Transplantation and Cellular Therapy 28 (2022) 365.e1–365.e7

Transplantation and Cellular Therapy

journal homepage: www.tctjournal.org

ASTCT American Society for Transplantation and Cellular Therapy

Full Length Article
Cellular Therapy

A Clinically Applicable Prediction Model to Improve T Cell Collection in Chimeric Antigen Receptor T Cell Therapy

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Article history:
Received 2 March 2022
Accepted 14 April 2022

Key Words:
CAR T cell therapy
Collection efficiency
Lymphapheresis

A B S T R A C T

As chimeric antigen receptor (CAR) T cell therapy targeting CD19 has shown favorable outcomes in patients with relapsed or refractory (r/r) mature B cell lymphomas and B cell acute lymphoblastic leukemia (B-ALL), an increasing number of patients are waiting to receive these treatments. Optimized protocols for T cell collection by lymphapheresis for chimeric antigen receptor (CAR) T cell therapy are urgently needed to provide CAR T cell therapy for patients with refractory and progressive disease and/or a low number of lymphocytes owing to prior chemotherapy. The predicted efficiency of $CD3^+$ cell collection in apheresis can guide protocols for apheresis, but a clinically applicable model to produce reliable estimates has not yet been established. In this study, we prospectively analyzed 108 lymphapheresis procedures for tisagenlecleucel therapy at 2 centers. The apheresis procedures included 20 procedures in patients with B cell acute lymphoblastic leukemia and 88 procedures in patients with diffuse large B cell lymphoma, with a median age at apheresis of 58 years (range, 1 to 71 years). After lymphapheresis with a median processing blood volume of 10 L (range, 3 to 16 L), a median of 3.2×10^9 $CD3^+$ cells (range, .1 to 15.0×10^9 cells) were harvested. Collection efficiency 2 (CE2) for $CD3^+$ cells was highly variable (median, 59.3%; range, 11.0% to 199.8%). Multivariate analyses revealed that lower hemoglobin levels, higher circulating $CD3^+$ cell counts, and higher platelet counts before apheresis significantly decreased apheresis CE2. Based on multivariate analyses, we developed a novel formula that estimates CE2 from precollection parameters with high accuracy ($r = .56$; $P < .01$), which also suggests the necessary processing blood volume. Our strategy for lymphapheresis should help reduce collection failure, as well as achieve efficient utilization of medical resources in clinical practice, thereby allowing delivery of CAR T cell therapy to more patients in a timely manner.

INTRODUCTION

Chimeric antigen receptor (CAR) T cell therapy targeting CD19 has shown favorable outcomes in patients with relapsed or refractory (r/r) mature B cell lymphomas and B cell acute lymphoblastic leukemia (B-ALL) [1,2]. As several CD19-directed CAR T cell therapeutic formulations, including tisagenlecleucel, axicabtagene ciloleucel, and lisocabtagene maraleucel, have entered clinical practice, an increasing number of patients are waiting to receive these treatments.

Successful CAR T cell therapy requires harvesting of T cells, the source of CAR T cells, from patients via lymphapheresis in a timely manner [3,4]. However, because candidates for CAR T cell therapy often have T cell depletion resulting from

Financial disclosure: See Acknowledgments on page 365.e6.

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https://doi.org/10.1016/j.jtct.2022.04.013

protracted chemotherapy, collecting a sufficient quantity of T cells by lymphapheresis may be difficult [3,5,6]. Furthermore, because of the refractory and progressive nature of tumors and frequent complications, including infections, the appropriate window for successful lymphapheresis is highly limited in most CAR T cell therapy candidates. Although flexible scheduling of lymphapheresis is necessary, considering the state of tumor control and complications in each patient, apheresis centers are often unable to adjust schedules based on a patient's unstable condition due to overbooked appointments, which can deprive patients of opportunities to receive CAR T cell therapy. Therefore, an optimized protocol for collecting T cells is urgently needed, especially for patients with depleted circulating T cells. This situation can be improved by predicting the necessary processing blood volume and number of apheresis procedures for each patient, considering individual characteristics, as well as by improving lymphapheresis collection efficiency, to maximize the limited opportunities for patients as well as the efficient utilization of finite medical resources.

