A multicenter, prospective validation of disseminated intravascular coagulation diagnostic criteria for critically ill patients: Comparing current criteria*

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Objectives: **To validate scoring algorithm criteria established by the Japanese Association for Acute Medicine (JAAM) for disseminated intravascular coagulation (DIC) and to evaluate its diagnostic property by comparing the two leading scoring systems for DIC, from the Japanese Ministry of Health and Welfare (JMHW) and International Society on Thrombosis and Haemostasis (ISTH).**

Design: **Prospective, multicenter study during a 3-month period.**

Setting: **General critical care center in a tertiary care hospital.**

Patients: **Two hundred seventy-three patients with platelet counts $<150 \times 10^9$/L were enrolled.**

Intervention: **None.**

Measurements and Main Results: **The JAAM, JMHW, and ISTH DIC scoring algorithms were prospectively applied within 12 hrs of patients meeting the inclusion criteria (day 0) to days 1–3, by global coagulation tests. The numbers of systemic inflammatory response syndrome (SIRS) criteria and Sequential Organ Failure Assessment (SOFA) scores were determined simultaneously. Mortality associated with any cause was also assessed 28 days after the enrollment. All global coagulation tests and SIRS criteria adopted in the JAAM criteria and their cutoff points were validated with use of SOFA scores and mortality rate. DIC diagnostic rate of the JAAM DIC scoring system was significantly higher than that of the other two criteria ($p < .001$). The JAAM DIC algorithm was the most sensitive for early diagnosis of DIC ($p < .001$). Patients who fulfilled the JAAM DIC criteria included almost all those whose DIC was diagnosed by the JMHW and ISTH scoring systems. The JAAM DIC scores showed significant correlation with SOFA scores ($\rho = 0.499$; $p < .001$). SOFA score and mortality rate worsened in accordance with an increase in the JAAM DIC score. Fibrinogen criteria had little effect in predicting outcome for the DIC patients, and a total score of 4 points in the JAAM scoring system without fibrinogen was closely related to poor prognosis. According to the results, we revised the JAAM criteria by excluding fibrinogen and confirmed that the DIC diagnostic properties of original criteria remained unchanged in the revised JAAM criteria.**

Conclusions: **The JAAM scoring system has an acceptable property for the diagnosis of DIC. The scoring system identified most of the patients diagnosed by the JMHW and ISTH criteria. Revised JAAM DIC criteria preserved all properties of the original criteria for DIC diagnosis. The revised scoring system can be useful for selecting DIC patients for early treatment in a critical care setting. (Crit Care Med 2006; 34:625–631)**

KEY WORDS: criteria; critical illness; diagnosis; disseminated intravascular coagulation; systemic inflammatory response syndrome

Disseminated intravascular coagulation (DIC) is characterized by the widespread activation of coagulation, which results in the intravascular formation of fibrin and ultimately thrombotic occlusion of vessels, followed by derangement of oxygen supply and demand to cells and tissues (1). It is now accepted that DIC is an important disorder that can originate from and cause damage to the microvasculature. If damage to the microvasculature is sufficiently severe, organ dysfunction can result (2).

Although there is recognition of the clinical importance of DIC, no clear and universally accepted diagnostic algorithm has existed until recently. The Japanese Ministry of Health and Welfare (JMHW) proposed criteria for the diagnosis of DIC a decade ago (3). The subcommittee of the International Society on Thrombosis and Haemostasis (ISTH) has proposed an overt and nonovert DIC scoring system (2). The ISTH score is partly based on a modification of the former criteria. A remarkable similarity in the ability of the JMHW DIC and ISTH overt DIC definitions to identify DIC patients has been reported (4). Re-

*See also p. 899.

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Table 1. Scoring system for disseminated intravascular coagulation (DIC) by the Japanese Association for Acute Medicine

	Score
Systemic inflammatory response syndrome criteria	
≥3	1
0–2	0
Platelet count ($\times 10^9$/L)	
<80 or >50% decrease within 24 hrs	3
≥80 and <120 or >30% decrease within 24 hrs	1
≥120	0
Prothrombin time (value of patient/normal value)	
≥1.2	1
<1.2	0
Fibrinogen (g/L)	
<3.5	1
≥3.5	0
Fibrin/fibrinogen degradation products (mg/L)	
≥25	3
≥10 and <25	1
<10	0
Diagnosis	
Five points or more	DIC

cent prospective assessment of the diagnostic accuracy of the ISTH overt criteria showed that the scoring system could be useful in clinical practice (5). However, several issues to be solved in application of the ISTH scoring system have been proposed (6).

