

# Persistent aggregates in apheresis platelet concentrates are commonly collected from donors with a history of aggregate donation

H. B. Feys,<sup>1</sup> H. Pottel,<sup>2</sup> J. Coene,<sup>3</sup> G. Vandewalle,<sup>3</sup> P. Vandekerckhove<sup>3,4,5</sup> & V. Compennolle<sup>1,3,4</sup>

<sup>1</sup>Transfusion Research Center, Belgian Red Cross-Flanders, Ghent, Belgium

<sup>2</sup>Department of Public Health and Primary Care, KU Leuven, KULAK, Kortrijk, Belgium

<sup>3</sup>Blood Service of the Belgian Red Cross-Flanders, Mechelen, Belgium

<sup>4</sup>Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

<sup>5</sup>Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium

## Vox Sanguinis

Platelet apheresis sometimes causes persistent aggregates (PA). This study ( $n = 211$ ) shows that changing the apheresis settings to reach fixed product volumes instead of yields does not influence PA incidence, even though PA products on average contain more platelets than controls. Furthermore, logistic regression was used to model if PA can be predicted on the basis of certain predonation parameters. PA donation history was the only parameter retained, proving a strong determinant of predictability [AUC = 0.735 (SE = 0.022)]. Consequently, donations from a donor with previous PA history are 7.8 times more likely to contain PA than from a donor without preceding history.

**Key words:** apheresis - donation, Blood collection, Platelet concentrates.

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## Introduction

Apheresis procedures may cause platelet aggregation. These generally dissipate, but some persist throughout the entire storage period [1]. Products with persisting aggregates (PA) may be quarantined, destroyed or distributed in which case an evaluation procedure can be used as a guideline [2]. Concentrates with PA contain more platelets than aggregate-free (AF) ones [3]. Moreover, mildly increased storage lesion was observed in PA products versus AF controls [3, 4]. Our previous study included 180 donations with PA and an equal number of AF controls. These were collected using an apheresis protocol that projected a fixed platelet yield. However, the introduction of pathogen inactivation (Intercept, Cerus Corporation, Concord, CA) at our blood institute prompted revision of that particular protocol to comply with the inclusion criteria. Now, defined volume ranges are projected, resulting in

(more) variable platelet yields instead. This raised the following questions: Does the new collection protocol influence the incidence of PA? Does it affect the previously observed differences between PA and AF products? We furthermore questioned whether the occurrence of PA can be predicted based on an algorithm containing only predonation parameters.

Single-donor platelet concentrates were collected by Trima Accel (Terumo BCT) with an inlet to anticoagulant (ACD-A) ratio of 11:1 at an infusion rate of 1.0 ml/min/l of estimated total blood volume. Additive solution was automatically supplemented following donation. Final product volumes between 300 and 420 ml were projected following the Intercept inclusion criteria. In case a larger collection was possible, volumes above 610 mL (double collection) were projected to allow splitting to the compliant volume range. All products were scored for PA presence by trained staff according to internal guidelines [2]. The AF group criteria were as described [3]. To define whether donors had donated PA prior to inclusion in this study, historical records of PA incidence were reviewed. These range from the start of systematically recording the problem (June 2012) until the end of this study period. Statistical analysis was with SAS (v9.3, SAS Institute Inc, Cary, NC).

Correspondence: Hendrik B. Feys, Belgian Red Cross-Flanders, Transfusion Research Center, Ottergemsesteenweg 413, 9000, Gent, Belgium

E-mail: [hendrik.feys@rodekruis.be](mailto:hendrik.feys@rodekruis.be)

The new collection protocol was installed by July 2014, and data collection was between November 2014 and April 2015. In that period, 211 donations with PA were registered on a total of 5664 successful procedures yielding a 3.7% incidence rate, which is not significantly different from the previous rate [3]. Concurrently, 204 AF controls were collected. On average, PA donations were from donors having higher circulating platelet counts ( $274 \pm 55 \times 10^3/\mu\text{l}$  vs.  $261 \pm 49 \times 10^3/\mu\text{l}$ , Fig. 1a), delivering products with a higher platelet concentration ( $1094 \pm 219 \times 10^3/\mu\text{l}$  vs.  $1041 \pm 205 \times 10^3/\mu\text{l}$ , Fig. 1b). The frequency of single and double donations was tabulated, and a significantly higher number of double donations were found in the PA group (Fig. 1c) confirmed by overall more high-yield products (Fig. 1d) in that arm. This indicates that independent of the collection protocol, PA incidence is higher in donors with high circulating platelet counts. Yet, the absolute difference in mean platelet concentration remains small and distributions overlap, suggesting that this parameter is not sufficient to predict the incidence of PA prior to donation.