Although T cell collection efficiency via lymphapheresis for CAR T cell therapy reportedly differs widely among patients, the factors affecting this collection efficiency are largely unknown [7–10]. Furthermore, most previous studies of lymphapheresis for CAR T cell therapy have been conducted in patients whose condition was favorable for phase I-II clinical trials, and thus their findings cannot always be applied to real-world clinical practice.

In this study, using real-world data, we sought to (1) identify factors that determine collection efficiency in lymphapheresis performed for CAR T cell therapy, (2) develop a novel model to estimate collection efficiency with high reliability, and (3) establish a ready-to-use protocol for clinical practice to estimate the necessary processing blood volume. Our findings should help deliver CAR T cell therapy to a wider range of patients by improving lymphapheresis procedures and by realizing successful T cell collection in patients with depleted circulating T cells. Moreover, these findings should expand the capacity of apheresis centers to perform lymphapheresis with smart scheduling, eventually contributing to improved prognosis for patients with r/r B cell malignancies.

METHODS

Patients

This prospective study was performed by analyzing all consecutive lymphocyte collections for CAR T cell therapy with commercialized tisagenlecleucel from patients with r/r diffuse large B cell lymphoma (DLBCL), or B cell acute lymphoblastic leukemia (B-ALL) at Hyogo College of Medicine Hospital and Kyoto University Hospital between October 2019 and May 2021. Patients with low performance status (defined as an Eastern Cooperative Oncology Group performance status ≥2) and patients enrolled in clinical trials at the time of apheresis were excluded. This study was approved by the Ethics Committee of each hospital and was conducted according to the principles set out in the Declaration of Helsinki.

Lymphapheresis and CD3$^+$Cell Measurement

All lymphapheresis procedures were performed using the Spectra Optia apheresis system (Terumo BCT, Tokyo, Japan) with either the MNC or cMNC program, as determined by the institution, according to procedural guidelines provided by Novartis. Acid citrate dextrose solution A (ACD-A) was used for anticoagulation. The processing blood volume was set to twice the calculated amount to target the collection of 1×10^9 CD3$^+$ cells, assuming a 20% to 40% collection efficiency for CD3$^+$ cells, with a maximum processed blood volume of .3 L/kg of body weight.

CD3$^+$ cell counts in peripheral blood and the collection bag were measured by flow cytometry after staining with fluorochrome-conjugated anti-CD3 antibody (clone SK7; BD Biosciences, San Jose, CA) at each facility. Collection efficiency 2 (CE2) for CD3$^+$ cells in lymphapheresis was calculated using the following equation [5]:

$$CE2(\%) = ([\text{product}CD3^+\text{cellcount} \times \text{productvolume}]/[\text{processingbloodvolume} \times \text{precollectionperipheralblood}CD3^+\text{cellcount}]) \times 100.$$

Statistical Analyses

Predictive factors of CE2 for CD3$^+$ cells were analyzed using the Pearson correlation coefficient and univariate and multivariate regression models. In regression analyses, all continuous variables were log-transformed to normalize skewed distributions. $P < .05$ was considered statistically significant. Statistical analyses were performed using EZR (Jichi Medical University, Saitama, Japan) [11] and Stata version 17 (StataCorp, College Station, TX).

RESULTS

Patient and Collection Characteristics

A total of 108 lymphapheresis procedures for tisagenlecleucel were performed in 98 patients. The median age at apheresis was 58 years (range, 1 to 71 years), including 13 apheresis procedures for children (<16 years) and 95 for adults (≥16 years) (Table 1, Supplementary Table S1). They included 56 procedures (51.9%) for male patients and 52 (48.1%) for female patients with a median body weight of 51.5 kg (range, 8.1 to 98.1 kg). The distribution of diseases was 18.5% B-ALL (n = 20) and 81.5% DLBCL (n = 88). The median precollection peripheral blood hemoglobin (Hgb) levels, circulating lymphocyte counts, CD3$^+$ cell counts, platelet counts, and lactate dehydrogenase (LDH) levels before lymphapheresis were 9.5 g/dL (range, 6.9 to 13.6 g/dL), 715/μL (range, 30 to 3702/μL), 593/μL (range, 23 to 3465/μL), 13.6 $\times$ 10^4/μL (range, 2.3 to 47.4 $\times$ 10^4/μL), and 229 IU/L (range, 138 to 6620 IU/L), respectively. Venous access for apheresis was via a central venous catheter (n = 92; 85.2%) or peripheral venous puncture (n = 16; 14.8%). Regarding