In the past few years, structural and functional studies have demonstrated an increasingly tight interplay between the coagulation and inflammatory systems (7). These studies support an important role of systemic inflammatory response syndrome (SIRS) in the development of DIC in these critically ill patients. The DIC in turn contributes to the development of multiple organ dysfunction syndrome and its complications in this patient group (7, 8). Wada et al. (9) suggested that rapid diagnosis and early treatment of DIC improve outcome for these patients. Dhainaut et al. (10) showed that therapeutic intervention directly against coagulation and inflammation in DIC associated with severe sepsis improves outcome. On the basis of this evidence, we have proposed a new Japanese DIC diagnostic criteria for critically ill patients (11).

In this report the Japanese Association for Acute Medicine (JAAM) DIC study group presents the results from a multicenter, prospective validation of criteria of the JAAM scoring system for DIC and evaluation of its clinical relevance in a critical care setting.

MATERIALS AND METHODS

Patients

We enrolled 273 patients in this prospective trial, conducted at 13 critical care centers in Japan between May 1 and August 15, 2004. The institutional review board of all institutions approved the protocol, and written informed consent from the patients or next of kin was obtained.

Selection Criteria. All patients admitted to the intensive care unit were eligible in this study when their platelet counts decreased to $<150 \times 10^9$/L. Patients who met the following criteria were excluded: <15 yrs of age; hematopoietic malignancy; liver cirrhosis classified as Child-Pugh grade C; concomitant treatment with carcinostatics or irradiation; and known clotting disorders or receipt of anticoagulant therapy.

Data Sampling and Evaluation of Patients. Blood samples were collected within 12 hrs after the patients were confirmed as meeting the inclusion criteria (day 0), as well as on days 1 to 3 at 24-hr intervals. Immediately after blood samples were taken, platelet counts, prothrombin time (PT), fibrinogen, and fibrin/fibrinogen degradation products (FDPs) were measured by electric impedance methods, scattered light detection method, and latex quantitative immunoassay, respectively. All patients were followed up for 28 days after enrollment in the study, and 28-day all-cause mortality was assessed. Acute Physiology and Chronic Health Evaluation (APACHE) II score was assessed at the time of enrollment (12). Daily Sequential Organ Failure Assessment (SOFA) score and SIRS criteria met by the patients were also determined (13). The coagulation score item was not used for assessment of the SOFA score.

DIC Diagnosis and Treatment. We used the JMHW DIC, ISTH overt DIC (ISTH DIC), and JAAM DIC diagnostic algorithms for scoring DIC. Scoring systems for the three DIC definitions are presented in Table 1 and elsewhere (2, 3). Bleeding symptoms and organ dysfunction in the JMHW criteria were defined as abnormal bleeding independent of original disease and SOFA score ≥2. FDP measurement was used for the fibrin-related marker in the ISTH criteria. No increase, moderate increase, and strong increase were defined as FDP values of <9, 10–24, and >25 mg/L, respectively. Management of DIC was with a combination of anticoagulants, plasma and platelet substitution therapy, and coagulation inhibitor concentrate. Standard treatments for the underlying disorders of DIC were administered simultaneously with these.

Statistical Analysis

Comparisons among the three groups were made using the Kruskal-Wallis rank test or the Friedman test. The Mann-Whitney U test was applied for two-group unpaired comparison. Proportions were compared with the chi-square test or Fisher's exact test when necessary. Correlation was examined by the Spearman's rank correlation coefficient.

The time lines of diagnosis by the three sets of DIC criteria were analyzed with the Wilcoxon signed-rank test. The relationships among the outcome and the following various factors were assessed by stepwise logistic regression analysis (backward elimination method, based on likelihood ratio), with use of outcome (survived, 0; dead, 1) as a criterion variate and age, gender (male, 0; female, 1), JAAM criteria (no, 0; yes, 1), revised JAAM criteria (no, 0; yes, 1) as explanatory variates. Results were reported as odds ratios (ORs) and 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curves were constructed for JMHW DIC criteria. As items, ISTH, JAAM, and revised JAAM scores were used. The areas under the ROC curve (AUC) with standard error (SE) were examined by a significance test for AUC.

For all reported results, a p value $<.05$ was considered statistically significant.

