Cell Saver device efficiently removes cell-derived microparticles during cardiac surgery

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At the end of cardiac procedures assisted by cardiopulmonary bypass (CPB), a large volume of diluted blood (0.75-1.5 L) remains within the extracorporeal circuit. To reduce transfusion requirements, this blood can be used for autotransfusion with or without processing. One of the options for processing is the use of a Cell Saver device (Haemonetics, Braintree, Mass) that concentrates erythrocytes and discards plasma. During CPB, elevated numbers of cell-derived vesicles, microparticles, are present that promote coagulation and inflammation.¹ The aim of this study was to determine the effects of a Cell Saver device on microparticle counts during a cardiac operation. Heparin and prothrombin fragment F₁₊₂ were measured as controls for the efficient removal of low-molecular-weight substances.

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Patients and Methods

Patients for elective coronary artery bypass grafting assisted by CPB (n = 13) were included after signed informed consent. This study was approved by the Medical Ethics Committee of the Academic Medical Center (Amsterdam, The Netherlands). Blood was collected before and after processing with a Cell Saver device (Cell Saver 5). Cell counts were determined on a CellDyn 4000 hematology analyzer (Abbott, Mijdrecht, The Netherlands). Microparticles, prothrombin fragment F₁₊₂, and heparin were determined as described previously.^{2,3} Concentrations of heparin, microparticles, and F₁₊₂ were corrected for hematocrit. Data were analyzed with SPSS version 11.0 (SPSS, Inc, Chicago, Ill) and presented as medians (interquartile range). The paired-samples *t* test or Wilcoxon signed rank test was used whenever appropriate.

Results and Discussion

All data are summarized in Table 1. Processing with the Cell Saver device decreased blood volume about 2-fold from 850 mL to 440 mL. As expected, the hematocrit value increased from 0.26 (before) to 0.55 (after cell salvage; *P* < .001). The recovery of the erythrocytes was almost 100% (*P* = .161). In contrast, about 89% of the platelets (*P* < .001) and 31% of the leukocytes (*P* < .001) were removed by the Cell Saver device. Small molecules like heparin and F₁₊₂ were removed efficiently by 100% (*P* < .001) and 98% (*P* = .003), respectively. The data demonstrating the efficiency of the Cell Saver device to recover erythrocytes and to remove platelets, leukocytes, and heparin are all in close agreement with data provided by the manufacturer in the Cell Saver 5 Equivalence Validation Report of September 20, 1993 (95.8%

TABLE 1. Cell Saver device data

	Cell Saver device		Removal (%)	<i>P</i> value
	Before	After		
Volume (mL)	850 (796-934)	440 (323-481)	53 (46-63)	<.001
Hematocrit (L/L)	0.26 (0.24-0.26)	0.55 (48-0.60)	NA	<.001
Erythrocytes (mL)	217 (199-246)	199 (178-253)	3 (-5-17)	.161
Thrombocytes (10 ⁹)	140 (85-179)	16 (10-21)	89 (79-91)	<.001
Leukocytes (10 ⁹)	4.7 (3.1-6.0)	3.8 (1.5-4.0)	31 (18-45)	<.001
Heparin (10 ³ IU)	1765 (1666-2053)	9 (4-11)	100 (99-100)	<.001
F ₁₊₂ (nmol)	2.47 (0.50-7.39)	0.04 (0.03-0.05)	98 (92-99)	.003
EryMP (10 ⁷)	128 (37-292)	5 (2-5)	97 (86-99)	.002
PMP (10 ⁷)	147 (93-191)	1 (1-2)	99 (98-99)	<.001

Data are presented as medians (interquartile ranges). NA, Not applicable; F₁₊₂, prothrombin fragment; EryMP, erythrocyte-derived microparticles; PMP, platelet-derived microparticles.

erythrocyte recovery; 82% and 24.3% for platelets and leukocytes, respectively; 97.8% for heparin).

Cell-derived microparticles are, on average, smaller in diameter than platelets and range in size from about 100 nm to 1.0 μ m. Thus, the largest microparticles may overlap in size with platelets, which on average range in from 1.0 μ m to 5.0 μ m. Both erythrocyte-derived microparticles and platelet-derived microparticles were removed efficiently (97% and 99%; $P = 0.002$ and $P < .001$, respectively). Interestingly, the efficiency of the Cell Saver device to remove platelet-derived microparticles as well as erythrocyte-derived microparticles was significantly increased compared with the efficiency to remove thrombocytes ($P = .019$ and $P = .002$, respectively; Wilcoxon signed rank test). Thus, cell-derived vesicles, which on average are smaller in diameter than thrombocytes, are removed more efficiently from blood by a Cell Saver device than thrombocytes in a clinical setting.

This study is the first to directly evaluate the efficiency of a Cell Saver device to remove cell-derived microparticles from patient

blood. Our data show that a Cell Saver device efficiently reduces the numbers of coagulation- and inflammation-promoting microparticles. From these data we cannot exclude that microparticles may bind to cells present within the blood or that low numbers of microparticles are generated by cell activation during the passage of blood through the Cell Saver device.

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Primary intrapulmonary thymoma associated with congenital hyperhomocysteinemia

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Primary intrapulmonary thymomas (PITs) are very uncommon, with 28 cases reported to date.¹⁻³ Because of the paucity of studies, the biologic behavior and pathologic features of these neoplasms are not well known. The C677T methylenetetrahydrofolate reductase (*MTHFR*) genotype is a congenital disorder leading to low folate levels; the resultant mild hyperhomocysteinemia is associated with increased risk of venous thromboembolism and malignancies.^{4,5}

We present a case of PIT associated with hyperhomocysteinemia caused by the C677T variant of *MTHFR*.

Clinical Summary

A 73-year-old woman was admitted for acute dyspnea with bronchospasm in a chronic obstructive pulmonary disease pathologic

substrate. Her medical history was marked by episodes of venous thrombosis caused by a mutation of the *MTHFR* gene that imposed a preventive anticoagulant therapy. Chest radiography revealed an 18-mm nodule in the right upper lobe, which was confirmed by a computed tomographic scan (Figure 1). A positron emission tomographic scan showed a moderate uptake in correspondence of the lesion (standardized uptake value, 2.2). The results of bronchoscopy and computed tomographic scanning of the brain were normal.

A primary pulmonary tumor was suspected. Thoracotomy was performed by one of us (E.B.), and a nodule was found in the right upper lobe close to the hilum. Frozen examination revealed cells of uncommon feature suspected for malignancy. A right upper lobectomy with full nodal dissection was performed.

Macroscopic examination showed a well-circumscribed and encapsulated nodule (Figure 2, a). Histologic evaluation revealed the presence of 2 cell populations: epithelioid and lymphocytic (Figure 2, b). The epithelioid component was predominant and admixed with scattered lymphocytes. No areas of necrosis and very few mitoses could be identified. Immunohistochemical analysis demonstrated strong staining for cytokeratin 5 and 6 and epithelial membrane antigen in the epithelioid component, with negative staining for cytokeratin 7, thyroid transcription factor 1, and calretinin. These histologic findings were consistent with mixed or type AB thymoma. All lymph nodes were free of tumor.

The postoperative course was uneventful, and the patient is free of recurrence 2 years after the operation.

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