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Correlation Between Degrees of Trauma and Volume of Rescission Fluids with Acute Coagulopathy in Multiple Trauma Patients at Prof. Dr. I.G.N.G Ngoerah Denpasar Hospital

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ABSTRACT

Background: Coagulopathy that occurs in trauma is known as Trauma Induced Coagulopathy (TIC). 1 in 7 deaths caused trauma, and 30% of all trauma patients who came to the hospital were in TIC condition. Prof. Dr IGNG Ngoerah Denpasar Hospital reported that coagulopathy occurred in 24 (39.3%) of 61 multiple trauma patients. ***Objective:*** Proving the correlation between the degree of trauma and volume of resuscitation fluid with the incidence of acute coagulopathy due to multiple trauma. ***Method:*** A retrospective cohort study conducted at Prof. Dr IGNG Ngoerah Denpasar Hospital with secondary data in a medical record from January 2020-December 2021. This study's data analysis consisted of univariate, bivariate, and multivariate analysis using SPSS IBM version 23. ***Results:*** There were 100 subjects where 40 respondents had coagulopathy, the median age was 33.5 years, the male gender was 80%, and the most type of trauma was a head injury. The results of the degrees of trauma with a NISS score (New Injury Severity Score) ≥ 41 increases the incidence of coagulopathy 17.7 times with $p<0.001$ of resuscitation fluid is more than 2 litres increases the risk of developing coagulopathy 27 times in multiple trauma patients with $p<0.001$. In addition, class 3-4 bleeding classification ATLS is known to be 17 times at risk of coagulopathy with $p<0.001$. ***Conclusion:*** There is a statistically significant correlation between an increase in the degree of trauma and NISS≥ 41 and the volume of resuscitation

Keywords: coagulopathy; fluid resuscitation; fluid volume; multiple trauma; NISS.

INTRODUCTION

Coagulopathy, also known as a bleeding disorder, is a condition in which the blood's ability to coagulate or clot to form a thrombus or clot, is impaired. This condition can lead to a tendency for prolonged or excessive bleeding (bleeding diathesis), which can occur spontaneously or after an injury or occur due to an incorrect medical procedure.[1] In Prof. Dr. I.G.N.G Ngoerah Hospital Denpasar showed that with a NISS *cut-off* score of 41, the sensitivity value of NISS was obtained in detecting acute coagulopathy in trauma with a value of 79.2% sensitivity and a specificity value of 91.8%.[2]

Meanwhile, volume handling resuscitation with a limit of 2 liters can increase the incidence of acute coagulopathy due to multiple trauma from research conducted by Wang et al., 2020 with meaningful results with a value of 86% sensitivity and a specificity value of 72%. [3]

There are several factors that influence the occurrence [3] of acute coagulopathy in trauma. The incidence of acute coagulopathy tends to increase as the degree of trauma increases. In addition, the administration of resuscitative fluids can also trigger hemodilution, hypothermia, and acidemia which are associated with the occurrence of acute coagulopathy in trauma. [4]

The gold standard for coagulopathy is a standardized coagulation test (SCT) consisting of *prothrombin time (*PT), *activated thromboplastin time* (aPTT), *platelet count* (PLT), and fibrinogen levels. However, some trauma centers agree on the use of INR > 1.5 and PLT < 100,000 to establish the presence of coagulopathy.[5] Given the high mortality rate of acute coagulopathy due to trauma and the limitations in confirming the diagnosis of coagulopathy using conventional examinations, where examinations such as PT, aPTT, and INR take a long time, efforts are needed to detect the incidence of acute coagulopathy due to trauma early. By describing the relationship between the degree of trauma and the amount of resuscitation fluid given with the incidence of acute coagulopathy due to trauma, it is hoped that data on these two predictor factors can be a reference in detecting acute coagulopathy in trauma early. Seeing this condition, the researcher is interested in knowing the effect of the degree of trauma and fluid administration with the occurrence of acute coagulopathy due to trauma, in addition to limited data and similar research has never been done in Bali, especially at Prof. Dr. I.G.N.G Ngoerah Hospital Denpasar.

