Evaluation of 4 Ts Score of Heparin Induced Thrombocytopenia as Predictive Value in Acute Lower Limb Ischemia Patients

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ABSTRACT

Background: Acute limb ischemia (ALI) is an abrupt, life-threatening reduction in limb perfusion, prothrombotic effect makes early immune-mediated heparin-induced thrombocytopenia (HIT) identification crucial.

Objective: To evaluate 4 Ts score of HIT; if it could serve as predictive value in acute lower limb ischemia patient. **Patients and Methods:** This prospective observational study included 54 patients with ALI, admitted to Emergency Hospital Mansoura University, who were divided into two groups according to platelet count after heparin therapy: Group I (n=31): normal platelet count after heparin therapy. Group II (n=23): Patients who developed thrombocytopenia after heparin therapy (platelet count <150 - 100×10^9 /L). Pretest scoring system for HIT: the 4 T's was done to all participants.

Results: Patients with thrombocytopenia had highly statistically significantly lower levels of platelet count, hemoglobin and hematocrit % when compared to patients with normal platelet count (at fifth day) after heparin therapy. There was highly statistically significantly of 4 Ts score among both studied groups thus, it was higher in thrombocytopenia group. Group II after heparin therapy: all cases complained of thrombocytopenia, bleeding in 8 (34.8%) and thrombosis in 8 (34.8%). Sensitivity, specificity, positive predictive value, and negative predictive value for heparin-induced thrombocytopenia as a predictor of outcome in patients with acute lower limb ischemia were 93.5%, 87.1%, 91.2%, and 92.3%, respectively, with an accuracy of 91.5% for this group of patients.

Conclusion: One easy, accurate, and inexpensive way to identify patients at varied risk of HIT is to apply a clinical model to evaluate the pretest probability of HIT.

Keywords: 4 TS score, HIT, Acute lower limb ischemia.

INTRODUCTION

Acute limb ischemia is an abrupt, life-threatening reduction in limb perfusion. New or increasing intermittent claudication, foot or leg discomfort at rest, paresthesias, muscular weakness, and paralysis of the afflicted limb develop over hours to days ⁽¹⁾. Weakness, poor sensation, cold, pale, or mottled skin, lack of pulses beyond the blockage, and diminished sensation. Paralysis, paresthesia, pain, pallor, pulselessness, poikilothermia (poor body temperature regulation, with the limb generally chilly), and compromised circulation are the six Ps of acute limb ischemia ⁽²⁾.

Trauma (from artery severing or thrombosis), dissection, embolism (in the heart or arteries), or arterial or bypass graft thrombosis are the main causes of acute limb ischemia. Thrombosis in the limb arteries is more common in atherosclerotic plaques ⁽³⁾.

Acute peripheral artery occlusion in the lower extremities may lead to amputation if not treated quickly. Thrombolytics may be administered alone, but recanalization leaves the vessel disease-free ⁽⁴⁾.

Immune-mediated HIT does not produce bleeding, rather a paradoxical prothrombotic state. This prothrombotic effect makes early HIT identification crucial ⁽⁵⁾. HIT often begins 5 to 10 days after heparin is given, both for new and re-exposed patients. IgG antibodies recognise neoepitopes on positively charged PF4 in PF4–polyanion complexes, causing HIT ⁽⁶⁾.

Immune complexes activate platelet (Fc RIIa) and monocyte (Fc RI) Fc receptors. Platelets and monocytes activated by endothelial cells stimulate thrombin production. Increased thrombin causes clinical issues, not thrombocytopenia ⁽⁷⁾.

The 4Ts, a grading system for HIT pretests, is one instrument that can enhance clinical diagnosis. Hemolytic thrombocytopenia (HIT) is characterized by a small platelet count, occurs at a specific time after heparin administration, can lead to thrombosis or other problems, and may have other causes ⁽⁸⁾. The approach indicates low, moderate, and high HIT pretest likelihood with scores 0-3, 4-5, and 6-8, respectively, on an integer scale from 0 to 8. The 4Ts have been observed in multiple single-center encounters. The generalizability of these studies to different settings and populations of patients is debatable ⁽⁹⁾.

