Prognostic value of a simple evolving disseminated intravascular coagulation score in patients with severe sepsis

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Abstract: Objective: to predict outcome in patients with severe sepsis using the simple evolving DIC score calculated in the first 48hrs from two readily available global coagulation markers, platelet count and prothrombin time, and comparing its accuracy with (SOFA) score. Patients and Methods: fifty patients with severe sepsis in an adult intensive care unit (ICU) in Critical Care Medicine Department Cairo University were included in the study. The SOFA score and our simple evolving DIC score were calculated in all patients just before enrollment in the study. Results: Patients with higher simple DIC score had the highest SOFA scores and were associated with worst outcome. Mortality rate increased from 0% for simple DIC score < 1 to 90,9% for simple DIC score 2 or 3 and reach 100% for simple DIC score 4. Conclusion: the simple evolving DIC score calculated in the first 48hr appears, besides its general availability and easy calculation at the bedside, to be a reliable and accurate tool in predicting patients' outcome. [Journal of American Science. 2011;7(1):101-107]. (ISSN: 1545-1003).

Keywords: Prognostic value; intravascular; coagulation; sepsis

1. Introduction

Patients with sepsis characteristically manifest an intense systemic inflammatory response that can result in activation of the coagulation system. This activation is initiated by microbial products, such as endotoxin, and amplified by proinflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-1[(1,2)]. Local thrombin generation can intensify the inflammatory response at sites of infection, but its spillover into the systemic circulation can result in disseminated intravascular coagulation (DIC) [(3)]. The presence of DIC has been associated with increasing risk of death from sepsis [(4)]. The International Society of Thrombosisn and Haemostasis (ISTH) has recognized that many patients who do not fulfill the criteria for overt DIC have an evolving coagulopathy manifest by worsening coagulation tests such as the platelet count and prothrombin time [(5,6)].

Over the past years, many scoring systems have been developed to describe the severity of illness of critically ill patients or to predict the outcome of intensive care units. As an example, the Acute Physiology and Chronic Health Evaluation (APACHE) score and the Simplified Acute Physiology Score (SAPS) are based on the first 24hr of ICU admission. Although the score on admission to the ICU provides useful information, it is clear that the pattern of change over time is a better indicator of the ultimate outcome [(7)]. The first Sepsis related Organ Failure Assessment score, later called the Sequential Organ Failure Assessment (SOFA) score, was introduced in 1994, the aim was to quantify the severity of the patients' illness based on the degree of organ dysfunction, and taking into account the time course of a patient's condition during the entire ICU stay. This enables physicians to follow the evolving disease process.

We are aiming to predict outcome in patients with severe sepsis using the simple evolving DIC score calculated in the first 48hrs from two readily available global coagulation markers, platelet count and prothrombin time, and comparing its accuracy with (SOFA) score.

2. Material and Methods

Patients &Methods

Fifty patients who had been admitted to the Critical Care Medicine Department, Cairo University during 2007 with the diagnosis of severe sepsis or septic shock were enrolled in the study. Patients included in this study were diagnosed to have severe sepsis according to the American College of Chest Physicians/Society of Critical Care Medicine (ACCP & SCCM) definitions [(8)].

Exclusion criteria:

Patients presenting with any of the following were excluded from the study:

1. Anticoagulant therapy.
2. Post cardiopulmonary resuscitation.
3. Presence of an advanced condition to withhold life-sustaining treatment e.g. (metastatic cancer).

All patients were subjected to*:* Full history taking including underling diseases, previous therapy and acute findings.

Routine monitoring and recording of heart rate HR, respiratory rate RR, temperature, mean arterial pressure MAP, urine output and Glasgow coma scale (GCS).

Daily recording of the need for: Mechanical ventilation (MV), adrenergic drugs was done.

Scoring system: The SOFA score [(9)] and the simple evolving DIC score [(10)] were recorded on admission and 48hr later. All patients were followed up until death or hospital discharge.

Routine laboratory investigations including: Complete blood count (CBC), Random blood sugar (RBS), kidney function, liver profile and arterial blood gases (ABG) was done.

Cultures: We performed Blood culture for all patients suspected to have sepsis. Tracheal aspirate from all ventilated patients and those suspected to have pneumonia was sent for sputum analysis and culture. A clean mid-stream sample of urine was sent for analysis and culture from all patients.

