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Autologous Platelet-rich Plasma Does Not Reduce Transfusion of Homologous Blood Products in Patients Undergoing Repeat Valvular Surgery

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Background: **Patients undergoing cardiac surgery employing cardiopulmonary bypass frequently require transfusion of homologous blood products and, therefore, are exposed to the risk of transfusions. Autologous platelet-rich plasma administration may reduce homologous transfusion and attendant risks.**

Methods: **In a blinded, randomized fashion, patients undergoing repeat sternotomy and valvular surgery received either a sham product (n = 28) or autologous platelet-rich plasma (n = 28) at the conclusion of cardiopulmonary bypass. Perioperative blood loss, coagulation profiles, and transfusion requirements were compared between the two groups.**

Results: **In the first 24 h postoperatively, both the platelet-rich plasma and sham groups received a median of 10.5 units of homologous blood products. Total median perioperative homologous transfusion requirements were 13 and 11.5 units for the platelet-rich plasma and sham groups, respectively. There was no significant difference in intraoperative or postoperative bleeding between the groups.**

Conclusions: **Autologous platelet-rich plasma did not reduce perioperative bleeding or transfusion requirements in repeat valvular surgery. (Key words: Blood: coagulation. Surgery: cardiac. Transfusion: plasmapheresis; plateletpheresis.)**

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PATIENTS undergoing cardiac surgery employing cardiopulmonary bypass (CPB) are at substantial risk for blood loss because of surgical trauma and a multitude of possible hemostatic defects.[1–3] Bleeding, which is commonly due to impairment of platelet function and defects in soluble coagulation factors, frequently requires transfusion of homologous blood products.[1,3] Intraoperative blood salvage is known to decrease the need for homologous transfusion by providing washed autologous erythrocytes.[4,5] Another intraoperatively collected product, autologous platelet-rich plasma, has the theoretical potential to decrease homologous transfusions by attenuating or eliminating the hemostatic defects. This technique involves the pre-CPB removal of approximately 20% of the patient's plasma volume and 25% of the circulating platelets with subsequent administration to the patient after CPB. A few nonblinded studies using platelet-rich plasma have documented increased numbers of circulating platelets after CPB, decreased bleeding, and decreased homologous transfusion requirements.[6–8] However, nonblinded trials may contain significant bias because transfusion practices are influenced by subjective criteria and by preconceived ideas regarding therapeutic effectiveness of certain procedures. It is unlikely that platelet-rich plasma would be beneficial and reduce transfusion requirements in all clinical situations.

Therefore, this prospective, randomized, and blinded study was instituted to determine the effect of autologous platelet-rich plasma on perioperative coagulation profiles, bleeding, and transfusion requirements. Patients undergoing repeat sternotomy and valvular surgery were selected because of their increased risk for

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bleeding, coagulopathy, and transfusion requirements as seen in our practice.††

Methods

After Institutional Review Board approval and written informed consent were obtained, 56 patients undergoing repeat valvular surgery were enrolled in the study. The patients were required to be older than 18 yr and to weigh more than 45 kg. Pregnant women were excluded. Patients also were excluded from the study if they were receiving thrombolytic therapy or had a history of a bleeding disorder. Patients with serum creatinine higher than 2.0 mg/dl or documented preexisting platelet dysfunction also were excluded. In patients in whom anticoagulation was in effect, the warfarin sodium was discontinued and the prothrombin time (PT) was allowed to return to normal in preparation for surgery.

Participants were randomized to one of two groups: sham procedure (control; n = 28) and autologous platelet-rich plasma procedure (study; n = 28). Anesthesia was induced and maintained with fentanyl (50–100 μg/kg), midazolam (0.2–0.5 mg/kg), and pancuronium or vecuronium. Isoflurane or enflurane (<0.25 MAC) was added to maintain hemodynamic stability. After tracheal intubation, all participants had a pulmonary artery catheter and an 8-Fr catheter inserted into the internal jugular vein. Once the patient was positioned and connections were made to the platelet-rich plasma instrument, the anesthesia personnel who had been involved in the case were replaced by different anesthesia personnel, of which one member was an anesthesiologist-investigator. This anesthesiologist-investigator was responsible for the management of the patient during the platelet-rich plasma or sham procedure. To blind all other operating room personnel to the identity of the procedure, the instrument used to collect the platelet-rich plasma and the autotransfusion personnel operating it were visually isolated by surgical drapes hung from intravenous poles. The autotransfusion personnel communicated only with the anesthesiologist-investigator during the collection period.

