

Platelet Additive Solutions: A Review of the Latest Developments and Their Clinical Implications

Pieter F. van der Meer · Dirk de Korte

Department of Product and Process Development, Sanquin Blood Bank, Amsterdam, The Netherlands

Keywords

Platelet additive solution · Platelet storage · Clinical effectiveness

Summary

Platelet additive solutions (PASs) have undergone many reformulations in order to further improve platelet storage. Studies of platelets stored in PAS-F (containing acetate, magnesium and potassium as key constituents) showed that platelets may be stored for 13 days with recovery and survival outcomes that are equal or even superior to 7-day stored platelets in plasma. Clinically, patients transfused with platelets in PAS have fewer allergic reactions, while for febrile reactions data are conflicting. Transfusion-related acute lung injury (TRALI) occurs less frequently if PAS is used for buffy coat-derived platelets, but for apheresis platelets there is no difference. For PAS-B and PAS-C, corrected count increments (CCIs) are lower than for platelets stored in plasma, but for PAS-E (like PAS-F also with acetate, magnesium and potassium but with additional phosphate), though limited data is available in the literature, the CCIs seem to be comparable to those observed for platelets in plasma. With platelets in PAS, there is an accumulated dilution effect of anticoagulant and PAS as well as a loss of number and function (due to storage and/or pathogen inactivation treatment) of platelets, of which it is not clear how this impacts clinical outcomes of patients undergoing massive transfusion. Worst-case in vitro studies, where the entire plasma fraction is replaced by supernatant of platelets in PAS, do show an effect on the ability of reconstituted whole blood to clot, but in a more realistic scenario, functional clotting parameters are not different. In this review, recent laboratory and clinical data are discussed, focusing on studies published after 2010.

© 2018 S. Karger GmbH, Freiburg

Introduction

Platelet additive solutions (PASs) were developed in the 1980s to have as little plasma as possible in a platelet concentrate, as plasma was suspected to contain harmful enzymes that caused the platelet storage lesion. Also, PAS was used to provide extra buffering capacity, at a time when platelet-rich plasma-derived platelet concentrates were stored in small gas-impermeable storage containers [1]. Techniques to isolate and store platelet concentrates changed, and nowadays high-volume pooled buffy coat-derived or apheresis platelets are stored in large gas-permeable bags, taking away some of these initial aims. However, more benefits have been identified, including having more plasma available for fractionation, causing fewer allergic reactions, and having a lower titer of anti-A and -B antibodies, to name a few. The benefits and disadvantages of the use of PAS, the latest developments, and their clinical implications will be discussed in this review. The papers discussed were selected based on a PubMed search with 'platelet additive solution' as keyword, and papers from 2010 onward were reviewed.

Room Temperature Platelet Storage

PASs contain ingredients to support platelet storage. Acetate has proven to be a key element in this respect for the following reasons: Acetate is negatively charged, and, in order to be oxidized, acetate has to be neutral to enter the mitochondrion [2]. Acetate derives a H⁺ ion from its environment, and thus de facto increases pH while being oxidized. Moreover, platelets switch their metabolism from oxidizing glucose as substrate (which generates lactic acid, causing lowering of the pH and subsequently causing the platelet storage lesion) to oxidizing a mixture of acetate and glucose, further reducing the generation of lactic acid [3].

Other important ingredients are potassium and magnesium [4] as well as phosphate [5], and comparative studies have shown superior in vitro quality of platelets stored in PAS containing acetate, potassium, magnesium, and phosphate [6–9]. Recent studies have