Statistical analysis:

Statistical Package for social science (SPSS) version 12 was used for analysis of data. For comparative purposes between groups in all continuous data unpaired t-test ANOVA test were performed.

Chi-square test for assessing association in categorical data.

Tools to assess the accuracy of diagnostic test have been calculated:

S ensitivity, specificity, positive and negative predictive values together with Odds ratio

3. Results:

This study included fifty Patients with mean Age of 61.2 ± 12.7 years, (23-87 years), thirty patients were males (60%), twenty patients were female and twenty sevens were diabetic (54%). Comparison between demographic data of septic patients in relation to outcome was shown in Table (1). 66% of our severely septic patients develop adult respiratory distress syndrome (ARDS) and managed by mechanical ventilator (MV). Patients without mechanical ventilation have 13 time chance to survive than those with mechanical ventilation (OR=13 and 95%confidence interval CI= 1.9-95; P<0.001). We also notice a trend towards increased mortality with prolonged periods of MV (P=0.001). Table (2) showed no significant difference regarding type of infecting microorganism in relation to outcome. A statistically significant difference was observed between length of stay, duration of mechanical ventilation and the mean difference in DIC score. While no significant difference was observed in age, Table (3). patients with simple evolving DIC score > 2 (calculated after 48 hours from admission) appear to have a shorter length of ICU stay, low PaO_2/FiO_2 ratio, prolonged period of MV and difficult weaning and higher values of liver enzymes (AST, ALT) in comparison to patients with simple DIC score < 2 (P < 0.05). Comparison between DIC score (calculated after 48 hours from admission) in septic patients in relation to outcome was shown in table 4. The accurate predictive value of the simple DIC score was 92% of died septic patients with DIC score > 2, and all who had score < 1 survive, while 65.7% of those with SOFA score > 5 died (table 5). Table (6) showed the high ability of the simple DIC score to predict SOFA score (calculated after 48 hours from admission), as all patients with DIC score > 2 had SOFA score > 5. While only 40% of those with DIC score < 1 had SOFA score > 5. Sensitivity, specificity, positive and negative predictive values and Odds ratio of SOFA score > 5 (calculated after 48 hours from admission) was 100 %, 55,6 %, 65,6%, 100 % and 2,9 respectively. While that of DIC > 2 (calculated after 48 hours from admission) was 100 %, 92,6 %, 92 %, 100 % and 12,5 respectively.

Table (1): Comparison between demographic data of septic patients in relation to outcome.

	Total N (%)	Survivors N (%)	Non-survivors N (%)	P. Value
Diagnosis				
Pneumonia	18 (36)	10 (55.6)	8 (44.4)	
Peritonitis	11 (22)	4 (36.4)	7 (63.6)	0.6
Skin & Soft tissue	13 (26)	8 (61.5)	5 (38.5)	
Urosepsis	8 (16)	5 (62.5)	3 (37.5)	
Culture :				
+ve organism	18 (36)	8 (44.4)	10 (55.6)	
-ve organism	26 (52)	14 (53.8)	12 (46.2)	0.4
Mixed	5 (10)	4 (80)	1 (20)	
Fungal	1 (2)	1 (100)	0 (0)	
Mechanical ventilator :				
- Ventilated	33 (66)	11 (33.3)	22 (66.7)	
- Non ventilated	17 (44)	16 (94.1)	1 (5.9)	0.001*
Diabetes :				
- Positive	23 (46)	7 (30.4)	16 (69.6)	0.002*
- Negative	27 (54)	20 (74.1)	7 (25.9)	

Table (2): Comparison between microorganisms of septic patients in relation to outcome

Organism	N (%)	Survivors N (%)	Non- Survivors N (%)	P value
+ ve organism				
• MRSA	9 (18)	4 (8)	5 (10)	
• Other staph	5 (10)	2 (4)	3 (6)	0.4
• Strepto	2 (4)	1(2)	1 (2)	
• Other (cocci, ..	2 (4)	1(2)	1(2)	
-ve organisms				
o E-coli	8 (16)	3 (6)	5 (10)	
o Pseudomonas	5(10)	3 (6)	2 (4)	
o Klebsiella	5 (10)	3 (6)	2 (4)	
o haemophilus	2 (4)	1(2)	1(2)	0.61
o Proteus	3(6)	2 (4)	1(2)	
o Actinobacter	3 (6)	2 (4)	1(2)	
Mixed	5 (10)	4(8)	1(2)	0.17
Fungal	1(2)	1(2)	none	---

MRSA: Methicillin resistant staph aureus

Table (3): Comparison between age, duration of MV and length of stay of septic patients in relation to outcome.

