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TRANSFUSION

The safety of COVID-19 convalescent plasma donation: A multi-institutional donor hemovigilance study

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Abstract

Background: Although the safety and therapeutic efficacy of COVID-19 convalescent plasma (CCP) has been extensively evaluated, the safety of CCP donation has not been explored in a multi-institutional context.

Study design and methods: Nine blood collection organizations (BCOs) participated in a multi-institutional donor hemovigilance effort to assess the safety of CCP donation. Donor adverse events (DAEs) were defined according to the Standard for Surveillance of Complications Related to Blood Donation, and severity was assessed using the severity grading tool. Multivariate analysis was performed to determine attributes associated with DAE severity.

Results: The overall DAE rate was 37.7 per 1000 donations. Repeat apheresis and apheresis-naïve donors experienced adverse event rates of 19.9 and 49.8 per 1000 donations, respectively. Female donors contributed 51.9% of CCP donations with a DAE rate of 49.4 per 1000 donations. The DAE rate for male donors was 27.4 per 1000 donations. Vasovagal reactions accounted for over half of all reported DAEs (51.1%). After adjustment, volume of CCP donated was associated with vasovagal reaction severity (odds ratio [OR] 6.5, 95% confidence interval [CI] 2.5–17.1). Donor age and donation history were also associated with DAE severity. Considerable differences in DAE types and rates were observed across the participating BCOs despite the use of standardized hemovigilance definitions.

Conclusion: The safety of CCP donation appears comparable to that of conventional apheresis plasma donation with similar associated risk factors for DAE types and severity.

Abbreviations: ARC, American Red Cross; BCO, blood collection organization; CCP, COVID-19 convalescent plasma; CI, confidence interval; COVID-19, Coronavirus disease 2019; DAE, donor adverse event; DHV, donor hemovigilance; EAP, expanded access protocol; HLA, human leukocyte antigen; LOC, loss of consciousness; ml, milliliter; OR, odds ratio; RR, rate ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SGT, Severity Grading Tool; SSCRBD, Standard for Surveillance of Complications Related to Blood Donation; UCLA, University of California, Los Angeles.

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1 | INTRODUCTION

Plasma donated by individuals recently recovered from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection facilitates the passive transfer of donor antibodies to the transfused recipient. Several studies indicate that COVID-19 convalescent plasma (CCP) with high titer SARS-CoV-2 neutralizing antibodies may be efficacious when transfused early in COVID-19 infection.[1-4] Conversely, several randomized controlled trials have concluded that CCP provides no therapeutic benefit in hospitalized COVID-19 patients.[5-7] Although initial studies demonstrated the safety of CCP transfusion in hospitalized COVID-19 patients, few have evaluated CCP donation safety and associated donor adverse events (DAEs).[8-10] Investigating the safety of CCP donation warrants a coordinated donor hemovigilance (DHV) effort.

DHV is the practice of organized surveillance of adverse events or outcomes associated with blood donation. The lack of uniform definitions and grading criteria for DAEs initially posed a significant impediment to multi-institutional collaborative DHV efforts. The Standard for Surveillance of Complications Related to Blood Donation (SSCRBD) now provides a common language to describe DAEs.[11] Shortly after adopting the SSCRBD, the need for improved DAE severity grading was recognized,[12] and in response, the severity grading tool (SGT) was developed (https://www.aabb.org/docs/default-source/default-document-library/resources/severity-grading-tool-for-donor-adverse-events.pdf?sfvrsn=ff563263_4).[13]

A survey study was developed by the AABB DHV Working Group and distributed to select non-profit blood centers and academic hospital-based donation centers in North America. The study aims were as follows: (a) to determine the rate of DAE for CCP donors in comparison to reported (historic) rates of DAE for conventional apheresis plasma donors, (b) determine and categorize the subtypes and severity of DAE experienced by CCP donors, and (c) to determine the donor attributes associated with DAE severity. In addition, this collaborative, multi-institutional DHV effort provided an opportunity to gain new insights on improving DHV studies.

