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Rapidly Establishing a Hospital-Based Convalescent Plasma Collection Center With the Alyx Apheresis Collection Device

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Abstract

The effort to collect convalescent plasma from individuals who recovered from COVID-19 began in earnest during the spring of 2020. Either whole blood or apheresis donations were obtained, the latter yielding higher numbers of units per donor per collection and more frequent collections. The NorthShore University HealthSystem blood donor center purchased 2 Alyx (Fresenius Kabi) apheresis plasma collection devices and quickly implemented them in order to collect COVID-19 convalescent plasma. Apheresis-experienced and inexperienced phlebotomists operated the instruments. Donors were collected >14 days from symptom resolution and all donors were negative by SARS-CoV-2 nasopharyngeal swab. Both internal metrics of performance as well as a post donation survey were used to evaluate the feasibility implementing this collection program. During the first 100 days of the collection program, 650 plasma units were collected. In particular, during the first week of the program, 38 units were collected and distributed to hospitals under the emergency investigational new drug and expanded access program. Fifty-one donors (15%) were deferred due to vital signs out of range or donor screening questions. Thirty-one donors (10%) were deferred due to positive nasopharyngeal swab. Lower than target yield occurred in 16.6% of collections due to donor reactions or flow errors. Donors rated the overall program lower, but not the staff, when they reported symptoms related to collection. In conclusion, a hospital-based apheresis convalescent plasma collection program can be rapidly implemented. Donor reaction rates and vein infiltration rates should be carefully monitored for each phlebotomist.

Keywords

convalescent plasma, COVID-19, blood collections, apheresis, donor reactions

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Introduction

The United States Food and Drug Administration (FDA) established guidelines for the manufacture and use of coronavirus disease 2019 (COVID-19) convalescent plasma (CP) in March 2020, using an emergency investigational new drug (eIND), expanded access program, or study-specific INDs.[1] Under this framework, units of CP could be obtained from whole blood or apheresis-based blood donations. By August 2020, CP was given an emergency use authorization by the FDA, likely increasing the demand for CP until a superior alternative therapy for COVID-19 is approved.[2]

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Both national blood collection centers and hospital blood banks have begun widespread local collection CP from donors, either by whole blood or apheresis collections.[3] Whole blood collections do not require collection instrument purchase; however, whole blood donations only yield 1 unit of CP (vs up to 4 units per collection by apheresis) and whole blood donors cannot donate more often than every 8 weeks (vs every 4 weeks or less for plasma donors).[4] On the other hand, venous access issues are more common, the cost is higher, and the collection time is longer for apheresis collections.[5]

Collection of plasma by apheresis can be performed either as part of an apheresis platelet collection as concurrent plasma, or as a stand-alone plasma collection procedure. There are 2 clear advantages to a stand-alone apheresis plasma collection. First, a limited amount of plasma can be collected by apheresis during a platelet collection (typically 1 unit, compared with up to 4 units per dedicated plasma collection). Second, the kit cost for apheresis plasma collections is lower than an apheresis platelet collection kit. On the other hand, dedicated apheresis plasma collection procedures cannot be performed using a platelet collection device, which are often already in-use at hospital-based blood centers.

Prior to the COVID-19 pandemic, the NorthShore blood donor center collected autologous stem cells and platelets using the Amicus apheresis instrument (Fresenius Kabi). Platelets were collected in platelet additive solution, and a unit of donor plasma was often concurrently collected during the procedure. As a result, multiple donor room staff phlebotomists were experienced performing apheresis collections as well as operating and validating the devices.

In order to collect COVID-19 CP, the NorthShore University HealthSystem purchased 2 Alyx (Fresenius Kabi) instruments in March 2020. The data presented here describe the challenges and opportunities associated with rapidly implementing these devices at a preexisting hospital-based blood center.

Materials and Methods

Installation and Qualification

An order for 2 Alyx devices was placed on April 3, 2020. These devices were selected in part due to their small physical footprint, light weight, and ability to sit on a standard table/cart, which facilitated their incorporation into an existing collection facility. Delivery and installation by a qualified Fresenius-Kabi Field Service Engineer took place on April 8. Operational performance qualification was completed prior to the first collection on April 16. Product performance qualification involved monitoring the actual versus target plasma yield for consecutive products, which was completed on April 29.