The platelet-rich plasma collection was performed with the Plasma Saver (Haemonetics, Braintree, MA) using a draw rate of 60 ml/min and a return rate of 80 ml/min through the 8-Fr catheter. Anticoagulant (adenine-citrate-dextrose, solution A) was added to the withdrawn blood at a ratio of 1:12. Approximately 15–20% of the patient's plasma volume (600–700 ml) was collected. Erythrocytes that were separated in the centrifugation process were returned to the patient immediately after the platelet-rich plasma collection and before initiation of CPB. Intravascular volume was maintained with administration of 5% albumin solution to offset the temporary loss of blood volume due to the platelet-rich plasma collection process. The volume of albumin infused was based on maintaining stable hemodynamics as indicated by the heart rate, cardiac output, arterial pressure, and pulmonary artery diastolic and capillary wedge pressures.

For the sham procedure (control group), the preparation of the patient was the same as for the platelet-rich plasma procedure (study group). However, in the control group, the patient's blood was drawn only through the collection tubing. Subsequently, both tubing ends were clamped and the internal jugular catheter was irrigated with saline to avoid clotting. The tubing remained filled with blood, thus simulating ongoing platelet-rich plasma collection. The instrument was operated to simulate the sound of standard collection while the operator prepared a sham product consisting of 5% albumin gently mixed with approximately 10 ml of the patient's blood, which was collected *via* the arterial catheter. The volume of albumin used in the sham product was calculated as 20% of the patient's plasma volume. The simulated collection was continued for a comparable amount of time based on previous experience with noninvestigational platelet-rich plasma procedures. All required supplies and the collection instrument were covered and removed before the return of the previous anesthesia personnel who started the case. The sham or platelet-rich plasma product was labeled "Platelet-rich Plasma Study Product" and, once collected, was placed in an insulated bag and remained undisturbed until after protamine neutralization of heparin.

In preparation for CPB, each participant received 300 units/kg heparin for anticoagulation. Anticoagulation was monitored by the activated clotting time. The activated clotting time was maintained at more than 400 s for the duration of CPB. A standardized pump prime was used. Cardiopulmonary bypass was instituted with the use of a Bentley 10 bubble oxygenator (Baxter-Bentley, Irvine, CA) at a flow of 2.4 $l \cdot min^{-1} \cdot m^{-2}$.

†† Santrach PJ, Oliver WC, Williamson KR: Three-year review of transfusion requirements for cardiac surgery at Mayo Clinic. Unpublished data. 1991.

After the successful discontinuation of CPB, heparin anticoagulation was neutralized with protamine (0.013 mg/unit heparin). The study product was administered to the patient in a standardized fashion 10 min after protamine administration.

Variables recorded included age, sex, body surface area, procedure, height, weight, percent plasma volume removed, and the duration of CPB and aortic cross clamp. Blood loss after administration of the study product was estimated intraoperatively by recording the volume of salvaged blood from the surgical field as measured and processed by the rapid cell salvage machine. Chest-tube drainage in the intensive care unit was recorded for the first 24 h postoperatively. Homologous blood product usage was recorded from the start of surgery, for the first 24 h postoperatively, and for the entire hospitalization period. Laboratory tests obtained included hemoglobin, PT, activated partial thromboplastin time, activated clotting time, platelet count, fibrinogen, and the thrombelastogram (TEG). These tests were drawn after induction of anesthesia, after the sham or study procedure (but before CPB), 10 min after protamine administration, 45 min after administration of the study product, and 18–24 h postoperatively.