2 | MATERIALS AND METHODS

The study protocol was approved by the Medical College of Wisconsin/Froedtert Hospital Institutional Review Board.

The survey was designed and developed using an online survey tool, Qualtrics (Provo, UT). Nine blood collection organizations (BCOs) participated in the study (Innovative Blood Resources, Mayo Clinic Blood Donor Center, American Red Cross (ARC)—Biomedical Services, OneBlood, Versiti Wisconsin, Versiti Illinois, New York Blood Center, UCLA Blood and Platelet Center, and Vitalant) and are hereafter referred to as "participants"—arbitrarily numbered 1 through 9. CCP donation and donor data from the start of collection in April 2020 through September 1, 2020, were requested. All participants, except for one that only provided data for the first 2 months of CCP collection provided the requested data.

Data were collected retrospectively as two parts (Table S1): (i) aggregate data points on donation and donor attributes and (ii) detailed inquiry form (reaction database) to collect donor attributes for each DAE. The donation history was categorized as previously never donated blood (first-time ever donors), previously donated whole blood only (first-time apheresis donors), and previously donated via apheresis collection (repeat apheresis donors). Data from only apheresis collections were included in the study. DAE were classified using the SSCRBD.[11] Severity grading classification was determined using the SGT.[13] Donations with more than one associated DAE were counted as separate events. Discrepancies in DAE type and category were harmonized to SSCRBD after follow-up with the participating organization. Missing donor attributes for biometric and clinical measurements in the detailed inquiry form for each DAE were not followed up (Table S2). DAE rates were calculated per 1000 donations. Stratified comparison for DAE types and categories were based on donation history.

Multivariable logistic model was developed to predict factors for reaction severity by comparing severity grade 1 (mild events) to severity grade 2 and above (moderate and severe events). Severity grades of 2 and 3 DAE were combined for analysis. Initial multivariable model included all donor attributes collected in the reaction database except

donor height. Donor height was not included in the model due to poor reporting (42.2%, Table S2). First-time ever and first-time apheresis donors were aggregated as a single category of "apheresis-naïve donors" and compared to repeat apheresis donors. CCP volume donated, age, and donation history were selected using stepwise backward elimination method in the final multivariate model, choosing the stopping rule at $p < .05$. A separate multivariate model was also run in a data set restricted to vasovagal reactions.

Comparator data included conventional apheresis plasma donation data from three large blood centers that provided their DHV data to the AABB DHV platform—DHV Analysis & Reporting Tool (DonorHART™) from 2014 to 2017.[14,15] DonorHART™ was discontinued in 2018. Donations identified as "Apheresis Plasma" under the data field "Procedure Type" in the DonorHART™ reaction database were classified as conventional plasma donations. Event type and category from this database was harmonized to the revised SSCRBD. Although attribute data included in the detailed inquiry portion of this study were available in the DonorHART™ reaction database, the denominator database collected aggregated data points only. Therefore, denominator data (total plasma collections) could not be further stratified into donor attributes. For estimates, 95% confidence intervals (95% CIs) not including 1.0 were selected as cutoff criteria for statistical significance. Statistical analysis was conducted using the computer software SAS (v9.4, SAS Institute).

3 | RESULTS

3.1 | Reporting participants

The participants included seven blood centers and two hospital-based donation centers. Six participants reported collecting CCP through apheresis procedure only, while three participants reported collecting CCP through both whole blood and apheresis procedure. Only apheresis data were included in analysis.

