Apheresis platelets are more frequently associated with adverse reactions than pooled platelets both in recipients and in donors: a study from French hemovigilance data

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BACKGROUND: Controversy exists regarding the safety of the different types of platelet (PLT) concentrates. This study was aimed at comparing the rate of adverse reactions associated with apheresis PLT concentrates (APCs) and pooled PLT concentrates (PPCs) both in donors and in recipients.

STUDY DESIGN AND METHODS: From the French national hemovigilance system, types and numbers of recipient adverse reactions were compared over a period from 2009 to 2011. Donor adverse reactions were available for 2010 and 2011. This study involved 23 of 26 French regions. Main outcomes were the rates of adverse reaction in recipients and serious adverse reaction in donors.

RESULTS: There were 790,854 PLT transfusions during the study period (477,747 [60%] with APCs, 313,107 [40%] with PPCs). APCs were associated with more adverse reactions (6244 vs. 2469 per 1,000,000, $p < 0.001$) and more severe and life-threatening reactions (respectively, 241 vs. 131 per 1,000,000, $p < 0.001$; and 182 vs. 121 per 1,000,000, $p = 0.04$). Mortality rates due to an adverse transfusion reaction were similar (15 vs. 6 per 1,000,000, $p = 0.5$). In donors, the number of whole blood (WB) donations was 4,722,685 whereas 266,095 apheresis procedures were performed. Serious adverse reactions were more frequent for apheresis procedures than for WB donations (5445 vs. 803 per 1,000,000, $p < 0.001$).

CONCLUSION: Our findings suggest that apheresis PLTs may be more hazardous than pooled PLTs both in recipients and in donors. This study calls for randomized trials to confirm or refute these results.

Platelet (PLT) transfusions are increasingly used to prevent bleeding in thrombocytopenia or to treat massive hemorrhage.[1] PLT concentrates are known to provide a higher rate of adverse recipients reactions than other blood components.[2] There are insufficient data to determine whether apheresis PLT concentrates (APCs) are preferable to pooled PLT concentrates (PPCs) regarding adverse reaction rates in recipients and donors.[3] APCs are known to provide a slightly higher increment in PLT count, but without any clinical outcome difference.[4] The rate of adverse reactions in recipients related to APCs or PPCs may also differ.[5] Infectious risk is theoretically higher with PPCs as they are usually prepared from four or five whole blood (WB) donations. Furthermore, APCs expose healthy donors to an apheresis

ABBREVIATIONS: APC(s) = apheresis platelet concentrate(s); EFS = Etablissement Français du Sang; PPC(s) = pooled platelet concentrate(s); WB = whole blood.

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procedure, which may include a supplementary risk without cost-effectiveness.[6]

Given the growing PLT demand, and the recurrent APC shortage, it seemed important to clarify the risk-benefit of PPCs and APCs. During the 2000s, a national comprehensive information system about transfused labile blood products and adverse reactions was put in place in France. By 2003 to 2004, reliable numerators, that is, adverse reactions of recipients, and denominators, that is, transfused blood components, both became available, and precise hazard rates could then be calculated for each sort of labile blood product and each sort of reaction. In 2008, donors' hemovigilance was put in place and embedded into the existing surveillance system. As the French national surveillance system allows checking all PLT transfusions and their potentially associated adverse reactions, this study was aimed at comparing: 1) the rate of PPC- and APC-associated adverse reactions in recipients and 2) the rate of serious side effects associated with WB or plateletpheresis donations.

MATERIALS AND METHODS

This study used data from the French national system, which is strictly anonymous. Consequently, patient informed consent was waived. This study was approved by the institutional review board of the Nîmes University Hospital (Nîmes, France; IRB No. 14/10.02).

PLTs and blood products

During the study period, in France, two major types of PLT concentrates were in use: 1) APCs from a single donor collected through an apheresis procedure and 2) buffy coat PPCs prepared from five WB donations. All PLT concentrates were leukoreduced during preparation either in process (APCs) or before storage (PPCs). A part of both types of components were prepared in additive solution (AS) or viro-attenuated. The amount of AS was identical for APCs and PPCs and corresponded to 68% of the initial plasma volume. Concerning PLTs and blood donations, neither therapeutic phlebotomies nor autologous donations were included.

Data collection

In the French national hemovigilance system, regional coordinators of hemovigilance actively take part in the collection and validation of data, both on hazard and on exposure. The surveillance system collects notifications of all adverse reactions of recipients and only serious adverse reactions of donors.