METHODS

The research design used was analytic observational with a retrospective cohort approach. This study was conducted at the Department of Surgery FK UNUD / RSUP Prof. Dr. I.G.N.G Ngoerah Denpasar from December 2021 to January 2022 by taking patient medical record data from January 2020 to December 2021. Inclusion Criteria: Patients over 16 years old and diagnosed with multiple trauma (ISS Score >15). Exclusion Criteria: (1) Patients with PTT ≥ 40 seconds or INR ≥ 1.4 on admission; (2) Patients with a history of congenital coagulation disorders; (3) Patients with a history of *chronic liver disease;* (4) Patients with a history of antiplatelet/anticoagulant drug use. Data analysis in this study consisted of univariate analysis (descriptive statistics), bivariate analysis and multivariate analysis assisted by the Statistical Product and Service Solutions (SPSS) program by IBM® Version 26.

RESULT

This study involved 100 patient respondents with multiple trauma with a division of 60 not experiencing coagulopathy and 40 respondents experiencing coagulopathy described based on age, gender, type of trauma, INR, PPT, NISS fluid volume obtained in Table 1 This study in the normality test tested with the *Kolmogorov Smirnov test* found that the data was not found from all variables normally distributed.

TABLE 1: Basic Characteristics of Research Subjects.

Variables		Incidence of coagulopathy			
		No n=60 (%)	**Normality Test***	**Yes n=40 (%)**	**Normality Test***
Age (year)	<30	38 (63,3)	<0.001	29 (72,5)	<0.001
	≥ 30	22 (36,67)		11 (27,5)	
	Median (IQR) min-max	31 (16) 18-60 years old		33.5 (12) 18-60	
Gender	Male	48 (80)	<0.001	32 (80)	<0.001
	Female	12 (20)		8 (20)	
Types of Trauma	Head injury	35 (58,3)	<0.001	25 (62,5)	<0.001
	Abdominal Trauma	8 (13,3)		11 (27,4)	
	Pelvic Trauma	7 (11,67)		2 (5)	
	Extremity trauma	19 (31,67)		15 (37,5)	
	Thoracic Trauma	6 (10)		5 (12,5)	
Arrival time from accident - ER	< 1 hour	37 (61,7)	<0.001	24 (60)	<0.001
	≥ 1 hour	23 (38,3)		16 (40)	
Classification of Hemorrhage	Class 1	31 (51,7)	<0.001	5 (12,5)	<0.001
	Class 2	16 (26,7)		2 (5)	
	Class 3	10 (16,7)		9 (22,5)	
	Class 4	3 (5)		24 (60)	
Hb	< 8	16 (26,7)	<0.001	17 (42,5)	<0.001
	≥ 8	44 (73,3)		23 (57,5)	
GCS	13-15	20 (33,3)	<0.001	8 (20)	<0.001
	9-12	28 (46,7)		15 (37,5)	
	≤ 8	16 (36,7)		17 (42,5)	
Hypothermia	Yes	11 (28,3)	<0.001	8 (20)	<0.001
	No	49 (81,6		32 (80)	
INR	<1,4	60 (100)	<0.001	-	<0.001
	≥ 1,4	-		40 (100)	
	Median (IQR) min-max	0.8 (0.6) 0.3-1.3		1,65 (0,5) 1,4-3	
PTT (seconds)	<40	60 (100)	<0.001	-	<0.001
	≥ 40	-		40 (100)	
	Median (IQR) min-max	30 (7) 20-38		45 (9) 40-60)	
NISS	<41	53 (88,3)		12 (30)	
	≥ 41	7 (21,7)		28 (70)	
	Median (IQR) min-max	35 (5) 20-40		41 (9) 20-50	
Liquid Volume (mL)	< 2000 mL	54 (90)	<0.001	10 (25)	<0.001
	≥ 2000 mL	6 (10)		30 (75)	
	Median (IQR) min-max	750 (700) 200-2500		(2200)250-3000	

Notes: ** Kolmogorov Smirnov*

Based on bivariate analysis using the Chi-squre test (Table 2), the results showed a significant relationship between the incidence of coagulopathy and the NISS score where OR = 17.7 (CI 95% = 6.3-49.9; p = <0.001) which means that NISS ≥ 41 in multiple trauma patients increases the risk of 17.7 times to experience coagulopathy with a range of 6.3-49.9 times compared to NISS scores < 41.

