Received: 8 December 2023 | Accepted: 24 February 2024

DOI: 10.1002/ams2.934

ACUTE MEDICINE & SURGERY WILEY

ORIGINAL ARTICLE

Accuracy of rapid blood coagulation testing device FibCare® in a tertiary emergency department

Yutaka Mihara | **Kenta Komoriya** | **Kei Hagiwara** | **Yasuhito Hatanaka** | **Keita Shibahashi** | **Mayu Hikone** | **Kazuhiro Sugiyama**

Tertiary Emergency Medical Center, Tokyo Metropolitan Bokutoh Hospital, Sumida-ku, Japan

Correspondence
Yutaka Mihara, Tertiary Emergency Medical Center, Tokyo Metropolitan Bokutoh Hospital, 4-23-15, Kotobashi, Sumida-ku, Tokyo 1308575, Japan.
Email: yutateni@gmail.com

Abstract

Aim: FibCare® is a novel point-of-care testing device enabling prompt evaluation of fibrinogen levels. This study aimed to investigate the accuracy of FibCare® at a tertiary emergency department.

Methods: Blood specimens obtained at a tertiary emergency medical center between October 1, 2021, and April 30, 2023, were evaluated. The correlation between the fibrinogen levels assessed via FibCare® and those via the Clauss method was evaluated using the Spearman's test. The discrepancy between the two measurement methods was assessed according to fibrinogen level and diagnosis.

Results: A total of 177 specimens from 147 patients were eligible for the analysis. The median age of the patients was 49 years, and 109 (61.6%) were men. The two measurements had statistically significant but moderate correlation ($p < 0.001$, $\rho = 0.76$). FibCare® missed 14 out of 35 cases from patients with hypofibrinogenemia (fibrinogen ≤150 mg/dL assessed by the Clauss method). The discrepancy between the two measurements was significantly greater in specimens with lower fibrinogen levels and those obtained from patients following trauma.

Conclusions: FibCare®, a novel point-of-care testing device, can be compatible with the Clauss method. However, clinicians should be aware of the risk that FibCare® may underestimate fibrinogen reduction, especially in severe cases and trauma cases.

KEYWORDS
blood coagulation, diagnosis, emergency room, fibrinogen, trauma

INTRODUCTION

Fibrinogen is a soluble plasma glycoprotein that circulates within the bloodstream. During the coagulation cascade, fibrinogen transforms into fibrin, which forms the structural framework of blood clots. This process depletes fibrinogen levels, resulting in low fibrinogen concentrations. Vigilant monitoring and prompt intervention for fibrinogen depletion are essential to ensure adequate hemostasis.

Conventional plasma fibrinogen assays commonly use the Clauss method, which requires 30–60 min for evaluation.[1] Given the time-sensitive nature of massive hemorrhage management, clinicians face challenges in making timely and well-informed decisions using laboratory tests with prolonged turnaround times. To ensure optimal patient care, rapid diagnostic tools and point-of-care tests are preferred. In 2019, a novel point-of-care testing device, FibCare® (Atom Medical), was developed. This device assesses blood fibrinogen levels within 2 min, allowing clinicians to promptly identify low fibrinogen levels and potentially improve the patient outcomes after hemorrhagic events.

Previous studies reported favorable agreement between FibCare® and the Clauss method measurements, while the correlation was diminished in the range of fibrinogen <150 mg/dL.[2,3] However, these studies were limited by small sample sizes. Furthermore, they focused only on obstetric

or cardiac surgery patients, thereby limiting the generalizability of their findings. Given the impact of the accuracy of rapid diagnostic tests on clinical practice, further study evaluating the usefulness of FibCare® is needed.

In this study, we aimed to examine the usefulness of FibCare® in patients who were treated at a tertiary emergency department.

MATERIALS AND METHODS

This cross-sectional study was conducted using laboratory test results at a tertiary emergency hospital. The study was approved by the Ethics Committee of the Bokutoh Metropolitan Hospital (approval number: 05–037). The requirement for obtaining informed consent from patients was waived as the study analyzed existing data that were anonymized before analysis.