Statistical Analysis

Previous studies have reported a 40–65% reduction in homologous blood product usage with platelet-rich plasma. From a retrospective review of repeat valvular surgery at this institution, median homologous blood product usage was estimated to be 14 units in the first 24 h. Therefore, to be 80% certain (statistical power) of detecting a 50% reduction in the median homologous blood product usage from 14 to 7 units, it was necessary to enroll 28 patients in each arm of the study. This assumes that a one-sided Wilcoxon rank sum test is used with a type 1 error rate of 5%.[9]

The distributions of blood loss, autologous blood returned, and number of units of homologous blood products (erythrocytes, fresh-frozen plasma, platelets, cryoprecipitate) transfused were compared between the platelet-rich plasma and sham groups with a Wilcoxon rank sum test and/or two-sample t test when appropriate. The distributions of age, preoperative blood values, and the percent change over time ([(post − pre)/pre] × 100) in laboratory results (hemoglobin, PT, activated partial thromboplastin time, activated clotting time, platelet count, fibrinogen, and the TEG values) also were analyzed in this fashion. Comparisons between the two groups for discrete variables such as gender, aspirin or dipyridamole usage, and reexploration for surgical bleeding were made with the chi-square analysis and/or Fisher's exact test where appropriate. Within each group, the Wilcoxon signed rank test and/or one-sample t test were used to assess whether the median percent change in laboratory values was significantly different from zero. Since the distributions of most of the variables were non-Gaussian, the data are presented as median and interquartile ranges. P values for comparisons between groups for both 24-h and total perioperative homologous blood product usage are reported in a one-sided and two-sided manner, whereas all other tests are two-sided. P values less than 0.05 were considered statistically significant.

Results

Complete transfusion and coagulation data were recorded on all 56 patients enrolled. The two groups did not differ significantly in demographic characteristics, duration of aortic cross clamping or CPB, or in preoperative coagulation studies (table 1). There was no significant difference between the two groups in the

Table 1. Perioperative Clinical Characteristics

	PRP (n = 28)	Sham (n = 28)
Male, n (%)	18 (64.3)	18 (64.3)
Age (yr)*	68 ± 11.1	66 ± 11.6
Height (cm)*	169 ± 10.5	170 ± 10.2
Weight (kg)*	76.6 ± 19.0	76.4 ± 15.3
Preoperative hemoglobin (g/dl)*	12.6 ± 1.3	12.8 ± 1.9
Preoperative platelets ($\times 10^3/mm^3$)*	229 ± 55.4	217 ± 72.6
Aspirin or dipyridamole usage, n (%)	6 (21.4)	14 (50.0)‡
PRP volume (ml)†	690 (499, 863)	NA
PRP platelet yield (units)†	2.7 (1.7, 3)	NA
Cardiopulmonary bypass total time (min)†	113 (68, 170)	108 (68, 148)
Aortic cross-clamp time (min)†	74 (58, 95)	62 (46, 77)
Reexploration for surgical bleeding, n (%)	1 (3.6)	1 (3.6)

PRP = platelet-rich plasma; NA = not applicable.

* Mean ± SD.

† Median (25th, 75th percentiles).

‡ $P < 0.05$, PRP *versus* sham.

percentage of patients who required intraaortic balloon pump insertion or reexploration for surgical bleeding or who suffered complications. The percentage of patients who underwent normothermic CPB in the platelet-rich plasma (32.1%) and sham (42.9%) groups was not significantly different.

We did not observe a significant difference in perioperative blood loss between the two groups (table 2). Transfusion requirements did not differ significantly between the two groups during the first 24 h or for the entire hospitalization period (fig. 1, table 2). During the first 24 h, the median of homologous units transfused was 10.5 units for both groups (one-sided $P = 1.0$, two-sided $P = 0.76$; Wilcoxon rank sum test). For the entire hospitalization period, the median units transfused also were not significantly different (one-sided $P = 1.0$, two-sided $P = 0.92$). A similar lack of significant difference between normothermic and hypothermic patients was seen.