focused on bicarbonate and calcium [10]. The specific effects of the addition of the various ingredients has been discussed in depth elsewhere [11, 12] and will not be repeated here, but the general thought is to 'tweak' the composition of PAS to improve platelet storage by playing with ingredients and concentrations. A good example of what the current status of platelet storage in PAS is, is the study by Slichter et al. [13]. They demonstrated that platelets stored in PAS-F (acetate, potassium, magnesium) had excellent storage properties until 13 days after apheresis collection. In a series of studies conducted in volunteers, using 51-chromium- and 111-indium-labeled platelets, 5-day-old apheresis platelets in plasma had a recovery of $59 \pm 7\%$ and a survival of 6.5 ± 0.6 days. During further storage of platelets in plasma, these parameters decreased, and 7-day-stored platelets had a recovery of $44 \pm 5\%$ and a survival of 4.9 ± 0.7 days. Similar values, with a recovery of $49 \pm 3\%$ and a survival of 4.6 ± 0.3 days, were found with PAS-F, but after a much longer storage period, namely 13 days. When stored for 7 days in PAS-F, outcomes were better maintained, with a recovery of $52 \pm 3\%$ and a survival of 6.0 ± 0.3 days as compared to plasma. These data show that for 7-day-stored platelets, recovery and survival of platelets stored in PAS are superior to those stored in plasma. However, recovery of fresh platelets is about 60%, and survival is a little under 8 days [13]; so further reformulations will be needed to ensure that platelets stored longer than 5 days have a clinical quality similar to freshly collected platelets.

PAS to Mitigate Lesions Caused by Pathogen Inactivation or Cold Storage

In addition to the storage lesions as described above, PASs can also be used to mitigate lesions induced by pathogen inactivation. Specifically, phosphate was added to PAS-B (acetate) to provide additional buffering capacity for the addition of amotosalen-HCl during the pathogen inactivation process (which has a pH of 4.0 to 6.0) [14], thus forming PAS-C (acetate, phosphate). Several studies have shown that PAS can prevent some of the effects induced by pathogen inactivation. Our group showed in a paired study that PAS-E (acetate, potassium, magnesium, phosphate) was able to drive down the apoptotic marker annexin A5 from $40 \pm 5\%$ in Mirasol-treated platelets in plasma on day 8 of storage to $23 \pm 4\%$ in Mirasol-treated platelets in PAS-E, a value not too different from the current standard untreated platelets in plasma, with an average of $18 \pm 4\%$ [15]. However, particularly activation marker CD62P was unchanged, with $43 \pm 4\%$ in Mirasol-treated platelets in plasma and $41 \pm 4\%$ in Mirasol-treated platelets in PAS-E, versus $17 \pm 2\%$ in untreated platelets in plasma. Also of note, lactic acid formation of Mirasol-treated platelets in PAS-E was in the same order as of untreated platelets in plasma, preserving pH to values above 6.8 in pathogen-inactivated platelet concentrates in PAS-E. This study showed that PAS can be used to optimize platelet storage if pathogen inactivation takes place, and more studies will follow.

Similarly, PAS could play a role in optimizing conditions for cold-stored platelets [16]. This study showed that at 4°C the GpIIb/IIIa fibrinogen receptor is activated by the cold and that the use of PAS resulted in less aggregate formation due to dilution of

fibrinogen. Whether or not PAS plays a role in maintaining in vivo quality of cold-stored platelets remains to be studied. Preliminary studies with the addition of adenine, lidocaine, and magnesium to PAS (presumably, PAS-F) showed some improvement of in vitro characteristics of cold-stored platelets [17]. Cold-stored platelets are currently not a product that is widely used, but there is renewed interest in this product for use in actively bleeding patients, because cold-stored platelets may support hemostasis more effectively than room temperature-stored platelets [18].

Clinical Outcomes

Corrected Count Increments, Bleeding

When it comes to clinical data, either corrected count increments (CCIs) or bleeding, there is scarce information available in the current literature. For a long time, it was true that PAS-stored platelets had a lower increment than plasma-stored ones. However, the reformulation of PAS-B to PAS-C already was a major improvement, for example prompting the Netherlands moving from 5- to 7-day storage of platelets in PAS [19]. This was based on the randomized clinical trial by Kerkhoffs et al. [20], that studied transfusion efficacy in hemato-oncological patients, revealing that buffy coat-derived platelets in plasma, stored for up to 7 days after collection, had a 1-hour CCI of 17.1 ± 7.3 , while those stored in PAS-C had a CCI of 15.3 ± 6.5 , i.e. 9% lower (95% confidence interval (CI) -22 to $+4\%$). The 24-hour CCI was 7% lower (95% CI -26 to $+12\%$). This had no effect on bleeding tendency of the patients, with 19% of the patients having a bleeding when receiving plasma-stored platelets versus 15% when receiving PAS-C-stored platelets. Similarly, Tobian et al. [21] showed in their general hospital population that for PAS-C the 1- to 4-hour CCI was 4.9 for apheresis platelets in plasma versus 3.8 in PAS-C (-24% , $p \leq 0.001$). The 12- to 24-hour CCI was 19% lower when stored in PAS.

