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—【Original】——原　著—

Utility of Non-invasive Monitering for Predicting Late-onset Adverse Reaction

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Late-onset adverse body reactions after blood donation are a serious problem when considering the safety of donors. However, predicting these reactions at the donation office can be difficult because their pathophysiology is poorly understood. We non-invasively monitored the cardiac output (CO) and stroke volume (SV) of 72 donors during autologous blood donation using an AESCULON mini device. The original preoperative autologous blood donation adverse reaction scale (PADARS) was used to estimate the severity of post-donation body reactions. The relationship between the total PADARS score and AESCULON mini measurements and other backgrounds was evaluated using a multivariate linear regression model. During the donation, the average decrease in CO and SV was 0.79±0.43*l*/min and 9.4±6.7m*l*, respectively. Among 30 donors who answered the questionnaire, 14 (47%) and 2 (7%) were aware of some subjective symptoms and suffered from relatively severe body reactions (score ≥ 5), respectively. A multivariate linear regression analysis revealed that age and SV value at the end of donation were inversely correlated with the total PADARS score ($p < 0.05$). In addition to younger age, a low post-donation SV value measured by AESCULON mini can be a risk factor for late-onset adverse body reactions.

Keywords: blood donation, electrical velocimetry, late-onset adverse body reaction

Introduction

Protecting blood donors from adverse body reactions during or after the donation is one of the most important subjects to ensure safe and effective blood transfusion therapy. A blood donation of 400-450m*l* is equivalent to acute blood loss of approximate 10% of the total blood volume and may cause various acute and late-onset adverse body reactions. Vasovagal reflex (VVR) is one of the commonest acute body reactions during donation. It is caused by physical or psychological stress inducing overstimulation of the brainstem vasomotor center and evokes typical symptoms (e.g., decreased blood pressure, bradycardia, and occasional syncope). Its pathophysiology is relatively clear and controllable to some extent by pre-donation water intake or leg exercises, although the prevalence of VVRs during blood donation is as high as approximately 1% of donors[1)2)]. VVRs can be a relatively manageable problem during bed rest and careful observation by the donation room staff can prevent donors from critical accidents, including falls. In contrast, late-onset adverse body reactions after blood donation are highly problematic. Reactions can show a wide variety of symptoms, including headache, dizziness, nausea, shortness of breath, fatigue, drowsiness, and presyncope/syncope. Although the symptoms are minor in most cases, serious head injuries due to falls have been reported[3)]. It is difficult for medical staff to deal with late-onset adverse body reactions, mainly because these reactions usually occur long after the donor departs from the donation room, which leads to uncertainty of the pathophysiology and lack of practical mitigation and prevention measures. Presently, informing donors of the possible delayed symptoms is the only available strategy to prevent serious accidents.

A haemodynamic change during blood donation is

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Table 1 Preoperative Autologous blood Donation Adverse Reaction Scale (PADARS)

Physical symptoms	Scale (point) [a]
Headache	0–3
Dizziness	0–3
Tinnitus	0–3
Nausea or vomiting	0–3 (vomiting, 3 points)
Loss of appetite	0–3
Shortness of breath	0–3
Fatigue	0–3
Drowsiness	0–3
Presyncope/syncope	0 or 3
Other symptoms	1 each symptom

[a]Four-point scale: 0, none; 1, mild; 2, moderate; and 3, severe

one of the probable causes of adverse body reactions. To support this hypothesis, the lower blood volume of young donors is associated with the risk of acute VVRs, syncopal reactions, and syncope-related complications[4)~7)]. The specific haemodynamic change related to the adverse reactions remains unclear. Although vital signs, such as blood pressure and heart rate, are conventionally used to estimate haemodynamic changes during blood donation, our previous studies have shown no association of these vital signs with any late-onset adverse body reactions[8)9)]. Continuous monitoring of either arterial or central venous pressure is undoubtedly useful in tracking haemodynamic changes in critically ill patients[10)], but is impractical to use in ambulatory blood donors because of their invasiveness. Non-invasive cardiac output (CO) monitoring using thoracic electrical bioimpedance (TEB), such as AESCULON mini (Osypka Medical, Berlin, Germany), has recently been introduced. AESCULON mini continuously measures thoracic electrical bioimpedance (TEB), an indicator of electrical conductivity changes induced by blood flow in the aortic arch, and non-invasively calculates stroke volume (SV) and CO from the TEB change. Although this technology has been applied to several clinical situations wherein patients suffered massive bleeding or severe heart failure[11)~14)], its utility in moderate amounts of bleeding, including blood donation, has never been examined.

In this study, we first attempted to capture the hemodynamic changes during and after autologous blood donation using a noninvasive CO monitor, AESCULON mini. Next, the severity of late-onset adverse body reactions was evaluated by our original scoring scale specifically adjusted for delayed reactions (Table 1, Fig. 1). Finally, we evaluated the association between late-onset adverse body reactions and AESCULON mini measurements as well as other physical and clinical features of autologous blood donors.

Materials and Methods

Study Design and Ethical Considerations

This prospective observational study was performed as part of a study on risk factors of adverse body reactions related to autologous blood donation. Ethical approval of the study was obtained from the institutional ethics committee of the Graduate School of Medicine, The University of Tokyo (10543).

Participants

Participants were selected from patients undergoing autologous blood donations at the University of Tokyo Hospital from June to October 2016. Pregnant women were excluded. Written informed consent was obtained from every participant or his/her representative.