There is a significant relationship between the incidence of coagulopathy and the volume of resuscitation fluid with OR = 27 (CI95% 8.9-81.6; p = <0.001) which means that a volume of more than 2 liters increases the risk of 27 times to experience coagulopathy in multiple trauma patients compared to resuscitation volume < 2 liters.

TABLE 2: Relationship between the incidence of coagulopathy with NISS score and total fluid volume.

Variables		Incidence of Coagulopathy		OR	CI 99%	P*
		No n= 60 (%)	Yes n= 40 (%)			
NISS	<41	53 (88,3)	12 (30)	17,7	6,3-49,9	<0,001†
	≥ 41	7 (21,7)	28 (70)			
Liquid Volume (mL)	< 2000	54 (90)	10 (25)	27	8,9-81,6	<0,001†
	≥ 2000	6 (10)	30 (75)			

Notes: * *Chi-Square;* † statistically significant

Other factors that are thought to affect the risk of coagulopathy are gender and age, the results of which are shown in Table 3.

TABLE 3: Bivariate analysis of other variables on risk factors for coagulopathy incidence.

Variables		Incidence of Coagulopathy		OR	CI 99%	P*
		No n= 60 (%)	Yes n= 40 (%)			
Age (year)	<30	38 (63,3)	29 (72,5)	0,6	0,3-1,6	0,341
	≥ 30	22 (36,67)	11 (27,5)			
Gender	Male	48 (80)	32 (80)	1	0,3-2,7	1.000
	Female	12 (20)	8 (20)			
Arrival time from accident - ER	< 1 hour	37 (61,7)	24 (60)	1,1	0,4-2,4	0,867
	≥ 1 hour	23 (38,3)	16 (40)			
Classification of Hemorrhage	Grades 1-2	47 (78,3)	7 (17,5)	17	6,1-47,3	<0.001
	Grades 3-4	13 (21,7)	33 (82,5)			
Hb grams/dL	≤8	16 (26,7)	17 (42,5)	0,4	0,2-1,2	0,101
	>8	44 (73,3)	23 (57,5)			
GCS	≤8	14 (23,3)	11 (27,5)	1,2	0,4-3,1	0,638
	> 8	46 (76,7)	29 (72,5)			
Hypothermia	Yes	11 (18,3)	8 (20)	1,1	0,4-3,1	0,835
	No	49 (81,7)	32 (80)			

Notes: †Statistically significant; **Chi-Square.*

The results of multivariate analysis with logistic regression were obtained in table 4 with the results the variable that is an independent risk factor for the occurrence of coagulopathy in multiple trauma patients is the volume of fluid with the Adj OR 27 (CI 95% 8.9-81.6; p = <0.001).

TABLE 4: Logistic Regression Multivariate Analysis.

Characteristics	Adjusted OR	95% CI	P*
Step 1			
NISS Score	0	0	0,999
Liquid Volume	339232525873	0	0,999
Classification of Hemorrhage	2,9	0,5-13,5	0,196
Step 2			
Liquid Volume	11,67	2,3-58,5	0,003
Classification of Hemorrhage	2,8	0,6-13,8	0,187
Step 3			
Liquid Volume	27	8,9-81,6	<0,001†

Notes: †Statistically significant; **Chi-Square.*

DISCUSION

This study found that men experienced more multiple trauma with an average age of 35 years. This is in accordance with data from WHO (*World Health Organization*) 2020 which states that multiple trauma occurs more in men, namely 78.6% with an average patient age of 32.5 years. This is because the majority of multiple trauma occurs in young men caused by traffic accidents.[2] The results of other studies are also the same as those of Simmons, Pittet and Pierce, 2014; Simmons and Powell, 2016; Chooi *et al.*, 2020 where most are men in their mid-30s.[6–8]

In this study, the most head injuries occurred. Damage to the parenchyma in the brain is extensive and thromboplastin enters the systemic circulation, causing uncontrolled activation of clotting factors and resulting in systemic coagulopathy or disseminated intravascular coagulation (DIC).[9]