Table 1
Patient Characteristics (N = 108)

Characteristic	Value
Patient precollection parameters	
Age, yr, median (range)	58 (1-71)
Sex, n (%)	
Male	56 (51.9)
Female	52 (48.1)
Body weight, kg, median (range)	51.5 (8.1-98.1)
Disease, n (%)	
B-ALL	20 (18.5)
DLBCL	88 (81.5)
Time between diagnosis to lymphapheresis, mo, median (range)	17 (2-226)
Hgb, g/dL, median (range)	9.5 (6.9-13.6)
Lymphocytes, /μL, median (range)	715 (30-3702)
CD3$^+$ cells, /μL, median (range)	593 (23-3465)
Platelets, $\times$ 10^4/μL, median (range)	13.6 (2.3-47.4)
LDH, IU/L, median (range)	229 (138-6620)
Apheresis parameters	
Venous access, n (%)	
Central venous catheter	92 (85.2)
Peripheral vein puncture	16 (14.8)
Collection mode, n (%)	
MNC	47 (43.5)
cMNC	61 (56.5)
Run time, min, median (range)	204 (69-330)
Total blood volume processed, L, median (range)	10 (3-16)

collection programs, an MNC collection program was selected in 47 procedures (43.5%) and a cMNC collection program was used in 61 procedures (56.5%) (Table 1).

Apheresis Results and Collection Efficiency for CD3⁺Cells

The median apheresis run time was 204 minutes (range, 69 to 330 minutes), and a median blood volume of 10 L (range, 3 to 16 L) was processed (Table 1). With respect to harvest yields, the median total cell, lymphocyte, and $CD3^+$ cell counts were 7.6×10^9 (range, 1.0 to 43.7×10^9), 4.2×10^9 (range, .2 to 15.9×10^9) and 3.2×10^9 (range, .1 to 15.0×10^9), respectively. The CE2 for $CD3^+$ cells exhibited a broad distribution, with a median of 59.3% (range, 11.0% to 199.8%) (Table 2). Only 1 patient had an insufficient $CD3^+$ cell harvest, even with 2 lymphapheresis procedures, owing to an extremely low $CD3^+$ cell count in peripheral blood ($23/\mu L$).

Identification of Predictive Factors for CD3⁺Cell Collection Efficiency

We next analyzed the correlation between CE2 for $CD3^+$ cells and patient precollection parameters to identify factors affecting CE2 for $CD3^+$ cells. Univariate analyses revealed that CE2 for $CD3^+$ cells was negatively correlated with precollection $CD3^+$ cell counts and platelet counts in peripheral blood, whereas CE2 for $CD3^+$ cells did not appear to be significantly associated with patient age, body weight, disease, Hgb level, or LDH level at apheresis (Figure 1, Supplementary Figure S1, Table 3). Multiple regression analysis revealed that lower Hgb level, higher circulating $CD3^+$ cell count, and higher platelet count were associated with significantly reduced CE2 for $CD3^+$ cells (Table 3). The relationship between CE2 and these 3 factors was similar when assessed by underlying disease, suggesting that these factors are predictive for CE2 irrespective of disease (Supplementary Tables S2 and S3).

Development of a Predictive Model for Collection Efficiency with Precollection Parameters

On the basis of the multiple regression model, the predicted CE2 for $CD3^+$ cells was calculated using the following formula (see also Supplementary Figure S2):

Predicted CE2 for $CD3^+$ cells (%) = $40.022 \times (\text{Age [years]})^{-.097} \times (\text{Body weight [kg]})^{.326} \times (\text{Hgb level [g/dL]})^{.923} \times (CD3^+ \text{ cell count } [/\mu L])^{-.238} \times (\text{platelet count } [10^4/\mu L])^{-.255} \times (\text{LDH [IU/L]})^{-.081}$ ($\times$ .989, if female) ($\times$ .885, if B-ALL).

