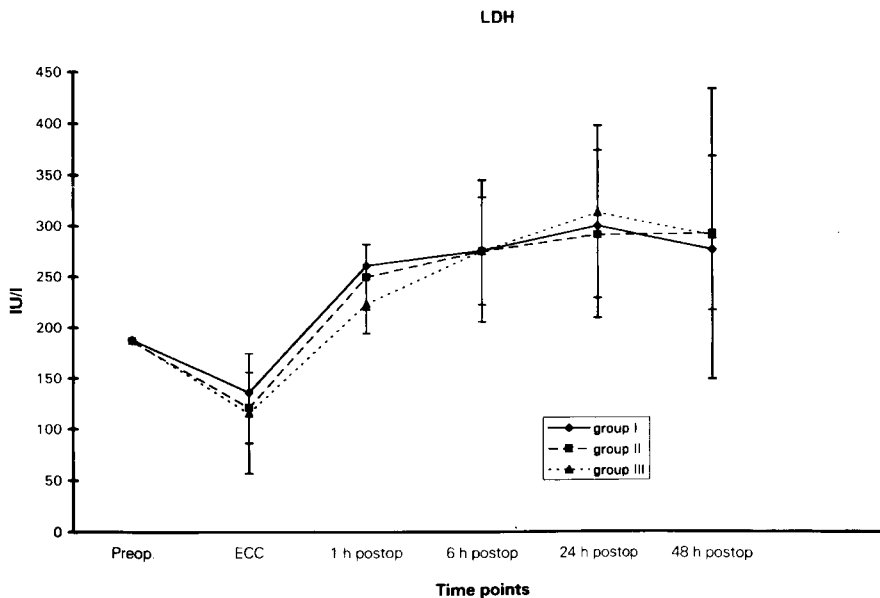
LDH

Figure 2 Lactic dehydrogenase (LDH) in group I, II and III

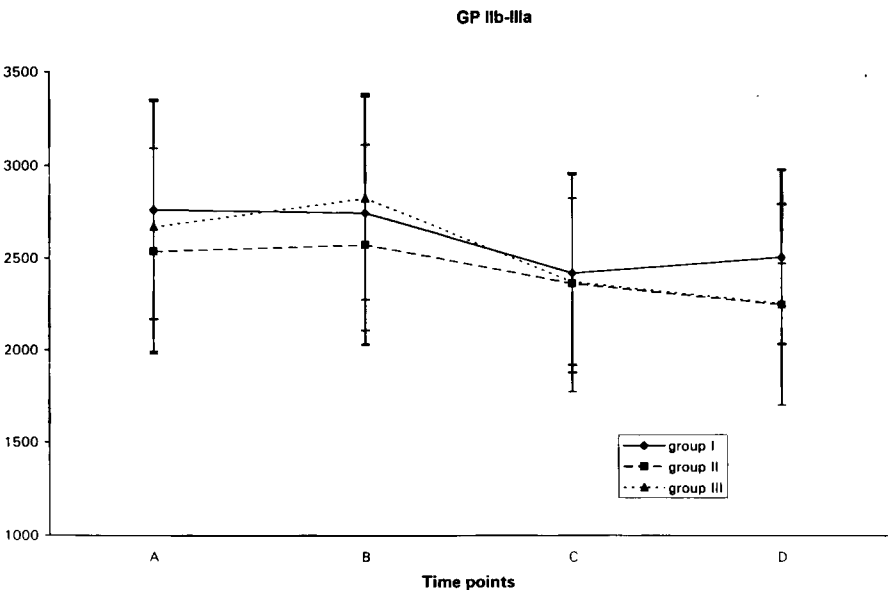**GP IIb-IIIa**

Figure 3   Expression of platelet surface glycoprotein IIb–IIIa in group I, II and III in arbitrary units
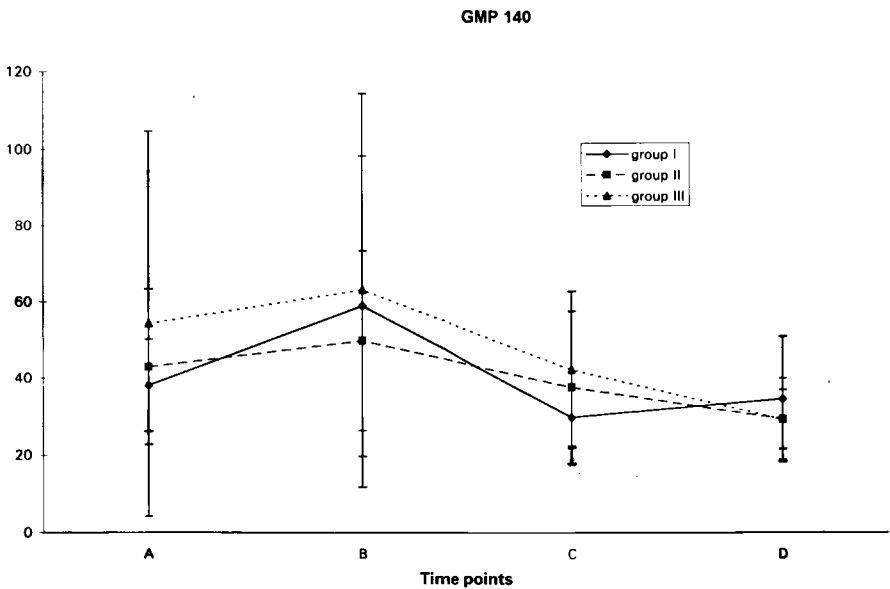
GMP 140