For PAS-E, because of the presence of potassium, magnesium and phosphate considered to be the best PAS at the current time [9], little information is available. Published as abstract, Vasse et al. [22] showed a 1- to 24-hour CCI of 10.2 for platelets in plasma, 8.6 for platelets in PAS-C, and 10.0 for platelets in PAS-E, indicating a 16% lower CCI for PAS-C ($p < 0.001$) and 2% lower CCI for PAS-E (not significantly different). In another, two-center clinical trial [23], evaluating Mirasol-treated platelets in PAS-C in one site and Mirasol-treated platelets in PAS-E in the other site, the outcomes showed a similar direction. In their untreated control groups, the authors showed a 1-hour CCI of 10.6 for platelets in PAS-C and of 11.8 for platelets in PAS-E; for the 24-hour CCI the difference was larger, with a 24-hour CCI of 2.4 for platelets in PAS-C and of 5.8 for platelets in PAS-E. The sample size was small (62 patients, 40 in the PAS-C arm and 22 in the PAS-E arm), so the study was underpowered to show any significant difference. Also, site-specific effects may play a role in the differences observed between PAS-C and PAS-E in this study, i.e. the difference may be caused by more than the difference in PAS alone.

Transfusion Reactions

Platelets in PAS still contain about 35% of plasma due to carry-over from the buffy coats. In fact, about 30% residual plasma is required for the current PASs, likely due to the glucose that is still needed by the platelets during storage [24]. Nonetheless, this by two-thirds lower plasma content reduces the incidence of allergic reactions by about 50%, as several studies have shown for platelets in first-generation PASs and as summarized elsewhere [11]. Kerkhoffs et al. [20] did not make a distinction between allergic, febrile and 'other' transfusion reactions and showed mostly mild reactions in 11% of the patients receiving platelets in plasma versus 9% in patients receiving platelets in PAS-C. Others [21] did separate out allergic and febrile reactions and showed that the incidence of allergic reactions in plasma-stored apheresis platelets was higher than in PAS-stored units, with an incidence of 1.85% for platelets in plasma versus 1.01% for platelets in PAS (risk ratio 0.54; 95% CI 0.30–0.99; $p = 0.04$). For febrile reactions, they showed no difference between platelets in plasma and in PAS, with an incidence of 0.70 and 0.59%, respectively. For transfusion reactions in general, Cohn et al. [25] reported an incidence of 1.37% for platelets in plasma, versus 0.55% for platelets in PAS-C, giving a relative risk of 0.403 with an upper confidence limit of 0.663. Allergic reactions were the most frequent, with a rate of 0.29% for platelets in PAS-C versus 0.82% for platelets in plasma. The frequency of febrile reactions was 0.17% for platelets in PAS-C, while it was 0.50% for plasma-stored platelet concentrates. Thus, overall far fewer transfusion reactions are observed when PAS is used.

Transfusion-Related Acute Lung Injury

Transfusion-related acute lung injury (TRALI) is a rare, but serious transfusion reaction. TRALI can be caused by human leukocyte antigen (HLA) and sometimes by human neutrophil antigens (HNA) antibodies in the donor plasma, reacting with donor leukocytes, ultimately resulting in capillary leak syndrome in the patient's lungs [26]. These HLA antibodies are generally found in persons who have received (non-leukocyte-reduced) blood products or have been pregnant, thus a common strategy is to use only plasma from a male donor that never received a blood transfusion when making platelet concentrates. In our country, where this policy was implemented in December 2009, the number of TRALI cases dropped from 20 to 30 per year to fewer than 10 [27]. Replacement of plasma for PAS should have the same effect. Because TRALI is so rare, the reported number of cases is generally small, which makes the comparison of TRALI cases with or without PAS difficult to interpret. Andreu et al. [28] presented 11 TRALI cases that were related to one specific transfusion with buffy coat-derived platelets, of which 3 occurred after a transfusion of platelets in plasma (1 antibody-positive TRALI and 2 possible TRALIs), and 8 occurred after a platelet transfusion in PAS (3 antibody-positive TRALIs, 4 antibody-negative TRALIs, and 1 possible TRALI). The total number of transfusions of platelets in plasma in the study period was 49,006, giving an incidence of 61 per million. There were many more transfusions of platelets stored in PAS, 653,001, giving an incidence of 12 per million ($p = 0.04$). Thus, relatively fewer