Recipient adverse reactions

For recipients, the surveillance was initiated in 1996 and improved several times. In 2004 the competent authority put a new Web-based reporting system in place. It allows hospital hemovigilance officers, who are physicians (usually part-time), to report all adverse reactions of recipients online. All data entered in the national Web system are strictly anonymous. Notification forms of adverse reactions include clinical data, severity grade, and imputability level, which ranges from not or unlikely related to transfusion (0) to possible (1), probable (2), or certain (3). Severity of reactions are classified according to clinical signs, regardless of the cause of the adverse reaction; severity grades are mild (Grade 1), severe (Grade 2), immediate life-threatening (Grade 3), and death (Grade 4). All blood components, transfused just before or during an adverse reaction, are entered using a code that describes precisely the type of blood component. For PPCs, the number of PLT concentrates used for analysis were doses (bags). The coding table of labile blood components first separates PPCs and APCs and then discriminates the different preparation processes, but for apheresis PLTs, it does not include all the precise kinds of apheresis: neither the machine brand nor the other obtained components. The most likely involved labile blood component is also identified in the form.

A large set of national detailed guidelines are provided as a reference for required clinical investigations, diagnosis, imputability, and severity criteria, to assure quality of collected data.[7] Definitions of recipient adverse reactions after PLT transfusion are summarized in Table 1. For each diagnosis, specific guidelines are issued to assess the severity grade. For example, an allergic reaction is categorized as Grade 1 if only cutaneous or mucosal signs are present, Grade 2 if two or more organs are affected, and Grade 3 if an anaphylactic shock occurs. For some diagnoses, such as serious allergic reactions, transfusion-associated circulatory overload, transfusion-related acute lung injury (TRALI), and transfusion-transmitted bacterial infection, complementary files are required and linked to the case report form. Forms are fulfilled gradually online, as long as data become available about each case, both by hospital and by regional hemovigilance officers.

To establish the study database, regional coordinators of hemovigilance transmitted data from 2009 to 2011. Adverse reactions unlikely related to transfusion (imputability level 0) were not included in this study. Notifications were discussed and validated by the regional hemovigilance coordinators and all severe adverse reactions were later reviewed by the hemovigilance department of the competent authority (Agence Nationale de Sécurité du Médicament, et des Produits de Santé ANSM) that supervised and maintained the whole system. In addition, for those specific diagnoses that need complementary forms, expert groups of the National Hemovigilance Commission performed a final validation every term during the studied period. Each case was reviewed with a

TABLE 1. Definitions of recipient adverse reactions after PLT transfusion*

Adverse reaction	Timing	Diagnosis criteria
Allergic transfusion reaction†	During transfusion or within 4 hr of cessation	Urticaria, rash, angioedema, pruritis Tachycardia, bradycardia, arrhythmia, hypotension, cardiocirculatory arrest Bronchospasm, respiratory distress, cough, hypoxemia, cyanosis Nausea, vomiting, diarrhea, abdominal pain Discomfort, anxiety Positive plasma histamine and tryptase
FNHTR	During transfusion or within 4 hr of cessation	Fever $\geq$38°C with increase $\geq$1°C from previous value Chills *No* evidence of other type of febrile reaction (infection, TRALI)
PLT transfusion refractoriness	24 hr after transfusion	Corrected count increment‡ $<$ 7 after transfusion of ABO-identical PLTs, dose adjusted to the patient's weight *No* evidence of disseminated intravascular coagulation, splenomegaly, hematopoietic stem cell graft
Transfusion reaction with alloantibody (HLA or HPA)	After the transfusion	FNHTR or PLT transfusion refractoriness (see above) *And* antibody against HLA Class I/II or HPA in recipient plasma
TACO†	During transfusion or within the 6 hr of cessation	Cough, respiratory distress, orthopnea, hypoxemia, cyanosis, wheezing, crackles Tachycardia, hypertension, gallop Discomfort, anxiety Radiographic signs of pulmonary edema Hypoxia on blood gas; elevated BNP Echocardiographic evidence of left heart failure or volume overload
TRALI†	During transfusion or within the 6 hr of cessation	Hypoxemia, cyanosis, cough Fever, hypotension Bilateral infiltrates on chest radiograph *No* evidence of left ventricular failure or fluid overload
Transfusion-transmitted bacterial infection†	During transfusion or within 24 hr of cessation	Fever $\geq$39°C or increase $\geq$2°C from previous value Chills, tachycardia $\geq$120 or increase $\geq$40, hypotension, or shock *And* identical pathogen in recipient blood culture and in the transfused component
Hypotensive	During transfusion or within the 2 hr of cessation	Decrease in systolic and/or diastolic blood pressure $\geq$30 mmHg *No* evidence of infection, allergy or any other cause of hypotension
Post-transfusion purpura	2 to 15 days after transfusion	Thrombocytopenia (PLT count $< 100 \times 10^9$/L, usually $< 20 \times 10^9$/L) Purpura, hemorrhage *And* alloantibody against HPA