Study population and data collection

We reviewed fibrinogen levels of consecutive patients who were treated at the emergency room of a tertiary emergency medical center and underwent fibrinogen level analysis using both FibCare® and Clauss methods for the same specimen between October 1, 2021, and April 30, 2023. Patients with fibrinogen values outside the upper or lower limits of the measurement range (<80 or ≥300 mg/dL for FibCare® and <20 mg/dL for the Clauss method) were excluded because concordance between the two measurements could not be evaluated. Collected data included age, sex, diagnosis, fibrinogen levels, the amount of fresh frozen plasma (FFP) or cryoprecipitate transfusion, and the timing of the fibrinogen test (on arrival or after blood transfusion). The diagnosis was classified as trauma, postpartum hemorrhage, gastrointestinal hemorrhage, cerebral hemorrhage, or others.

Fibrinogen tests

Fibrinogen measurement using FibCare® was performed by health-care professionals in the emergency department in accordance with the following operating procedures: (i) citrate whole blood (no need for dilution procedure) was employed, (ii) after inversion and thorough mixing, the sample was deposited into the designated sample wells, and (iii) input the hematocrit value for measurement calibration. The hematocrit value was typically acquired from concomitant blood gas analysis, whereas it was set at 30% in the absence of such information. The measurement principle of FibCare® is a type of viscoelastic test. The coagulation reaction is initiated by bringing the sample into contact with the lyophilized reagent packed in the reaction cell on the card. The viscosity increase in the reaction cell is monitored in terms of the amount of change in scattered light, which is then analyzed to determine the coagulation time.

Fibrinogen measurement using the Clauss method was performed by a clinical laboratory technician. The Clauss method is the standard fibrinogen concentration test. Briefly, plasma obtained from the blood specimen was mixed with an excess of thrombin, and the time taken for clot formation was determined and converted into a measurement of the functional fibrinogen concentration using calibration standards.[4]

Analysis

First, fibrinogen values measured using FibCare® were plotted over those measured using the Clauss method. The correlation between the two measurements was assessed using the Spearman's rank correlation coefficient and a linear regression analysis. Second, we visually explored the dispersion of the discrepancy between fibrinogen values measured by FibCare® and those measured by the Clauss method over fibrinogen levels using a scatter plot. Subsequently, a generalized additive model was applied to explore the association between the measurement error and fibrinogen levels. The mean and standard deviations (SDs) of the aforementioned discrepancy were calculated across four categories based on fibrinogen levels (≤150, 151–200, 201–250, and ≥251–300 mg/dL), diagnosis (trauma, postpartum hemorrhage, gastrointestinal bleeding, and cerebral hemorrhage), and the timing of specimen collection (on arrival or after clotting factor transfusion). Third, we analyzed the characteristics of patients in whom hypofibrinogenemia (fibrinogen ≤150 mg/dL measured using the Clauss method) was missed by FibCare®. Variables included age, sex, disease category, and timing of specimen collection.

RESULTS

A total of 217 pairs of fibrinogen measurements from 182 patients were identified during the study period. After excluding 40 pairs of measurements with fibrinogen levels outside the upper or lower limits of measurement, 177 pairs of tests from 147 patients were eligible for the analysis. The hematocrit value was missing in 11 (6.2%) pairs of samples. Of the 147 patients, 83 had clotting factor transfusion within 24 h. Table 1 summarizes the characteristics of the blood specimen. The median age of the patients was 49 (interquartile range: 33–61) years, and 109 (62%) were men. The diagnosis was trauma, postpartum hemorrhage, gastrointestinal hemorrhage, cerebral hemorrhage, and others for 109 (62%), 18 (10%), 22 (12%), 8 (5%), and 20 (11%) tests, respectively. Further, 112 patients (63%) needed subsequent FFP or cryoprecipitate transfusion in 24 h.

Figure 1 shows a scatterplot of fibrinogen measurements via FibCare® and the Clauss method. The two measurements had statistically significant but moderate correlation ($p < 0.001$, $\rho = 0.76$). Out of 35 specimens assessed via the Clauss method (fibrinogen level ≤150 mg/dL), fibrinogen level

TABLE 1 Characteristics of blood specimen.