Using this formula, predicted CE2 value for $CD3^+$ cells showed a significant correlation with the actual CE2 values ($r = .56$; $P < .01$) (Figure 2). The estimation formula predicted CE2 within a 20% error in 77 apheresis procedures (71.3%), and among the remaining 31 procedures, the estimated CE2 was lower than the actual CE2, with an error of $\geq$20% (overestimation) in only 13 procedures (12.0%), suggesting that our estimation equation is suitable for CE2 prediction (Supplementary Table S4). When thresholds of CE2 were set at 40%, 50%, or 60%, poor CE2 (defined as under each threshold value) was plausibly predicted with accuracies of 87.5%, 72.4%, and 64.4%, respectively, whereas the positive predictive values of rich CE2 (ie, exceeding each threshold value) were 88.0%, 83.5%, and 65.3%, respectively (Table 4, Supplementary Table S5).

Table 2
Apheresis Yields

Variable	Value, median (range)
Total cell count, $\times 10^9$	7.6 (1.0-43.7)
Lymphocytes, %total cell counts	61.1 (2.8-92.5)
Counts, $\times 10^9$	4.2 (.2-15.9)
CE2 for lymphocytes, %	59.8 (7.3-195.3)
$CD3^+$ cells, %total cell counts	47.1 (2.0-87.0)
Counts, $\times 10^9$	3.2 (.1-15.0)
CE2 for $CD3^+$ cells, %	59.3 (11.0-199.8)

Application of the Estimation Model to Clinical Practice

To implement this CE2 estimation formula in clinical practice, we created a CE2 calculation nomogram based on the estimation formula (Figure 3). For example, for a 60-year-old male patient weighting 60 kg with r/r DLBCL and precollection Hgb level, $CD3^+$ cell count, platelet count, and LDH level of 10 g/dL, $600/\mu L$, $10 \times 10^4/\mu L$, and 300 IU/L, respectively, scores corresponding to the respective factors—3 points for age, 1 point for sex, 10 points for disease, 52.5 points for body weight, 28 points for Hgb level, 38 points for $CD3^+$ cell count, 32.5 points for platelet count, and 21 points for LDH level—were obtained using the nomogram. Then an estimated CE2 of 65%, corresponding to a total score of 186 points, was obtained quickly and easily.

In addition, based on the estimation formula, reference diagrams were developed to quickly determine the processing blood volume needed to harvest 1×10^9 $CD3^+$ cells, based on precollection Hgb level and $CD3^+$ cell count, according to clinical setting (Figure 4A,B, Supplementary Figure S3A,B). The processing blood volume necessary to obtain 1×10^9 $CD3^+$ cells corresponding to a precollection $CD3^+$ cell count according to Hgb level in the case of a 60-year-old male patient weighing 60 kg with r/r DLBCL is described in Figure 4A. For instance, when the precollection $CD3^+$ cell count is as low as $100/\mu L$, the diagram shows that the required processing blood volume differs widely depending on Hgb level, with a necessary processing volume of 12.4 L for an Hgb level of 8 g/dL, 10.1 L for 10 g/dL, and 8.4 L for 12 g/dL. Although age has little effect on the necessary processing volume in patients with adult DLBCL, younger age was associated with increased processing volume in patients with B-ALL, with adjustment for the average body weight at each age (Supplementary Figure S3C, D).

These nomograms and diagrams enable rapid prediction of the blood volume to be processed for apheresis without complicated calculations, which not only facilitates scheduling of lymphapheresis, but also makes it possible to take timely preemptive measures, such as erythrocyte transfusion, to reduce the processed blood volume and minimize the possibility of collection failure by enhancing CE2 in apheresis.

DISCUSSION

In this prospective study, we evaluated 108 lymphocyte collections by lymphapheresis for CAR T cell therapy in patients with r/r DLBCL and B-ALL and found that precollection lower Hgb level, higher peripheral blood $CD3^+$ cell count, and higher platelet count before apheresis were associated with significantly reduced CE2 for $CD3^+$ cells. We have developed a novel model to estimate CE2 for $CD3^+$ cells based on patient characteristics and laboratory data before apheresis. The necessary blood volume for acquisition of the required number of $CD3^+$ cells can be determined using nomograms and diagrams based on this model, suggesting that the model can be implemented in clinical practice without complicated calculations.