RESULTS

Baseline Characteristics of the Patients. The 13 centers participating in the study collected 1072 samples from 273 patients. The patients were aged 59 ± 19 years, and the male-to-female ratio was 179:94. APACHE II score was 17.8 ± 8.6, and 43 patients died. Clinical conditions of the enrolled patients are presented in Table 3.

Validation of the JAAM Criteria. Rate of platelet decrease and SIRS criteria are newly cited criteria in the JAAM DIC scoring system. The maximum rate of platelet decrease and SIRS category showed significant impacts both on the maximum SOFA score and on mortality at 28 days (Figs. 1 and 2). Table 4 demonstrates that mortality, maximum SOFA score, and maximum JAAM score during observation gradually worsened, depending on the increase in SIRS scores. We confirm the same results in platelet counts, PT ratio, and FDP levels in Table 5. Patients' mortality, organ dysfunction by SOFA score, and JAAM DIC score significantly worsened, depending on the cutoff points in the respective criteria.

Comparison of the Three Sets of Criteria. Markedly different DIC diagnostic rates were observed for the JAAM criteria (184/273; 67.4%), JMHW criteria (110/273; 40.3%), and ISTH criteria (77/273; 28.2%) ($p < .001$). These relations are shown in Figure 3. Table 6 shows the number of patients on the day of DIC diagnosis per the diagnostic criteria and demonstrates that the JAAM DIC criteria could detect DIC earliest ($p < .001$).

We observed deterioration of organ function and progression of mortality rate with an increase in the maximum JAAM DIC score during the study period (Fig. 4). Significant correlations were found between maximum DIC scores for the three sets of criteria and the maximum SOFA scores ($p < .001$) (Table 7). There was no difference in the SOFA scores on the day of DIC diagnosis among the three sets of diagnostic criteria. The results are shown in Table 7.

Revision of the JAAM Criteria. We found that minimum fibrinogen levels during the study period had no effect on prediction of outcome (crude OR, 0.999; $p = .213$; CI, 0.997–1.001). On the basis of this finding, we revised the JAAM score, removing fibrinogen. Maximum DIC scores of the revised JAAM criteria had significant impacts on the maximum SOFA score and mortality (Fig. 5). When we determined total score points for DIC diagnosis of the revised criteria, a total score of 4 demonstrated a higher DIC diagnostic rate (178/273, or 65.2%, vs. 153/273, or 56.0%; $p = .035$) and earlier DIC diagnosis ($p < .001$) than a total score of 5 points. However, no differences were observed between total scores of 4 and 5 points in the other diagnostic properties and SOFA on the day of DIC diagnosis (7.3 ± 3.7 vs. 7.8 ± 3.8; $p = .294$).

Table 2. Revised scoring system for disseminated intravascular coagulation (DIC) by the Japanese Association for Acute Medicine

	Score
Systemic inflammatory response syndrome criteria	
≥3	1
0–2	0
Platelet count ($\times 10^9$/L)	
<80 or >50% decrease within 24 hrs	3
≥80 and <120 or >30% decrease within 24 hrs	1
≥120	0
Prothrombin time (value of patient/normal value)	
≥1.2	1
<1.2	0
Fibrin/fibrinogen degradation products (mg/L)	
≥25	3
≥10 and <25	1
<10	0
Diagnosis	
Four points or more	DIC

Table 3. Clinical conditions of the patients

Condition	No. of Patients
Trauma/burn/surgery	109
Sepsis/severe infection	93
Vascular abnormalities	21
Ischemia/hypoxia/shock	20
Organ destruction (severe pancreatitis)	9
Heat stroke/malignant syndrome	5
Severe toxic or immunologic reactions	5
Severe hepatic failure	4
Malignancy	3
Other	4
Total	273

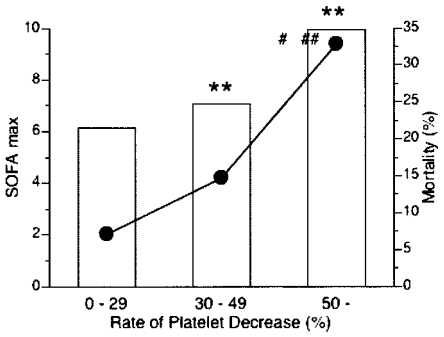

Figure 1. Sequential Organ Failure Assessment (*SOFA*) score and mortality by rate of platelet decrease. Bar graph shows maximum SOFA scores during study period (**$p < .001$ vs. 0–29%, 30–49%). Line graph shows mortality (#$p < .05$ vs. 30–49%; ##$p < .001$ vs. 0–29%).