Variables	Total	Diagnosis category				
		Trauma	Postpartum hemorrhage	Gastrointestinal hemorrhage	Cerebral hemorrhage	Others
n (%)	177	109 (62)	18 (10)	22 (12)	8 (5)	20 (11)
Age, year, median (IQR)	49 (33–61)	39 (23–58)	39 (36–41)	55 (50–60)	63 (58–83)	72 (53–78)
Men, *n* (%)	109 (62)	72 (66)	0 (0)	19 (86)	3 (38)	15 (75)
Fibrinogen[a], mg/dL, median (IQR)	205 (172–235)	200 (168–226)	193 (172–250)	164 (113–223)	184 (182–218)	197 (160–225)
Subsequent FFP or cryoprecipitate transfusion in 24 h, *n* (%)	112 (63)	72 (66)	10 (56)	13 (60)	3 (38)	14 (70)

Abbreviation: IQR, interquartile range.

[a]Fibrinogen level assessed via the Clauss method.

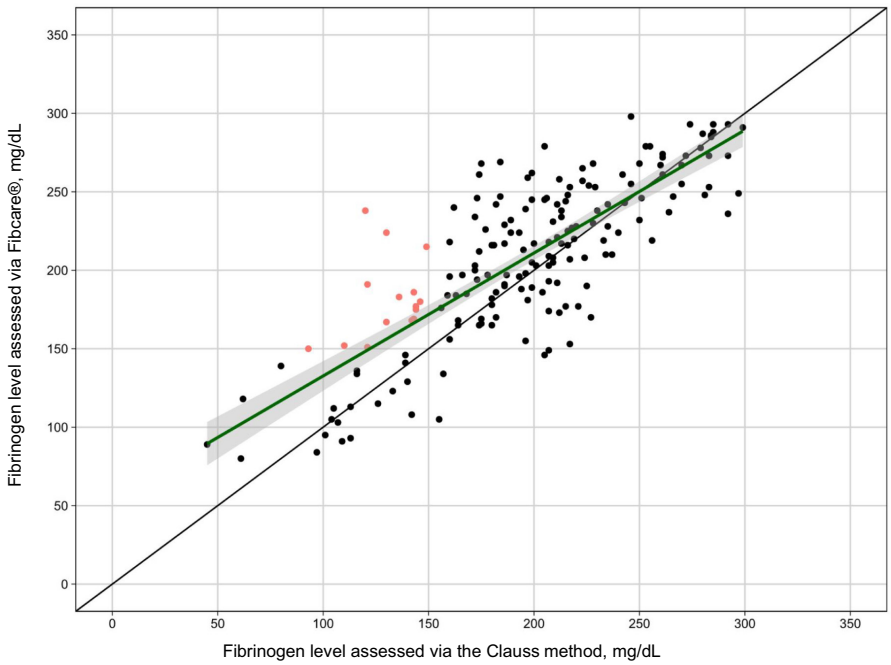

FIGURE 1 Scatterplot of fibrinogen measurements via FibCare® and the Clauss method. Each circle represents one specimen. The solid green line depicts the linear regression least-squares fit for the relationship between fibrinogen measured via FibCare® and the Clauss method. Shaded bands represent the 95% confidence interval. The 14 test pairs in which hypofibrinogenemia (fibrinogen ≤150 mg/dL measured using the Clauss method) was missed by FibCare® are shown in red circles.

via FibCare® was ≥150 mg/dL in 14 measurements. The discrepancy between the two measurements was significantly greater in specimens with lower fibrinogen levels (Figure 2).

In patients with fibrinogen levels assessed using the Clauss method (≤150, 151–200, 201–250, and ≥251–300 mg/dL), the mean of the discrepancy between the two measurements was 24.6 mg/dL (SD, 33.4 mg/dL), 24.7 mg/dL (SD, 30.1 mg/dL), 2.0 mg/dL (SD, 29.9 mg/dL), and −6.7 mg/dL (SD, 20.2 mg/dL), respectively. When patients were categorized based on diagnoses as trauma, postpartum hemorrhage, gastrointestinal bleeding, and cerebral hemorrhage, the mean of the discrepancy between the two measurements was 17.2 mg/dL (SD, 33.7 mg/dL), 8.9 mg/dL (SD, 25.5 mg/dL), −1.2 mg/dL (SD, 24.2 mg/dL), and 10.9 mg/dL (SD, 30.8 mg/dL), respectively. The mean of the discrepancy between the two measurements was 11.3 mg/dL (SD, 32.0 mg/dL) and 14.1 mg/dL (SD, 33.6 mg/dL) for specimens obtained on hospital arrival and those obtained after clotting factor transfusion, respectively.