Autologous Blood Donation

Autologous blood donations from patients with scheduled elective surgeries were carried out in the autologous blood donation room at the transfusion service of the University of Tokyo Hospital. Prior to autologous donation, each patient was given written and oral information on preoperative donation and its perioperative use, after which written informed consent was obtained. Autologous blood donation was contraindicated in patients with active infection, active or uncontrollable bleeding (e.g., heavy genital bleeding), severe heart disease, pre-donation dental treatment with continuous bleeding on the donation day, and pre-donation haemoglobin (Hb) levels of $<10\,g/dl$. There was no age restriction for autologous blood donation.

A maximum single donation volume was set at 400 m*l*, following the national criteria of allogeneic blood donation and the guidelines of the Japanese Society of Autologous Transfusion (JSAT). This volume was adjusted in 50-m*l* decrements considering the donor's estimated blood volume (EBV) and Hb value. In principle, single donation volume was restricted to <12% of EBV, and the maximum limit was set at 13%. If the Hb level of the donor was $<11\,g/dl$, the collection volume was adjusted by deducting the theoretical blood loss volume, which was presumed when the donor's Hb level decreased from $11\,g/dl$ to the actual measurement value by blood collection. The EBV of the donor was

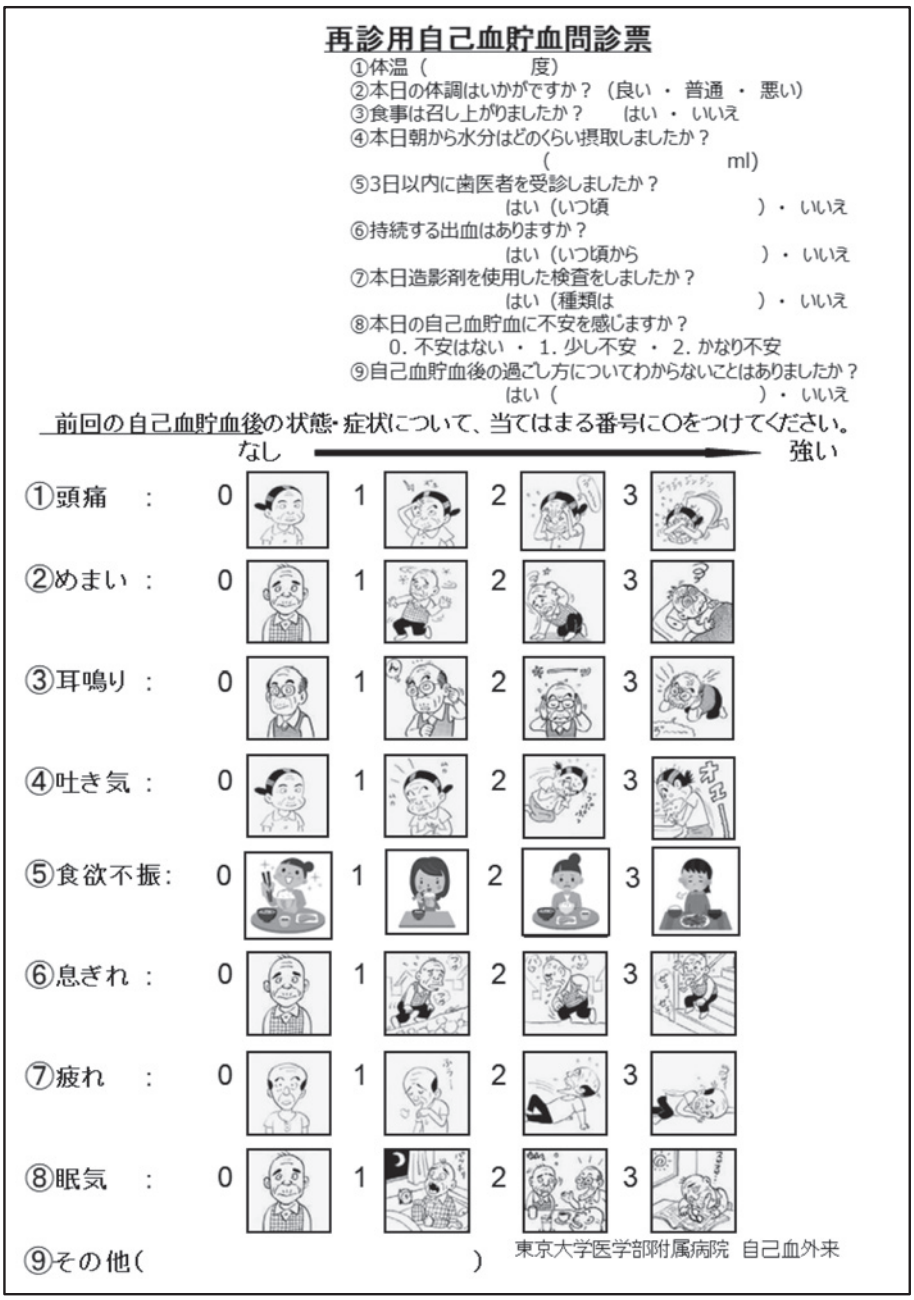

Fig. 1
Interview sheet to evaluate PADARS score. Late-onset adverse body reactions other than presyncope are routinely self-checked by donors on subsequent visits to the outpatient donation office. Since presyncope is a rare and critical event, the donation room doctor directly interviews the donor in detail and estimates it.

calculated using Ogawa-Fujita's formula[3)15)]:

(*male*) 0.168 $H3 + 0.050\ W + 0.444$, (*female*) 0.250 $H3 + 0.0625\ W - 0.662$

*H, height (m); W, weight (kg).