HIT is effectively excluded with an unlikely 4Ts score. Overdiagnosis, overtreatment, and overtesting of HIT may all be reduced by implementing the 4Ts. It is necessary to compare this approach with diagnostics based on gut feelings. A standardized clinicopathologic reference standard, clinical provider ratings instead of study personnel, and a standardized 4Ts protocol are all ways to improve upon previous trials ⁽¹⁰⁾.

Objectives: To evaluate 4 TS score of HIT; if it could serve as predictive value in acute lower limb ischemia patient.

PATIENTS AND METHODS

This prospective observational study included 54 cases who had ALI and were admitted to Emergency Hospital Mansoura University from July 2023 till February 2024. They were classified into two groups

according to platelet count after heparin therapy: Group I (n=31): normal platelet counts after heparin therapy. Group II (n=23): Patients who developed thrombocytopenia after heparin therapy (platelet count $<150 - 100 \times 10^9$ /L).

Inclusion criteria: Patients of both genders over 18 years old, with symptoms of acute lower-limb ischemia: the 5 Ps-acute onset of progressive pain in the affected limb, pain on passive extension of the affected limb, pulselessness, pallor, paresthesia, paralysis. Arteriographically confirmed complete occlusion of arteries of lower limb.

Exclusion criteria: People who suffer from severe, uncontrolled hypertension and whose blood pressure readings consistently show a systolic of 180 mm Hg or higher or a diastolic of 110 mm Hg or higher, previous ischemic strokes (TIAs) within the last two months or cerebrovascular accidents within the last six months, severe internal hemorrhage within a week, within the past fourteen days, patients have experienced severe internal bleeding, undergone major surgery, had an organ biopsy, perforated non-compressible veins, or suffered severe trauma. In cases where angiography, intraarterial thrombolytic treatment, or surgery would be inappropriate, platelet count below 150 to $100 \times 10^9/L$ in pregnant women.

All cases had been subjected to the following: A.Full history taking: Name, age, sex, precipitating factor including duration of lesions, the patient's history of treatment, the patient's response to treatment, the patient's diabetes type (non-insulin requiring or insulin requiring), the patient's current cigarette use, the patient's COPD severity, the patient's current heart failure, the patient's blood pressure, the patient's disseminated cancer, the patient's chronic steroid use, the patient's weight loss (greater than 10% within six months prior to the operation), and the patient's bleeding disorder.

Complete general examination: With a mercury sphygmomanometer, we measured each patient's blood pressure as they lay in bed with one arm supported and one foot on top of their heart. We also carefully noted each patient's temperature, respiration rate, pulse, and mental status as part of our thorough physical examination. Body mass index, height, and weight were all examples of anthropometric measures.

Vascular examination: All patients were examined for the end level of pulsation, hard and soft signs.

Laboratory investigations:

The clinical pathology and laboratory procedures followed by the hospitals affiliated with Mansoura University, were the basis for all of these investigations, which comprised: Fully automatic blood counter for complete blood count. The term "thrombocytopenia" was used to describe a platelet count below 150×10^{9} /L. Patients with this condition were categorized into several severity levels based on the extent of their thrombocytopenia: mild ($<150 - 100 \times 10^9/L$), moderate $(<100 - 50 \times 10^{9}/L)$, severe $(<50 - 20 \times 10^{9}/L)$, and very severe ($<20 \times 10^{9}$ /L). Laboratory evaluations of liver and renal function, including blood creatinine and urea levels Information on the rate of bleeding: international normalized ratio (INR), prothrombin time (PT), partial thromboplastin time (PTT), and random blood glucose. On days one, five, and ten, platelet counts were taken $^{(11)}$.