Logistic regression analysis identified revised JAAM criteria using a total of 4 points as a significant independent predictor of death (OR, 12.380; $p = .001$; CI, 3.021–54.489). In addition, gender was also an independent factor, but it was not significantly related to outcome (OR, 0.506; $p = .099$; CI, 0.225–1.137). A JAAM criterion was omitted in the results because of the removal of multicollinearity from the formula of logistic regression analysis, i.e., revised JAAM criteria were related to outcome more than the original criteria. On the basis of these results, the JAAM decided to revise the JAAM DIC diagnostic criteria (Table 2).

ROC Curve Analysis. The ROC curves for the JMHW DIC by the JAAM DIC and ISTH DIC scores and then by the JAAM DIC and revised JAAM DIC scores were analyzed. AUC (SE) were as follows: JAAM DIC, 0.930 (0.008), vs. ISTH DIC, 0.913 (0.01), $p = .770$; and JAAM DIC, 0.930 (0.008), vs. revised JAAM DIC, 0.920 (0.009), $p = .629$. The results demonstrated that there were no differences in the AUCs for the JMHW criteria between the ISTH, JAAM, and revised JAAM criteria.

DISCUSSION

Scoring systems are successful if clinicians can use them at the bedside, if they are readily available, and if they are easy to use. The criteria should be simple so that clinicians will not resist their commitment to memory or application. The JAAM DIC criteria aimed at high sensitivity and sufficient specificity with use of laboratory assays that are commonly available at all hospitals; early diagnosis and treatment to improve outcome; coincidence of diagnosis and treatment; and evaluation of the disease process and severity by scoring system. The criteria consist of clinical conditions that may be associated with DIC, clinical conditions

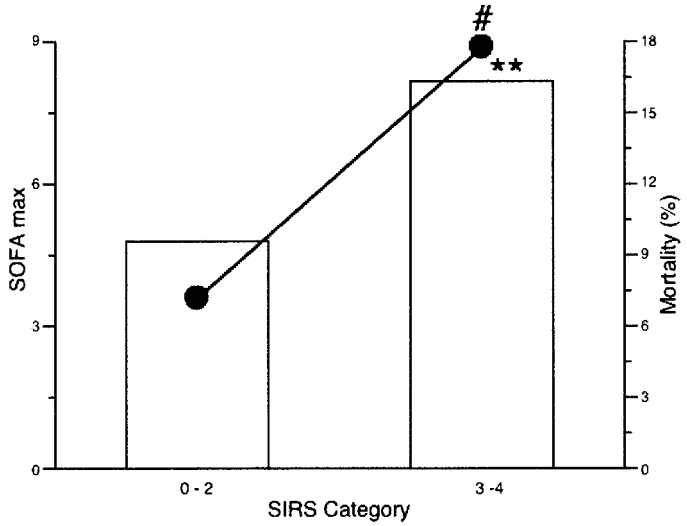

Figure 2. Sequential Organ Failure Assessment (*SOFA*) score and mortality by systemic inflammatory response syndrome (*SIRS*) category. Bar graph shows maximum SOFA scores during study period (**$p < .001$). Line graph shows mortality (#$p = .03$).

Table 4. Changes in mortality, SOFA score, and JAAM score by maximum SIRS criteria

SIRS criteria	0	1	2	3	4
Mortality (%)	0	6.7	8.2	13.1	22.9[a]
SOFA, max	2.3 ± 1.2	3.1 ± 2.9	5.6 ± 3.3[b]	7.4 ± 3.7[c]	9.0 ± 4.1[d]
JAAM, max	2.2 ± 0.8	3.7 ± 2.8	3.9 ± 2.3	5.3 ± 2.3[e]	5.9 ± 2.3[f]

SOFA, Sequential Organ Failure Assessment score; JAAM, Japanese Association for Acute Medicine; SIRS, systemic inflammatory response syndrome; Max, maximum score during the study period.

[a]$p < .05$ vs. 2; [b]$p < .01$ vs. 0, 1; [c]$p < .001$ vs. 0, 1, 2; [d]$p < .001$ vs. 0, 1, 2, 3; [e]$p < .01$ vs. 0, 1, 2; [f]$p < .001$ vs. 0, 1, 2.