Each Alyx disposable plasma collection kit comes with 3 preattached satellite plasma storage bags, which can be used to collect 3 plasma units of approximately 220 mL each. Depending on the donor input parameters, the Alyx machine defaults to 450 mL, 650 mL, or 825 mL plasma collection volume. Since a 4-unit ($\sim$825 mL) collection would have required welding a fourth plasma storage bag, only 3 unit (650 mL) collections were performed using the standard 3 attached plasma storage bags.

Staff Training

Three NorthShore staff were initially trained by Fresenius Kabi trainers. Prior to the first in-person training session, Alyx Participant Workbooks links to training videos, the instrument owner's manual, and the Administration guide were sent to NorthShore for staff review. On April 14, 2020, a Fresenius Kabi Field Service Engineer and Clinical Consultant arrived on site for training, along with a remote Clinician Consultant who connected via teleconferencing. Six hours were spent reviewing key Alyx training modules. In addition, each trainee completed a successful saline run using the instrument along with a final knowledge assessment. Supplemental materials were also provided including a butterfly venipuncture job aid and a guide on how to manage alarms on the Alyx instrument. Both on-site trainers returned for the first 2 days of CP donor collection procedures in order to observe and answer questions.

Donor Recruitment and Scheduling

Donor recruitment for the NorthShore CP collection program consisted primarily of listing NorthShore on a national website as a collection center (http://www.ccpp19.org) and messaging NorthShore physicians with contact information about the collection program that they could disseminate to their patients. Donors initially contacted the NorthShore Blood Donor Center either by phone or email, then study personnel contacted them by phone for initial screening to ensure that they met eligibility requirements, which included being >14 days from the resolution of symptoms and documentation of a positive COVID-19 test result (polymerase chain reaction (PCR) or serology).

During the period of time reported in this manuscript, all consented donors were then screened by nasopharyngeal swab (NP) PCR using the Abbott ID NOW rapid test in a negative pressure area of the Evanston Hospital Emergency Department or the Evanston Hospital phlebotomy area. NP swab samples were collected by phlebotomy or Emergency Department nursing staff wearing appropriate personal protective equipment. Similar precautions were taken at other blood centers, however it remains unclear whether this approach is useful for individuals beyond 14 days from symptom resolution, to prevent viral transmission in the donor room or via the blood product.[6] Donors who tested negative for the virus were immediately invited to the donor room to complete a donor history screening form, vital sign check, and collection.

In order for the collection to proceed, the donor must have passed the donor history screening and vital sign criteria, however COVID-19 antibody levels were not measured prior to donation. Updated guidance for donor deferral criteria (published April 2, 2020, by the FDA) was implemented and the FDA was notified that the normal 28-day interdonation interval