There were minor differences between the two groups with respect to coagulation function (table 3). Before the platelet-rich plasma or sham procedure, there was no significant difference between the two groups in coagulation function except that the median TEG angle of divergence (α) value was significantly higher in the platelet-rich plasma group ($P < 0.001$; Wilcoxon rank sum test). Within the sham group, the median percent change in coagulation parameters before and after the sham collection was significantly different from 0 for hemoglobin, activated partial thromboplastin time, platelet count, and the TEG reaction time (R), coagulation time (R + K), and α values ($P < 0.05$; one-sample t test and/or Wilcoxon signed rank test; table 4). The median percent change from before to after platelet-rich plasma collection was significantly elevated for PT and reduced for hemoglobin, platelet count, fibrinogen, and the TEG R value ($P < 0.05$). When comparing the percent change in coagulation parameters between the two groups following the platelet-rich plasma or sham collection, some significant differences were noted (fig. 2, table 4). In the platelet-rich plasma group, the median percent change in the PT was significantly prolonged ($P = 0.043$), the fibrinogen was significantly reduced ($P < 0.001$), the maximal amplitude of the TEG value was significantly

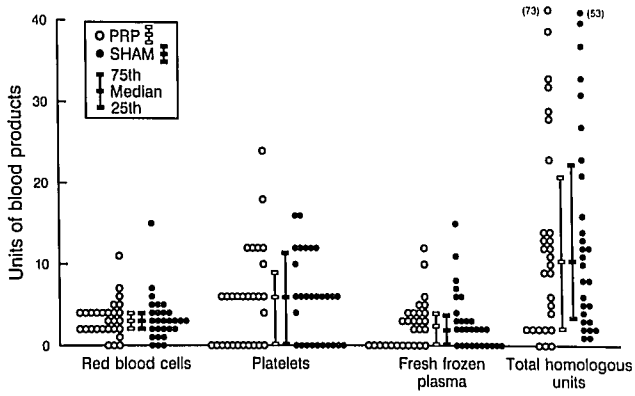

Fig. 1. Distribution of homologous blood product usage during the first 24 h after platelet-rich plasma or sham infusion. Median and interquartile ranges (25th and 75th percentiles) are indicated for each group. There were no significant differences in blood product usage between the patients who received the platelet-rich plasma and sham product.

Table 2. Blood Loss and Transfusion Requirements in PRP *Versus* Sham Groups

	First 24 h		Total Perioperative Transfusion Requirements	
	PRP	Sham	PRP	Sham
Intraoperative blood loss (ml)	2,650 (1,493, 2,950)	1,975 (1,550, 2,950)	—	—
Chest tube drainage first 24 h (ml)	950 (463, 2,029)	975 (690, 1,520)	—	—
Autologous transfusion (units)	5.2 (3.7, 6.4)	5.0 (4.0, 5.8)	5.4 (3.8, 6.9)	5.0 (4.0, 6.0)
Homologous transfusion (total)	10.5 (2.0, 20.8)	10.5 (3.3, 22.5)	13.0 (4.0, 22.8)	11.5 (4.0, 22.5)
Erythrocytes (units)	3.0 (2.0, 4.0)	3.0 (2.0, 4.0)	4.0 (3.3, 6.0)	4.0 (2.0, 5.0)
Fresh-frozen plasma (units)	2.5 (0, 4.0)	2.0 (0, 3.8)	2.5 (0, 4.0)	2.0 (0, 4.8)
Platelets (units)	6.0 (0, 9.0)	6.0 (0, 11.5)	6.0 (0, 11.5)	6.0 (0, 11.5)
Cryoprecipitate (units)	0 (0, 0)*	0 (0, 4.5)†	0 (0, 0)	0 (0, 4.5)

Data are reported as median (25th, 75th percentiles). No significant differences between PRP and sham groups.

PRP = platelet-rich plasma.

* Four patients had 10 units; 1 patient had 34 units.