We initially analyzed precollection factors affecting CE2 for $CD3^+$ cells and found that precollection lower Hgb level, higher circulating $CD3^+$ cell count, and higher platelet count were

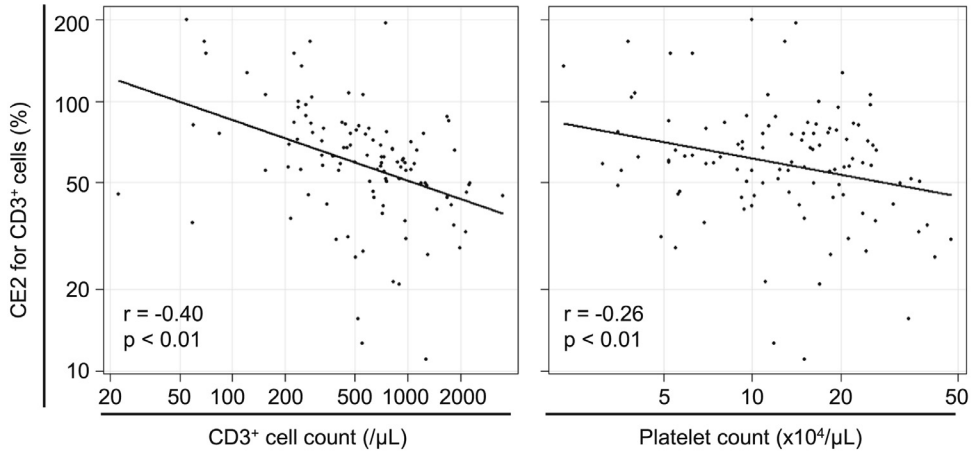

Figure 1. Correlation between CE2 of $CD3^+$ cells and parameters. Axes are logarithmic.

associated with significantly reduced CE2 for $CD3^+$ cells in lymphapheresis for CAR T cell therapy. In the univariate analysis, the correlation between Hgb level and CE2 was nonsignificant. Hgb level was correlated with other parameters; for instance, there was a trend toward higher Hgb levels in patients with higher circulating $CD3^+$ cell counts and higher platelet counts (Supplementary Figure S4). Therefore, we evaluated the effects of these parameters in the multivariate analysis, adjusting for potential confounding. According to a previous report indicated that older age was associated with lower CE2 [9], we included age in the multivariate analysis and found a trend toward lower CE2 in older patients, consistent with that previous report. In cases of B-ALL (mostly pediatric cases), older age was not associated with lower CE2 (Supplementary Figure S3D); the relationship between age and CE2 merits further study, especially in pediatric cases.

Our finding that anemia is associated with lower CE2 in lymphapheresis for CAR T cell therapy is consistent with previous studies of peripheral blood stem cell (PBSC) collection with apheresis in which low hematocrit levels resulted in poor separation of the mononuclear cell layer during blood centrifugation [12,13].

Given previous studies of PBSC collection suggesting that higher $CD34^+$ cell counts in peripheral blood can decrease CE2 due to the thicker layer of $CD34^+$ cells during centrifugation, resulting in insufficient recovery of targeted cells from the collection port of the machine with the standard collection flow rate [13], it can be speculated that a similar mechanism may underlie the reduced CE2 in lymphapheresis for CAR T cell therapy. Consequently, optimization of collection flow rate in lymphapheresis for CAR T cell therapy warrants further study.

There are 2 possible mechanisms for the decreased CE2 in patients with high precollection platelet counts as suggested by PBSC collection. First, because the high-G-force centrifuge of the Spectra Optia positions platelets in the buffy coat, higher platelet counts can interfere with the separation of mononuclear cells in patients with high platelet counts [14]. Second, because the Spectra Optia has an intermediate collection chamber for separating platelets from mononuclear cells in the MNC program, high platelet counts can fill the intermediate collection chamber with platelets, leaving less space for mononuclear cells and thereby reducing CE2 in the MNC program [13]. Indeed, in this study, a more prominent negative correlation between platelet count and CE2 was observed in the MNC program compared with the cMNC program (Supplementary Figure S5), whereas a different collection program (cMNC versus MNC) itself was not associated with CE2 (data not shown). The negative correlation between platelet count and CE2 observed in the present study is congruent with a previous report [9].