* Each reported case was later discussed and validated by the regional hemovigilance coordinators and the hemovigilance department of the competent authority (Agence Nationale de Sécurité du Médicament, ANSM).
† Supplementary validation required by a national expert group.
‡ Corrected count increment = increment in PLT count (10^9) $\times$ body surface area (m^2)/number of PLT transfused (10^{11}).
BNP = brain natriuretic peptide; FNHTR = febrile nonhemolytic transfusion reaction; TACO = transfusion acute circulatory overload.

reappraisal of severity grade, imputability, and compliance with case definition of the guidelines.[7,8]

Donor adverse reactions

In 2008, notification of serious adverse reactions of donors was established and, in the last months of 2009, the Web-based system extended to collect them. The only difference is that hospital hemovigilance officers are not involved. So reliable data on donors have been available since year 2010 only.

This study included all apheresis procedures providing at least one PLT concentrate and all WB donations, since any of them might have been used to prepare pooled buffy coat PLT concentrates. Apheresis procedures not intended to produce any PLT concentrates (plasma and/or red blood cell [RBC] only donations) were excluded.

Serious adverse reactions only were notified and registered online by the hemovigilance physicians of the blood services (Etablissement Français du Sang [EFS]). Hospital hemovigilance officers were not involved.

Statistical analysis

Qualitative variables are expressed in absolute numbers and percentage and were compared using the Fisher's exact test. To identify independent risk factors for adverse reaction in recipients, a multivariable analysis was performed using a stepwise logistic regression model (Logit). Potential explicative variables with a p value of 0.20 or less in univariate analysis were included in the analysis.

As the proportion of APCs and PPCs and the reporting of adverse reactions could vary between regions, we compared adverse reaction rates in recipients for each participating region. Mantel-Haenszel chi-square test adjusted on the proportion of AS PLTs was used for this purpose. P values of less than 0.05 were considered significant. Statistical analyses were performed using computer

TABLE 2. Number and type of PLT concentrates transfused in 23 of 26 French regions by year

	Year							
	2009 (n = 249,874)		2010 (n = 263,654)		2011 (n = 277,326)		2009-2011 (n = 790,854)	
PLT concentrate type	Number	% PC	Number	% PC	Number	% PC	Number	% PC
APCs								
WCS	126,353	50.6	102,426	38.8	41,564	15.0	270,343	34.2
IA	7,082	2.8	6,939	2.6	6,575	2.4	20,596	2.6
AS	43,062	17.2	50,923	19.3	92,823	33.5	186,808	23.6
Total	176,497	70.6	160,288	60.8	140,962	50.8	477,747	60.4
PPCs								
WCS	12,644	5.1	8,270	3.1	3,559	1.3	24,473	3.1
IA	11,751	4.7	12,208	4.6	13,214	4.8	37,173	4.7
AS	48,982	19.6	82,888	31.4	119,591	43.1	251,461	31.8
Total	73,377	29.4	103,366	39.2	136,364	49.2	313,107	39.6

IA = Intercept amotosalen treated; PC = PLT concentrate; WCS = without conservative solution.

software (R, Version 3.0.2, https://cran.r-project.org/bin/windows/base/old/3.0.2/).

RESULTS

Of 26 French regions, 23 participated in the study, gathering together 96% of the French population. From 2009 to 2011, a total of 790,854 PLT concentrates (477,747 APCs and 313,107 PPCs) were transfused. The proportion of PLTs prepared with AS was lower in APC (186,808/477,747, 39%) than in PPCs (251,461/313,107, 80%; $p < 0.001$). More PPCs were prepared with Intercept amotosalen (37,173/313,107, 12%) than APCs (20,596/477,747, 4%; $p < 0.001$), but only one participating region used this process. Number and type of PLT concentrate transfused by year are displayed in Table 2. In 2010 and 2011, a total of 266,095 apheresis procedures intended to produce PLTs, and 4,722,685 WB donations were performed in 23 of 26 French regions.