TRALI cases were seen when PAS is used. For apheresis platelets, about equal TRALI numbers were seen for platelets in PAS or in plasma in this study. While the amount of plasma is approximately the same for both types of platelet products, buffy coat-derived platelet concentrates contain about 20 ml from 4 or 5 individual donations, while for apheresis, the entire volume of 150 ml plasma comes from the same donor. The large volume of plasma coming from one donor may explain the difference in TRALI incidence between buffy coat-derived platelets and apheresis platelets.

Sepsis

There is evidence that platelets in PAS are more susceptible to bacterial contamination. The assumption is that plasma contains bactericidal proteins, and so there is a risk of bacterial outgrowth when PAS is used. Greco et al. [29] showed that in PAS-E, *Serratia liquefaciens* grows faster than in spiked platelet concentrates in plasma, while the growth rate was unaffected for *Staphylococcus epidermidis* when comparing plasma- and PAS-stored platelets. While it may seem contra-intuitive, a quicker growth will result in earlier detection when performing a bacterial screening. Also, there was an increased likelihood of biofilm formation of these bacteria in plasma-stored platelets, which is associated with lower numbers of colony-forming units, which in turn may result in false-negative bacterial screening assays. Thus, while PAS-stored platelets appear to be more at risk than those in plasma, in reality, this may result in faster or better detection of contaminated platelet units in PAS, although biofilm formation may counteract this. In our own 100% screening of platelet concentrates, the frequency of positives is similar for buffy coat-derived platelet concentrates in plasma or in PAS-C, 0.37% versus 0.34% (data 2015–2016). The percentage of confirmed positives is significantly lower for PCs in PAS-C (0.25%, as opposed to 0.34% for platelets in plasma). Transfusion-transmitted bacterial infection is a rare complication if bacterial screening is applied, but the higher risk of false-positive results seems to be reflected in Dutch hemovigilance data, where more bacterial infections were observed in patients that received PAS-B or PAS-C-stored platelets [30]. This study found that the relative risk was 4.6 (95% CI 1.4–16.2), i.e. infections in patients receiving platelets in either PAS-B or PAS-C were more likely when compared to patients receiving platelets in plasma. The overall incidence of transfusion-transmitted bacterial infections was 22.2 per million (95% CI 12.1–37.2 per million) transfused buffy coat platelet concentrates.

Clinical Outcomes in Surgical Patients

Since hemato-oncological patients use the majority of platelets in high-income countries, the focus has been on developing platelet products that have high platelet increments, contain platelets that circulate for a long time, and have few adverse reactions. However, in recent years, the focus has been put on patients that require massive transfusions (trauma, surgery), since these patients need platelets that function right away in a storage solution that still allows adequate clotting. These patients are often supported with a 1:1 transfusion strategy, i.e. 1 unit of red cells, 1 unit of plasma and

1 unit of platelets, to come to a transfused product as close to whole blood as possible. Mays and Hess [31] mathematically showed that blood collection and subsequent component therapy results in dilution of blood cells, in loss of the number of cells, and loss of potency of these cells. For example, collection of whole blood in anticoagulant immediately results in a 1:7 dilution of the concentration of every cell and every clotting factor. They calculated that a reconstituted unit of whole blood in the 1:1:1 ratio results in a 38% lower concentration of clotting factors and a 56% loss of platelets. Storage for up to 7 days, and/or performing a pathogen inactivation step, leads to further loss of the clinical efficacy of the transfused products. Particularly replacement of two-thirds of the plasma for PAS will impact the amount of clotting factor given to the patient. While the above example is purely mathematical and needs further clinical confirmation, *in vitro* studies showed that the dilution effect of platelets in PAS may be true, or at least warrants further investigation. Van Hout et al. [32] reconstituted whole blood and used either platelets stored in plasma or in PAS-C. Their *in vitro* study showed that platelet aggregation responses as measured with the Multiplate aggregation assay with ADP and TRAP as stimulus declined during 7 days of storage and were always lower in PAS-stored platelets; collagen and ristocetin responses also declined over time, but no difference was seen between plasma- or PAS-stored platelets. Thromboelastographic parameters (measured with the TEG device), showing the overall ability of this reconstituted whole blood to clot, were not affected. In this case, also the clotting factors of the supernatant should be taken into account. If the plasma fraction was completely replaced by platelet concentrate supernatant (as would be the case in massive transfusion where the entire volume of circulating blood was replaced by transfusion products), then TEG clot strength (maximum amplitude) was weaker, the initial clot formation time (R-time) was longer, and the clot growth rate (alpha angle) was slower. Although in cases of massive transfusion it is unlikely that the entire volume of circulating blood will be replaced by transfusion products, this has never been investigated in clinical cases. Because worst-case *in vitro* experiments do show the effect of PAS supernatant dilution, evaluations in patients need to be performed to investigate if these effects are of clinical relevance.