3.2 | Prescreening measures

Five out of nine participants reported performing prescreening measures prior to scheduling a CCP donor. Of the participants performing prescreening measures, three implemented the Donor History Questionnaire (either full length or modified), one implemented a vein assessment, one assessed hemoglobin, one implemented human leukocyte antigen antibody screen for female donors with a history of pregnancy, and one performed

TABLE 1 Donor demographics and donor adverse event (DAE) by donations

	Number of DAE	Number of donations	DAE per 1000 donations
CCP DHV project (overall)	1402	37,174[a]	37.7
Gender			
Male	476	17,390	27.4
Female	926	18,754	49.4
Transgender/other/nonbinary	–	3	–
Age			
16–20	55	773	71.2
21–24	113	1784	63.3
25–44	536	14,616	36.7
45–64	534	15,445	34.6
65+	164	3490	47.0
Prior donation history			
Apheresis-naïve donor	1156	23,200	49.8
First-time ever donor	660	12,481	52.9
First-time apheresis donor	496	10,719	46.3
Repeat apheresis donor	246	12,380	19.9
DonorHART™: 2014–2017 data (overall)	1205	52,952	22.8

Note: Data are presented as reported by the participants.

Abbreviations: CCP, COVID-19 convalescent plasma; DHV, donor hemovigilance.

[a]Total complete and incomplete donations.

qualitative COVID-19 antibody testing. Four participants did not perform any prescreening measures.

3.3 | Data elements

All DAE data elements were reported at greater than 99.0% except for donor height that was reported at 42.2%. Incompletely reported data elements in the DonorHART™ database are shown in Table S2.

3.4 | Donation information, donor demographics, and event rates

The aggregate number of complete and incomplete reported CCP donations was 37,174 (complete donation = 34,891) (Table 1). Of which, 25,402 donors completed 1 or more CCP donations. The mean of completed donations per donor was 1.6 (participant mean range: 1.02–2.22). A total of 104,918 CCP units were manufactured from total complete donations. The mean number of CCP units yielded per completed donation was 3.01 (participant mean range: 2.27–3.45). Distributions of donor history, gender, and age are shown in Table 1 and Figures S1, S2A, and S2B.

A total of 1402 DAEs were reported and the overall DAE rate was 37.7 per 1000 donations. In comparison, the DAE rate for plasma donation in the DonorHART™ database was 22.8 per 1000 donations. Female donors contributed 18,754 (51.9%) donations and had a DAE rate of 49.4 per 1000 donations. Male donors had a DAE rate of 27.4 per 1000 donations. Donor demographics and DAE rates by donation are presented in Table 1.

The overall rate of DAE for apheresis-naïve donors (49.8 per 1000 donations) was significantly higher than that for repeat donors (19.9 per 1000 donations, Table 1). Donors aged 16–20 years old accounted for highest DAE rate per age group (71.2 per 1000 donations). Donors in the 45–64 years of age group donated 42.8% of all CCP donations (Figure S2B), and in the age-based comparison, this age group had the lowest DAE rate (34.6 per 1000 donations, Table 1).

Vasovagal reaction (717) was the most commonly reported DAE followed by hematoma (471) (Figure 1, Table 2). The event rate of vasovagal reaction among apheresis-naïve donors (24.6 per 1000 donations) was 2.1 (95% CI 1.7–2.5) times higher than for repeat apheresis donors (11.9 per 1000 donations). When considering vasovagal reactions without loss of consciousness (LOC), the incidence of DAE for apheresis-naïve donors is 2- to 3-fold higher than in repeat apheresis donors (rate ratio [RR] 2.9, 95% CI 2.3–3.6). Surprisingly, the event rate of vasovagal reaction with LOC is lower in apheresis-naïve donors relative to repeat apheresis donors (RR 0.7, 95% CI 0.5–0.9), although based on unadjusted data and a low number of adverse events (Table 2). The event rate of hematoma was also significantly higher among apheresis-naïve donors (18.1 per 1000 donations) than in repeat apheresis donors (4.0 per 1000 donations). Citrate reactions occurred nearly 4 times more frequently with apheresis-naïve donors (3.5 per 1000 donations) relative to repeat apheresis donors (0.9 per 1000 donations).