The time of arrival from the incident to the emergency treatment room is known in this study most of them are still with a duration of <1 hour, known from Brohi's research (2007) that the time of injury experienced greatly affects the estimation of thromboplastin and prothrombin time, prothrombin fragment 1-2, fibrinogen, thrombomodulin, protein C, plasminogen activator inhibitor-1, and D-dimer.[10] Basis deficit (BD) was used as a measure of tissue hypoperfusion. Similar results to Brohi's (2007) study found 208 patients had a median time from injury to emergency department arrival of 28 minutes with a min-max (23-29 minutes). The mean time from injury to blood sampling was 32 minutes, there was no use of vasopressors or colloids and patients received an average of 150 - 100 mL of intravenous crystalloid before specimen collection. Acute coagulopathy presents on arrival at the emergency department in approximately one quarter of major trauma patients. Patients presenting with coagulopathy are 4 times more lCIely to die compared to those with normal coagulopathy. This effect is independent of the severity of injury and is therefore unlCIely to be exclusively due to tissue injury and consumption of coagulation factors.[10]

In this study, Hb was still above 8. It is known in Simmon's research, 2016 that hemoglobin <11 is known to affect the incidence of coagulopathy and the risk of mortality. Based on the latest guidelines, red blood cell transfusions should target a hemoglobin between 7-9 grams/dL.

In this study, all were at GCS > 8 and were in moderate consciousness more. In Rau's (2017) study GCS was significantly lower for polytrauma patients than non-polytrauma patients (9.2± 4.6 vs 11.8± 4.2, respectively; P < 0.001).[11] Significantly more polytrauma patients had GCS≤. 8 than non-politrauma patients. The addition of physiologically relevant conditions or pathophysiological changes in the combined AIS/ISS significantly increased the predictive power of mortality. Age, systolic blood pressure (SBP) and Glasgow Coma Scale (GCS) have been reported to have good predictive power for mortality.

An international consensus meeting in 2012 first attempted to define polytrauma by combining the concept of injury in different body regions and physiological response parameters with the addition of at least one of the five standard physiological responses of hypotension ([SBP ≤. 90 mmHg], unconsciousness [GCS score ≤. 8], acidosis [base excess ≤. 6.0], coagulopathy [partial thromboplastin time ≥. 40 seconds or INR≥1.4], and age [≥. 70 years]) in this new "Berlin definition" with the definitions of ISS ≥. 16 and AIS ≥. 3 for at least two body regions, a better definition of polytrauma was determined. Notably, in studies that defined polytrauma as AIS≥. 3 points for two or more different body regions, mortality was 11.4% and 11.0% in polytrauma and non-polytrauma patients, respectively. A mortality rate of 18.7% was found when polytrauma was defined using ISS≥. 16 and the mortality rate increased to 35-38% as soon as one other physiological parameter was added.[11]

Hypothermia in this study only occurred in 8 people who experienced coagulation, hypothermic events can increase bleeding because it disrupts platelet adhesion (due to decreased thromboxane production), dysregulation of coagulation factors and interferes with fibrinolysis. The effect of hypothermia in vivo on coagulation is often not reflected in the parameters of coagulation tests (prothrombin*, activated partial thromboplastin time* and *bleeding time*) because prior to performing the above tests, blood samples are heated in vitro at 37°C. Clinically, hypothermia in trauma can exacerbate coagulation disorders, metabolic acidosis, heart rhythm disturbances and severe electrolyte disturbances.[12]

In this study, it is known that NISS and fluid volume are statistically significant where the results of both with p < 0.001. The results of a significant relationship between the incidence of coagulopathy and the NISS score where OR = 17.7 (CI 95% = 6.3-49.9; p = <0.001) which means that NISS ≥ 41 in multiple trauma patients increases the risk of 17.7 times to experience coagulopathy events with a range of 6.3-49.9 times compared to NISS scores < 41.41 and there is also a significant relationship between the incidence of coagulopathy and the volume of resuscitation fluid with OR = 27 (CI 95% 8.9-81.6; p = <0.001) which means that a volume of more than 2 liters increases the risk of 27 times to experience coagulopathy in multiple trauma patients compared to resuscitation volume < 2 liters.