Cost Effectiveness

Kacker et al. [33] published a cost-benefit analysis in 2013 where they compared their current standard of apheresis platelets in plasma, combined with pre-transfusion medication to prevent transfusion reactions, with a number of scenarios where platelets in PAS were used. In a cost calculation where platelets in plasma

would be entirely replaced by platelets in PAS, their model showed a USD 6.30 reduction in cost per unit transfused, mainly due to transfusion reactions occurring less frequently. The cost to prevent one transfusion reaction was estimated at USD 701.95, and switching from plasma to PAS would be cost neutral if no pre-transfusion medication would be used and if PAS cost less than USD 11.90 per unit. This paper used the hospital perspective for calculation of costs and did not take into account the yield of saving one unit of plasma for fractionation. From a blood bank perspective, the saving is much more, with a price of about USD 100 per kilogram of plasma. While the cost calculation will differ from place to place, in general, a switch from plasma to PAS for storage of platelets is cost-effective.

In summary, the current generation of PAS allow excellent storage of platelets during at least 7 days after collection, as shown by CCI data for PAS-E and recovery and survival data for PAS-F. PASs should be further reformulated, in order to keep the platelet quality close to that when blood is freshly collected. In addition, PASs can be used to support storage of pathogen-inactivated as well as cold-stored platelets. The current PASs probably do not require a 30% plasma carry-over [34]. With a lower percentage of plasma, it is probable that the number of transfusion reactions will further decrease. Possibly, using advanced apheresis-like technologies to produce platelet concentrates, the plasma carry-over could be driven down to only a few percent. TRALI caused by HLA antibodies thus can be prevented. Bacterial contamination of platelets in PAS may be a concern. There is not much literature, but there is a plausible explanation (bactericidal proteins in plasma), and the data that is available does show an increased risk. The risk and severity of a transfusion-transmitted bacterial infection should be weighed against the cost of e.g. introducing a post-storage bacterial screening assay. Another concern is patients undergoing massive transfusions who need clotting factors and do not tolerate dilution of their circulatory volume with PAS. However, no clinical data is available, and only under worst-case laboratory conditions an effect could be observed. Nevertheless, clinical evaluations need to be performed.

As with other things in life, every benefit has its disadvantages. Whether or not the benefits of PAS outweigh the disadvantages depends on specific conditions of the patient, hospital, and geography and may differ from blood provider to blood provider.

Disclosure Statement

The authors declare no conflicts of interest.