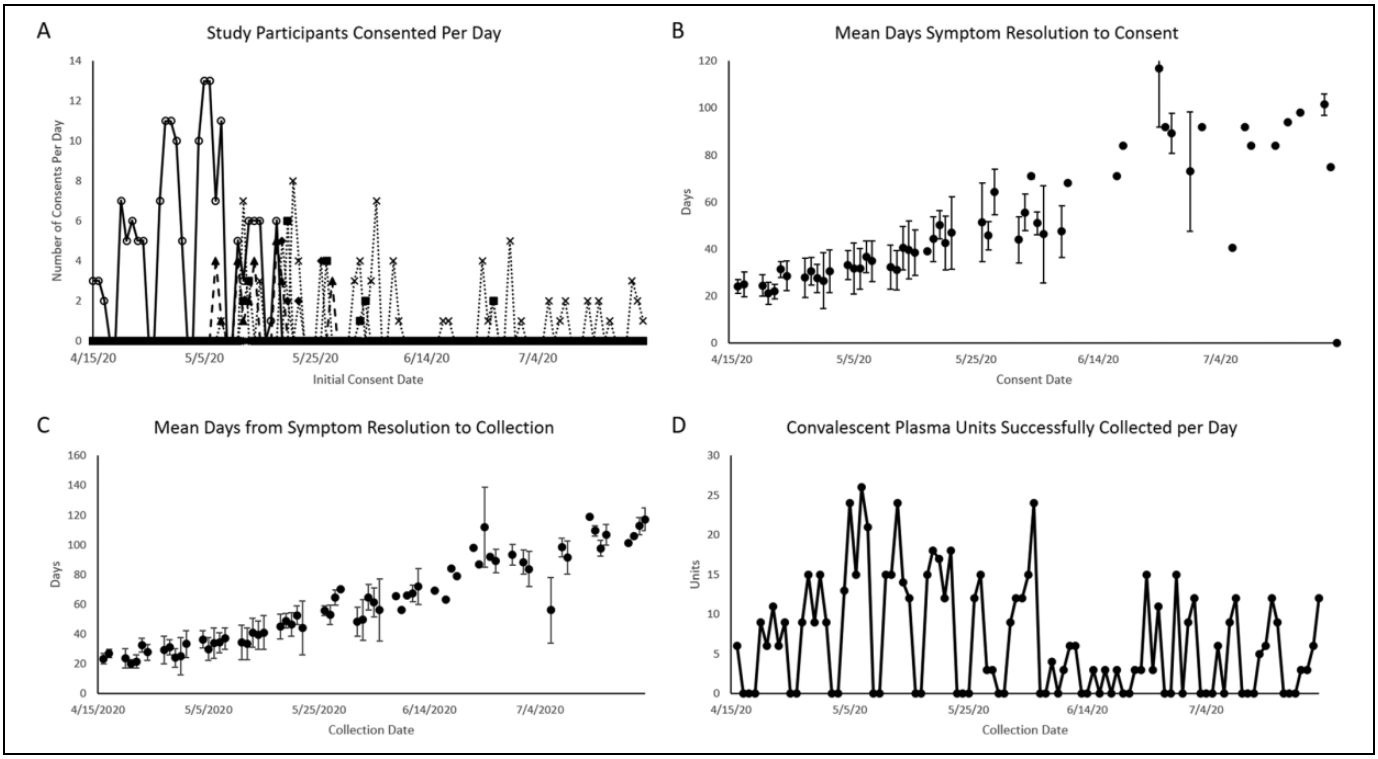

Figure 1. Consenting of participants. A, the number of individuals consented per day by each research staff member who performed consents (indicated by point shape). B, For each day, the mean number of days from resolution of symptoms to consent, for all donors consenting on that day. C, The mean days from symptom resolution to collection for all collections. D, The total number of successfully collected and labeled units per day. Error bars show $\pm$ standard deviation.

would be suspended for CP donors, with donations permitted as frequently as once every 14 days. Additionally, plasma was collected from any female donor and males who had been transfused in the past, with anti-human leukocyte antigen (HLA) antibody testing performed after the collection in order to mitigate the risk of transfusion-related acute lung injury. Medical supervision was provided by onsite pathologists boarded in Transfusion Medicine (T.J.G. and J.K.).

Donor Reaction Management

Historically, the NorthShore blood donor center stopped apheresis collections whenever a donor reaction occurred, including mild vasovagal symptoms or vein infiltration. This practice continued for CP collections.

Post-Donation Survey

As part of ongoing quality improvement activities, donors were contacted after their donation in order to provide post-donation feedback by phone or email. The survey began 76 days after the first patient was consented for donation. Donors were asked if they ever donated blood prior to volunteering as a CP donor and if so, whether they donated whole blood or platelets/plasma (apheresis) and whether they recall any complications during a previous donation. In addition, participants were asked how they would rate the CP collection procedure and CP donor room staff (scale of 1 to 10, with 10 being the best). Finally, they were asked if they experienced any symptoms after CP donation, whether there

Table 1. Deferrals.*

Donors with positive NP swab	Number
Total	31 (10%)
>28 days from symptom resolution	21 (7%)
Returned to donate	17 (6%)
Never donated CP	14 (5%)
Deferral or disqualification reason	**Number**
Recent needle stick	1 (0.3%)
Positive ID screening test	2 (0.7%)
Travel	5 (2%)
Vital signs out of range	19 (6%)
Medications / medical history	24 (8%)
Anti-HLA, male (% of males)	5 (4%)
Anti-HLA, female (% of females)	29 (18%)

Abbreviations: CP, convalescent plasma; HLA, human leukocyte antigen; NP, nasopharyngeal.