	Survivors mean ± SD	Non-survivors mean ± SD	P. Value
Age (years)	59.9 ± 13.0	62.8 ± 12.5	0.42
Duration of MV(Days)	2.4 ± 3.1	6.3 ± 3.7	0.001
Length of stay(Days)	11.1 ± 4.1	8.2 ± 3.5	0.01
Mean Difference in DIC*	- 0.33 ± 1.03	1.73 ± 0.915	0.001

*The change from simple DIC score calculated on admission to that calculated 48hr later.

Table (4): Comparison between DIC score (calculated after 48 hours from admission) in septic patients in relation to outcome

	Survivors N (%)	Non-survivors N (%)	P. Value
Simple DIC Score (calculated after 48 hours from admission)			
0			
1	12 (100)	None	
2	13 (100)	None	
3	1 (9.1)	10 (90.9)	0.001
4	1 (9.1)	10 (90.9)	
	None	3 (100)	

Table (5): DIC and SOFA scores of septic patients in relation to outcome

	Survivors	Non-survivors
DIC < 1	25 (100%)	None (0%)
DIC≥ 2	2 (8%)	23 (92%)
SOFA < 5	15 (100%)	None (0%)
SOFA ≥ 5	12 (34,3%)	23 (65,7%)

Table (6): The correlation between the simple DIC score & SOFA (calculated after 48 hours from admission)

	(N) of patients	
	SOFA < 5	**SOFA ≥ 5**
DIC < 1	15 (60%)	10 (40%)
DIC ≥ 2	None	25 (100%)

4. Discussion:

The aim of this present study was to predict outcome in patients with severe sepsis using the simple evolving DIC score calculated in the first 48hrs from two readily available global coagulation markers, platelet count and prothrombin time, and comparing its accuracy with (SOFA) score.

In our study, pneumonia was the most frequent cause of sepsis in ICU (36%), followed by skin and soft tissue infection (26%), then peritonitis (22%) and finally, urosepsis (16%).

The later findings go with Vincent et al, [9], who reported that in patients with severe sepsis, the lung was the most common site of infection 68% followed by the abdomen 22%. Alberti et al,[11] reported that pneumonia contributed to 62% of infections with intra-abdominal infections contributing to 15% of infections. Angus et al.,[7] reported that the lung was the site of infection for 44% of patients with severe sepsis with abdominal infections involved in only 9%. Some earlier studies reported a higher incidence of abdominal infection. Brun- Buisson et al., [12] noting abdominal infection in 32% of 1.052 patients with microbiologically documented infection however pneumonia still contributed to 40% of infections.

In our study, patients with urosepsis had the lowest mortality rate (37, 5%) compared to patients with peritonitis who had the highest mortality rate (63, 6%). Although this finding is statistically insignificant (p=0.5) it can be explained by the PIRO (Predisposing factor, Infectious organism, host Response, Organ dysfunction). Concept in which characters of Infectious insult such as, the site of infection, can influence severity of sepsis response and the patient's likely response to therapy [13].

This go with the data from PROWESS trial of patients with urinary tract infection as a cause of severe sepsis had mortality rate (21%) while patients with pneumonia had a mortality rate (34%) [14].

In our study, all cultures showed growth of an organism with slightly higher frequency of Gram-negative organisms (52%) than Gram-positive organisms (36%) and polymicrobial infection in 10%

of cases. The type of the organism had no impact on the outcome (p=0.4).

These data are comparable to the data of Vincent et al.,[10] (SOAP) study in which cultures showed almost equal frequency of Gram negative and Gram-positive organisms and 18% of infections were polymicrobial but about one third of cultures showed no growth in the SOAP study, this may be attributed to our inclusion criteria which necessitate a documented infection to diagnosis sepsis.