Radiological evaluation: diagnostic imaging procedures, such as a pelviabdominal ultrasonography, a CT angiography of the lower extremities, or an arterial duplex ultrasound of the diseased leg performed by radiology professionals. While in the hospital, any additional tests that may be necessary was done. **4 Ts Score:**

Table (1): Pretest scoring system for HIT: the 4 T's ⁽¹²⁾ .							
4Ts category	2 points	1 point	0 points				
Thrombocytopenia	Platelet count fall $> 50\%$ and	Platelet count 30%-50% or platelet	Platelet count fall < 30%				
	platelet nadir ≥ 20	nadir 10-19	or platelet nadir < 10				
Timing of platelet	Clear onset days 5-10 or	Consistent with days 5-10 fall, but not	Platelet count \leq 4 days				
count fall	platelet fall ≤ 1 day (prior	clear (eg, missing platelet counts);	without recent exposure				
	heparin exposure within 30	onset after day 10; or fall ≤ 1 day					
	days)	(prior heparin exposure 30-100 days					
		ago)					
Thrombosis or other	New thrombosis (confirmed);	Progressive or recurrent thrombosis;	None				
sequelae	skin necrosis; acute systemic	non-necrotizing (erythematous) skin					
	reaction postintravenous	lesions; suspected thrombosis (not					
	unfractionated heparin bolus	proven)					
Other causes of	None apparent	Possible	Definite				
thrombocytopenia							

When all four categories' scores are added together, the result is the 4Ts score. A low risk of HIT is indicated by a score of 1-3, whereas an intermediate probability is indicated by 4-5. 6-8 is thought to indicate a significant likelihood of HIT $^{(12)}$.

Ethical approval:

The Ethics Committee of the Faculty of Medicine at Mansoura University approved the study. Each participant received a full summary of the study's aims prior to signing an informed consent form. The Helsinki Declaration was followed at all stages of the inquiry.

Statistical analysis

Software developed by SPSS Inc. of Chicago, Illinois, USA, specifically for Windows, version 25.0, was used to analyze all of the data. Quantitative data were presented as mean, standard deviation (SD) and were compared by independent t-test to compare 2 groups and by one-way ANOVA test to compare more than 2 groups. Qualitative data were presented as frequency and percentage and were compared by Chisquare test and Fisher's exact test as needed. Dependent variables were analyzed using binary logistic regressions. We utilized Pearson's product-moment correlation coefficient to evaluate the relationship between continuous parametric variables and Spearman's rank correlation coefficient (Spearman's rho) to determine the relationship between nonparametric criteria. A significant p-value was considered when it is equal or less than 0.05.

RESULTS

Given that the two groups were comparable with respect to age, sex, and all comorbidities considered, it is clear from the data that no statistically significant difference existed between them. When looking at the groups side by side, history of antiplatelet therapy and anticoagulant therapy were significantly different (Table 2).

Variables	Normal Platel Group I (No	et count ().= 31)	Thrombocytopenia Group II (N=23)		t-test	P value
	Mean ±S	SD		Mean ±SD		
Age	55.3 ± 6 .	7 1		52.8 ± 10.21	0.785	0.47
Sex	Ν	%	N	%	\mathbf{X}^2	p-value
Male	23	74.1	18	78.2		
Female	8	25.9	5	21.8	Fisher	1.0
Smokers	18	58	15	65.2	0.284	0.594
Diabetic cases	26	83.8	19	82.6	Fisher	1.0
Hypertensive	17	54.8	14	60.8	0.196	0.657
Dyslipidemia	29	93.5	21	91.3	Fisher	0.643
Respiratory disorder						
No	27	87	20	86.9		
COPD	4	13	2	8.6	Fisher	0.647
ILD	0	0.0	1	4.4		
Cardiac disease	20	65.5	9	39.1	3.42	0.064
Liver disease						
No	26	83.8	22	95.6	3.04	0.034
Fatty liver	5	16.1	0	0.0		
Cirrhosis	0	0.0	1	4.4		
History of antiplatelet	4	13	9	39.1	4.97	0.026
therapy						
History of	5	16.1	15	65.2	13.64	< 0.001
anticoagulant therapy						