* The reasons for deferral for consented individuals who did not attempt to donate are shown. Donors who previously tested negative by rapid NP swab PCR (Abbott ID NOW) were not retested if they presented for a subsequent donation. "Positive ID Screening Test" refers to standard blood donor infectious disease testing, excluding COVID-19.

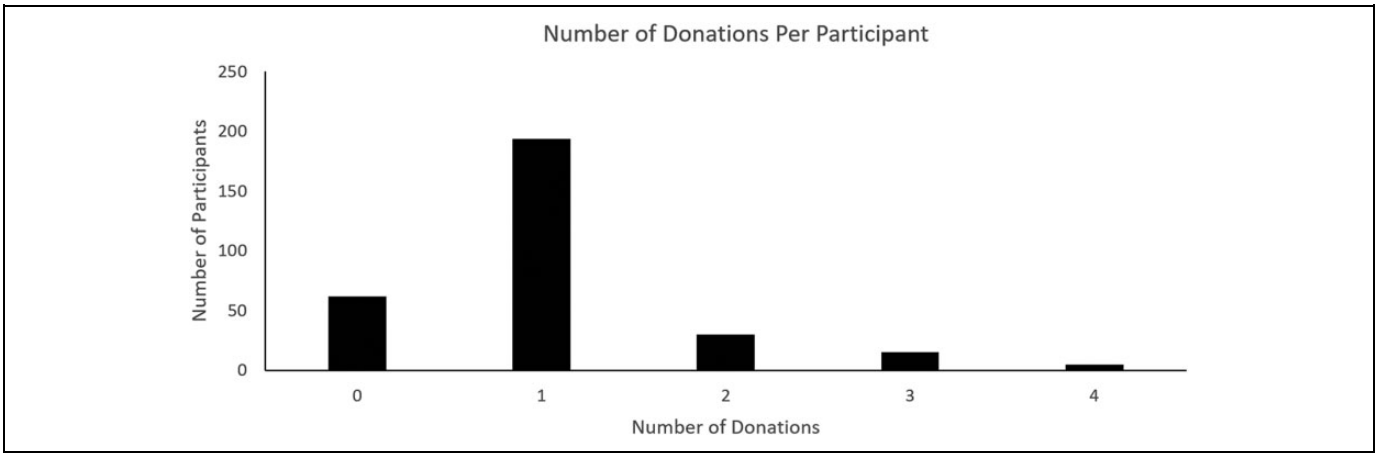

Figure 2. Donation frequency and daily yield. Histogram of the number of donations per donor (within the first 100 days of the collection program).

Table 2. Donor Reactions and Instrument Alarms.*

			Instrument alarms			
Collection yield (Product volume)	Total	Donor reaction	Flow errors	Air errors	User errors	Instrument errors
>600 mL	267	3%	35%	6%	8%	3%
400-600 mL	7	29%	71%	14%	0%	0%
200-400 mL	3	67%	67%	0%	0%	0%
<200 mL	43	84%	47%	12%	2%	0%

* The target plasma yield for each collection was set at 650 mL. The rate of staff-reported donor reactions (all types) is shown for collections of various actual yield, in addition to the rate of instrument alarms (grouped by type).

was any trouble obtaining venous access, and whether they were interested in donated CP again.

Results

Donor Screening and Consent

Donor screening and consent began on April 15 and within the first hundred days of the program, 305 individuals were consented. Consent, donor history, and NP swab screening was performed by T.J.G. with NP swab collection done by phlebotomy and nursing for the first 3 weeks of the program, with a peak of 13 donors consented per day during the fourth week (Figure 1A). There was a positive correlation between day of consent and days from symptom resolution to consent, Pearson correlation coefficient = 0.896, $P < .00001$ (Figure 1B). In other words, the time from symptom resolution to donation increased during the course of the study (Figure 1C).

