

Supplemental File 5: Study Characteristics Tables

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3.1.a. Heparin discontinuation vs parenteral non-heparin anticoagulant

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Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on--- ?	Laboratory test for diagnosis	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT, etc.)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Al-Eidan 2018	Retrospective Cohort	General HIT	39 Fondaparinux, 56 Argatroban	NA	95	ELISA results	ELISA, CrCl	Yes \geq 1.0 was considered positive	Isolated HIT	Death, Major bleeding, Limb amputation, Thromboembolic complication (DVT, PE, DVT&PE, Arterial thrombosis)
Al-Rossaies 2011	Retrospective Cohort	General HIT	Fondaparinux, lepirudin	NA	Fondaparinux (n = 5) Lepirudin (n = 7)	Platelet count	Immune assay test	NR	Acute HIT	Death not related to HIT, No recurrent thrombotic events
Bethea BT 2017	Case Report	Hypertrophic cardiomyopathy, coronary artery disease, hypertension, chronic diastolic heart failure, and atrial flutter and a large thrombus in the main and descending pulmonary arteries.	Argatroban, and converting to Rivaroxaban	Cardio-vascular catheterization	1	Reduced platelet count, 4Ts score	ELISA, SRA	Optical density ratio of 2.838 (a positive result is defined as an optical density ratio of >1)	HITT	Increasing size of thrombus

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Chong 2001	RCT	General HIT	Danaparoid: 25, Dextran 70: 17	NA	42	Platelet count	Immune assay test	NR	Acute HIT	New Thrombosis, Deaths, Major Bleeding, adverse events
Davis 2017	Case Series	General HIT (VTE prophylaxis, AF and Dialysis)	apixaban, dabigatran, rivaroxaban.	NA	12	4T score ≥ 4	positive IgG-specific anti-PF4/heparin complex assay, SRA	Mean OD using the anti- PF4 assay was 1.66 units (range 0.24-3.34 units) (Positive OD= >0.4 and $>50\%$ inhibition with heparin. Negative=OD <0.4 or $<5\%$ heparin inhibition considered normal		Eleven patients continued DOAC following hospital discharge. One patient discontinued DOAC prior to discharge. No patients experienced thrombotic related event or major bleed while receiving DOAC therapy.
Ezekwudo 2017	Case Report	Endocarditis and Cardiac surgery	Argatroban and apixaban	Cardiac surgery	1	Drop in Platelet count	4Ts score, ELISA. SRA	positive value of 1.131 (OD)(negative reference range 0.000–0.399)	HITT	no reported bleeding or thrombosis 3 months later.
Fraielli 2019	Case Report	Factor V Leiden undergo neurosurgery and post surgery PE	Argatroban, Fondaparinux to warfarin	NA	1	Drop in Platelet count	4Ts score, SRA	NR	HITT	No bleeding nor new thrombotic complications were noted throughout the hos-

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Gleichgerricht 2017	Case Report	Post surgery HIT plus ITP	Argatroban, Warfarin and IVIG	NA	1	Drop in Platelet count	4Ts score, ELISA, SRA	optical density of 3.032 absorbance units (normal<0.4OD)	HITII	Intracranial thrombosis, at the time of discharge all neurologic and cognitive problem resolved
Gonzales 2019	Case Report	Post mastectomy surgery HIT	IVIG, Argatroban, bivalirudin, methylprednisolone and warfarin	NA	1	Drop in Platelet count	4Ts score, ELISA, SRA	(2.69 OD)	HIT II	Discharged
He 2018	Case Report	General HIT	Fondaparinux, Argatroban	Orthopedic surgery	1	Drop in Platelet count	4Ts score	NR	HIT II	Platelet recovery and no bleeding
Ito 2018	Case Report	ECMO and	Argatroban, Warfarin	NA		Drop in Platelet count	4Ts score, anti-PF4/heparin enzyme immunoassays		HITT	3 month FU normal Plt count,
Joseph 2014	Retrospective Cohort	critically ill, dialysis dependent.	Bivalirudin	Dialysis	461	Serologic testing for PF4-heparin antibodies, SRA, HIPA	Immunogenic assays utilized anti-PF4-heparin ELISA	Yes, ≥ 0.400	Suspected 262, confirmed 124 and previous history of HIT 75	Death all cause, , New thrombosis, amputation, Major bleeding,
Kang 2015	Retrospective Cohort	Adult men and nonpregnant, non-breast-	(fondaparinux 5 133, danaparoid 5 59, and	NA	239	4T scores	ELISA test, SRA	NR	Acute HIT	thrombosis or thrombosis-related death and major bleeding