The most common organisms in our study were Staphylococcus aureus (28%, including 18% methicillin-resistant), Escherichia coli (16%), Pseudomonas (10%) and Klebsiella (10%). Inspite of wide variations in microorganism's virulence factors and their susceptibility to antibiotics, no organism in our study appear to be independently associated with increased mortality rate.

Similar results were obtained by Vincent et al., [10] (SOAP) study who reported that, Staphylococcus aureus (30%, including 14% methicillin-resistant), Pseudomonas (14%), Escherichia coli (13%). But in contrast to our finding, Pseudomonas species were independently associated with increased mortality rate. This could be explained by the emerging of more resistant strains of that organism.

This go with data of Antonis et al., [15] who reported that in severe sepsis, gram-positive, gram-negative and other microorganisms produce identical impairment of coagulation.

In our study, about 66% of our severely septic patients develop ARDS defined as ($PaO_2/FiO_2 \leq 200$, bilateral infiltrates on chest radiograph and pulmonary artery wedge pressure $\leq$18mmHg when measured or no evidence of left atrial hypertension) and managed by MV. 66.7% of them died while 94.1% of patients without MV survive their episode of sepsis.

Patients without mechanical ventilation have 13 time chance to survive than those with mechanical ventilation (OR=13 and 95% confidence interval CI= 1.9-95; P<0.001). We also notice a trend towards increased mortality with prolonged periods of MV (P=0.001). This could be explained by higher incidence of complication with prolonged periods as ventilator-associated pneumonia (VAP), the need for tracheostomy and deep venous thrombosis (DVT) with embolization.

Similar results were obtained by Vincent et al., [10] (SOAP) study as patients with MV has increased mortality rate (OR = 7, 95%CI=4.1-12; p<0.001).

These finding go also with the data of Danner et al., [16] and Hudson et al., [17] who reported that incidence of ARDS is 37% and 41% respectively in severely septic patients .

In our study, diabetes mellitus was among the most important risk factors for mortality in septic patients where mortality rate was 69.6% in diabetics while it was 25% in non diabetics (p=0.002).

In the contrary, Leonidou et al., [18] reported that no statistically significant difference in mortality between diabetics and non diabetic patients with severe sepsis. This may be attributed to the inclusion criteria of his study as;

- All diabetic patients included in his study suffered from type II diabetes mellitus.
- Patients with septic shock or diabetic ketoacidosis were excluded from the study.

Also our results contrasted the work of Vincent et al., [10], who reported that the effect of diabetes mellitus on septic patients was statistically insignificant and was associated with just a trend towards higher mortality (p=0.1). This controversy may be attributed to the tight glycemic control strategy applied in the SOAP study which can lessen the deleterious effects of hyperglycemia. But in our study, we still follow the sliding scale regimen.

Our study shows that non- survivors have a shorter length of ICU stay (8.2±3.5 days) compared with survivor (11.1±4.1days). This may be explained by the rapid progression that occurs in some patients.

These finding go with the data of Bertrand et al., [19] who reported that the ICU length of stay was significantly longer in surviving patients (21.8±23.5) than in non surviving patients (18.5±21.6) p<0.001 .

Edbrooke et al., [20], reported an increasing length of ICU stay with increasing severity of septic process, severe sepsis versus sepsis (13.3 versus 12.7 days). However, they found a shorter duration of ICU stay in shock patients (11.6 days).

Our study stated that, the change in simple DIC score from admission to 48hr later (mean difference in DIC) was an accurate predictor of clinical course and may reflect improving or worsening septic process (p=0.001). We chose to award points even when the absolute values of PT and /or platelet count were within normal range but moving in the direction that suggest an underlying coagulopathy. This may highlight the value of change over time rather than single admission score.

This go with the data of Dhainaut et al., [21] who noted that a worsening coagulopathy augers a worse outcome in patients with severe sepsis.

In our study, patient group with simple evolving DIC score $\geq$ 2 (calculated after 48 hours

from admission) appear to have a shorter length of ICU stay which may reflect the severity of the underlying condition. Also they show significant hypoxia (low PaO2/FiO2 ratio) and those who were managed with MV suffer from prolonged period of MV and difficult weaning in comparison to patients with simple DIC score < 2 (P < 0.05).