Table 1 shows the incidence of reasons for deferral or inability to use the CP units collected. Positive NP swab was a reason for deferral for 10% of donors during their initial visit, with the majority of those individuals presenting again at >28 days from resolution of symptoms; 15 male donors who had been previously transfused and 20 female donors were found to be positive for anti-HLA antibodies after collection. In addition, 4 donors did not donate for scheduling reasons. Note that donors who previously tested negative by rapid NP swab PCR (Abbott ID NOW) were not retested if they presented for a subsequent donation.

Productivity. Collection yield per day rose quickly during the first few weeks of the collection program, peaking on May 7, then decreased in June due to lower demand and storage limitations (Figure 1D). Most participants donated once (Figure 2). During the first 100 days of the collection program, a total of 650 CP units were collected, labeled, and frozen at −80 °C (Table 2). Collections that yielded less than 3 units (<600 mL product volume) had a higher rate of donor reactions and flow-related instrument alarms (Table 2).

Staff Performance

The 3 phlebotomists with experience collecting platelets by apheresis had a significantly higher percentage of successful collections during their first dozen procedures, when compared with the 2 phlebotomists who did not have experience with apheresis collections (mean 97 vs 83%, $P = .038$). The yield of >600 mL collections did not vary significantly between the first dozen collections and the second dozen

Table 3. Yield per Phlebotomist.*

			>600 mL Yield per collection				Instrument alarms		
Staff	Apheresis experience	Total CP	1st Dozen	2nd Dozen	Total	Needle site reactions	Flow error	Air error	User error
A	Yes	82	92%	50%	83%	2%	44%	9%	8%
B	Yes	36	100%	83%	89%	6%	58%	3%	8%
C	Yes	82	100%	67%	87%	5%	33%	7%	2%
D	No	40	83%	83%	85%	5%	25%	8%	5%
E	No	77	83%	67%	78%	13%	34%	6%	11%

Abbreviation: CP, convalescent plasma.
* The number of collections, actual yield (units), needle site reaction rate, and instrument alarm rate is shown for each of the 5 phlebotomists who performed convalescent plasma collections. Two phlebotomists had not previously performed apheresis-based blood collections.

Table 4. Post-Donation Survey Results.*

Donor category	Respondents, N (%)	Collection rating	Staff rating
Donated blood previously			
Yes	91 (52%)	8.99	9.67
No	83 (48%)	9.07	9.80
Symptoms from collection			
Yes	48 (28%)	7.81	9.78
No	127 (73%)	9.50	9.72
Apheresis performed by experienced staff			
Yes	117 (67%)	9.20	9.74
No	57 (33%)	8.69	9.73

* A summary of the post-donation quality survey is shown for individuals who responded. Donors were asked to rate the overall collection and the staff on a scale of 1 to 10 (1 being the worst and 10 the best). "Symptoms from Collection" includes donor-reported symptoms during or immediately after collection. Experienced staff include those who had prior experience collecting blood products using an apheresis instrument.

collections performed by each phlebotomist. However, one of the apheresis-inexperienced phlebotomists in particular had a lower overall rate of >600 mL product collections, a higher rate of needle-site reactions, and a higher rate of instrument alarms related to user error (Table 3).

Donor Feedback

A total of 174 donors responded to post-donation feedback questions, of those 143 had initial collections that yielded >600 mL of CP (82%, compared with 83% for all donors). Three of these individuals donated more than once; only the feedback relative to their first collection was included. Whether a donor had previously donated blood did not correlate with their rating of the overall CP collection experience or the donor room staff, however donors who had symptoms related to collection tended to rate the overall collection experience lower, $P = .0005$ (see Table 4). For donors undergoing apheresis performed by phlebotomy staff without prior apheresis collection experience, there was a slightly lower overall collection experience rating that was not statistically significant ($P = .17$).