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		feeding women who received a non-heparin anticoagulant for suspected HIT	argatroban 547)							
Kunk 2017	Case Series	General HIT	Bivalirudin & Argatroban switch to Apixaban, Rivaroxaban	CABG, PE, DDVT prophylaxis	12	Thrombi(9), Thrombocytopenia (3)	ELISA and SRA	NR	Acute HIT and HITII	Severe bleeding, Recurrent thrombi
Lewis 2001	Prospective Cohort	General HIT	Lepirudin	NA	138	Platelet count	Immune assay test	NR	isolated HIT	Limb Amputation , New Thrombosis, Major Bleeding
Lewis 2003	Prospective Cohort	General HIT	Lepirudin	NA	138	Platelet count	Immune assay test	NR	Acute HIT	Limb Amputation , New Thrombosis, Major Bleeding
Lubenow 2005	Prospective Cohort	General HIT	Lepirudin	NA	205	HIPA test	ELISA	NR	Acute HIT	Death , New Thrombosis, Major Bleeding
Magnani 2006	Cross-sectional	General HIT, Renal failure patients	Danaparoid	Dialysis	1,291 /1,478	Platelet count	Immune assay test, platelet aggregation test (PAT, or HIPA	NR	isolated HIT, Past HIT, Current HIT	Death all cause, New thromboses, Adverse events, Major bleeding, Amputation

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on--- ?	Laboratory test for diagnosis	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT, etc.)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Ong SY 2017	Case Series	Thromboembolic, (DVT, PE)	Rivaroxaban	NR	9	4Ts score 4 or more	IgG-specific anti-PF4/heparin complex assay HPIA-IgG anti-PF4 kit (Diagnostic a Stago, France) or GTI-PF4 IgG ELISA	Mean OD reading using the anti-PF4/heparin assay was 2.34 OD units (range 1.13 to 3.21)	HIT	thrombosis, death or major bleeding
Rouge 2017	Case Report	Hemodynamic compromised requiring ECMO	Argatroban switch to Danaparoid and then changed to VKA	ECMO	2	Drop in Platelet count	anti-PF4 antibodies measured by ELISA (IgG) was 0.775 (.)	positivity threshold value at 0.146	HIT II	One patient died
Samos 2019	Case Report	Post cardiac surgery	Apixaban	NA	1	Drop in Platelet count	rapid immunoanalysis, HITALert® flow cytometric analysis (HITALert assay,	NR	Acute HIT (Isolated)	No bleeding, no thrombosis, 1-month FU in good condition
Sin 2017	Case Report	ECMO	Argatroban	NA	1	Drop in Platelet count	ELISA, SRA	(OD) of .146, OD of 1.392. On day 19, a third anti-PF4 was	HITT II	No thrombosis, no bleeding