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Table	(7).	Domogra	nhia data	omong	hoth	atudiad	GHOIDG
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Patients with thrombocytopenia had much lower platelet counts than the general population. On the fifth day following heparin treatment, individuals with thrombocytopenia had considerably lower levels of platelets, hemoglobin, and hematocrit % compared to those with normal platelet counts. At the tenth day following heparin treatment, patients with thrombocytopenia had significantly lower levels of hemoglobin, hematocrit %, and platelet count compared to individuals with normal platelet count (Table 3).

Table (3): Baseline of CBC (at first day), changes CBC (at fifth day) and changes CBC (at 10^{th} day) in the two studied groups after heparin therapy.

	Normal Platelet count Group I (No.= 31)	Thrombo- cytopenia Group II (N=23)	Т	Р			
	Mean± SD	Mean± SD					
PLT (× 10 ⁹ /L)	294 ±72.4	283 ±69.1	0.563	0.283			
Hb (g/dl)	10.6 ± 2.3	10.9 ± 2.1	0.492	0.625			
HCT %	31.4 ± 7.4	33.3 ± 7.6	0.922	0.361			
WBC (× 10 ⁹ /L)	13.6 ± 3.2	14.3 ± 3.4	0.774	0.442			
Changes CB	C (at fifth day after hepari) in the two st n therapy	udy gi	oups			
PLT (× 10 ⁹ /L)	284 ±69.3	190 ±45.3	5.662	0.001			
Hb (g/dl)	10.3 ± 2.2	10.8 ± 2.6	0.764	0.448			
HCT %	30.1 ± 7.4	33.3 ± 7.6	1.553	0.126			
WBC (× 10 ⁹ /L)	12.6 ± 3.1	14.3 ± 3.5	1.886	0.065			
Changes CBC (at 10 th day) in the two study groups after heparin therapy							
PLT (× 10 ⁹ /L)	254 ±61.8	90 ±21.6	12.69	<0.001			
Hb (g/dl)	9.7 ± 2.2	8.8 ± 2.1	1.515	0.136			
HCT %	29.9 ± 6.9	30.3 ±7.2	0.207	0.837			
WBC (× 10 ⁹ /L)	14.6 ± 3.4	14.3 ± 3.3	0.325	0.747			

Hb: hemoglobin, PLT: platelets, HCT: hematocrit, WBCs: white blood cells.

There was highly statistically significant decrease of platelet count, hemoglobin concentration and hematocrit value in Group II after heparin therapy (Table 4).

Table (4):	Changes	of	CBC	findings	in	Group	II
after hepar	in therap	y.					

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	At first	At fifth	At tenth		
	day	day	day		
	(M±S.D)	(M±S.D)	(M±S.D)	Т	Р
Platelets	283	190	00 121 6	1 79	-0.001
$(\times 10^{9}/L)$	±69.1	±45.3	90 ± 21.0	4.70	<0.001
Hemoglobin	10.9 ±	10.8 ±	00101	5.0	-0.001
(g/dl)	2.1	2.6	0.0 ± 2.1	5.0	<0.001
Hematocrit	33.3	33.3	30.3	5.05	-0.001
%	±7.6	±7.6	±7.2	5.05	<0.001
WBC	14.3 ±	14.3 ±	14.3 ±	0.05	0.001
$(\times 10^{9}/L)$	3.3	3.5	3.3	0.95	0.891

There was highly statistically significant difference of 4 Ts score among both studied groups thus, the score was higher in thrombocytopenia group (Table 5).

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4 Ts Score	Group I	Group II
	(No.= 31)	(N=23)
Low (1-3)	31(100%)	2(8.6%)
Intermediate (4-5)	0(0%)	11(47.8%)
High (6-8)	0 (0%)	10 (43.6%)
Total (%)	31(100%)	23(100%)

As regard clinical manifestations of HITs in Group II after heparin therapy, all cases had thrombocytopenia (Table 6).