† One patient had 6 units, 5 patients had 10 units, and 1 patient had 11 units.

Table 3. Coagulation Data in PRP and Sham Groups at Five Perioperative Intervals

Coagulation Parameter	Baseline	After Collection	After Bypass and Protamine	Post Product Infusion	18–24 h Postoperation
HgB PRP (g/dl)	11.6 (10.3, 12.3)	10.8 (9.9, 11.7)	8.1 (7.4, 9.4)	8.5 (7.7, 9.9)	8.4 (7.6, 9.4)
HgB sham (g/dl)	11.7 (10.2, 12.9)	11.2 (9.4, 12.2)	8.2 (7.8, 9.3)	8.8 (8.3, 9.7)	8.9 (7.8, 9.6)
PT PRP (s)	12.9 (12.2, 13.4)	13.2 (12.7, 13.7)	18.9 (16.4, 20.9)	17.1 (15.2, 18.7)	14.0 (12.8, 15.0)
PT sham (s)	13.4 (12.3, 14.6)	13.5 (12.4, 14.7)	18.3 (16.3, 20.4)	17.6 (16.4, 18.9)	14.8 (13.4, 16.4)
aPTT PRP (s)	34 (31, 42)	37 (29, 45)	64 (50, 78)	58 (46, 65)	45 (38, 60)
aPTT sham (s)	35 (28, 44)	38 (34, 45)	58 (49, 75)	60 (45, 70)	46 (35, 58)
ACT PRP (s)	136 (126, 150)	147 (127, 160)	140 (128, 150)	138 (123, 149)	154 (128, 167)
ACT sham (s)	146 (129, 161)	147 (131, 165)	140 (125, 155)	137 (122, 153)	149 (137, 159)
Platelet PRP ($\times 10^3/mm^3$)	198 (160, 243)	179 (146, 211)	95 (70, 138)	138 (100, 181)*	119 (84, 163)
Platelet sham ($\times 10^3/mm^3$)	178 (147, 236)	160 (133, 220)	113 (75, 151)	121 (98, 141)	114 (87, 134)
Fibrinogen PRP (mg/dl)	299 (263, 358)	271 (218, 288)	146 (109, 191)	163 (129, 223)*	246 (208, 291)
Fibrinogen sham (mg/dl)	263 (239, 328)	262 (232, 318)	164 (134, 189)	155 (116, 170)	248 (196, 297)
Thromboelastogram					
R PRP (s)	18 (16, 19)	16 (15, 17)	17 (13, 19)	15 (13, 19)	14 (13, 16)
R sham (s)	18 (15, 21)	17 (14, 19)	16 (13, 20)	15 (12, 19)	15 (12, 16)
R + K PRP (s)	24 (22, 26)	23 (21, 26)	26 (21, 29)	22 (18, 27)	22 (18, 25)
R + K sham (s)	26 (22, 30)	25 (20, 28)	24 (20, 31)	23 (19, 34)	22 (19, 23)
MA PRP (mm)	55 (52, 59)	56 (49, 57)	47 (43, 50)	51 (44, 57)	50 (44, 59)
MA sham (mm)	54 (50, 58)	54 (49, 61)	49 (43, 53)	48 (42, 53)	53 (48, 56)
α PRP (°)	50 (48, 54)*	49 (41, 52)	40 (34, 48)	46 (37, 52)*	48 (39, 56)
α sham (°)	43 (38, 48)	46 (39, 53)	41 (33, 48)	40 (31, 46)	49 (41, 52)

Data are reported as median (25th, 75th percentiles).

PRP = platelet-rich plasma; HgB = hemoglobin; PT = prothrombin time; aPTT = activated partial thromboplastin time; ACT = activated coagulation time; R = reaction time; R + K = coagulation time; MA = maximal amplitude; α = angle of divergence.

* PRP *versus* sham, $P < 0.05$.

reduced ($P = 0.03$), and the TEG α value was significantly reduced ($P = 0.003$).