Autologous blood was collected from the donor in the supine position on the blood collection chair or on a standard hospital bed. Throughout the donation, trained nurses, including those with JSAT accreditation, carefully observed the donors, and any adverse reactions were adequately treated and recorded. All patients were administered 500m*l* of crystalloid solution after donation through the same blood access of the blood collection to complement the loss of extracellular fluid. Hemostasis and the donor's physical condition were checked by a nurse 10min after intravenous line removal, and the donor was permitted to leave the au-

tologous blood donation room. Blood pressure and heart rate were measured before and after blood collection and after intravenous line removal.

Evaluation of Late-Onset Adverse Body Reactions

For semi-quantitative and appropriate evaluation of late-onset adverse body reactions after blood donation, a preoperative autologous blood donation adverse reaction scale (PADARS) (Table 1 and Fig. 1) was generated by modifying the Blood Donation Reactions Inventory (BDRI)[16]. Donors were requested to indicate their perceived levels of late-onset symptoms on a four-point scale (0 (none) to 3 (severe) for each item). This PADARS was composed of nine items: headache, dizziness, tinnitus, nausea or vomiting, loss of appetite, shortness of breath, fatigue, drowsiness, presyncope, and other symptoms. Different from BDRI, subjective symptoms were mainly adjusted to actual late-onset symptoms that autologous blood donors frequently experienced at the second visit. For example, acute adverse body reactions, including weakness, facial flush, visual disturbance, lightheadedness, rapid or pounding heartbeat, and sweating, were eliminated from PADARS; instead, these symptoms were evaluated by nurses at the bedside in the donation room. Drowsiness and fatigue are the most common late-onset post-donation body reactions and will be useful as screening markers to estimate a donor's susceptibility to more severe adverse body reactions. Headache and loss of appetite are less frequent but constantly reported symptoms among autologous blood donors and sometimes cause donors to decline a second donation. These four symptoms were added to the PADARS. To rapidly estimate adverse body reactions in a busy clinical practice, the 6-point scale on the BDRI was simplified to a 4-point scale. The scale with the mini-illustrations that comprehensively explain each symptom (Fig. 1) has been routinely presented to second-time donors and is used to rapidly self-check the late-onset adverse body reactions after first-time donation[9]. All reactions that occurred after the donors left the donation room and were subjectively related to donations by the donors were evaluated and recorded as late-onset adverse body reactions. In this study, this scale was handed to the donors as a questionnaire and collected upon hospital admission. The total PADARS score was used as a parameter to represent the severity of late-onset adverse body reactions.

Haemodynamic Changes during Blood Donation

The AESCULON mini device was used to evaluate the donors' haemodynamic changes during blood donation (Fig. 2a). Four surface electrodes were attached to the donor, two on the left side of the upper and lower neck and two on the left lower thorax and abdomen (Fig. 2b). Pulse, SV, and CO were measured every minute until crystalloid administration was finished and venous access was removed entirely. The reliability of the data acquired from AESCULON mini was evaluated using a signal quality indicator (SQI), ranging from 0 to 100. SQI is the sum of several measured values (echocardiogram, ultrasonic bioimpedance, respiratory status, etc.) and indicates the reliability of the data. Data with an SQI value < 80 were excluded from the analyses. The SV and CO measurements at the start and end of the donation were used for the multivariate linear regression analysis described below. The maximum changes in SV, CO, and pulse (Δ SV, Δ CO, and Δ pulse) and changes in blood and pulse pressures were also measured and used for statistical analyses.

Clinical and Physical Features of Donors

Information on age, gender, body mass index (BMI), pre-donation Hb value, and history of allogeneic and autologous blood donation was recorded for each donor. The donation volume was corrected by the donor's EBV and shown as the relative blood donation volume (in percentage) to adjust for differences in physique among donors as:

$$\textit{Relative blood donation volume}\ (\%) = (\textit{Donation volume}\ [ml]/\textit{EBV}\ [l] \times 1{,}000) \times 100$$

Information on the total volume of pre-donation oral fluid on the donation day, on-site acute body reactions during and just after the donation, and total donation time was also recorded for each donor. All these data were used for the analysis as confounding factors that may affect late-onset adverse body reactions. Information on the clinical department performing the donor's elective surgery was also examined but not used for the analysis.