References

- 1 Rock G, Swenson SD, Adams GA: Platelet storage in a plasma-free medium. *Transfusion* 1985;25:551–556.
- 2 Murphy S: The oxidation of exogenously added organic anions by platelets facilitates maintenance of pH during their storage for transfusion at 22 degrees C. *Blood* 1995;85:1929–1935.
- 3 Shimizu T, Murphy S: Roles of acetate and phosphate in the successful storage of platelet concentrates prepared with an acetate-containing additive solution. *Transfusion* 1993;33:304–310.
- 4 De Wildt-Eggen J, Schrijver JG, Bins M, Gulliksson H: Storage of platelets in additive solutions: effects of magnesium and/or potassium. *Transfusion* 2002;42:76–80.
- 5 Gulliksson H, Larsson S, Kumlien G, Shanwell A: Storage of platelets in additive solutions: effects of phosphate. *Vox Sang* 2000;78:176–184.
- 6 Fijnheer R, Veldman HA, van den Eertwegh AJ, Gouwerok CW, Homburg CH, Boomgaard MN, de Korte D, Roos D: In vitro evaluation of buffy-coat-derived platelet concentrates stored in a synthetic medium. *Vox Sang* 1991;60:16–22.
- 7 Ringwald J, Walz S, Zimmermann R, Zingsem J, Strasser E, Weisbach V, Eckstein R: Hyperconcentrated platelets stored in additive solution: aspects on productivity and in vitro quality. *Vox Sang* 2005;89:11–18.
- 8 Cardigan R, Sutherland J, Garwood M, Bashir S, Turner C, Smith K, Hancock V, Wiltshire M, Pergande C, Williamson LM: In vitro function of buffy coat-derived platelet concentrates stored for 9 days in CompSol, PASII or 100% plasma in three different storage bags. *Vox Sang* 2008;94:103–112.
- 9 Van der Meer PF, Kerkhoffs JL, Curvers J, Scharenberg J, de Korte D, Brand A, de Wildt-Eggen J: In vitro comparison of platelet storage in plasma and in four platelet additive solutions, and the effect of pathogen reduction: a proposal for an in vitro rating system. *Vox Sang* 2010;98:517–524.
- 10 Skripchenko A, Turgeon A, Thompson-Montgomery D, Awatefe H, Wagner SJ: Value of calcium and phosphate in a bicarbonate-containing platelet additive solution with low plasma levels in maintaining key in vitro platelet storage parameters. *Transfusion* 2017;57:349–356.
- 11 Van der Meer PF, De Korte D: Platelet additive solutions; in: Lozano M, Sweeney J (eds): *Platelet Transfusion Therapy*. Bethesda, AABB Press, 2013, pp 75–118.
- 12 Van der Meer PF: PAS or plasma for storage of platelets? A concise review. *Transfus Med* 2016;26:339–342.
- 13 Slichter SJ, Corson J, Jones MK, Christoffel T, Pellham E, Bailey SL, Bolgiano D: Exploratory studies of extended storage of apheresis platelets in a platelet additive solution (PAS). *Blood* 2014;123:271–280.
- 14 Picker SM, Speer R, Gathof BS: Functional characteristics of buffy-coat PLTs photochemically treated with amotosalen-HCl for pathogen inactivation. *Transfusion* 2004;44:320–329.
- 15 Van der Meer PF, Bontekoe IJ, Daal BB, de Korte D: Riboflavin and UV light treatment of platelets: a protective effect of platelet additive solution? *Transfusion* 2015;55:1900–1908.
- 16 Getz TM, Montgomery RK, Bynum JA, Aden JK, Pidcoke HF, Cap AP: Storage of platelets at 4°C in platelet additive solutions prevents aggregate formation and preserves platelet functional responses. *Transfusion* 2016;56:1320–1328.
- 17 Bynum JA, Taylor AS, Peltier GC, McIntosh CS, Meleleo MA, Dobson GP, Cap AP: Evaluation of adenosine, lidocaine, and magnesium for enhancement of platelet function during storage. *J Trauma Acute Care Surg* 2017;83(1 suppl 1):S9–S15.
- 18 Apelseth TO, Cap AP, Spinella PC, Hervig T, Strandenes G: Cold stored platelets in treatment of bleeding. *ISBT Sci Ser* 2017;12:488–495.
- 19 Caram-Deelder C, van der Bom JG, Putter H, Leyte A, Kerkhof DV, Evers D, Beckers EA, Weerkamp F, Hudig F, Zwaginga JJ, Rondeel JMM, de Vooght KMK, Péquériau NCV, Visser O, Wallis JP, Middelburg RA: Age of platelet concentrates and time to the next transfusion. *Transfusion* 2018;58:121–131.