Table (6): Clinical manifestations of HITs in Group
II after heparin therapy(N=23).

Variable	Group II (N &%)
Thrombocytopenia	23(100%)
Bleeding	15(65.2%)
Thrombosis	8 (34.8%)
Timing of typical presentation	20(86.9%)
(5-9 days)	
Delayed-onset HIT following	3(13.1%)
withdrawal of heparin	

Most common complication of HITs in Group II after heparin therapy was infarction (Table 7).

Table (7): Complications of HITs in Group II after heparin therapy (N=23).

Variable	Group II (N &%)
Skin necrosis	7(30.4%)
limb gangrene	4 (17.4%)
Infarction	10(43.4%)
Death	1(4.3%)

Table 8 shows that age>60, history of antiplatelet therapy, history of anticoagulant therapy, platelet count<100.000, 4 Ts score, Rutherford's category, Fontaine's grade, and dyslipidemia were independent risk factor for unfavorable outcome on patients with acute lower limb ischemia (P<0.05) (Table 8).

Risk factor	95% CI		Expected	r	р
	Lower	Upper			
Age>60y	2.14	38.131	9.033	8.972	0.03
DM	0.327	4.353	1.193	0.71	0.789
HTN	0.784	37.38	5.413	2.935	0.087
History of antiplatelet	1.211	11.069	3.347	4.849	0.01
therapy					
History of anticoagulant	0.65	1.974	0.435	6.212	0.01
therapy					
Liver functions	0.415	4.824	1.414	0.306	0.58
Type of ischemic lesion	0.478	7.488	1.892	0.825	0.36
Dyslipidemia	1.313	15.059	4.447	5.749	0.01
Platelet count<100.000	0.77	1.784	0.245	5.612	0.001
4 Ts Score	0.011	2.079	0.154	1.986	0.003
Rutherford's category	1.412	14.059	5.447	6.849	0.01
Fontaine`s grade	0.65	1.984	0.415	4.682	0.01
Clinical presentations	0.292	1.539	0.676	0.872	0.35

Table (8): Cox regression	analysis for	risk factors	associated	with	unfavorable	outcome i	n patients	with acute
lower limb ischemia:								

The 4 Ts score of heparin-induced thrombocytopenia was found to be a valid predictor of outcome in patients with acute lower limb ischemia. The specificity, sensitivity, positive predictive value, and negative predictive value are shown in table 9 and figure 1.

 Table (9): Assessing the predictive value of the 4 Ts score of heparin-induced thrombocytopenia in patients with acute lower limb ischemia

Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
≥4	93.5	87.1	91.2	92.3	91.5%



Figure (1): Receiver-operating characteristic (ROC) curve for 4 Ts score of heparin-induced thrombocytopenia in prediction of outcome of acute lower limb ischemia patients.

DISCUSSION

Acute limb ischemia is an abrupt, life-threatening reduction in limb perfusion. New or increasing intermittent claudication, foot or leg discomfort at rest, paresthesias, muscular weakness, and paralysis of the afflicted limb develop over hours to days ⁽¹⁾. Immune-mediated heparin-induced thrombocytopenia (HIT) often begins 5 to 10 days after heparin is given, both for new and re-exposed patients. IgG antibodies recognise neoepitopes on positively charged PF4 in PF4– polyanion complexes, causing HIT ⁽⁶⁾.

Regarding patients' characteristics, in our study the age was distributed as 55.3 ± 6.71 and 52.8 ± 10.21 respectively between groups with no significant difference, also there was no significant difference regarding sex distribution (23 males and 8 females versus 18 males and 15 females in group I and group II respectively).

As regard to predisposing factors and medical history; in our study (83.8%) versus 82.6% were diabetic in the first and second group respectively, (54.8% versus 60.8%) were hypertensive in the first and second group respectively, (58% versus 65.2%) were smokers in first and second group respectively. As regard CVD (65.5% versus 39.1%) had cardiac disease in the first and second group respectively, and (93.5% versus 91.3%) had hyperlipidemia in the first and second group respectively.