Statistical Analysis

All collected data were analyzed using SPSS statistics for Windows, version 19.0 (IBM, Armonk, NY, USA). A chi-square test was used to evaluate categorical variables, and a Mann-Whitney U-test was used to evaluate quantitative variables. A Spearman's rank correlation test was used to evaluate the correlations between the AESCULON mini measurements (Δ SV and Δ CO)

(a)　(b)

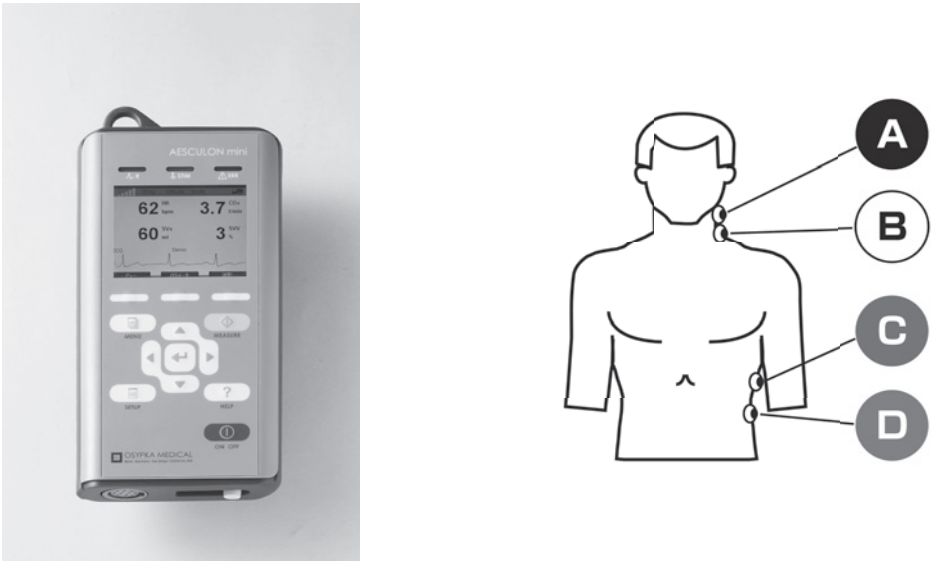

Fig. 2
a The AESCULON mini device used for thoracic electrical bioimpedance (TEB) measurement. b A schema of the electrodes' position for monitoring TEB by the device. Four surface electrodes were attached to the donor, two on the left side of the upper and lower neck (A, B) and two on the left lateral body trunk at the xiphisternum level (C) and 10~15cm below it (D) (Reprinted with permission from the manufacturer)

Table 2　Patient characteristics ($n=65$)

Variables	Median [min–max]
Age (years)	54 [11–78]
Female	38 (58%)
Height (cm)	160 [147–190]
Weight (kg)	57 [40–90]
BMI (kg/m/m)	22.1 [16.8–32.6]
Total blood volume (m*l*)	4,037 [2,719–6,235]
Blood donation volume (m*l*)	400 [200–400]
Relative amount of blood donation (%)	9.8 [5.7–12.6]
Pre-donation haemoglobin (g/d*l*)	13.2 [11.0–18.0]
History of autologous blood donation	7 (11%)
History of allogeneic blood donation	27 (42%)
Department, *n* (%)	
Gynaecology	23 (35%)
Orthopedics	23 (35%)
Neurosurgery	10 (15%)
Dental and oral surgery	5 (8%)
Cardiovascular surgery	2 (3%)
Urology	1 (2%)

Data were presented as median [minimum–maximum] or number (in percentage).

and the changes in systolic and diastolic blood pressures and pulse (Δ sBP, Δ dBP, and Δ pulse) before and after blood donation as well as the relative blood donation volume. Multivariate linear regression analysis was performed to estimate the association between the total PADARS score and the AESCULON mini measurements, as well as the donor's other clinical and physical features. A stepwise selection method was applied to determine useful explanatory variables. Model fit was evaluated using Hosmer-Lemeshow statistics. A two-sided p value <0.05 was considered statistically significant.

Results

A total of 72 donors consented to participate in the study. Seven patients were excluded because of trouble with blood collection or AESCULON mini measurements, such as disconnection of electrodes and a low SQI value. Consequently, 65 donors participated in the study. Table 2 shows the demographic data. The median age of the donors was 54 years old, and 58% (n = 38) were women. Most patients (n=56; 86%) donated 400m*l*, with a median relative blood donation volume of 9.8%. No patient developed acute VVR during donation.

Typical sequential changes in CO, SV, and pulse measured using the AESCULON mini are shown in Fig. 3. As the donation progressed, CO and SV showed downward trends, and the pulse showed an upward trend, reflecting the reduction of circulating blood volume of the donor. These values gradually returned to