Table 5. Validation of cut-off points for platelet counts, PT ratio, and FDPs

	Mortality (%)	SOFA Max	JAAM Max
Platelet count (10^9/L)			
1. ≥120	3.6	4.6 ± 3.0	2.4 ± 1.9
2. ≥80 <120	6.1	5.6 ± 3.2	4.1 ± 1.8[a]
3. <80	25[b]	9.4 ± 3.8[b]	6.8 ± 1.5[b]
p Value	<.001	<.001	<.001
PT ratio			
1. <1.2	1.8	5.2 ± 3.2	2.8 ± 2.0
2. ≥1.2	18.4[b]	7.8 ± 4.1[b]	5.7 ± 2.2[b]
FDPs (g/L)			
1. <10	9.8	6.6 ± 4.1	3.2 ± 2.1
2. ≥10 <25	7.9	6.5 ± 3.8	4.6 ± 1.8[a]
3. ≥25	25.5[b]	8.5 ± 4.1[b]	7.1 ± 1.6[b]
p Value	<.001	<.001	<.001

PT, prothrombin time; FDPs, fibrin/fibrinogen degradation products; SOFA, Sequential Organ Failure Assessment score; Max, maximum score during study period; JAAM, Japanese Association for Acute Medicine; *p* value, Kruskal-Wallis rank test among the three criteria sets.

[a]$p < .001$ vs. 1; [b]$p < .001$ vs. 1 and 2.

that should be carefully ruled out, and a scoring algorithm.

The JAAM DIC criteria are characterized by the adoption of SIRS criteria and rate of platelet reduction in the algorithm. The molecular links between inflammation and coagulation that progress before vascular injury and multiple organ dysfunction syndrome are now commonly accepted (7). Rangel-Frausto et al. (14) demonstrated higher proportions of organ dysfunction, including DIC, in the hierarchy from SIRS to sepsis. The platelet counts in DIC strongly correlated with markers of thrombin generation, because thrombin-induced platelet aggregation is largely responsible for platelet consumption (15). In addition to low platelet counts, assessment of a rapid and continuous decrease in the count more accurately reflects both consumption and thrombin generation and is helpful in establishing the presence and severity of DIC (1, 2). The above-mentioned studies validate the adoption of SIRS criteria and the rate of platelet decrease in the JAAM DIC scoring algorithm.

The JAAM defined the scores in the algorithm such that a score of 1 correlates with presence of DIC and a score of 3 correlates with the onset of organ dysfunction or with death. In the present study, we observed significant stepwise increases in mortality, SOFA score, and JAAM DIC score in accordance with increases in scores of SIRS criteria, platelet counts and reduction rate, PT ratio, and FDP (Tables 4 and 5). This was especially true for a score of 3, for which the highest mortality rate and SOFA score were demonstrated. The results support the validation of weighing for scores in our criteria.

For therapeutic intervention, identifying the harbingers of DIC that progress to multiple organ dysfunction syndrome and death is critical. For the purpose of this discussion, the ISTH has proposed two categories of DIC: overt and nonovert DIC (2, 16). The diagnosis of nonovert DIC should be of value for identifying patients who are at risk before they develop uncompensated DIC. The ISTH suggested that when nonovert DIC is present, therapeutic intervention is most efficacious (2, 16, 17). The concept of nonovert DIC and the study in Japan (9) have an impact on early diagnosis and treatment of DIC. The finding in the present study that JAAM DIC criteria could diagnose DIC earliest, with a high DIC diagnostic rate, means that our criteria may be judged successful.

Fibrinogen is highly specific but has very low sensitivity in diagnosis of DIC. A low level of fibrinogen reflects the late, severe consumptive stage of DIC, because fibrinogen is an acute-phase reactant and will remain at falsely normal or even higher levels until the late stage (18). Thus hypofibrinogenemia is not common except in the most severe cases of DIC. The findings of the present study and this characteristic of fibrinogen led us to remove fibrinogen criteria from the JAAM DIC scoring system. A recent study by the ISTH supports our decision by hypothe-

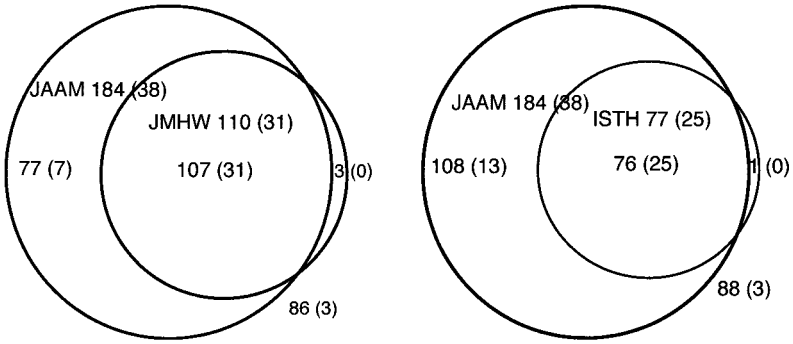

Figure 3. Distribution of patients according to the three diagnostic criteria. *Left,* comparison between the Japanese Association for Acute Medicine (*JAAM*) disseminated intravascular coagulation (DIC) and Japanese Ministry of Health and Welfare (*JMHW*) DIC diagnoses; *right,* comparison between the JAAM DIC and International Society on Thrombosis and Haemostasis (*ISTH*) DIC diagnoses. Numbers in parentheses are of nonsurvivors.