After protamine neutralization of heparin anticoagulation, there were no significant differences between the two groups with regard to coagulation parameters (table 3). The median percent change in a few of the coagulation parameters after administration of the study product compared with the previous time differed significantly between the two groups. In the platelet-rich plasma group, there was a greater median percent reduction in PT, increase in platelet count and fibrinogen, and increase in maximal amplitude of the TEG, compared to the sham group ($P < 0.01$; fig. 2, table 4).

At the end of the surgical procedure (*i.e.*, after product infusion), however, there was no significant difference between the control and study groups when comparing the median percent change in coagulation function from the baseline results (table 4).

Discussion

In this prospective, randomized, and blinded evaluation of platelet-rich plasma, we did not demonstrate a significant reduction in perioperative blood loss or homologous blood product transfusion requirements in patients who underwent repeat valvular surgery. Furthermore, there were minor changes in the coagulation profile associated with collection and administration of platelet-rich plasma. This previously unstudied group of patients was chosen because they are at risk for blood loss, perioperative coagulopathy, and increased transfusion requirements.

One challenge in evaluating the efficacy of a technique such as platelet-rich plasma is removing bias from the investigation. Previous evaluations of platelet-rich plasma have been performed without blinding of the participating clinicians[7,8,10] and have demonstrated that the use of autologous platelet-rich plasma reduces requirements for erythrocytes, fresh-frozen plasma, platelets, and cryoprecipitate.[6–8] The transfusion of blood products is influenced greatly by the subjective appearance of the surgical field and individual preferences in transfusion practice. However, the absence of blinding could lead to bias in transfusion practices based on preconceived notions of the effectiveness of platelet-rich plasma in reducing homologous blood

Table 4. Percent Changes in Coagulation Function between PRP and Sham Groups

	Before to After Collection		Before to After Product Infusion		Before Collection to After Infusion	
Coagulation Parameter	PRP	Sham	PRP	Sham	PRP	Sham
HgB (g/dl)	−3.5	−4.9	2.8	4.5	2.8	4.5
	(−9.9, 1.7)	(−9.6, −0.5)	(0, 15.1)	(−6.5, 13.7)	(0, 14.7)	(−6.5, 13.3)
Prothrombin time (s)	2.7	0*	−9.3	−2.1*	30.6	27.3
	(0.6, 5.8)	(−4.2, 3.3)	(−12.8, −5.4)	(−9.4, 2.8)	(19.9, 41.7)	(20.4, 39.0)
aPTT (s)	9.8	7.1	−10.7	−5.4	66.1	56.3
	(−7.5, 22.2)	(−5.9, 23.9)	(−21.1, 1.3)	(−20.2, 4.5)	(22.2, 106.4)	(31.3, 110.5)
ACT (s)	5.1	0	−2.3	4.6	0	−4.0
	(−5.4, 13.0)	(−10.5, 8.2)	(−12.6, 5.3)	(−10.5, 9.3)	(−15.8, 11.1)	(−17.9, 5.8)
Platelet ($\times 10^3/mm^3$)	−12.0	−5.1	34.8	3.6*	−32.0	−31.2
	(−17.7, −6.4)	(−12.2, −0.9)	(13.6, 68.2)	(−7.8, 21.1)	(−47.0, −15.4)	(−45.9, −26.0)
Fibrinogen (mg/dl)	−15.8	−4.1*	13.4	−11.6*	−41.8	−49.0
	(−21.0, −10.0)	(−8.4, 2.8)	(6.5, 26.2)	(−21.4, −5.6)	(−50.7, −37.9)	(−56.9, −38.6)
Thromboelastogram						
R (s)	−7.5	−10.8	−7.5	−6.2	−19.1	−20.0
	(−21.1, 5.9)	(−25.3, 7.3)	(−25.7, 22.0)	(−22.1, 13.2)	(−31.3, 13.3)	(−38.9, 6.7)
R + K (s)	−4.2	−13.5	−13.7	1.2	−6.3	−8.3
	(−16.5, 7.4)	(−29.7, 4.9)	(−23.8, 5.6)	(−22.4, 22.3)	(−28.0, 16.7)	(−34.6, 12.0)
MA (mm)	−4.1	0*	6.6	−5.1*	−6.6	−12.7
	(−7.8, 1.8)	(−4.6, 8.6)	(−0.4, 18.6)	(−11.1, 7.0)	(−19.1, −1.6)	(−17.8, −2.0)
α (°)	−4.2	9.5*	2.8	0	−11.6	−8.5
	(−13.8, 2.4)	(−1.1, 26.6)	(−7.0, 41.1)	(−17.2, 15.0)	(−29.3, 4.2)	(−20.0, 6.4)