In agreement with **our results, Naoum** *et al.* ⁽¹³⁾ found that heparin-induced thrombocytopenia (HIT) was found in 29% of diabetic patients compared to 25% of non-diabetic patients; this finding suggests that diabetes increases the risk of HIT. Because of the increased risk of peripheral arterial disease and vascular complications in diabetic patients, as well as the fact that these patients may be in a more advanced stage of platelet aggregation and cytokine activation, this finding may impact the decision to use anticoagulation in these patients. The incidence of DM patients who had HIT in this study is lower than our study. This may due to difference in patients' groups as in previous study the populations were DM with ESRD undergoing hemodialysis,

Also, **Kaur** *et al.* ⁽¹⁴⁾ found that overweight, a history of cancer, diabetes, renal failure, major surgery, congestive heart failure, autoimmune diseases, and significant bleeding are additional risk factors for HIT in adults hospitalized for a variety of medical conditions.

In the current study, as regard clinical manifestations of HITs in Group II after heparin therapy; all cases complain of thrombocytopenia, bleeding occurred in 8 (34.8%) and thrombosis in 8 (34.8%)

Smith *et al.* ⁽¹⁵⁾ reported that patients diagnosed with HIT often experienced several thrombotic episodes in both veins and arteries. Nearly half of all HIT patients initially experienced a thrombosis; deep vein

thrombosis (DVT) accounted for 48% of these sequelae, while percutaneous embolism (PE) accounted for 25%.

Medical and surgical patients might develop thrombocytopenia for several reasons. But now, depending on the clinical syndrome, a prediction scale can assess the probability of HIT ⁽¹⁶⁾.

The 4 Ts score for heparin-induced thrombocytopenia was found to be valid in this study with sensitivity of 93.5%, specificity of 87.1%, positive predictive value of 91.2%, and negative predictive value of 92.3% in patients with acute lower limb ischemia, and an accuracy rate of 91.5%.

According to a meta-analysis and systematic review of the 4Ts' predictive value, a low likelihood score (≤ 4) was associated with a high net present value (NPV) of 99.8 percent for HIT. With a positive predictive value of 95.8% and a negative predictive value of 97.4%, the sensitivity was 94.4% and the specificity was 88.1% ⁽¹⁷⁾.

Conversely, the prevalence rate has little effect on specificity and sensitivity. In the group with 4 T \geq 4, the sensitivity of the 4 Ts score for detecting thrombocytopenia caused by heparin was 82.4% (95% Ci 56.6-96.2) ⁽¹⁸⁾. Although the overall specificity for 4Ts \geq 4 was only 41.6%, a previous prospective study indicated a sensitivity of 97% (95% CI 86.2-99.8). 4Ts \geq 6 had a significantly better specificity of 84% and overall accuracy of 78%, proving the vital usefulness of clinical grading ⁽¹⁹⁾.

Linkins *et al.* ⁽²⁰⁾ found the reverse to be true for a prospective study that examined the reliability of the 4Ts score estimation in conjunction with the HIT antibody test. Among those with low 4Ts scores, 1.9% were diagnosed with HIT; among those with intermediate scores, 6.7%; and among those with high scores, 36.6%.

Results showed that 4Ts 0-3 and negative HIT Ab had a PPV of 0, indicating a more effective criterion for ruling out HIT, in addition to being in the low-risk category alone. In a prospective study of MICU patients, this finding was in agreement with those of **Nagler** *et al.* ⁽²¹⁾. According to our findings, patients with 4Ts values of 4 or 6 did not necessarily have a positive HIT Ab test, and the reverse was also true. This finding brings to light an additional issue with the present testing protocol, which suggests not doing any additional SRA tests if a patient tests negative for HIT Ab ⁽²²⁾.