Table 6. Number of patients on day of DIC diagnosis by the three sets of diagnostic criteria

	JAAM	JMHW	ISTH	*p* Value
DIC patients				
Day 0	161	79	50	
Day 1	19	13	17	
Day 2	1	12	7	
Day 3	3	6	3	
Non-DIC patients	89	163	196	
				$<.001^a$

DIC, disseminated intravascular coagulation; JAAM, Japanese Association for Acute Medicine; JMHW, Japanese Ministry of Health and Welfare; ISTH, International Society on Thrombosis and Haemostasis.

[a]Friedman test among the three groups; $p < .001$ between all groups by paired Wilcoxon signed-rank test.

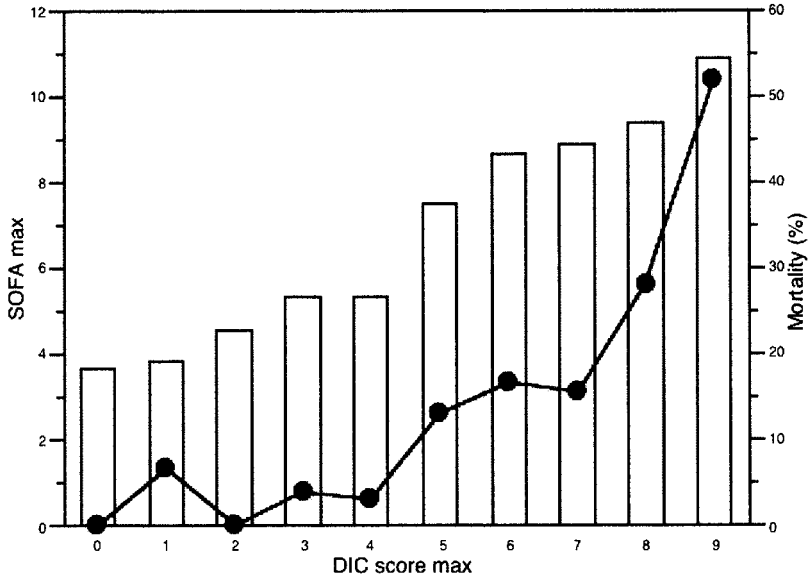

Figure 4. Sequential Organ Failure Assessment (*SOFA*) score and mortality by the Japanese Association for Acute Medicine disseminated intravascular coagulation (*DIC*) score. Bar graph shows SOFA score and line graph shows mortality. Maximum scores for SOFA and DIC criteria were used for analysis.

sizing that exclusion of all fibrinogen levels from the calculation of the ISTH DIC score would hardly affect the accuracy of the scoring system (5).

We examined total-score diagnosing of DIC in the revised JAAM criteria with use of 4 and 5 total points. A total score of 4 points could diagnose DIC earlier and more sensitively than a score of 5 points, without changing diagnostic properties and mortality among the patients with DIC. In accordance with the results, the JAAM adopted a total score of 4 points. We validated that the DIC diagnostic property of the revised JAAM criteria remained unchanged, using stepwise logistic regression. The revised JAAM DIC criteria demonstrated good prediction of organ dysfunction and poor outcome. As presented in Figure 5, the good correlations between revised DIC scores, SOFA scores, and mortality suggest that the revised algorithm can evaluate disease process and severity of DIC.

Prospective validation showed that the ISTH criteria diagnosed 34% of cases of DIC in 217 intensive care patients with clinically suspected DIC (5). Taylor et al. (17) estimated the actual incidence of DIC might have been as high as 45% among patients with severe sepsis or 75% among those with septic shock, citing the former study (19). The incidences of DIC on the basis of the JMHW and ISTH criteria in the present study were 40.3% and 28.2%, respectively. Taken together, these two sets of criteria could diagnose DIC in approximately 30% to 40% of critically ill patients.