Next, based on multivariate regression analyses, we developed a quantitative predictive formula for CE2 in lymphapheresis for $CD3^+$ cells using 8 parameters, including precollection Hgb level, $CD3^+$ cell count, and platelet count, suggesting that CE2 for $CD3^+$ cells is estimated according to precollection parameters (Figure 2). Although the estimated value calculated

Table 3
Univariate and Multivariate Analyses of CE2 for $CD3^+$ Cells

Variable	Univariate			Multivariate		
	Coefficient	95% CI	*P* Value	Coefficient	95% CI	*P* Value
Age	.034	−.081 to .148	.56	−.097	−.346 to .153	.44
Sex (female vs male)*	.889	.732 to 1.079	.23	.989	.815 to 1.199	.91
Body weight	.159	−.076 to .394	.18	.326	−.061 to .713	.10
Disease (B-ALL vs DLBCL)*	1.006	.783 to 1.294	.96	.885	.584 to 1.340	.56
Hgb level	.272	−.408 to .952	.43	.923	.249 to 1.597	<.01†
$CD3^+$ cell count	−.225	−.324 to −.126	<.01†	−.238	−.333 to −.143	<.01†
Platelet count	−.203	−.346 to −.060	<.01†	−.255	−.396 to −.114	<.01†
LDH level	−.111	−.267 to .045	.16	−.081	−.222 to .059	.25

* Binary variable.
† Significant *P* value (<.05).

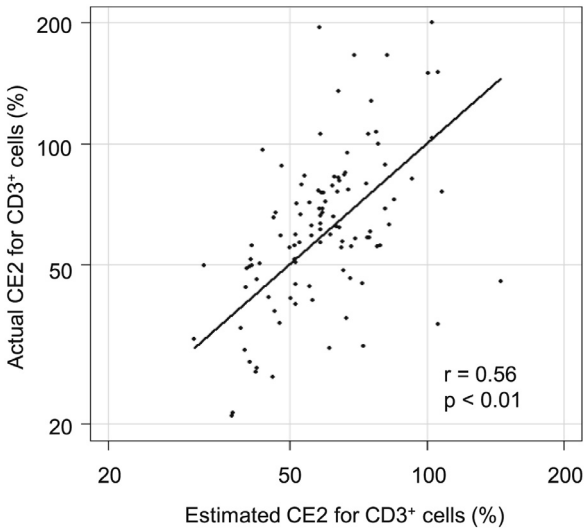

Figure 2. Correlation between actual CE2 and estimated CE2 of $CD3^+$ cells. Axes are logarithmic.

Table 4
Predictive Value of Estimation of CE2 for $CD3^+$ Cells

Actual CE2	Estimated CE2		Total
	<50%	≥50%	
<50%	21 (72.4)	13 (16.5)	34 (31.5)
≥50%	8 (27.6)	66 (83.5)	74 (68.5)
Total	29 (100.0)	79 (100.0)	108 (100.0)

by the formula showed accurate prediction for CE2, a novel strategy that simplifies the calculation process is needed to use the formula in clinical practice. Accordingly, we developed a nomogram and a diagram to estimate the necessary blood volume at the bedside, depending on patient characteristics (Figures 3 and 4, Supplementary Figures S2 and S3A-D). Notably, this nomogram and diagram underscore the importance of precollection Hgb level; for instance, assuming that the required processing blood volume for a Hgb level of 8 g/dL is 100%, the required processing blood volume for Hgb levels of 10 g/dL and 12 g/dL are 81.4% and 68.8%, respectively (Figure 4, Supplementary Figure S3A,B), suggesting that the necessary processing volume can be reduced by increasing the Hgb level. Therefore, erythrocyte transfusion before apheresis not only reduces the processing blood volume and run time required to obtain sufficient T cells, but also may allow for CAR T cell therapy in patients with a low lymphocyte count who previously were considered ineligible for this therapy owing to the high risk of collection failure. Indeed, we found that a sufficient $CD3^+$ cell count of 1×10^9 can be harvested even in patients with a $CD3^+$ cell count as low as $100/\mu L$ in a single lymphapheresis procedure and in patients with a $CD3^+$ cell count as low as $50/\mu L$ in 2 lymphapheresis procedures, if the Hgb level is maintained above 10 g/dL. These findings suggest that it is worth performing lymphapheresis after appropriate preparation even if circulating $CD3^+$ cell counts are very low.

As for the negative correlation between precollection $CD3^+$ cell count and CE2 observed in this study, although the blood volume required to collect the necessary $CD3^+$ cells in patients with higher circulating $CD3^+$ cell counts is smaller than that required in those with lower $CD3^+$ cell counts, we suggest that the processing blood volume should be planned based on proper estimation even with abundant $CD3^+$ cells in peripheral blood. To avoid a negative effect of precollection platelet count on CE2, sufficient blood volume should be processed in patients with high platelet counts, especially when the MNC program is selected.