We further analyzed the characteristics of 14 patients in whom hypofibrinogenemia (fibrinogen ≤150 mg/dL measured using the Clauss method) was missed by FibCare®. The mean age of these patients was 44 years and eight (57%) were men. The diagnosis was trauma in 11 (78%) patients. The

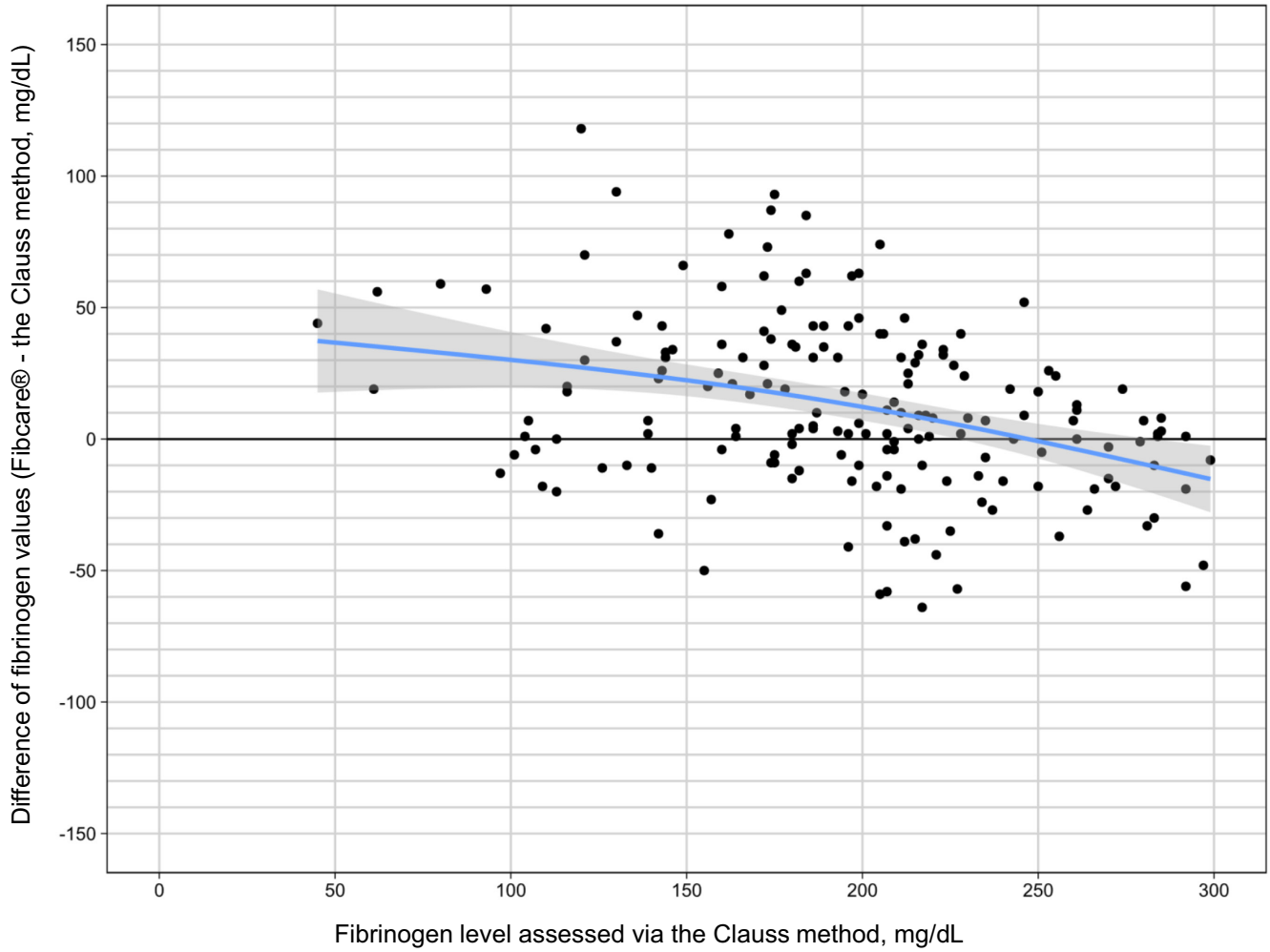

FIGURE 2 Scatterplot of the discrepancy between fibrinogen values measured by FibCare® and the Clauss method over fibrinogen levels. The solid line depicts the generalized additive model curve to assess the degree of discrepancy between fibrinogen values measured by FibCare® and the Clauss method based on the values of fibrinogen levels. Shaded bands represent the 95% confidence intervals for the estimated points.

specimen was obtained after clotting factor transfusion for eight (57%) patients. The discrepancy between the two measurements was <50 mg/dL in 10 (71%) patients.

DISCUSSION

In this study, we aimed to examine the usefulness of FibCare® in patients who were treated at a tertiary emergency department. Our analysis revealed that fibrinogen measurements using FibCare® correlated with the Clauss method, whereas FibCare® tended to overestimate the fibrinogen level in patients with hypofibrinogenemia. To the best of our knowledge, this was the largest study to investigate FibCare® and focused on the patients treated at an emergency department of a tertiary emergency medical center.

Our findings of a large variance of the difference between FibCare® measurement and the Clauss method were consistent with those of previous studies that evaluated other types of point-of-care fibrinogen tests, such as thromboelastography, viscoelastic test, and rotational thermoelectrometry.[5] We found that FibCare® values were more likely to deviate to higher values in patients with hypofibrinogenemia. Previous studies that evaluated the accuracy of ROTEM® also reported that the accuracy was reduced in cases with fibrinogen levels <100 mg/dL.[6]

We cannot definitively conclude the underlying mechanism of these findings. However, our results suggested several potential explanations. First, the deviations between the FibCare® value and the Clauss method were larger in patients who had FFP/cryoprecipitate transfusion, suggesting that transfusing coagulation factors may affect the test accuracy.[7] There are subclasses of fibrinogen, with high molecular weight fibrinogen (Fib-420) accounting for 1%–3% and low molecular weight fibrinogen (Fib-340) for 97%–99%. Fib-420 has a higher maximum amplitude than Fib-340.[8] Variations in the Fib-420 subclass proportions between exogenous and endogenous fibrinogen may underlie disparities in both the dynamic and static assessments of fibrinogen subsequent to transfusion.[9] Second, the deviations between FibCare® and the Clauss method were larger in patients with severe trauma. Severe trauma leads to inflammation, thrombogenesis, and fibrinolysis,[10] where the αEc domain of Fib-420 acts