Those in the study who would have tested positive for HIT Ab were partially overlapped with those who were deemed to be at intermediate or high risk according to clinical criteria. Accordingly, these two tests may be able to generate separate predictions. Patients with HIT were included in the study if they met the selection criteria of having $4 \text{ T} \ge 4$ or a positive HIT Ab test. Therefore, we advise that in cases where an HIT antibody test comes back negative, patients in the intermediate or high-risk category who are suspected of having HIT should still undergo SRA testing ⁽²²⁾.

The particle immuno-filtration assay (PIFA) found that a large percentage of the individuals in this study had an antibody against heparin/platelet factor 4 (HPF4). When compared to an ELISA assay (statistics found on the package insert), the assay has a sensitivity of 91.3%, specificity of 98%, and overall agreement of 97.2%; furthermore, it offers the benefit of quick sameday data turnover. To this day, the study's sensitivity remains at 60% and its NPV is at 96.7%. Because of its poor PPV (only 10%) and rapid turnover rate, this test requires an ideal NPV to compensate. It won't outperform the ELISA test till then. Since the rapid test incorrectly identified two patients as having HIT, it is evident that it is not as good as the ELISA assay ⁽²²⁾, a positive ELISA assay (OD >0.4) had a sensitivity of 100% and NPV, whereas the subgroup with $OD \ge 1$ had a PPV of 50% and an overall accuracy of 91.1%. According to these findings, a negative result for HIT antibodies by the PIFA fast test cannot be relied upon as conclusive proof that HIT is not present.

Based on our research, the 4Ts score has the potential to guide the first assessment and treatment of individuals suspected of having HIT, while also reducing the likelihood of unnecessary testing and treatment. We suggest that individuals with a low probability 4Ts score may be able to continue taking heparin without HIT testing or therapy, given the strong NPV of the model.

Since **Cuker** *et al.* ⁽¹⁷⁾ found a low likelihood 4Ts score in their meta-analysis, which is consistent with the current study, it is likely that implementing such a decision rule will significantly reduce testing and unneeded treatment. Withdrawal of heparin, start of an alternate anticoagulant, and acquisition of HIT laboratory tests are recommendations for patients with intermediate or high likelihood scores.

Thrombocytopenia was associated with a higher 4 Ts score, which was statistically significant in the present study.

In 2011, researchers in Egypt looked at heparininduced thrombocytopenia (HIT) in patients to see how well the 4Ts clinical scoring system worked as a pretest probability strategy for detecting HIT. Of the patients surveyed, 16 (or 32% of the total) had low 4T scores, 26 (or 52% of the total) had intermediate scores, and just 8 (16%) had high scores. In order to rule out HIT, they discovered that a low 4T's score had a negative predictive value of 100%. The likelihood of HIT is low when the 4Ts score is low ⁽²³⁾.

CONCLUSION

Improving the process of identifying individuals at various risk of HIT, using a clinical model to predict the pretest probability of HIT is easy, accurate, and inexpensive. Incorporating the 4Ts into the examination and beginning management of patients suspected of having HIT may decrease the likelihood of overtesting, overdiagnosis, and overtreatment of this condition, as our results indicate that a low probability score for the 4Ts can be used to rule out HIT.