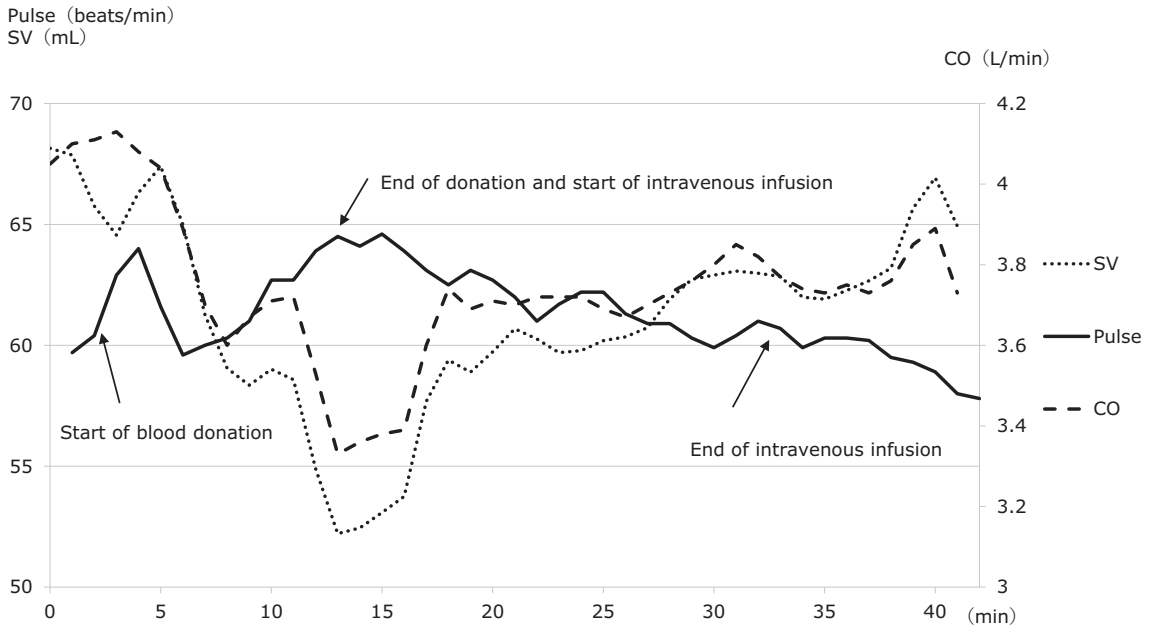

Fig. 3

Sequential changes in CO, SV, and pulse in one patient monitored with the TEB device. The continuous line indicates pulse, and the short and long broken lines indicate SV and CO, respectively. The patient was a 49-year-old woman who donated 400m*l* of autologous blood.

the pre-donation level after crystalloid infusion. However, in some cases, SV and CO exhibited no apparent change or even a slight increase. The mean (±SD) of the maximum decreases in CO and SV were 0.79±0.43 *l*/min and 9.5±6.7m*l*, respectively.

Next, the relationships between the AESCULON mini measurements and the value of conventional vital signs were evaluated. The correlations between these hemodynamic parameters and the relative blood donation volume were also evaluated. Although Δ CO and Δ SV had a strong correlation with each other ($r = 0.7$; data not shown), Δ CO and Δ SV during donation did not exhibit any significant correlation to Δ sBP, Δ dBP, or Δ pulse (Fig. 4a, b). They also showed no correlation with relative blood donation volume (Fig. 4c). Moreover, any rational linear regression models could not be generated to explain the relative blood donation volume using these conventional and TEB-based hemodynamic parameters as explanatory variables (data not shown).

Thirty of the 65 participating donors (46%) answered the questionnaire. The distribution of the responding donor's total modified PADARS score is shown in Fig. 5a. Approximately half of the donors (n=14; 47%) experienced some late-onset adverse body reactions, of whom 50% (n=7) were female. This ratio was comparable to that of all participants in this study (58%) and that of participants who responded to the questionnaire (63%). Although most of the donors perceived relatively mild reactions (scores 1-3), two donors (7%) experienced moderate to severe reactions (scores 5 and 9). Among various late-onset adverse body reactions reported by donors, fatigue and drowsiness were the most frequent reactions, followed by dizziness. No donors experienced presyncope (Fig. 5b).

Finally, the risk factors affecting the severity of the late-onset body adverse reactions after donation were evaluated. A multivariate linear regression model that explained the total PADARS score was generated using a stepwise selection method (Table 3). Three cases were eliminated from the analysis because of a lack of data on pre-donation oral fluid intake. Age and post-donation SV values were inversely and significantly associated with the total PADARS score ($p = 0.0010$ and 0.045, respectively). Although BMI and the relative blood donation volume also exhibited positive marginal associations ($p < 0.1$), they were not selected for the final model ($p = 0.08$ and 0.09, respectively). Donor gender, other hemodynamic parameters, and the experience of blood donation had no association with late-onset adverse body reactions.