Discussion

These results demonstrate the feasibility of rapidly implementing a CP collection program using dedicated apheresis plasma collection instruments and a hospital-based blood donor center with prompt technical support from the device manufacturer. NorthShore is a 738 bed community hospital system in a metropolitan setting. Similar rapid implementation programs have been reported during prior epidemics, including Ebola.[7]

This CP collection program succeeded in collected an ample supply of plasma during the spring of 2020, when national availability of CP was limited. Assuming an adequate supply of materials, it is likely that hospital-based CP collection program will continue to benefit organizations by minimizing the impact national CP shortages. In addition, having an in-house collection program shortened the time between CP order and transfusion, since the hospital itself maintained a standing inventory, that is, immediately available. Finally, NorthShore became a site for outpatient COVID-19 early disease treatment and prophylaxis trials using CP collected in this program. If these trials (or trials like them) prove that CP is useful to treat early COVID-19 disease or as a prophylaxis, it is likely that the demand for CP will increase markedly along with the value of a hospital-based collection program.

In response to the increased donor room activity, 2 phlebotomists who had no prior experience collecting blood products by apheresis were trained to collect CP. One of those individuals demonstrated rates of needle-site reactions and alarms similar to experienced phlebotomists, however the other individual had a slightly higher rate of instrument errors, needle-site reactions, and incomplete collections. Going forward, these findings will be used to better monitor which phlebotomists, especially new staff members, might benefit most from additional phlebotomy training. Nevertheless, even the new phlebotomist was able to yield a significant number of products.

Additional efforts to increase collection efficiency might include collecting 825 mL of plasma per donor (when possible), prescreening donors for anti-SARS-CoV-2 antibody strength prior to donation, and prescreening donors for anti-HLA antibodies. Furthermore, efforts to continue collections despite even mild symptoms of a vasovagal reaction were not implemented and might be used to increase unit yield.

Finally, a major area of potential quality improvement remains phlebotomy skills training in order to decrease the number of needle site reactions and infiltrations.

Factors critical to the success of this program were prompt availability of collection instruments, including delivery and on-site and remote training provided by the supplier during this pandemic with its strict regulations, making customer interactions very challenging. In addition, there were no shortages of the collection kits, although supply chain was a major concern and should be considered in any future pandemic situations. Rapidly changing demand and limited freezer storage space were challenges that would likely recur in any future situation as well.

Authors' Note

The Alyx apheresis collection device is sold by Fresenius Kabi.

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Technical assistance in preparation of this manuscript was provided by staff of Fresenius Kabi.

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References

1. Marano G, Vaglio S, Pupella S, et al. Convalescent plasma: new evidence for an old therapeutic tool? *Blood Transf*. 2016;14: 152-157.
2. Centers for Disease Control (CDC). Recommendations for investigational COVID-19 convalescent plasma. Published 2020. Accessed September 4, 2020. Version updated September 2, 2020. https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma
3. Budhai A, Wu AA, Hall L, et al. How did we rapidly implement a convalescent plasma program? *Transfusion*. 2020;60:1348-1355. doi:10.1111/trf.15910
4. Zeger G, Selogie E, Shulman IA. Blood donation and collection. In: Hillyer CD, Silberstein LE, Ness PM, Anderson KC, Roback JD, eds. *Blood Banking and Transfusion Medicine*. 2nd ed. 2007:157-182.
5. Despotis GJ, Goodnough LT, Dynis M, Baorto D, Spitznagel E. Adverse events in platelet apheresis donors: a multivariate analysis in a hospital-based program. *Vox Sang*. 1999;77:24-32.
6. Kutner JM, Bonet-Bub C, Yokoyama APH, et al. Convalescent plasma for Covid19—how long should a donor be excluded from donation? *Transfus Apher Sci*. 2020;59:102873. doi:10.1016/j.transci.2020.102873
7. Brown JF, Rowe K, Zacharias P, et al. Apheresis for collection of Ebola convalescent plasma in Libera. *J Clin Apher*. 2017;32: 175-181.