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REFERENCES

- 1. McNally M, Univers J (2018): Acute limb ischemia. Surgical Clinics, 98(5): 1081-1096.
- 2. Olinic D, Stanek A, Tătaru D *et al.* (2019): Acute limb ischemia: An update on diagnosis and management. J Clin Med., 8(08):1215-19.
- **3.** Kolte D, Parikh S, Piazza G *et al.* (2019): Vascular teams in peripheral vascular disease. Journal of the American College of Cardiology, 73(19): 2477-2486.
- 4. Osawa E, Brandão A, Américo A *et al.* (2022): Fondaparinux for systemic anticoagulation during continuous hemofiltration in a patient with heparininduced thrombocytopenia and limb ischemia-a case report. Hematology, Transfusion and Cell Therapy, 44: 108-111.
- 5. Hogan M, Berger J (2020): Heparin-induced thrombocytopenia (HIT): Review of incidence, diagnosis, and management. Vascular Medicine, 25(2): 160-173.
- 6. Warkentin T, Greinacher A (2022): Heparin-induced thrombocytopenia. Practical Transfusion Medicine, 22: 187-205.
- 7. Rauova L, Arepally G, Poncz M *et al.* (2018): Molecular and cellular pathogenesis of heparin-induced thrombocytopenia (HIT). Autoimmunity Reviews, 17(10): 1046-52.
- 8. Bloom M, Johnson J, Volod O *et al.* (2020): Improved prediction of HIT in the SICU using an improved model of the Warkentin 4-T system: 3-T. The American Journal of Surgery, 219(1): 54-57.
- **9.** Avila L, Amiri N, Yenson P *et al.* (2020): Heparininduced thrombocytopenia in a pediatric population: implications for clinical probability scores and testing. The Journal of Pediatrics, 226: 167-172.
- **10.** Brodard J, Alberio L, Angelillo-Scherrer A *et al.* (2020): Accuracy of heparin-induced platelet aggregation test for the diagnosis of heparin-induced thrombocytopenia. Thrombosis Research, 185: 27-30.
- **11.** Sharma B, Sharma M, Majumder M *et al.* (2007): Thrombocytopenia in septic shock patients--a prospective observational study of incidence, risk factors and correlation with clinical outcome. Anaesth Intensive Care, 35(6):874-880.
- 12. Warkentin T, Heddle N (2003): Laboratory diagnosis of immune heparin-induced thrombocytopenia. Curr Hematol Rep., 2: 148-57.
- **13.** Naoum J, Chamoun N, Patel M *et al.* (2014): Elevated heparin-induced antibodies are more common in diabetic patients with vascular disease. Thrombosis, 14: 649652. doi: 10.1155/2014/649652.
- 14. Kaur J, Arsene C, Yadav S *et al.* (2021): Risk factors in hospitalized patients for heparin-induced thrombocytopenia by real world database: A new role for primary hypercoagulable states. J Hematol., 10(4): 171-177.
- **15.** Smith B, Joseph J, Park P (2017): Heparin-induced thrombocytopenia presenting as unilateral lower limb

paralysis following lumbar spine surgery: case report. J Neurosurg Spine, 26: 594–597.

- **16.** Cuker A (2014): Clinical and laboratory diagnosis of heparin-induced thrombocytopenia: an integrated approach. Semin Thromb Hemost., 40:106–114.
- **17.** Cuker A, Gimotty P, Crowther M *et al.* (2018): Predictive value of the 4Ts scoring system for heparininduced thrombocytopenia: a systematic review and meta-analysis. Blood, 120: 4160-67.
- **18. Pishko A, Fardin S, Lefler D** *et al.* (2018): Prospective comparison of the HEP score and 4Ts score for the diagnosis of heparin-induced thrombocytopenia. Blood Advances, 2(22):3155–3162.
- **19.** Lo G, Juhl D, Warkentin T *et al.* (2006): Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. J Thromb Haemost., 4(4):759–765.

- **20.** Linkins L, Bates S, Lee A *et al.* (2015): Combination of 4Ts score and PF4/H-PaGIA for diagnosis and management of heparin-induced thrombocytopenia: prospective cohort study. Blood, 126(5):597-603.
- **21.** Nagler M, Bachmann L, Cate H *et al.* (2016): Diagnostic value of immunoassays for heparin-induced thrombocytopenia: a systematic review and meta-analysis. Blood, 127(5): 546-557.
- 22. Greinacher A (2015): Clinical practice. Heparininduced thrombocytopenia. N Eng J Med., 373(3): 252– 261.
- **23.** Tawfik N, Hegazy M, Hassan E *et al.* (2011): Egyptian experience of reliability of 4T's score in diagnosis of heparin induced thrombocytopenia syndrome. Blood Coagul Fibrinolysis, 22(8): 701-705.