The results mentioned in the above paragraph may force us to consider that nonovert DIC criteria could identify more than 40% of patients as having nonovert DIC in a population of critically ill patients. Toh et al. prospectively analyzed a non-overt DIC template using a score of ≥5 for diagnosis in a general intensive care unit over a period 12 months. The study sufficiently identified nonovert DIC with increased mortality, but the nonovert DIC algorithm could not predict overt DIC, which suggests nonovert DIC is independent of overt DIC (20). On the contrary, patients who fulfilled the revised JAAM criteria (65.2%) included >97% of those diagnosed by the JMHW DIC and ISTH overt DIC criteria, which means the revised JAAM DIC criteria constitute a dependent continuum of those two sets of criteria. The results demonstrate that the revised JAAM DIC scoring system can be used as a predictor of full-blown DIC.

We close our discussion by addressing a possibility of false-positive DIC diagnosis by the JAAM criteria. In the present study, we carefully excluded patients who may have had false-positive high DIC scores, such as those with hematopoietic

Table 7. Prediction of organ dysfunction by three sets of diagnostic criteria for disseminated intravascular coagulation (DIC)

	JAAM	JMHW	ISTH	*p* Value
Organ dysfunction				
SOFA[a]	0.499[c]	0.521[c]	0.334[c]	
(n)	(1017)	(1017)	(990)	
SOFA[b]	7.2 ± 3.8	8.1 ± 3.8	8.3 ± 4.1	.051
(n)	(184)	(110)	(77)	

JAAM, Japanese Association for Acute Medicine; JMHW, Japanese Ministry of Health and Welfare; ISTH, International Society on Thrombosis and Haemostasis; SOFA, Sequential Organ Failure Assessment score, except coagulation.

[a]Correlation coefficient between DIC scores and SOFA scores during study period; [b]SOFA score on the day of DIC diagnosis; [c]$p < .001$, examined by a significance test for each correlation coefficient.

The revised scoring system can be useful for selecting patients with disseminated intravascular coagulation for early treatment in a critical care setting.

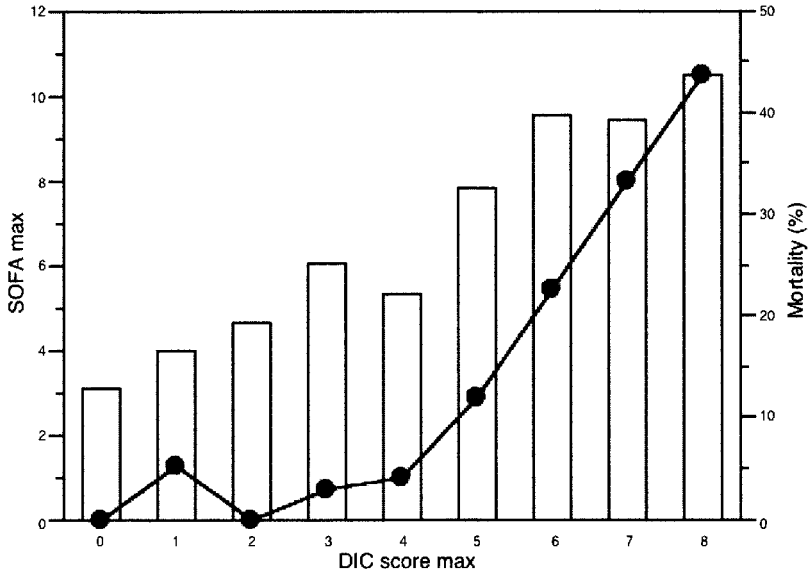

Figure 5. Sequential Organ Failure Assessment (*SOFA*) score and mortality by the revised Japanese Association for Acute Medicine (JAAM) disseminated intravascular coagulation (*DIC*) score. Bar graph shows SOFA score and line graph shows mortality. Maximum scores for SOFA and DIC criteria were used for analysis.

malignancy, severe liver cirrhosis, and concomitant treatments with carcinostatics or irradiation. The exclusion criteria used in the present study led us to confirm the validity of the results in our study. Thrombocytopenia and the other coagulation disorders observed in these diseases or conditions have no relation to the development of DIC. Therefore, we should exercise extreme caution in diagnosing DIC by means of the JAAM criteria in patients with these diseases or conditions.