3.5 | Severity grading analysis

The percentages of DAEs with severity grading 1, 2, and 3 were 95.7%, 3.7%, and 0.6%, respectively (Figures 1 and

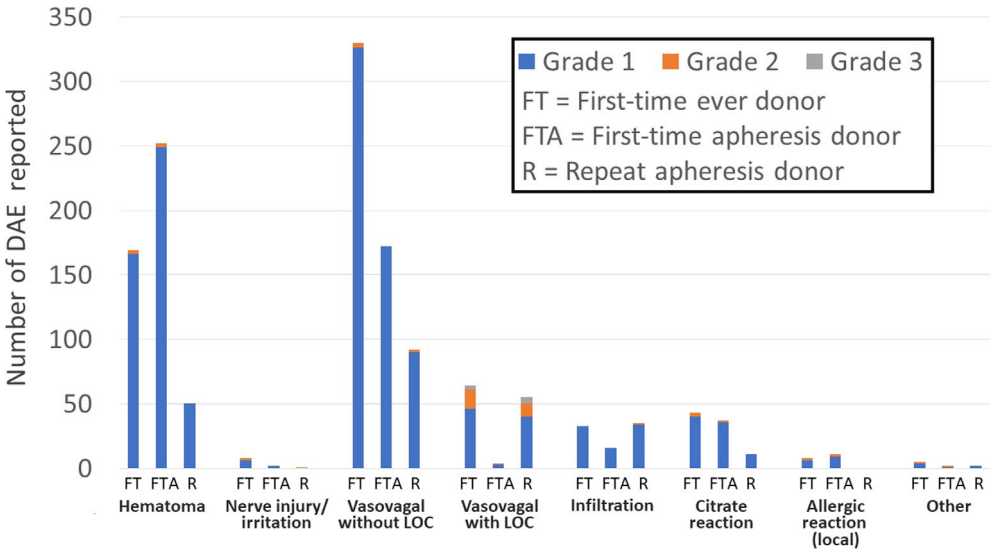

FIGURE 1 Distribution of donor adverse event types and severity [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Comparison of DAE rates among CCP donors based on donor history

DAE type/category	Apheresis-naïve[a] donors		Repeat apheresis donors		
	DAE (*N*)	Rate (per 1000 donations)	DAE (*N*)	Rate (per 1000 donations)	Rate ratio (95% CI)
Overall	1156	49.8	246	19.9	2.5 (2.2–2.9)
Hematoma	421	18.1	50	4.0	4.5 (3.4–6.0)
Nerve injury/irritation	10	0.4	1	0.1	5.3 (0.7–41.7)
Superficial thrombophlebitis	1	<0.1	0	0	–
Vasovagal reaction	570	24.6	147	11.9	2.1 (1.7–2.5)
No LOC	502	21.6	92	7.4	2.9 (2.3–3.6)
LOC	68	2.9	55	4.4	0.7 (0.5–0.9)
Related to apheresis	129	5.6	46	3.7	1.5 (1.1–2.1)
Citrate reaction	80	3.5	11	0.9	3.9 (2.1–7.3)
Infiltration	49	2.1	35	2.8	0.7 (0.5–1.2)
Allergic reaction	20	0.9	0	0	–
Local allergic	19	0.8	0	0	–
Generalized (anaphylactic)	1	<0.1	0	0	–
Other	5	0.2	2	0.2	1.3 (0.3–6.9)

Abbreviations: CCP, COVID-19 convalescent plasma; CI, confidence interval; DAE, donor adverse event; LOC, loss of consciousness.
[a]Includes first-time ever donors and first-time apheresis donors.