Adverse reactions in recipients

There were 3756 adverse reactions in recipients during the study period (overall incidence rate, 4749 per 1,000,000). In 3539 (94%) of adverse reactions, the PLT concentrate was the only labile blood component transfused. Overall adverse reaction rate was higher with APCs (6244 per 1,000,000) than with PPCs (2469 per 1,000,000; $p < 0.001$). More severe and life-threatening reactions were notified with APCs (respectively, 241 vs. 131 per 1,000,000, $p < 0.001$; and 182 vs. 121 per 1,000,000, $p = 0.04$). Death rates (severity Grade 4) were not different (Table 3).

A significant difference in overall adverse reactions was observed both in teaching and in nonteaching hospitals. Adverse reaction rates with APCs versus PPCs were, respectively, 5640 versus 2185 per 1,000,000 ($p < 0.001$) and 7310 versus 2830 per 1,000,000 ($p < 0.001$; Table 4).

Multivariable analysis using logistic regression (Table 5) revealed that APCs were independently associated with more adverse reactions in recipients than PPCs (odds ratio [OR], 2.39; 95% confidence interval [CI], 2.21-2.58). The presence of AS was not a confounding factor of adverse reaction (OR, 1.05; 95% CI, 0.99-1.12), whereas transfusion occurring in a university hospital was associated with a decrease in adverse reaction risk (OR, 0.80; 95% CI, 0.75-0.85).

The comparison between APCs and PPCs by region, adjusted on the proportion of AS, revealed a significant association between APCs and adverse reactions in 12 among the 20 analyzed regions that delivered both components. No significant association was found in the remaining eight regions (Fig. 1).

Donor serious adverse reactions

The overall rate of donor serious adverse reactions was higher for plateletpheresis than for WB: 5545 versus 803 per 1,000,000 ($p < 0.001$) (Table 6). Apheresis donor referrals to a physician and hospitalization rates were higher compared to WB donors, respectively, 909 versus 115 per 1,000,000 ($p < 0.001$) and 225 versus 39 per 1,000,000 ($p < 0.001$). Numbers and types of donor adverse events and management are reported in Table 5.

DISCUSSION

Main findings

In this large study involving 790,854 transfused PLT concentrates, APC transfusion was associated with a higher rate of overall, severe, and immediate life-threatening adverse reactions, although the majority of these adverse reactions were mild. Multivariable analysis demonstrated that this association was independent of the AS PLT proportion and of transfusion in a university hospital. Moreover, the analysis by region showed the same significant association between APC use and adverse recipient reactions in most regions. There was no significant impact on deaths related to PLT transfusion. Concerning the analysis of 4,988,780 donations, there were more serious adverse reactions during apheresis procedures than during WB donations.

TABLE 3. Comparison of recipient adverse reactions after PLT transfusion between APCs and PPCs

	APCs (n = 477,747)		PPCs (n = 313,107)		
Adverse reactions	Number of adverse reactions	Rate/10^6	Number of adverse reactions	Rate/10^6	p value
Overall reported	2983	6244	773	2469	<0.001
Severity grade*					
Grade 1 (mild)	2774	5806	692	2210	<0.001
Serious reactions	209	437	81	259	<0.001
Grade 2	115	241	41	131	<0.001
Grade 3	87	182	38	121	0.04
Grade 4 (death)	7	15	2	6	0.50
Imputability level					
Possible (1)	1059	2217	376	1201	<0.001
Probable (2) or certain (3)	1924	4027	397	3127	<0.001
Type of adverse reaction					
Allergic transfusion reaction	1917	4013	310	990	<0.001
FNHTR	453	948	207	661	<0.001
Transfusion reaction with alloantibody (HLA or HPA)	230	481	110	351	0.007
PLT transfusion refractoriness	80	167	29	93	0.006
TACO	34	71	13	42	0.1
TRALI	25	52	9	29	0.16
Transfusion-transmitted bacterial infection	13	27	8	26	0.99
Hypotensive	7	15	10	32	0.14
Posttransfusion purpura	4	8	0	0	0.16
Miscellaneous	220	460	77	246	<0.001

* Severity grades: Grade 1, mild; Grade 2, severe reaction; Grade 3, immediate life threat; Grade 4, death; serious adverse reaction, adverse reaction from Grade 2 to 4.
FNHTR = febrile nonhemolytic transfusion reaction; TACO = transfusion acute circulatory overload.