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on--- ?	Laboratory test for diagnosis	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT, etc.)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
								also positive with an OD of 1.590		
Topliceanu, 2018	Case Report	post cardiac surgery	1 patient received Bivalirudin and converted to Warfarin	Mitral valve repair, Tricuspid valve repair and ASD closure with AF	1	Platelet reduction	ELISA heparin PF4 complex, SRA	optical density of 2.295 (normal <0.400)	Acute HIT	A follow-up trans esophagus echo cardiography (TEE) performed approximately 2months later revealed, no LA thrombus. no embolic events during hospital stay and during the available 3-year follow-up.
Vavlukis 2017	Case Report	Pulmonary Emboli	Rivaroxaban	NA	1	Drop in Platelet count	4Ts score, ELISA	NR	Subacute HIT A	rise in the PLT, thrombotic material resolution
Warkentin 2011	Case Series	Acute HIT	Fondaparinux	NA	16	SRA	SRA	Optical density of 2.53 (normal <0.45 units)	Acute HIT	New or recurrent thrombosis, bleeds, necrosis, amputation
Warkentin 1996	Case Series	General HIT	Heparin discontinued	NA	127	Platelet count	Immune assay test	NR	with Thrombosis 65; with Isolated with Thrombosis Thrombocytopenia 62	Death all cause, Death due to thrombosis, New Thrombosis

4Ts score is not a Lab test but some components defined based on the Lab Test

3.1.b. DOAC vs DOAC

1. Warkentin TE, Pai M, Linkins LA. Direct oral anticoagulants for treatment of HIT: update of Hamilton experience and literature review. *Blood*. 2017;130(9):1104-1113
2. Bethea BT, Elliot JW, Richardson JB, Ahmed MI. Treatment of pulmonary embolism with argatroban and ultrasound-assisted catheter-directed thrombolysis with alteplase in a patient with heparin-induced thrombocytopenia. *American Journal of Health-System Pharmacy*. 2017;74(15):1153-7.
3. Davis KA, Davis DO. Direct acting oral anticoagulants for the treatment of suspected heparin-induced thrombocytopenia. *European Journal of Haematology*. 2017;99(4):332-5.
4. Ezekwudo DE, Chacko R, Gbadamosi B, Batool S, Gaikazian S, Warkentin TE, et al. Apixaban for treatment of confirmed heparin-induced thrombocytopenia: A case report and review of literature. *Experimental Hematology and Oncology*. 2017;6(1):21.
5. Samos M, Bolek T, Skornova I, Benko J, Stasko J, Kubisz P, et al. Apixaban: a novel agent to treat heparin induced thrombocytopenia and to prevent embolism in patient with atrial fibrillation after multiple valve replacement? *Journal of Thrombosis and Thrombolysis*. 2019.
6. Vavlukis M, Kotlar I, Taravari H, Poposka L, Kedev S. Can rivaroxaban be a drug of choice for treating heparin-induced thrombocytopenia in a patient with pulmonary thromboembolism? *Anatolian Journal of Cardiology*. 2017;18(1):77-9.

Characteristics of included studies

Author/Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Warkentin 2017	prospective study	General HIT	DOACs (rivaroxaban, apixaban, dabigatran, edoxaban)	NR	46	4Ts score ≥ 4 points; positive platelet factor 4 [PF4]	heparin immunoassay, positive serotonin-release assay	NR	confirmed HIT; acute HIT	New progressive, or recurrent thrombosis, major hemorrhage,
Bethea BT 2017	Case Report	Hypertrophic cardiomyopathy, coronary artery	Argatroban, and converting to Rivaroxaban	Cardio-vascular catheterization	1	Reduced platelet count, 4Ts score	ELISA, SRA	Optical density ratio of 2.838 (a positive result is defined as an optical density ratio of >1)	HITT	Increasing size of thrombus