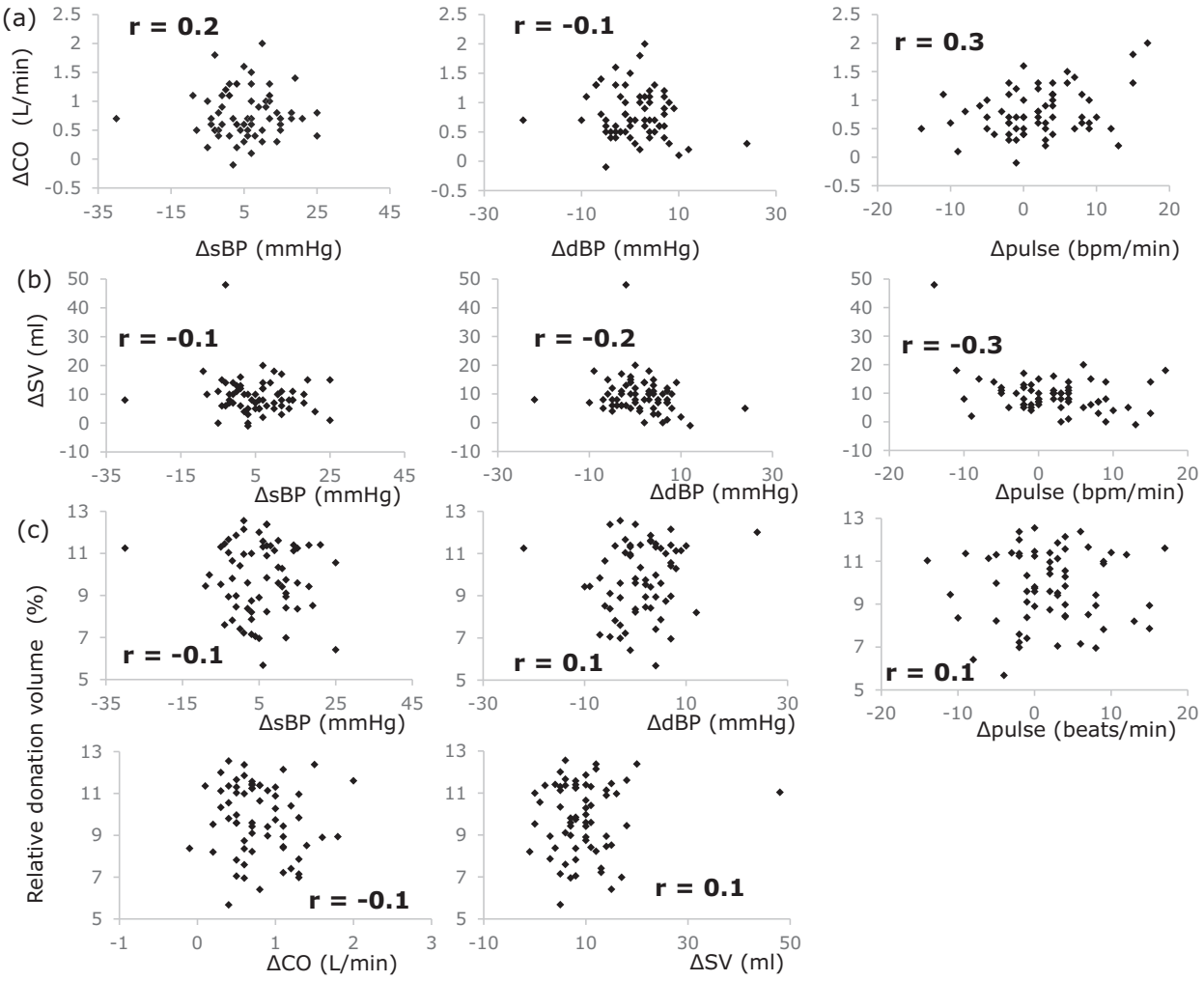

Fig. 4

Scatter diagrams to show the correlations among TEB measurements, vital signs, and relative donation volume. Correlation coefficient of each combination is shown on the graph. a Correlation between ΔCO and vital signs. b Correlation between ΔSV and vital signs. c Correlation between relative donation volume and vital signs (upper column) or monitor measurements (lower column). SV = stroke volume, sBP = systolic blood pressure, dBP = diastolic blood pressure, CO = cardiac output.

Discussion

This study monitored haemodynamic changes during blood donation using a non-invasive TEB device, AESCULON mini, and examined the relationship between the objective measurements by the device and the subjective scores of late-onset adverse body reactions after donation. First, the AESCULON mini measurement results were noted to reflect the decrease in the donor's circulatory volume independently from the conventional vital signs (e.g., blood pressure and pulse). Next, the low SV value at the end of the donation and younger age were found to be risk factors for late-onset adverse body reactions after donation.

The noninvasive TEB estimates CO and SV by TEB, which reflects changes in red blood cell orientation. TEB accuracy and validity have been examined by several previous studies that compared it with cardiac magnetic resonance imaging[17], subxiphoidal Doppler flow measurement[12], pulmonary arterial thermodilution[11], and transthoracic echocardiography (TTE)[13)18)19]. There are some disagreements about the degree of correlation with other evaluation methods, and, as a consequence, its accuracy and validity are still controversial[20]. Some trials reported that the measurements of TEB were comparable with those of TTE[13)18)19] and reliable in clinical applications[11)21]. TEB technology is expected to be less accurate than direct measurements such as pulmonary arterial thermodilution using a pulmonary artery catheter. On the other hand, it would be useful for prehension of sequential trends of each pa-

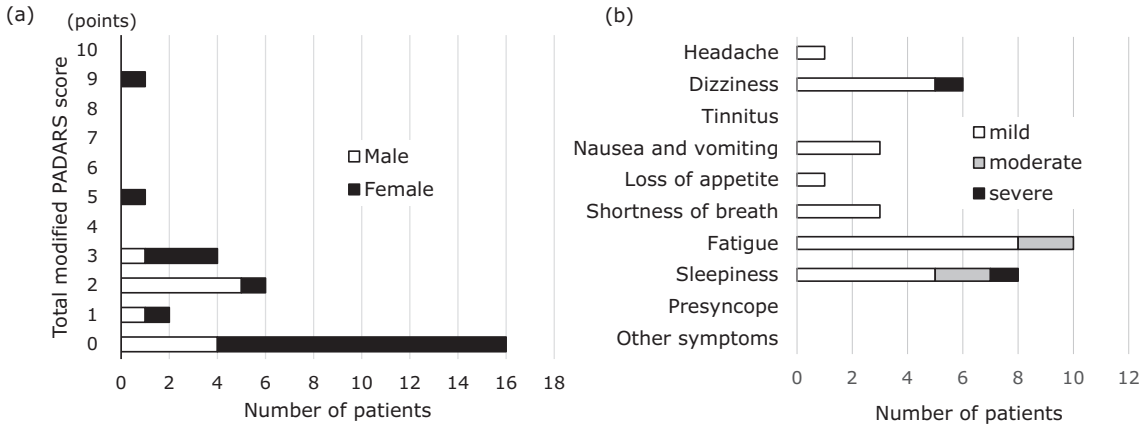

Fig. 5

Late-onset adverse body reactions of donors (n = 30). (a) Distribution of the total PADARS scores. The number of males and females are shown by black and white bars, respectively. (b) Number of observed symptoms and their severity. The numbers of mild, moderate, and severe symptoms are indicated by white, gray, and black bars, respectively.