TABLE 4. Comparison of overall recipient adverse reactions after PLT transfusion between APCs and PPCs according to the type of hospital (teaching vs. nonteaching)

University hospital					Nonteaching hospital				
APC (n = 314,879)		PPC (n = 158,938)			APC (n = 165,110)		PPC (n = 151,927)		
Number	Rate/10^6	Number	Rate/10^6	p value	Number	Rate/10^6	Number	Rate/10^6	p value
1937	61.52	472	29.71	<0.001	1250	75.70	544	35.80	<0.001

TABLE 5. Results of multivariable analysis

Variable	OR (95% CI)	p value
APCs	2.39 (2.21-2.58)	<0.001
AS	1.05 (0.99-1.12)	0.11
University hospital	0.80 (0.75-0.85)	<0.001

The main strength of this study resides in a large database obtained from the notification systems of 23 of 26 French regions (96% of the French population, >1400 hospitals, >250 donation centers). To our knowledge, this study is the largest report on the topic of adverse reactions related to PLT transfusion. Moreover, the use of a mature, well-established, and organized notification system, with several validation stages, allowed a high quality of data.

Recipient adverse reactions

The mechanisms of transfusion reactions to PLTs remain incompletely elucidated.[9] In this study, adverse reactions were more frequent with APCs for febrile nonhemolytic transfusion reaction, transfusion reaction with anti-human leukocyte antigen (HLA) or anti-human PLT antigen (HPA) alloantibodies and PLT transfusion refractoriness. The later reactions are associated with HLA or HPA alloantibodies in the recipient.[10] Allergic transfusion reactions have a different mechanism, which involves recipients immunoglobulin (Ig)E or IgG against transfused plasma proteins as well as the donors' plasma component.[2] Thus, an immunologic mechanism may be suspected to explain the observed difference between APCs and PPCs. Another explanation could have been the higher proportion of PPCs prepared with AS during the study period in France (Table 2), as AS has been associated with less adverse reactions in some studies,[11] but when eliminating this potentially confounding factor, the difference between the two components remained significant.

The findings of this study are consistent with one previous study that reported an increase in adverse reactions with APCs.[12] However, two other studies reported no difference,[13,14] while two more noted an increase in allergic transfusion reactions with PPCs.[5,15] PLT concentrate

TABLE 6. Comparison of serious adverse reactions occurring during whole blood donation (WBD) and apheresis PLT donation (APD) with doctor's referral and hospitalization

	APD (n = 266,095)		WBD (n = 4,722,685)		
Serious adverse reactions	Number of serious adverse reactions	Rate/10^6	Number of serious adverse reactions	Rate/10^6	p value
Total	1449	5445	3791	803	<0.001
Systemic complications*					
Myocardial infarction	4	15	0	0	<0.001
Angina pectoris	1	4	4	1	0.24
Pulmonary embolism	2	8	0	0	0.028
Immediate vasovagal reaction	647	2431	2748	582	<0.001
Delayed vasovagal reaction	117	440	442	94	<0.001
Local complications					
Thrombophlebitis	7	26	10	2	<0.001
Nerve wound	12	45	38	8	<0.001
Tendon wound	1	4	2	0	0.15
Hematoma	308	1157	230	49	<0.001
Local infection	3	11	13	3	0.051
Arterial puncture	12	45	127	27	0.09
Other local pain	14	53	17	4	<0.001
Allergic complications					
Generalized allergic reaction	6	23	0	0	<0.001
Local allergic reaction	1	4	5	1	0.28
Citrate reaction	220	827	0	0	<0.001
Others	94	353	155	33	<0.001
Doctor's referral and hospitalization*					
Doctor's referral	242	909	544	115	<0.001
Hospitalization	60	225	186	39	<0.001

* Systemic complications, doctor referral, and hospitalization are not risk adjusted.

characteristics might be implicated in these discordant results. Plasma-rich pooled PLTs were used in discordant studies, while in France, during the study period, PPCs were prepared from buffy coat (as in most European countries and more recently in Canada). This technique is known to provide PLTs of better quality than the PLT-rich plasma protocol.[16]

The lower rate of adverse reactions in university hospitals has, to the authors' knowledge, not been reported previously. We hypothesized that this might be the consequence of either differences in patients' profiles, which may be less at risk for adverse reactions, or a less comprehensive reporting of adverse reactions. This point deserves further investigation.