In our study, higher values of liver enzymes (AST, ALT) were detected in patient group with simple evolving DIC score ≥ 2 (calculated after 48 hours from admission) which demonstrates the strong link between evolving DIC and liver dysfunction which can be summarized in the following points;

- The increase in α-1antitrypsin and α-2-macroglobulin inhibits protein C [(22)].
- C4-binding protein is increased, lowering the levels of free protein S [(22)].
- The synthesis of antithrombin is decreased; In addition, tissue factor expression is increased [(22)].

In our study, almost all patients with simple DIC score ≤ 1 survive their episode of sepsis, while 92% of those who had simple DIC score ≥ 2 develop multiple organ failure and died.

These results are consistent with the work of Kinasewitz et al, [(23)] who reported that a majority (55%) of those with a score ≤1 had a rapid recovery, and overall 86% of these patients survived their episode of sepsis. In contrast, 85% of those with a score of ≥ 2 developed multiple organ failure and about half of those patients died from sepsis.

In our study, we compare the SOFA score with the simple DIC score using cut level 5 for SOFA and 2 for simple DIC score

Simple DIC score ≥ 2 (calculated after 48 hours from admission) shows sensitivity 100% and specificity 92.6% while SOFA score ≥ 5 shows sensitivity 100% and specificity 55.6%. This indicate that simple DIC score is more accurate in predicting mortality in septic patients.

This high sensitivity may be explained by data from the PROWESS trial which indicated that activation of coagulation and inflammatory pathways are virtually universal phenomena in patients with severe sepsis. And this is consistent with experimental primate studies of E.coli sepsis that have demonstrated a strong link between procoagulant activities and inflammation [(24)].

A higher odds ratio 12.5 (OR=12.5, 95% CI=3.3-47.1) was observed in patients with DIC score > 2(calculated after 48 hours from admission). This indicate that patients with simple DIC score > 2 have 12.5 times increased risk to die than those who had DIC < 2, compared to 2.9 times increased risk of death in patients with SOFA score > 5 than those with SOFA score < 5 where odds ratio was just 2.9, (95% CI=1.8-4.6).

In the current study, all patients with simple DIC score ≥ 2 had SOFA score ≥ 5 (calculated after 48 hours from admission), indicating an association between the subtle evolving coagulopathy and the extent of organ dysfunction. The behavior of the coagulation system is a part of the pathophsiology of the septic process not an isolated organ which may fail or not.

This go with the data of Dhainaut et al [(21)] who have suggested that coagulopathy preceded multiple organ failure and that continued coagulopathy during the first day of severe sepsis increases the risk of new organ failure and, ultimately, death.

Shorr et al., [(25)] stated that coagulopathy results in microvascular fibrin deposition responsible for multiple organ failure in severe sepsis.

5. Conclusion:

The simple evolving DIC score calculated in the first 48hrs from two readily available global coagulation markers, platelet count and PT was an accurate predictor of clinical course and outcome in patients with severe sepsis. The power of the simple evolving DIC score may be related to that it scores for the change over time in platelet count and PT, not only for the absolute values of these markers. The simplicity of this score, as it can easily be applied at the bedside as well as the wide availability of its components may help physicians to follow up their patients on daily basis.

References:

1. Levi M, Van Der Poll T, Ten Cate H, et al: The cytokine-mediated imbalance between coagulant and anticoagulant mechanisms in sepsis and endotoxaemia. Eur J Clin Invest; 27:3-9, 1997.
2. Vervloet MG, Thijs LG, Hack CE: Derangements of coagulation and fibrinolysis in critically ill patients with sepsis and septic shock. Semin Thromb Hemost; 24: 33-44, 1998.
3. McGilvray ID. Rotstein OD: Role of the coagulation system in the local and systemic inflammatory response. World J Surg; 22:179-186, 1998.
4. Levi M, Ten Cate H: Disseminated intravascular coagulation. N Engl J. Med; 341: 586-592, 1999.
5. Taylor FB Jr, Toh C-H, Hoots WK, et al: Towards definition, clinical and laboratory criteria and a scoring system for disseminated