Figure 4   Expression of platelet surface granule membrane protein 140 in group I, II and III in arbitrary units
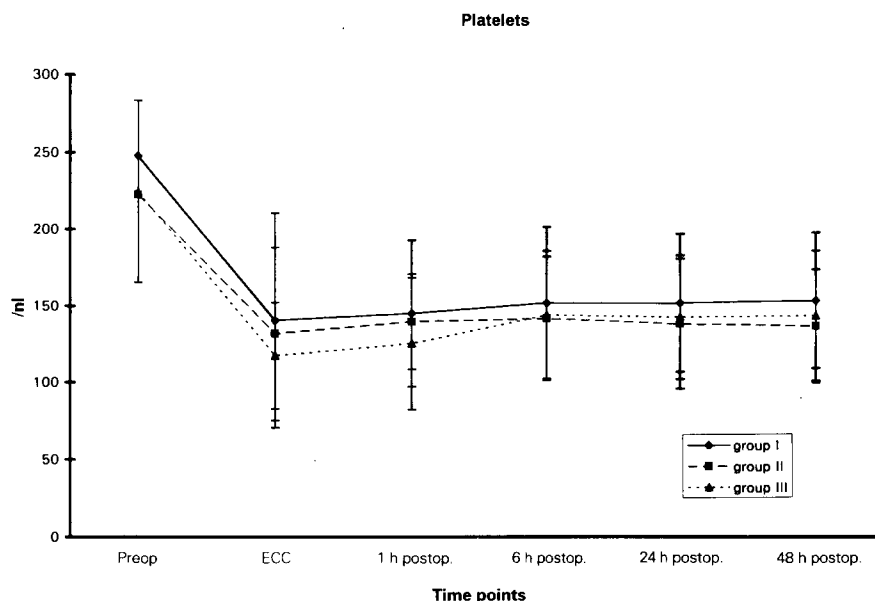
Platelets

Figure 5 Platelet count in group I, II and III

found to be reduced in ECC.[18] it was suggested that this contributes to the platelet function defect of CPB.[18] We also found a significant reduction in GP IIb–IIIa expression during ECC ($p < 0.05$). GMP 140, a marker of platelet activation, was significantly reduced during ECC in groups I and II. The decrease in GMP 140 in group III did not reach statistical significance. This may be related to the small number of cases in each group.

Our data on platelet surface antigens support the hypothesis that centrifugal blood pumps do not improve platelet function in routine CPB. We found no effect of aprotinin on platelet count and surface antigen expression. Van Oeveren *et al.* published similar results for platelet count and GP IIb–IIIa.[19] In addition, they found a preservation of GPIb expression,[19] which was not measured in this study. There was no difference in the length of stay (LOS) in the intensive care unit or time on ventilator between any of the groups. Similar results were reported by others.[14,15] However, total hospital stay was reported to be shortened by the use of centrifugal blood pumps.[2] Total hospital stay was not investigated here because patients were transferred to medical wards in our

hospital and elsewhere as soon as appropriate, usually on the fifth to seventh postoperative day. We suggest that LOS is not a sensitive indicator of performance, at least in continental hospitals, since the discharge of patients is influenced by a number of administrative variables. Moreover, the LOS in ICU and in the hospital may be influenced by patient-independent factors like the availability beds on the ward. In our institution, patients are discharged routinely from ICU on the first postoperative morning. This may explain the difference in LOS in ICU between our data and others (1.1 versus 3.0 days for roller pump).[14]

Postoperative deaths were nil in groups I and II. Two patients in group III died. In one patient with a preoperative ejection fraction of 20%, the cause of death was multiorgan failure that developed unexpectedly on the first postoperative day. The other patient had a reduced myocardial contractility preoperatively and severe diffuse peripheral coronary artery disease. He was shown to have occlusion of all five bypass grafts on the second postoperative day and died, despite reoperation, from congestive heart failure on the seventh postoperative day. Another patient in group III

required reoperation for unexpected occlusion of one of two bypass grafts, three months following the initial operation. Although statistical significance was not reached, the question should be raised whether aprotinin may increase mortality and early graft failure. This has been suggested previously, in particular when profound hypothermia was employed.[20,21] This effect may be mediated by a phase of hypercoagulability during ECC when aprotinin is used.[22] Several double-blind randomized studies on the influence of aprotinin on early graft failure with postoperative angiographic control have been conducted. An influence of aprotinin on graft patency could not be shown.[23,24] Further investigations with larger numbers of patients need to be performed to answer this question finally. Another disadvantage of routine use of aprotinin may arise through allergic reactions. Therefore, at present, we reserve the use of aprotinin to patients who have an increased risk of bleeding after heart surgery.

In conclusion, we were unable to show a beneficial effect of the centrifugal blood pump on a number of postoperative variables in elective coronary artery bypass grafting. The routine use of these pumps is currently not recommended in respect of higher costs. In contrast, aprotinin significantly reduces postoperative blood loss and the requirements for blood products. This must be weighed against potential adverse effects of this drug.

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