Historically, limiting the infectious risk has been one of the major arguments for preferring APCs. Nevertheless, this particular risk may be overestimated. Prevention programs around the world led to a spectacular drop in viral risk related to labile blood components since the 1990s, to a level that can be considered low nowadays.[12] For instance, the current cumulative viral residual risk (for all known viruses) was assessed to less than 1 per 1,000,000 per donation in 2005 to 2007 in France.[17] Consequently, the PPC hazard could be estimated to 5 per 1,000,000, as a PPC is commonly prepared from five buffy coats. Interestingly, this rate is 36-fold smaller than the absolute difference of pooled severe and life-threatening adverse reactions rates between APCs and PPCs in this study. Similarly, pooling five donors to produce a PPC would theoretically increase the bacterial risk by the same factor. However, concordantly with previous studies, we did not find any increase in transfusion-transmitted bacterial infection with PPCs.[18,19]

Serious adverse reactions in donors

Serious adverse reactions in donors were more frequently reported during apheresis procedures than during WB donations. In France, apheresis donations are performed after a donor has experienced several successful WB donations. So no apheresis donors are first-time donors, although a small part of them experience apheresis for the first time. On the other hand, first-time donors account for one-fifth of WB donations. As a consequence, a higher rate of adverse reactions might be expected in WB donors. This was, however, not the case in this study. The rate of the most common adverse reaction (vasovagal reaction) was fourfold greater with apheresis. Citrate reactions obviously never occurred for WB donations, but were the second more frequent hazard in apheresis. These observations are consistent with data published by the International Hemovigilance Network.[20] In 2 years, 340 serious adverse reactions related to apheresis procedures were considered severe (Grade 3), 242 previously healthy donors were referred to a doctor, and 60 more were admitted to the hospital. Theoretically, in the French health system, where components are collected and prepared at a county level by a single national institution (EFS), the current annual 2.3 millions of WB donations could provide the nearly 300,000 requested PLT concentrates, as 5 WB