- 20 Kerkhoffs JL, van Putten WL, Novotny VM, Te Boekhorst PA, Schipperus MR, Zwaginga JJ, van Pampus LC, de Greef GE, Luten M, Huijgens PC, Brand A, van Rhenen DJ; Dutch-Belgian HOVON Cooperative Group: Clinical effectiveness of leucoreduced, pooled donor platelet concentrates, stored in plasma or additive solution with and without pathogen reduction. *Br J Haematol* 2010;150:209–217.
- 21 Tobian AA, Fuller AK, Uglik K, Tisch DJ, Borge PD, Benjamin RJ, Ness PM, King KE: The impact of platelet additive solution apheresis platelets on allergic transfusion reactions and corrected count increment. *Transfusion* 2014;54:1523–1529.
- 22 Vasse J, Gaucheron S, Lebaudy JP, Tardivel R, Sémana G: Étude comparative de l'efficacité transfusionnelle plaquettaire biologique entre les concentrés de plaquettes d'aphérèse conservés en plasma, les concentrés de plaquettes d'aphérèse et les mélanges de concentrés de plaquettes conservés en solution de conservation SSP+. *Transfus Clin Biol* 2012;19:280–310.
- 23 Drawz SM, Marschner S, Yañez M, García de Coca A, Feys HB, Deeren D, Coene J: Observational study of corrected count increments after transfusion of platelets treated with riboflavin pathogen reduction technology in additive solutions. *Transfusion* 2015;55:1745–1751.
- 24 Klinger MH, Josch M, Klüter H: Platelets stored in a glucose-free additive solution or in autologous plasma – an ultrastructural and morphometric evaluation. *Vox Sang* 1996;71:13–20.
- 25 Cohn CS, Stubbs J, Schwartz J, Francis R, Goss C, Cushing M, Shaz B, Mair D, Brantigan B, Heaton WA: A comparison of adverse reaction rates for PASC versus plasma platelet units. *Transfusion* 2014;54:1927–1934.
- 26 Gajic OI, Rana R, Winters JL, Yilmaz M, Mendez JL, Rickman OB, O'Byrne MM, Evenson LK, Malinchoc M, DeGoey SR, Afessa B, Hubmayr RD, Moore SB: Transfusion-related acute lung injury in the critically ill: prospective nested case-control study. *Am J Respir Crit Care Med*. 2007;176:886–891.
- 27 TRIP Foundation: TRIP Report 2015, Hemovigilance, Extended Version. www.tripnet.nl/pages/en/documents/Trip.HEMO_ENG_19.04.2017def.pdf (last accessed February 20, 2018).
- 28 Andreu G, Boudjedir K, Muller JY, Pouchol E, Ozier Y, Fevre G, Gautreau C, Quaranta JF, Drouet C, Rieux C, Mertes PM, Clavier B, Carlier M, Sandid I: Analysis of transfusion-related acute lung injury and possible transfusion-related acute lung injury reported to the French Hemovigilance Network from 2007 to 2013. *Transfus Med Rev* 2018;32:16–27.
- 29 Greco CA, Zhang JG, Kalab M, Yi QL, Ramirez-Arcos SM, Gyongyossy-Issa MI: Effect of platelet additive solution on bacterial dynamics and their influence on platelet quality in stored platelet concentrates. *Transfusion* 2010;50:2344–2352.
- 30 Kreuger AL, Middelburg RA, Kerkhoffs JH, Schipperus MR, Wiersum-Osselton JC, Van der Bom JG: Storage medium of platelet transfusions and the risk of transfusion-transmitted bacterial infections. *Transfusion* 2017;57:657–660.
- 31 Mays JA, Hess JR: Modelling the effects of blood component storage lesions on the quality of haemostatic resuscitation in massive transfusion for trauma. *Blood Transfus* 2017;15:153–157.
- 32 Van Hout FMA, Bontekoe IJ, de Laleijne LAE, Kerkhoffs JL, de Korte D, Eikenboom J, Van der Bom JG, Van der Meer PF: Comparison of haemostatic function of PAS-C-platelets vs. plasma-platelets in reconstituted whole blood using impedance aggregometry and thromboelastography. *Vox Sang* 2017;112:549–556.
- 33 Kacker S, Ness PM, Savage WJ, Frick KD, McCullough J, King KE, Tobian AA: The cost-effectiveness of platelet additive solution to prevent allergic transfusion reactions. *Transfusion* 2013;53:2609–2618.
- 34 Kosteljik EH, Klomp AJ, Engbers GH, Gouwerok CW, Verhoeven AJ, van Aken WG, Feijen J, de Korte D: Improved platelet compatibility of water vapour glow discharge treated non-woven poly(ethylene terephthalate) leukocyte-reduction filters for different types of platelet concentrates. *Transfus Med* 2001;11:199–205.