CONCLUSION

The JAAM DIC Study Group prospectively assessed the diagnostic property of the JAAM criteria for the diagnosis of DIC in critically ill patients. We validated the criteria adopted and their cutoff points. The JAAM DIC algorithm can diagnose DIC early, at a high diagnostic rate, with use of global coagulation markers. The scoring system precisely evaluates the DIC process and its severity and can predict organ dysfunction and outcome for the critically ill patients with DIC. Those DIC diagnostic properties remained unchanged in the revised JAAM criteria.

Almost all the patients who developed DIC as defined by the JMHW and ISTH criteria could be identified by the revised JAAM DIC criteria in the early stage. This result demonstrates that the revised JAAM DIC criteria constitute a dependent continuum to the two major criteria and can predict full-blown DIC. We believe that the JAAM criteria have an advantage for selection of patients for early DIC treatment in a critical care setting.

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REFERENCES

1. Levi M, ten Cate H: Disseminated intravascular coagulation. *N Engl J Med* 1999; 341: 586–592
2. Taylor FB Jr, Toh CH, Hoots WK, et al: Toward definition, clinical and laboratory criteria, and a scoring system for disseminated intravascular coagulation. *Thromb Haemost* 2001; 86:1327–1330
3. Kobayashi N, Maekawa T, Takada M, et al: Criteria for diagnosis of DIC based on the analysis of clinical and laboratory findings in 345 DIC patients collected by the Research Committee on DIC in Japan. *Bibl Haematol* 1987; 49:848–852
4. Levi M, Joyce DE, Sundin DP, et al: Disseminated intravascular coagulation in patients with severe sepsis: Comparing current definitions. *Intensive Care Med* 2003; 29(Suppl 1):S33
5. Bakhtiari K, Meijers JC, De Jonge E, et al: Prospective validation of the International Society of Thrombosis and Haemostasis scoring system for disseminated intravascular coagulation. *Crit Care Med* 2004; 32: 2416–2421
6. Rason D, Dwyre L, Heyland D, et al: Issues arising in application of the ISTH disseminated intravascular coagulation (DIC) scoring system: The need for modification before prospective validation. *J Thromb Haemost* 2003; 1(Suppl 1):0583
7. Esmon CT: Inflammation and thrombosis. *J Thromb Haemost* 2003; 1:1343–1348
8. Members of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definition for sepsis and organ failure and guidelines for the use innovative therapies in sepsis. *Crit Care Med* 1992;20: 864–874
9. Wada H, Wakita Y, Nakase T, et al: Outcome prediction of disseminated intravascular coagulation in relation to the score when treatment was begun. *Thromb Haemost* 1995; 74:848–852
10. Dhainaut JF, Yan SB, Joyce DE, et al: Treatment effects of drotrecogin alfa (activated) in patients with severe sepsis with or without overt disseminated intravascular coagulation. *J Thromb Haemost* 2004; 2:1924–1933
11. Gando S, Wada H, Asakura H, et al: Evaluation of new Japanese diagnostic criteria for disseminated intravascular coagulation in critically ill patients. *Clin Appl Thromb Hemost* 2005; 11:71–76
12. Knaus WA, Draper EA, Wanger DP, et al: APACHE II: A severity classification system. *Crit Care Med* 1985; 13:818–829
13. Vincent JL, de Mendonça A, Cantraine F, et al: Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. *Crit Care Med* 1998; 26: 1793–1800
14. Range-Frausto MS, Pittet D, Costigan M, et al: The natural history of the systemic inflammatory response syndrome (SIRS): A prospective study. *JAMA* 1995; 273: 117–123
15. Akca S, Haji-Michael P, de Mendonça A, et al: Time course of platelet counts in critically ill patients. *Crit Care Med* 2002; 30:753–756
16. Hoots WK: Non-overt disseminated intravascular coagulation: Definition and pathophysiological implications. *Blood Rev* 2002; 16(Suppl 1):S3–S9
17. Taylor FB Jr, Kinasewitz GT: The diagnosis and management of disseminated intravascular coagulation. *Current Hematol Rep* 2002; 1:34–40
18. Toh CH: Laboratory testing in disseminated intravascular coagulation. *Semin Thromb Haemost* 2001; 27:653–656
19. Fourrier F, Chopin V, Goudemand J, et al: Septic shock, multiple organ failure, and disseminated intravascular coagulation: Compared pattern of antithrombin III, protein C, and protein S deficiencies. *Chest* 1992; 101:816–823
20. Toh CH, Downey C: Performance and prognostic importance of a new clinical and laboratory scoring system for identifying non-overt disseminated intravascular coagulation. *Blood Coagl Fibrinolysis* 2005; 16:69–74