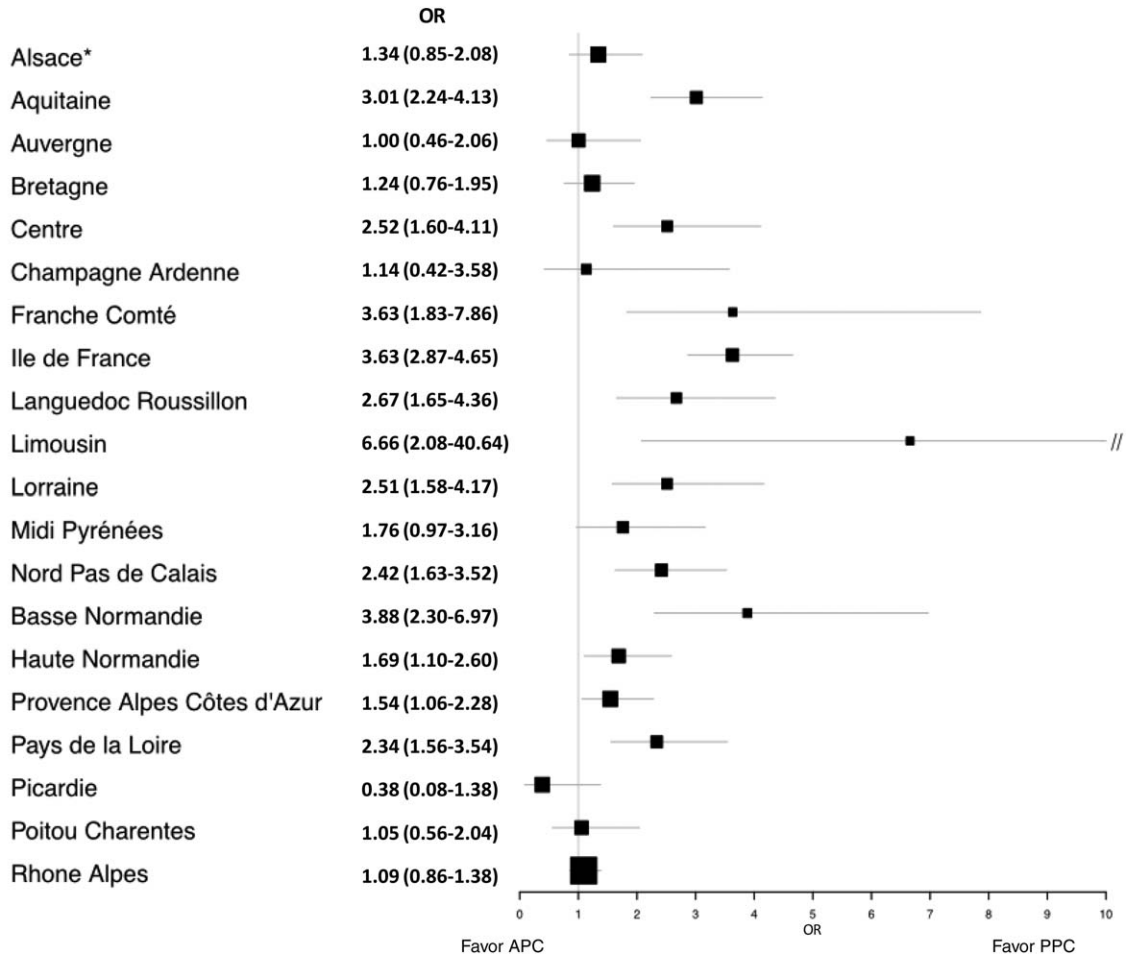

Fig. 1. Forest plot displaying the OR of adverse reactions by type of PLT concentrate (APC vs. PPC) in 20 of 23 participating French regions. Three regions have been excluded from the analysis because they used only one type of PLT concentrate. All ORs have been adjusted on the proportion of AS PLT concentrates using Mantel-Haenszel chi-square test. Region-specific ORs (95% CI) are denoted by black squares (black lines). Square sizes are inversely proportional to the magnitude of the CI.

units are necessary to prepare a PPC and this would not alter the risk for WB donors.

In other circumstances (e.g., a self-sufficient blood bank) where the PLT need would be greater than one-fifth of RBCs, and the blood components prepared locally, a supplementary exposure of donors would theoretically be necessary to provide PPCs instead of APCs. However, even multiplying by five the risk of WB donors would not make it superior to the risk of apheresis. These data are of concern about an excess risk caused by avoidable apheresis procedures, which should be further investigated by future studies.

Limitations of the study

Due to its observational design, this study cannot prove causality. Besides, it suffers from several limitations.

The database was anonymous for reactions and aggregated at a hospital level for exposure to transfusion and regional level for exposure to donation. It did not provide a comprehensive description of individual characteristics of patients receiving transfusion or donors. Consequently, identification of demographic confounding factors associated with a higher rate of adverse reaction could not be performed. Moreover, the choice of the type of PLT concentrate (APC or PPC) might have been made according to physicians' specific request leading to potential selection bias. Patients considered more at risk for adverse reactions (e.g., pregnancy or multiple transfusions) may have been transfused preferentially with APCs. For instance, patients experiencing PLT refractoriness may have received HLA-identical or cross-matched APCs.[20] However, the scarce supply allowed a limited choice, and the EFS, who delivers the PLTs, being independent from hospitals, had no access to patients' files. Therefore, it was difficult to choose the PLT component according to the specific patient's condition.

Notification of transfusion-related adverse reactions is mandatory in France, although it is a passive surveillance system and reported rates of adverse reactions are lower than those of prospective studies.[13] The difference in rates of adverse reactions in recipients between APCs and PPCs could also result from a selection of patients between university hospitals and nonteaching hospitals; patients attending university hospitals are supposed to be more seriously ill and more at risk of adverse reactions. Yet APCs were associated with an increased risk of recipient adverse reactions in both types of hospitals, which limits this potential bias.

In conclusion, in this large observational study aggregating more than 790,000 PLT transfusions and nearly five million donations, recipient adverse reactions were less frequently associated with PPCs than with APCs. In the meantime, partly avoidable apheresis procedures were associated with an increased risk of donor adverse reactions. These results question the wide use of APCs and might lead to recommend their prescription for specific indications.

However, due to its methodologic weakness, this study calls for future prospective studies to confirm or refute these results. Future studies should focus on the global risk-to-benefit ratio associated with transfusion of the different types of PLT concentrates, taking into account precise demographic characteristics of patients.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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