Table 3 Multivariate linear regression analyses on the explanatory variables of the PADARS score ($n = 27$)

Variables	β (95% confidence interval)	Standardized β	p value
Age	− 0.097 (− 0.15 to − 0.045)	− 0.67	0.0010*
Post-donation SV	− 0.084 (− 0.17 to − 0.0010)	− 0.37	0.045*
Excluded variables			
Gender		0.18	0.31
BMI		0.29	0.08
Pre-donation Hb		0.18	0.30
History of autologous blood donation		− 0.17	0.33
History of allogeneic blood donation		− 0.22	0.19
Blood collection time		− 0.13	0.45
Relative donation volume		− 0.33	0.09
Pre-donation fluid intake		0.15	0.40
Body reactions during blood donation		− 0.05	0.79
Δ sBP		0.13	0.44
Δ dBP		− 0.17	0.32
Δ pulse		0.03	0.86
Pulse pressure change		0.19	0.26
Pre-donation CO		− 0.19	0.32
Pre-donation SV		0.26	0.66
Post-donation CO		0.38	0.17
Δ CO		− 0.08	0.92
Δ SV		− 0.02	0.62

Explanatory variables were selected by a stepwise method. The pre/postdonation AESCULON mini parameters were measured at the start and the end of donation, respectively. *SV* stroke volume, *Hb* haemoglobin, *sBP* systolic blood pressure, *dBP* diastolic blood pressure, *CO* cardiac output

*$p < 0.05$, statistically significant.

tient. TEB measurement is safer, easier to operate, less expensive to conduct, less invasive, and has fewer associated complications than other more invasive and complicated technologies, such as pulmonary artery thermodilution. Hence, TEB was applied to autologous blood donors who develop moderate bleeding. The expected change of CO and SV during donation was successfully observed, although autologous blood donors were expected to have a more stable haemodynamic status than previously reported cases, which included patients with severe heart failure and massive bleeding situations. As expected, the changes in conven-

tional vital signs during donation were small and did not correlate with ΔSV or ΔCO, implying that the vital signs would be insufficient for estimating haemodynamic change by blood donation.

On the contrary, we failed to prove that the relative blood donation volume correlated to Δ CO and Δ SV (Fig. 4c). The low variation in relative blood donation volume among donors because of the strict criteria for donation volume and elaborate adjustment of donation volume might have affected these results. Additionally, the high heterogeneity in physiological reactions among donors might have resulted in a nonlinear relationship between ΔSV/ΔCO and relative donation volume (Fig. 4a, b, Table 3).

Several risk factors for acute body reactions during and just after blood donation, including acute VVRs and pre-fainting/fainting reactions, have been identified by previous observational studies focused mainly on allogeneic blood donors[22)~24)]. Younger age, female gender, and first-time donation have been repeatedly reported as common risk factors. Low blood volume has also been reported to elevate the risk of acute body reactions, including VVR as an indicator of haemodynamic change. In contrast, the role of pre-donation vital signs as a predictor of acute body reactions is controversial. Ogata et al. reported that lower pre-donation dBP was associated with acute VVRs on in-hospital 200-m*l* allogeneic blood donation[25)]. Furthermore, Nishimori et al. examined autologous blood donors and found that lower pre-donation sBP and higher pulse, as well as a first-time donation, were associated with acute VVRs[24)]. On the other hand, Odajima et al. reported that higher pre-donation sBP was a risk factor for acute VVRs in 400-m*l* allogeneic blood donors[26)].

As described above, many studies of acute adverse body reactions related to blood donations have had conflicting results. The number of studies that examined late-onset adverse body reactions after blood donation is relatively small. Narbey et al. found that the female gender was associated with late-onset adverse body reactions in a study of allogeneic blood donors[22)]. However, information on late-onset adverse body reactions in that study was collected from the donors' self-reports, and cases were restricted to severe ones. Kamel et al. also reported that low blood volume and female gender were associated with delayed adverse reactions in a study on allogeneic blood donors of a similar design[5)]. Newman et al. conducted interviews with 1,000 donors three weeks after donation and found that female gender and first-time donation were associated with late-onset adverse body reactions[27)]. Inaba et al. performed a large-scale study on 98,389 allogeneic blood donors using questionnaires and concluded that lower body weight, younger age, history of presyncope, and pre-donation anxiety were risk factors of late-onset adverse body reactions[3)]. In a preliminary questionnaire survey of 72 autologous blood donors, younger age, lower pre-donation Hb, and lower relative donation volume were the risk factors of late-onset adverse body reactions[8)].