This study is similar to research by Maegele et al (2007) showing that multiple trauma patients who experience acute coagulopathy have a mean ISS (*injury severity* score) of 30 (±SD 15), while the mean ISS score in patients without coagulopathy is 21 (±SD 12). Coagulopathy occurred in 26% of patients with ISS 16-24), in 42% of patients with ISS 25-49, and in 70% of patients with ISS >50.[4]

New Injury Severity Score (NISS) is a predictor of acute coagulopathy in trauma patients. Research by Antara et al (2017) on 61 multiple trauma patients at Prof. Dr. I.G.N.G Ngoerah Hospital in Denpasar showed that with a NISS *cut-off* score of 41, the sensitivity value of NISS in detecting acute coagulopathy in trauma was 79.2% and a specificity value of 91.8%. Antara, 2017 which is the same as this study.[2]

In this study and the study conducted by Cohen *et al.* (2012), it was found that the amount of resuscitation fluid needed was associated with the presence of coagulopathy. Unbalanced transfusion in patients with massive bleeding will also cause *dilutional coagulopathy* which results in increased bleeding. When a diagnosis of massive bleeding is made, administration of blood products other than red blood cells can prevent the onset of trauma-induced coagulopathy.[13]

The pragmatic, randomized optimal platelet and *plasma ratio* (PROPRR) 2015, conducted on 680 patients at 12 trauma centers in North America, compared plasma, platelet and red blood cell transfusion ratios of 1:1:1 with 1:1:2. Results from this study showed no significant difference in total mortality in the first 24 hours and after 30 days. However, more patients reached hemostatic status in the 1:1:1 group, fewer patients died from exsanguination and it was evident that this transfusion ratio was safe to administer. There was also no difference in the incidence of inflammatory complications such as ARDS, thromboembolism, sepsis and *multiple organ failure.*[12]

In trauma centers, the development and systematic application of transfusion delivery through the development of a *massive* transfusion protocol is essential. In patients known or suspected to require massive transfusion, immediate activation of this protocol will not only result in systematic, efficient, timely and balanced administration of blood and blood products, but will also result in a reduction in the amount of blood used and improve patient prognosis and survival. [12]

Aggressive fluid resuscitation results in poor coagulation, excessive trauma-related *systemic inflammatory response syndrome* (SIRS), increased incidence of adult respiratory distress syndrome (ARDS), pulmonary edema, compartment syndrome, anemia, thrombocytopenia, pneumonia, electrolyte disturbances and overall poor survival. In this study, the most important result was the appropriateness of fluid volume in resuscitation and prevention of acute coagulation based on the results of multivariate analysis which obtained an OR of 27 (95% CI 8.9-81.6; p = 0.001).

This study used a 2-year retrospective cohort study data design with complete data, detailed information from medical records. We have also excluded acute illnesses that may reflect an increase in PTT and INR resulting in coagulopathy. Fluid resuscitation management and NISS score assessment are predictors of coagulopathy and can be used as a prognosis for increased mortality in multiple trauma patients.

The limitation of the study was not recording mortality or survival in patients with coagulopathy after fluid resuscitation and NISS assessment. Researchers also did not include the use of fluids used to perform resuscitation even though it is known that the use of fluid types does not affect the risk of coagulopathy.[14] This study used subjects in certain populations and was conducted in certain places, so the results of this study cannot describe the same conditions in different populations and places. The data obtained is not homogeneous and normal so further research is needed with a prospective cohort.

CONCLUSSION

(1) There was a significant relationship between the degree of trauma and the NISS (*New Injury Severity Score*) score of more or equal to 41 which increased the incidence of acute coagulopathy where NISS ≥ 41 increased the incidence of coagulopathy 17.7 times with p<0.001.

(2) There was a significant relationship between the incidence of coagulopathy and the volume of resuscitation fluid where more than 2 liters of resuscitation fluid increased the risk of coagulopathy 27 times in multiple trauma patients with p<0.001.

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