Data are reported as median percent change (25th, 75th percentiles).

NS = no significant differences in the distribution of the percent change between the groups; PRP = platelet-rich plasma; HgB = hemoglobin; aPTT = activated partial thromboplastin time; ACT = activated coagulation time; R = reaction time; R + K = coagulation time; MA = maximal amplitude; α = angle of divergence.

* PRP *versus* sham, $P < 0.05$.

product transfusion requirements and could lead to erroneous conclusions. In the present investigation, a blinding procedure was developed and applied in an effort to minimize any biases in transfusion practices. Effectively blinding all individuals in the operating room to the knowledge of whether the patient was undergoing the platelet-rich plasma or sham procedure was vital. One might argue that a better blinding procedure would be to withdraw platelet-rich plasma in both groups of patients to be followed by the immediate reinfusion of the product into the sham patient and subsequent preparation of a sham product. It is possible that some degree of platelet inactivation or disruption may occur during the platelet-rich plasma collection procedure.[11] This potentially detrimental effect in that blinding design could handicap the sham group, exaggerate the differences between the two groups, and contribute to erroneous conclusions. The effectiveness of the blinding procedure was not formally investigated in this study. We believe that careful management of volume status and hemodynamics adequately disguised the identity of the study group. Interviews with the participating cardiac surgeons and anesthesiologists supported that conclusion.

The criteria for transfusion of blood products were not specifically outlined. This may have resulted in some variability with respect to the transfusion practice of the individual clinicians. We chose not to include specific transfusion criteria because our goal was to simulate standard clinical practice as closely as possible. Assigning artificial or limiting criteria for transfusion would introduce restrictions not present in normal clinical practice. The differences concerning transfusion practices between individual anesthesiologists and cardiac surgeons were minimized by the prospective, randomized, and blinded nature of this study.

Postoperative blood loss was obtained from the chest-tube drainage collected in the first 24-h period in the intensive care unit. Each patient admitted to the cardiac surgery intensive care unit routinely is monitored with an hourly determination of chest-tube output, an important factor involved in determination of blood product transfusion.

Minor changes in coagulation function were noted with collection and administration of platelet-rich plasma. As one might expect in the platelet-rich plasma group, the removal of platelets and plasma resulted in an increase in the PT and a decrease in platelet count and fibrinogen. Subsequent administration of platelet-rich plasma after CPB slightly improved coagulation function. The PT in the platelet-rich plasma group was shortened to a greater extent than in the sham group, and as one would expect, the number of platelets and fibrinogen increased to a significantly greater degree in the platelet-rich plasma group. Administration of platelet-rich plasma also resulted in an increase in the maximal amplitude of the TEG. However, when comparing the baseline values to those at the end of the surgery, there were no significant differences between patients in the platelet-rich plasma and sham groups. Perhaps administration of platelet-rich plasma merely corrected the minor reduction in coagulation function that occurred as a result of its collection.

Medications that could potentially affect platelet function and blood loss in either group were evaluated. Fifty percent of the patients in the sham group had received either aspirin or dipyridamole preoperatively compared to only 21.4% of the patients in the platelet-rich plasma group ($P = 0.026$). These drugs could result in an inhibition of platelet activity, and one would anticipate a small decrease in coagulation function and possibly increased blood loss. A reduction in platelet function in the sham group would have exaggerated differences in homologous transfusion requirements between the control and study groups, yet the data did not demonstrate any significant differences.