S3). No life-threatening or fatal reactions (severity grade 4 or 5) occurred. Donation history, donor age, and CCP volume donated were independent predictors for more serious reactions (severity grading 2 and above compared to severity grading 1). All comparisons were adjusted for these factors. When compared to the reference group aged 45–64 years, the adjusted odds ratio (OR) of developing more serious reactions requiring outside medical attention (i.e., DAE of severity grading 2 or 3, Table 3) for donors aged 25–44 years is 0.5 (95% CI 0.3–1.0) indicating a trend toward lower risk. Although risk of grade 2 or 3 DAE was higher in donors of 65+ years, the adjusted OR (1.6) was not significant (95% CI 0.8–3.1). Apheresis-naïve donors were at significant higher risk of developing a severe reaction compared to repeat apheresis donors (adjusted OR: 1.8, 95% CI 1.1–3.3). Donors who donated more than 560 ml CCP were about three times more likely to develop a grade 2 or 3 reaction (adjusted OR: 3.0, 95% CI 1.6–5.4) compared to donors who donated ≤560 ml CCP. Based on the unadjusted OR, females were at greater risk of more serious reactions compared to male donors.

Restricting the database to vasovagal reactions revealed that donors in the age group 16–44 years had a significantly lower risk of developing grade 2 or 3 vasovagal reaction compared to donors in age group 45–64 years (adjusted OR: 0.3, 95% CI 0.1–0.7) (Table 3). Compared to repeat donors, apheresis-naïve donors were at higher risk of developing grade 2 or 3 vasovagal reactions (adjusted OR: 2.4, 95% CI 1.2–4.8). Similarly, donors who donated more than 560 ml CCP were at significantly higher risk of developing more serious vasovagal reactions (adjusted OR: 6.5, 95% CI 2.5–17.1) than that of donors who donated ≤560 ml CCP.

3.6 | Donor hemovigilance

The overall DAE rates, the DAE rates relative to donation history, and distribution of DAEs reported for CCP donors varied significantly between participants (Figures 2 and S4A). A 10-fold difference in DAE rates was observed with participant 1 reporting a rate at 140.3 DAEs per 1000 donations and participant 4 reporting a DAE rate of 13.9 per 1000 donations (Figure 2). The variability in the DAE rates relative to donation history is illustrated in Figure 2. The distribution of DAE types and categories reported by each participant is shown in Figure S4A.

4 | DISCUSSION

The current multi-institutional DHV study affirms the safety of CCP donation relative to conventional apheresis plasma donation and demonstrates the utility of the SGT for uniform DAE severity grading. We report an overall DAE rate for CCP donation that appears in line with the historical rate of DAE for apheresis plasma donation,

TABLE 3 Comparing odds ratio (OR) for donor attributes by reactions with severity grading 2 and 3 versus with severity grading 1

	Severity grade 1	Severity grades 2 and 3	Unadjusted OR (95% confidence interval [CI])	Adjusted OR[a] (95% CI)
All reactions				
Age group (years)				
16–24[c]	165	3	0.3 (0.1–1.1)	0.4 (0.1–1.2)
25–44	521	15	0.5 (0.3–1.0)	0.5 (0.3–1.0)
45–64	506	28	1	1
65+	150	14	1.7 (0.9–3.3)	1.6 (0.8–3.1)
Donation history				
Apheresis naïve[b]	1115	41	0.4 (0.3–0.8)	1.8 (1.1–3.3)
Repeat apheresis	227	19	1	1
COVID-19 convalescent plasma (CCP) volume donated (ml)				
≤560	653	15	1	1
≥561	689	45	2.8 (1.6–5.2)	3.0 (1.6–5.4)
Gender				
Female	881	45	1.6 (0.9–2.8)	
Male	461	15	1	
Vasovagal reactions only				
Age group (years)				
16–44[c]	410	10	0.3 (0.1–0.6)	0.3 (0.1–0.7)
45–64	213	18	1	1
65+	54	12	2.6 (1.2–5.8)	2.2 (1.0–5.0)
Donation history				
Apheresis-naïve[b]	547	23	0.3 (0.2–0.6)	2.4 (1.2–4.8)
Repeat apheresis	130	17	1	1
CCP volume donated (ml)				
≤560	330	35	1	1
≥561	347	5	0.1 (0.1–0.4)	6.5 (2.5–17.1)
Gender				
Female	471	32	1.7 (0.8–3.9)	
Male	206	8	1	