As none of these previous studies reported that vital signs during donation were associated with delayed adverse body reactions, we previously tried to evaluate haemodynamic changes during donation by echography of the right jugular vein. Although intravascular blood volume and CO could be estimated by measuring variation in the cross-sectional area of the vein, and the measured variation was significantly associated with late-onset adverse body reactions, measurements were not appropriately accomplished in approximately half of the cases due to technical problems. In this study, we used a TEB monitor and successfully found its usefulness as a potential predictor of late-onset adverse body reactions after blood donation. The obtained data suggest that a lower post-donation SV value may cause more severe delayed adverse reactions. This result seems rational if the hemodynamic status of donors is assumed to be one of the causes of delayed post-donation adverse reactions. In addition to this, TEB measurements were appropriately obtained in $>$ 90% of participants, and this rate will be expected to increase in clinical practice in proportion to the measurer's experience. Although monitoring TEB in all healthy volunteer blood donors is not realistic, it may be useful for high-risk donors (e.g., female, younger, smaller allogeneic blood donors, and autologous blood donors who suffered surgery-indicated diseases and potential comorbidities). We could not determine a specific threshold of post-donation SV value strongly related to late-onset post-donation adverse body reactions. Instead, the measured SV was $<$ 55m*l*, the mean of the donors who did not suffer any adverse body reactions; donors should be comprehensively educated on post-donation safety behaviors to prevent critical accidents, including falling. A decrease in second-time donation volume also may be considered.

BDRI has been reported and used to evaluate the severity of blood donation-related adverse body reactions and the risk of fainting and falling[16)28)29)]. The original BDRI is an 11-item five-point scale to estimate the donor's subjective symptoms. France et al. reported that four of 11 items, i.e., faintness, dizziness, weakness, and lightheadedness, were useful in assessing the donor's subjective perception of mild presyncopal symptoms. In contrast, typical late-onset post-donation adverse body reactions include other symptoms such as fatigue, sleepiness, and headache[3)9)27)]. Because these symptoms are not included in BDRI, we developed a different scoring scale, the modified PADARS, to specifically estimate late-onset adverse body reactions after autologous blood donation[30)]. In this study, we used the total modified PADARS score as a quantitative variable to estimate delayed post-donation adverse reactions and successfully established a linear regression model to show the association with SV and late-onset adverse body reactions. We believe that this scale may also be useful in evaluating the severity of relatively mild late-onset reactions after donation compared to estimation with BDRI.

There is still room for improvement in weighing each symptom in the modified PADARS. One strategy is to give higher points to clinically important symptoms such as headache, nausea, and dizziness, which often cause a donor to decline the second donation. However, to completely resolve this problem, we need to know what type of late-onset adverse body reactions specifically relate to low SV values and other risk factors. We hypothesize that psychological factors will cause adverse body reactions as well as physiological factors. Although we predicted that fatigue, sleepiness, and headache would be more dependent on physiological factors, no specific symptoms showed a significant association with peri-donation SV or CO values, probably because of sample size limitation. To resolve the relationship between specific late-onset adverse body reactions and various risk factors, including low post-donation SV value by further analyses, a more effective weighing of each symptom may be established.

This study has several limitations. First, the sample size was relatively small, and confounding factors, such as donors' clinical background and psychological status, were not considered in this study. Some significant risk factors may be overlooked or ignored by this limitation. Second, the modified PADARS score is a subjective questionnaire, and the completion rate of the questionnaire was about half, which may have introduced bias. Third, the TEB monitor measurements may be influenced by patient's hydration status and obesity, and we could not compare the results with other SV/CO measurement devices since invasive methods are not feasible for autologous blood donation. Although we evaluated BMI as a possible confounding factor and used SQI to prove the reliability of the measurements, it cannot be denied that this inaccuracy might have affected the results. Finally, the number of explanatory variables in the multivariate linear regression model is large compared to the number of cases, although the multivariate analysis was performed using the forward stepwise method. Further analysis will be needed to confirm the reliability of these data and reveal the pathophysiology of late-onset post-donation adverse body reactions.

In conclusion, we observed haemodynamic change during autologous blood donations using the TEB device, AESCULON mini, and evaluated its association with late-onset adverse body reactions. Low SV values at the end of the donation and younger age were significantly associated with late-onset post-donation adverse body reactions. TEB monitoring may be useful for predicting the risk of late-onset adverse body reactions after blood donation.

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自己血貯血後の遅発性有害症状予測のための非侵襲的心拍出量モニタリングの有用性

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要旨：

献血や自己血貯血後に遅発性に生じる有害な身体症状は病態生理がよくわかっておらず，かつ有効な予防策もないため，献血者/自己血貯血患者の安全を担保する上での残された課題となっている．今回，72 人の自己血貯血患者を対象に，非侵襲的に心拍出量（CO）と 1 回拍出量（SV）をリアルタイムで測定できるエスクロンミニを用いて貯血中の変化を測定した．アンケート紙法を用いて，独自に開発した preoperative autologous blood donation adverse reaction scale（PADARS）を使用し，貯血後の遅発性身体症状の重症度を推定した．合計 PADARS スコアとエスクロンミニの測定値，および貯血患者の臨床的背景との関係を，多変量線形回帰モデルを使用して評価した．結果として，貯血後，CO と SV はそれぞれ 0.79±0.43*l*/分，9.4±6.7m*l* と減少しており，アンケートに回答した 30 人の貯血患者のうち，14 人（47%）が何らかの遅発性身体症状を自覚し，2 人（7%）は比較的重度の身体症状（スコア≥5）を認めた．解析の結果，年齢と貯血終了時の SV 値が，合計 PADARS スコアと逆相関していることが明らかになった（$p<0.05$）．若年齢に加えて，エスクロンミニによって測定された貯血後の SV 値の低値は，遅発性有害症状の危険因子となる可能性があることが示された．

キーワード：
自己血貯血，非侵襲的心拍出量モニター，遅発性身体症状