as a chaperon.[11] Fib-420 may increase in such conditions by escaping degeneration; thus, affecting the dynamic measurement of fibrinogen.

Considering the much shorter time to obtain fibrinogen level, it is reasonable that point-of-care fibrinogen test, such as FibCare®, acquires popularity among clinicians caring for critical patients as rapid measure is mandatory to address fibrinogen deficiency. However, our results show that clinicians should be aware that the test overestimates the fibrinogen concentration with respect to the Clauss method. Current guidelines recommend treatment with fibrinogen concentrate or cryoprecipitate if major bleeding is accompanied by hypofibrinogenemia which is defined as plasma Clauss fibrinogen level ≤150 mg/dL.[12] As our result highlighted the even larger difference in the measurements between FibCare® and the Clauss method, clinicians need to search for conversion methods between FibCare® and the Clauss method. FibCare® tended to overestimate the fibrinogen levels, especially in patients with hypofibrinogenemia, although the discrepancy between the two methods was mostly <50 mg/dL; therefore, it is advisable that clinicians who care for patients with major bleeding set a relatively higher threshold to determine hypofibrinogenemia when FibCare® is used.

Limitations

This study has some limitations. First, this was an observational study. Our results showed a statistically significant but moderate correlation between FibCare® and the Clauss method measurements. However, the clinical benefit of FibCare® in a tertiary emergency department cannot be determined. Second, we could not address the underlying mechanisms of our findings. Although we considered some hypotheses based on collateral evidence, further research is needed to elucidate them. Third, the Clauss method was used as the golden standard for the reference value of fibrinogen levels; however, the Clauss method is not a perfect measurement as it can be influenced by heparin use and the calibration process.[13]

CONCLUSIONS

We examined the usefulness of FibCare® in a tertiary emergency department. FibCare® can be compatible with the Clauss method; however, it may underestimate fibrinogen reduction, especially in severe cases and trauma cases.