[a]Adjusted OR includes age group, donation history, and CCP volume donated as covariates. Gender was not included in the multivariate model, and therefore, adjusted OR is not reported.
[b]Includes first-time ever donor and first-time apheresis donor.
[c]Age groups were combined due to low/absent number of grade 2 or 3 events in these age categories.

although direct statistical comparison was not performed against the comparator apheresis data (DonorHART™). Our study represents the first collaborative DHV effort to utilize the SGT for uniform grading of DAE severity across multiple, independent institutions and to assist in identifying risk factors associated with event severity. Additionally, this study provides insights on the range of DAE types and event rates observed by independent BCOs.

The DAE rate associated with CCP donation appears to fall within the reported range for conventional apheresis plasma donation. In comparison, the historical incidence of DAE for plasma donors from DonorHART™ is 22.8 per 1000 donations.[14,15] Covariates known to influence occurrence of DAE could not be adjusted in the DonorHART™ data to match CCP donor demographics. Individual-level data were not collected for all donors in the current study, precluding adjustment of CCP donor data to match DonorHART™ data. Thus, direct statistical comparison between the two groups could not be performed. Nonetheless, it should be noted that DonorHART™ data were comprised of 84.0% repeat donors, which further supports that the DAE rate for CCP donation, with a high percentage of