Although strengths of this study include our detailed analyses using real-world data and including patients with various baseline characteristics, some limitations of the study also must be acknowledged. First, because the study includes real-world data from 2 facilities, differences in patient characteristics and collection procedures at the 2 facilities could potentially affect the CE2 for $CD3^+$ cells. However, the differences

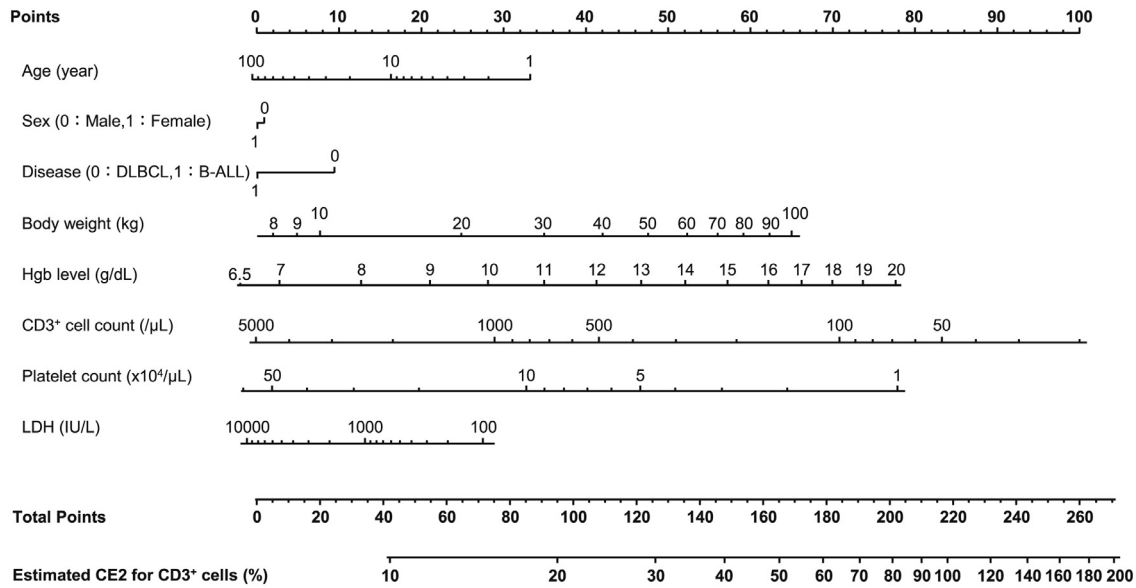

Figure 3. Nomogram for predicting CE2 of $CD3^+$ cells. Instructions: Locate the patient's age on the age axis. Draw a line straight upward to the points axis to determine the number of points toward the CE2 for age. Repeat the process for all predictive factors. Sum the points achieved for all predictive factors. Locate the final sum for age, sex, disease, body weight, Hgb level, $CD3^+$ cell count, platelet count, and LDH level on the total point axis. Draw a line straight down to find the estimated CE2 for $CD3^+$ cells.