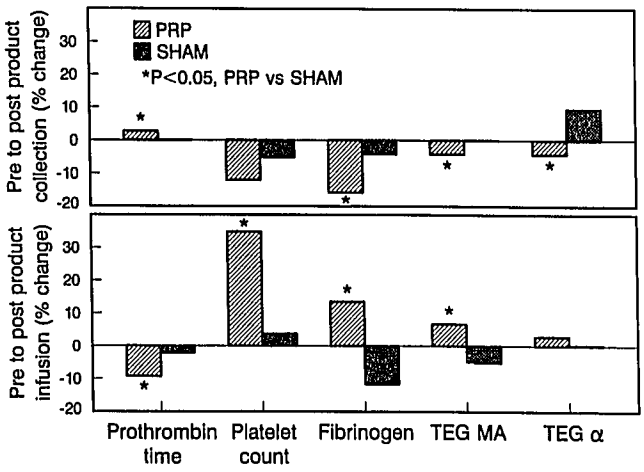

Fig. 2. Median percent changes in coagulation function for patients who received the platelet-rich plasma or sham product. (*Top*) Changes from before to after product collection. (*Bottom*) Changes from before to after product infusion. α = angle of divergence; MA = maximal amplitude; TEG = thrombelastogram.

In addition to the previously reported beneficial effects of platelet-rich plasma on homologous blood product requirements and perioperative blood loss after CPB, a recent study demonstrated an improvement in pulmonary function and arterial oxygen tension following tracheal extubation in patients who received platelet-rich plasma in comparison to those who did not receive platelet-rich plasma.[12] Removal of leukocytes in the platelet-rich plasma may decrease the amount of elastase, a neutrophil-derived enzyme implicated as a cause of pulmonary dysfunction, which is released during CPB.[13,14] Review of our patients' arterial oxygen tension immediately after tracheal extubation revealed no significant difference between the two groups.

Recently, there has been increased interest in normothermic CPB.[15] This study was conducted under normothermic or mild-to-moderate hypothermic CPB conditions. It is possible that hypothermic CPB may affect platelet function differently than normothermic CPB; however, quantitative and qualitative alterations in platelets during CPB are more likely related to interactions between the platelets and the synthetic surfaces of the extracorporeal circuit.[16,17] The patients in this study were fully rewarmed before emergence from CPB, and analysis of the thermal subgroups within the platelet-rich plasma and sham groups was not informative.

Because so many factors influence blood transfusion, certain therapies, such as platelet-rich plasma, may prove effective in some situations but not in others. For example, prolonged CPB, severe preoperative platelet dysfunction, or the type of surgery may render a blood conservation technique minor in comparison with the coagulation insult. Furthermore, platelet-rich plasma may not result in the collection of the very large and most potent platelets that remain in the packed erythrocyte layer during platelet-rich plasma separation.[18]

A procedure such as platelet-rich plasma collection, which requires the insertion of a dedicated, large-bore central venous catheter and has the potential for hemodynamic instability during the collection process, is not without risk. The identification of groups of patients who may benefit from platelet-rich plasma with the lowest risk seems warranted. Although this study

did not identify any beneficial effect from platelet-rich plasma, we cannot conclude that other groups of patients in other clinical situations may not benefit. Further studies are needed to clarify these issues. The combination of platelet-rich plasma and various pharmacologic approaches to reduce blood loss such as desmopressin acetate, prostacyclin, tranexamic acid, epsilon aminocaproic acid, and aprotinin also may warrant investigation.[19–23]

In conclusion, this study demonstrated that platelet-rich plasma did not reduce blood loss or homologous transfusion requirements in patients who underwent repeat valvular surgery. This was a prospective and randomized study designed to also blind the anesthesiologist and cardiac surgeon as to whether the patient received the platelet-rich plasma technique of blood conservation. Additional studies using blinded methodology should be conducted to better define the efficacy of these blood conservation therapies and the conditions for optimal clinical response, especially in patients undergoing other types of cardiac surgery.

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