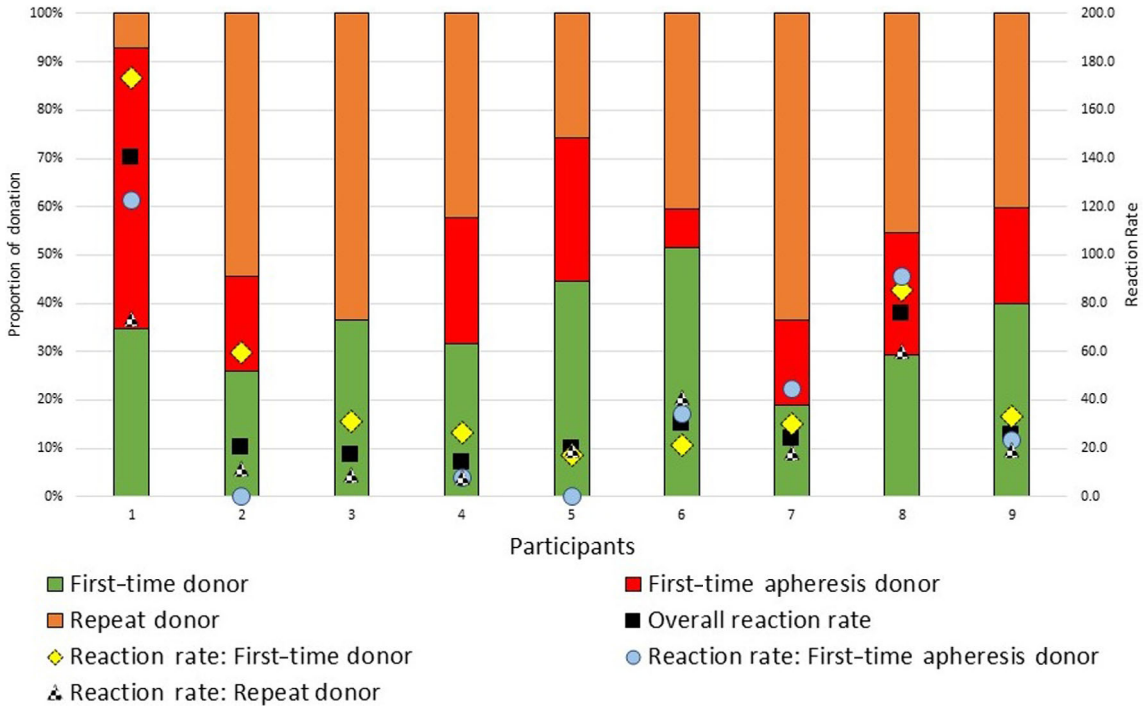

FIGURE 2 Comparison of proportion of donation and donor adverse event (DAE) rates among the participants based on donation history. Participant 3 did not report any first-time apheresis donors. Participants 2 and 5 did not report any DAEs for first-time apheresis donors [Color figure can be viewed at wileyonlinelibrary.com]

first-time donors, is within the range of conventional apheresis plasma donation.

Two studies on CCP donors, which included DAE incidence, were recently published.[9,10] The first study involved CCP donors at two transfusion centers in Italy and reported an incidence of DAE at 25.8 per 1000 CCP donations.[9] While in line with our incidence of DAE, the small size of the Italian study with only 504 CCP donations makes it vulnerable to sampling bias. The second study recently published by the ARC included 14,272 CCP donations.[10] The incidence of DAE reported by the ARC was approximately 137 per 1000 donations. Interestingly 52.1% of CCP donors in the ARC study were first-time ever donors compared to 35.1% of donors in the current CCP donor study. The larger fraction of first-time ever donors likely contributed to the higher incidence of DAE among CCP donors observed in the ARC study compared to the current study. However, different reporting thresholds for adverse events, alternative interpretations of the SSCRBD definitions, variations in collection practice, and other unaccounted for donor variables cannot be excluded. Previously reported DAE rates by the ARC for standard apheresis donors were between 53.8 and 57.8 per 1000 donations, which is closer to the incidence reported in our study of CCP donors.[16]

Our study includes several notable observations. The incidence of vasovagal reaction without LOC is significantly higher in first-time donors relative to repeat apheresis donors (RR 2.9, 95% CI 2.3–3.6). However, when considering vasovagal reaction with LOC the incidence is lower in apheresis-naïve donors compared to repeat apheresis donors (RR 0.7, 95% CI 0.5–0.9), although confounding variables (e.g., gender, age) were not adjusted for in this comparison (Table 2). The very low number (4 of 10,719) of vasovagal reaction with LOC reported in first-time apheresis donors (Figure 1) suggests that lack of apheresis experience does not contribute to an increased risk of LOC for CCP donors. The frequency of hematoma and nerve injury/irritation is increased in apheresis-naïve donors relative to repeat apheresis donors (hematoma RR 4.5 and nerve injury RR 5.3, respectively) (Table 2). Likewise, the rate of citrate reaction is around 4 times greater in apheresis-naïve donors than that in repeat donors (RR 3.9, 95% CI 2.1–7.3). It is tempting to speculate that this reflects self-selection of individuals with easy phlebotomy access and citrate tolerance toward repeat donation. Indeed, prior research demonstrates that adverse events with blood donation significantly lower the odds of future donation.[17] Whether additional factors increase hematoma, nerve injury/irritation, and citrate reaction rates in apheresis-naïve CCP donors relative to repeat apheresis CCP donors remains to be determined.

Our DHV study revealed substantial variation in the incidence of specific DAE types reported across the nine study participants relative to DonorHART™ (Figures S4A and S4B). With respect to the variability in

infiltration rates, our findings suggest that some of the reported hematomas were infiltration events. This is supported by the absence of infiltration event reporting combined with a high number of reported hematoma events by participant 1. Given that a hematoma can result from infiltration of red blood cells into the soft tissue during the return phase of apheresis, the potential for misclassification is understandable. Revisiting the definitions of hematoma in the setting of apheresis and infiltration could benefit the consistency of DAE classification in future DHV efforts. Other anomalous findings included the observation by participant 5 of more vasovagal reactions with LOC compared to vasovagal reactions without LOC (Figure S4A) while participant 4 did not report a single vasovagal reaction with LOC, despite a substantial number of vasovagal reactions without LOC. Although variability is to be expected with inter-institutional studies, the substantial difference among participants observed in our study suggests a need to further standardizing DHV practice.