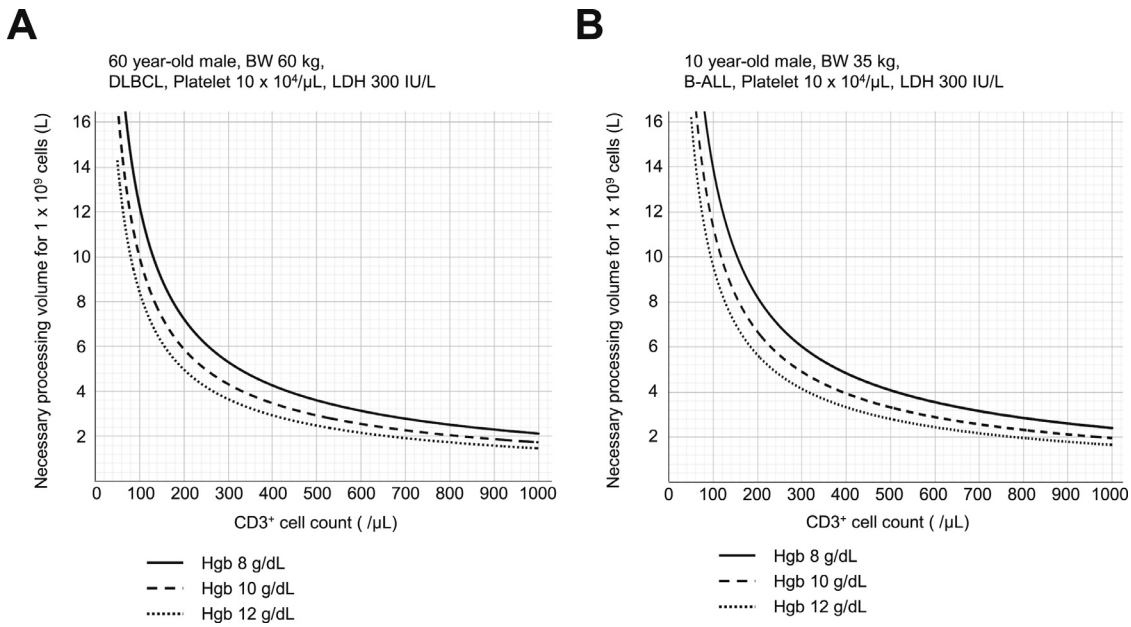

Figure 4. Quick reference diagrams predicting the required processing blood volume. Precollection $CD3^+$ cell counts and the estimated processing blood volumes necessary to obtain 1×10^9 cells per Hgb level are described in the text. Solid, dashed, and dotted lines indicate 8, 10, and 12 g/dL of Hgb, respectively, in the case of a 60-year-old male weighing 60 kg with DLBCL and an LDH level of 300 IU/L (A), and a case of a 10-year-old male weighing 35 kg with B-ALL and an LDH level of 300 IU/L (B).

between the facilities were not significantly associated with CE2. Second, in this study, disease (B-ALL versus DLBCL) had no significant effect on CE2, but patients with DLBCL and B-ALL had significantly different parameter distributions, including age and body weight. Given the small number of patients with B-ALL in this study, the effects of underlying disease should be interpreted with caution. Third, because apheresis parameters were considered intermediate variables between precollection parameters and collection yields, effects of apheresis parameters on CE2 were not evaluated in this study. Fourth, because both the development and validation of the model were performed using the same cohort, the potential for overfitting cannot be excluded. Therefore, despite suitable prediction accuracy, our model requires external validation to ensure generalizability.

In conclusion, the present study provides information on lymphapheresis for CAR T cell therapy in a clinical setting, and a ready-to-use collection protocol applicable to clinical practice. Optimization of lymphapheresis through reliable estimation of CE2 and appropriate preemptive measures, such as erythrocyte transfusion, are beneficial for maximizing the probability of collecting enough T cells, especially in patients with depleted T cells. We believe that our study results and discussion not only can help reduce the risk of collection failure, which deprives patients of the chance to receive CAR T cell therapy, but also can promote more efficient use of medical resources, both of which will allow CAR T cell therapy to be offered in timely fashion to a wider range of patients, ultimately contributing to improvement of unfavorable prognoses of patients with r/r malignancies.

ACKNOWLEDGMENTS

The authors thank the clinical engineers and nurses at the apheresis sites, the transplantation coordinators, and all clinicians at the Hyogo College of Medicine Hospital and Kyoto University Hospital, as well as the patients who contributed to this research.

Financial disclosure: This work was supported in part by the MSD Life Science Foundation, the Lotte Foundation, and the Program for the Development of Next-Generation Leading Scientists with Global Insight (L-INSIGHT), sponsored by the Japanese Ministry of Education, Culture, Sports, Science and Technology (to Y.A.).

*Conflict of interest statement: The*re are no conflicts of *interest* to report.

Authorship statement: T.J., S.Y., A.H., and Y.A. designed the study and reviewed and analyzed data; T.J., A.H., S.Y., and Y.A. wrote the manuscript; T. Kitawaki, J.I., H.O., H.S., K.Y., J.K., T. Kondo, S.S., I.K., H.H., S.A., J.T., A.T.K., and M.N. interpreted data and revised the manuscript; and N.O., K.M., N.N., and Y.N. contributed to data collection and reviewed the manuscript. T.J. and S.Y. contributed equally to this work and should be considered co-first authors.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jtct.2022.04.013.

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