intravascular coagulation. J Thromb Haemost; 86:1327-1330, 2001.
6. Taylor FB Jr. Wada H, Kinasewitz GT, et al: Description of compensated and uncompensated disseminated intravascular coagulation (DIC) responses (non-overt and overt DIC) in baboon models of intravenous and intraperitoneal Escherichia coli sepsis and in the human model of endotoxemia: Toward a better definition of DIC. Crit Care Med; 28: S12-S19, 2000.
7. Angus DC, linde-zwirb WT, lidicker J, et al: Epidemiology of severe sepsis in the United states: analysis of incidence, outcome, and associated costs of care. Crit Care Med; 29:1303-1310, 2001.
8. .American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee: Definition of sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med; 20:864-874, 1992.
9. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, Moreno R, Carlet J, Le Gall JR, Payen D: Sepsis in European Intensive Care Units: Results of the SOAP study. Crit Care Med; 34(2):344-353, 2006.
10. Bakhtiari K. meijers JCM. De Jonge E, et al: Prospective validation of the International Society of thrombosis and Haemostasis scoring system for disseminated intravascular coagulation. Crit Care Med: 32: 2416-2421, 2004.
11. Alberti C, Brun-Buisson C, Goodman SV, et al: influence of systemic inflammatory response syndrome and sepsis on outcome of critically ill infected patients. Am J Respir Crit Care Med; 168:77-84, 2003.
12. Brun-Buisson C, Doyon F , Carlet J , et al: Incidence, risk factors, and outcome of severe sepsis and septic shock .A multicenter prospective study in intensive care units. *JAMA*; 274:968-974, 1995.
13. Han X, Fink MP, Delude RL, et al: Proinflammatory cytokine cause NO-dependent and independent changes in expression and localization of tight junction protein in intestinal epithelial cells. Shock; 19:229-237, 2003.
14. Petersen LC, Valentin S, Hedner U, et al: regulation of the extrinsic tissue factor pathway system in health and disease: the role of factor VIIa and tissue factor pathway inhibitor (TFPI). Thromb Res; 79:1-47, 1995.
15. Antonias C, Mavrommatis M, Thodoris T, et al: coagulation system and platelet are fully activated in uncomplicated sepsis. Crit Care Med; 28:451-457, 2000.
16. Danner RL, Elin RJ, Hosseini JM, et al: Endotoxiemia in human septic shock; Chest; 99:169-175, 1991.
17. Hudson LD, Milberg JA, Anardi D, et al: Clinical risks for development of the acute respiratory distress syndrome. Am Rev Respir Dis; 151:293-301, 1995.
18. Leonidou L, Mouzaki A, Michalaki M, et al: Cytokine production and hospital mortality in patients with sepsis-induced stress hyperglycemia. Journal of Infection; 55, 340-346, 2007.
19. Bertrand G,Philippe A, Remy G, et al:: Incidence and Impact of Organ Dysfunctions Associated With SepsisChest.;127:942-951, 2005.
20. Edbrooke DL, Hibbert CL, Kingsley JM, Bright NM, et al: The patient-related costs of care for sepsis patients in a United Kingdom adult general intensive care unit. Crit Care Med, 27:1760-1767, 1999.
21. Dhainaut J-F, shorr AF, Macias WL, et al: Dynamic evolution of coagulopathy in the first day of severe sepsis: relationship between mortality and organ failure. Crit Care Med; 33:341-348, 2005.
22. Christian P.,: Shock liver. Best Practice & Research Clinical Gastroenterology, Vol. 17, No. 3, pp. 369–381, 2003.
23. Kinasewitz GT,Yan SB, Basson B,et al: Universal changes in biomarkers of coagulation and inflammation occure in patients with severe sepsis, regardless of causative microorganism. Crit Care Med;8:R1-R10, 2004.
24. Tylor FB, Wada H, Kinasewitz GT, et al: description of compensated and uncompensated disseminated intravascular coagulation (DIC) response (overt and nonovert DIC) in baboon models of intravenous and intraperitoneal E.coli sepsis Crit Care Med;28:S12-S19, 2000.
25. Shorr AF, Thomas SJ, Alkins SA, et al: D-dimer correlates with proinflammatory cytokines levels and outcomes in critically ill patients. Chest; 121: 1262-1268, 2002.

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