ACKNOWLEDGEMENTS
None.

CONFLICT OF INTEREST STATEMENT
The authors declare no conflict of interests for this article.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT
This study was approved by the Ethics Committee of the Bokutoh Metropolitan Hospital (approval number: 05-037). Requirement for obtaining informed consent from patients was waived as the study analyzed existing data that were anonymized before analysis.

ORCID
Yutaka Mihara https://orcid.org/0009-0007-1004-9659
Kenta Komoriya https://orcid.org/0009-0009-9980-1185
Keita Shibahashi https://orcid.org/0000-0001-5651-1449
Mayu Hikone https://orcid.org/0000-0003-4104-386X

REFERENCES
1. Solomon C, Cadamuro J, Ziegler B, Schöchl H, Varvenne M, Sørensen B, et al. A comparison of fibrinogen measurement methods with fibrin clot elasticity assessed by thromboelastometry, before and after administration of fibrinogen concentrate in cardiac surgery patients. Transfusion. 2011;51:1695–706.
2. Ohno S, Mizobe K, Yanagi A, Ikeda A, Kakumoto S, Miyawaki H. Evaluation of the accuracy of fibrinogen concentration measurement by FibCare® in cardiovascular surgery with a cardiopulmonary bypass. Cardiovascular Anesthesia. 2021;25:37–42.
3. Imai K, Kotani T, Nakano T, Ushida T, Kikkawa F. Clinical utility and limitations of FibCare® for the rapid measurement of fibrinogen concentrations: the first clinical experience. Taiwan J Obstet Gynecol. 2018;57:899–900.
4. Stang LJ, Mitchell LG. Fibrinogen. Methods Mol Biol. 2013;992:181–92.
5. Ranucci M, Di Dedda U, Baryshnikova E. Trials and tribulations of viscoelastic-based determination of fibrinogen concentration. Anesth Analg. 2020;130:644–53.
6. Seo H, Choi JH, Moon YJ, Jeong SM. FIBTEM of Thromboelastometry does not accurately represent fibrinogen concentration in patients with severe hypofibrinogenemia during liver transplantation. Ann Transplant. 2015;20:342–50.
7. David JS, Durand M, Levrat A, Lefevre M, Rugeri L, Geay-Baillat MO, et al. Correlation between laboratory coagulation testing and thromboelastometry is modified during management of trauma patients. J Trauma Acute Care Surg. 2016;81:319–27.
8. Mosesson MW, DiOrio JP, Hernandez I, Hainfeld JF, Wall JS, Grieninger G. The ultrastructure of fibrinogen-420 and the fibrin-420 clot. Biophys Chem. 2004;112:209–14.
9. Ranucci M, Baryshnikova E. Fibrinogen supplementation after cardiac surgery: insights from the zero-plasma trial (ZEPLAST). Br J Anaesth. 2016;116:618–23.
10. Moore FA, Moore EE, Read RA. Postinjury multiple organ failure: role of extrathoracic injury and sepsis in adult respiratory distress syndrome. New Horiz. 1993;1:538–49.
11. Tang H, Fu Y, Zhan S, Luo Y. Alpha(E)C, the C-terminal extension of fibrinogen, has chaperone-like activity. Biochemistry. 2009;48:3967–76.
12. Rossaint R, Afshari A, Bouillon B, et al. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. Crit Care, 6th edn. 2023;27:80.
13. Mackie IJ, Kitchen S, Machin SJ, Lowe GD. Haemostasis and thrombosis task force of the British Committee for Standards in Haematology. Guidelines on fibrinogen assays. Br J Haematol. 2003;121:396–404.

How to cite this article: Mihara Y, Komoriya K, Hagiwara K, Hatanaka Y, Shibahashi K, Hikone M, et al. Accuracy of rapid blood coagulation testing device FibCare® in a tertiary emergency department. Acute Med Surg. 2024;11:e934. https://doi.org/10.1002/ams2.934