Several distinguishing qualities make CCP donors an important segment of plasma donors. First, although the acute symptoms and disease course of COVID-19 infection are well documented, the sequelae of this disease specifically pertaining to blood donation risk remain unknown.[18] Second, a large portion CCP donors, 35.1% in this study, were first- time ever blood donors. Collection via an apheresis machine usually occurs after a donor has successfully donated whole blood. In contrast, first-time ever donors in this study underwent apheresis collection as their introduction to blood donation. Third, a significant fraction of CCP donors donated more than once (mean number of donations completed per donor = 1.6 within <5 months), suggesting a highly motivated group of donors. Finally, the federally mandated order to collect, stockpile, and distribute CCP during the pandemic bolstered the importance of ascertaining CCP donation risk and identifying which individuals could safely donate CCP.[19] Given the attributes of CCP donors and the unique circumstances with the COVID-19 pandemic, it is not surprising that five out of the nine participants in our study utilized prescreening measures to aid in the selection of CCP donors.

Strengths of this study include the robust representation of early CCP donation events, the multi-institutional participation in the study, the large geographic area from which donors were represented, and use of the SGT. By analyzing 37,174 CCP donations resulting in 104,918 units collected within the 5 months of data collection, we have confidence that these data provide ample representation of the CCP collected in the United States during this time frame. To put the number of CCP units collected into context, the Mayo Clinic, under whose expanded access protocol (EAP) most hospitals in the United States administered CCP, reported that from April 3, 2020 to September 7, 2020, the number of patients transfused one or more units of CCP under the EAP was 94,287.[20] The participants in our study included five of the largest nonprofit blood centers with a collection footprint spanning all regions of the United States. To our knowledge, this is the first multi-institutional DHV study to employ the SGT since its introduction.[13]

This study has several limitations. First, as a survey study with few participants, we acknowledge the potential for sampling bias toward the experience of CCP collection at nonprofit blood centers. Second, only CCP donors who donated by apheresis were included in this study; whole blood CCP donors were not included. Therefore, the findings of our study may not be generalizable to CCP donors collected via whole blood. Third, this study was limited to BCOs in the United States and did not include any international CCP collection efforts. Fourth, while use of the DonorHART™ database allowed a comparison of our study findings to conventional apheresis plasma donors, the data could not be adjusted for covariates known to affect DAE incidence.[14,21] Furthermore the data set collected for the current study did not allow adjusting for covariates. In light of the limitations, statistical comparison of DAE incidence between the two donor groups was not performed. Finally, the SGT helped identify risk factors associated with event severity; however, for more granular analysis, future studies of larger sample size will be needed.

Despite uniform employment of the SSCRBD and SGT, wide variability in DAE reporting existed between participants. The reason for the variability in DAE types and event rates reported between participants is likely multifactorial. Future prospective studies should include training in using the SSCRBD and SGT to standardize data collection. The importance of consistent DAE reporting between BCOs will continue to increase as efforts to establish a national DHV system in the United States progress.

5 | CONCLUSIONS

Our multi-institutional DHV study finds that the safety of CCP donation appears comparable to that of conventional apheresis plasma donation with similar associated risk factors for DAE types and severity. By using the SGT and performing multivariate analysis, we find that donation history, donor age, and volume of CCP donated are risk factors for DAE severity. This multi-institutional study also reveals wide variations in the types and rates of DAE reported across the participating BCOs. Although the reason for these variations is likely multifactorial, it also illustrates the importance of standardized procedures

for conducting DHV collaborative studies. Our CCP study affirms the safety of convalescent plasma collection from individuals recently recovered from COVID-19.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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