Consequently, we used additional predonation data to build a logistic regression model to predict PA incidence. Mean platelet volume, gender, whole-blood platelet concentration, haematocrit, PA donation history, apheresis product platelet concentration and volume were included as variables in a backward-selection logistic regression. Only PA donation history ( $P < 0.0001$ ) was retained in the final model, proving a strong determinant of predictability [AUC = 0.735 (SE = 0.022)]. Based on the odds ratio, a donation from a donor with PA history is thus 7.8 times

more likely to contain PA than from a donor without preceding history. The other parameters were not substantially improving the model. Of note, all 204 donors with a PA donation history (154/211 in the PA, 50/204 in the AF arm) had significantly ( $P < 0.0001$ ) higher whole-blood platelet concentrations ( $278 \pm 54 \times 10^3/\mu\text{l}$ ) than those without ( $257 \pm 48 \times 10^3/\mu\text{l}$ ).

For blood institutions worldwide, products with PA pose a problem. Medical staff performing transfusion are required to visually inspect prior to administration in order to prevent transfusion of aberrantly appearing products. If transfusion of PA is tolerated, operators may become accustomed to aberrantly looking products, thus jeopardizing good practice. Moreover, it is not entirely clear whether PA containing platelet concentrates are safe for transfusion or whether the quality is sufficiently high. These products therefore often go to waste. At 4% incidence, this wastage is a significant economic cost for (blood) communities. The current update from our longitudinal survey now shows that PA history is a strong determinant of future donations with PA. Our data suggest that this may be caused by the inherent difference in whole-blood platelet concentration between donors. A practical consequence of the higher platelet concentration in PA donor's whole blood is the larger products these donors provide, but it is unclear whether collection of smaller products from such donors would help driving back PA incidence. To mitigate PA incidence, previous reports have suggested to increase the anticoagulant to inlet ratio, but additional research is required to confirm utility and investigate the consequences for donor and

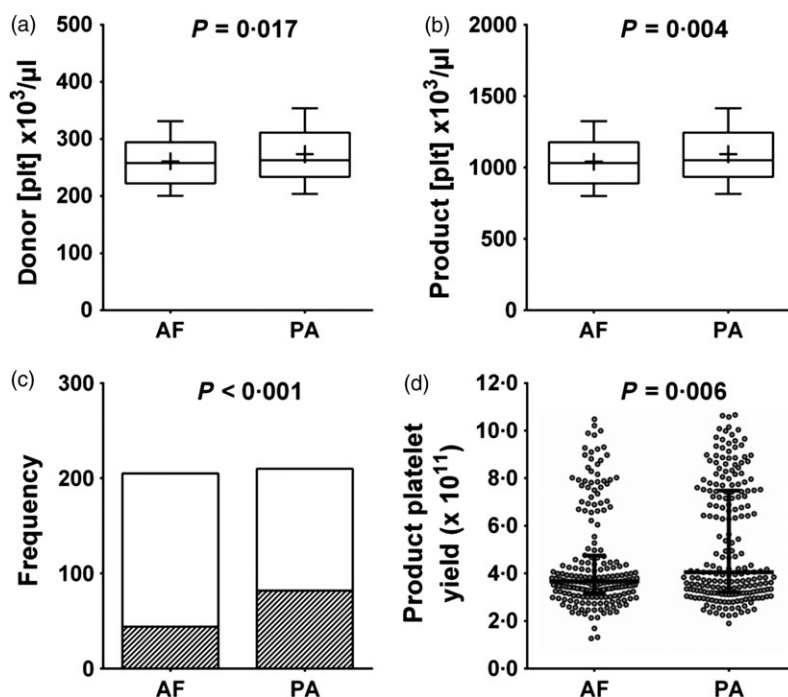


Fig. 1 Donor and donation variables in donations with PA compared to AF controls. (a) Whole-blood platelet concentration of the donor and (b) platelet concentration in the final product, following the addition of additive solution. Boxes represent median with interquartile ranges, (+) indicates data mean, and whiskers indicate the 10–90 percentile. (c) The absolute frequency of double-apheresis platelet concentrates ( $\geq 600$  ml) is shown by the hatched bars, while single donations by open bars. (d) The product platelet yield is shown by plotting all individual data with the median (line) and interquartile ranges (whiskers) embedded.

operators [1, 5]. With the adoption of Intercept pathogen inactivation, PA have disappeared in our blood institution. This can be attributed to the additional filtration in the Intercept pathogen inactivation process which is intended to remove putative *compound adsorption device* beads but coincidentally retains platelet aggregates. Therefore, the mere visual aspect of PA in Intercept-treated products is no longer preventing product issuance. However, removal of aggregates does not necessarily guarantee that the (small) increase in storage lesion observed in products with PA [3, 4] will normalize.

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## Author contributions

HBF designed and managed research, performed experiments, interpreted data and wrote the manuscript; HP designed research, performed statistical analysis and interpreted data; GV, JC, PV provided essential raw data and interpreted data; VC conceptualized, designed and managed research and interpreted data. All authors critically reviewed the manuscript.

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