		disease, hypertension, chronic diastolic heart failure, and atrial flutter and a large thrombus in the main and descending pulmonary arteries.								
Davis 2017	Case series	General HIT (VTE prophylaxis, AF and Dialysis)	apixaban, dabigatran, rivaroxaban	NA	12	4T score ≥ 4	positive IgG-specific anti-PF4/heparin complex assay, SRA	Mean OD using the anti-PF4 assay was 1.66 units (range 0.24- 3.34 units) (Positive OD= ≥ 0.4 and $>50\%$ inhibition with heparin. Negative=OD <0.4 or $<5\%$ heparin inhibition considered normal	Acute HIT	Eleven patients continued DOAC following hospital discharge. One patient discontinued DOAC prior to discharge. No patients experienced thrombotic related event or major bleed while receiving DOAC therapy.
Ezekwudo 2017	Case Report	Endocarditis and Cardiac surgery	Argatroban and apixaban	Cardiac surgery	1	Drop in Platelet count	4Ts score, ELISA. SRA	positive value of 1.131 (OD)(negative reference range 0.000–0.399)	HITT	no reported bleeding or thrombosis 3 months later.
Samos 2019	Case report	Post cardiac surgery	Apixaban	NA	1	Drop in Platelet count	rapid immunoanalysis, HITAlert® flow cytometric analysis (HITAlert assay,	NR	Acute HIT (Isolated)	No bleeding, no thrombosis, 1-month FU in good condition

Vavlukis 2017	Case Report	Pulmonary Emboli	Rivaroxaba n	NA	1	Drop in Platelet count	4Ts score, ELISA	NR	Subacute HIT A	rise in the PLT, thrombotic material resolution
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3.2 Therapeutic vs prophylactic dosing

1. Schindewolf M, Scheuermann J, Kroll H, et al. Application, tolerance and safety of fondaparinux therapy in a German hospital: a prospective single-centre experience. *Thrombosis Research*. 2012;129(1):17-21.
2. Greinacher A, Janssens U, Berg G, et al. Lepirudin (recombinant hirudin) for parenteral anticoagulation in patients with heparin-induced thrombocytopenia. *Circulation*. 1999;100(6):587-593.
3. Farner B, Eichler P, Kroll H, Greinacher A. A comparison of danaparoid and lepirudin in heparin-induced thrombocytopenia. *Thrombosis and Haemostasis*. 2001;85(6):950-957.

Characteristics of included studies

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Farner 2001	Prospective trials	General HIT	Danaparoid 126 Lepirudin 175	NA	301	Platelet count	Immune assay test, HIPA	NR	Active HIT	new thromboembolic complications (new TECs), amputations, death, and major bleeding
Greinacher 1999	2 Cohorts	General HIT	Lepirudin	NA	419	Platelet count	Immune assay test	NR	HITT	Death, Limp Amputation, New thrombosis, Major bleeding
Schindewolf 2012	prospective observational cohort study	General HIT	Fondaparinux	NA	231	Platelet count	Immune assay test	NR	Acute HIT	Death, Major bleeding, Adverse events

3.3 DOAC vs DOAC plus platelets

1. Palatianos GM, Foroulis CN, Vassili MI, et al. Preoperative detection and management of immune heparin-induced thrombocytopenia in patients undergoing heart surgery with iloprost. *Journal of Thoracic and Cardiovascular Surgery*. 2004;127(2):548-554.
2. Palatianos G, Michalis A, Alivizatos P, et al. Perioperative use of iloprost in cardiac surgery patients diagnosed with heparin-induced thrombocytopenia-reactive antibodies or with true HIT (HIT-reactive antibodies plus thrombocytopenia): An 11-year experience. *American Journal of Hematology*. 2015;90(7):608-617.

Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Palatianos 2004	Longit udinal data	Patients with immune heparin- induced thrombocyt openia undergoing cardiac surgery	Iloprost	cardiac surgery	32/1518	Platelet count	Immune assay test	NR	HITT	Mortality, Major Bleeding,
Palatianos 2015	Longit udinal data for 11 years	cardiac surgery patients with HIT	Iloprost (n=110) Controls (n=118)	cardiac surgery	228	Platelet count	Immune assay test	OD <0.300	Acute HIT	Adverse events, 30- Day mortality, Thromboembolism, Bleeding

3.4: IVC filter

1. Hong AP, Cook DJ, Sigouin CS, Warkentin TE. Central venous catheters and upper-extremity deep-vein thrombosis complicating immune heparin-induced thrombocytopenia. *Blood*. 2003;101(8):3049-3051.
2. Jung M, McCarthy J, Baker K, Rice L. Risks of IVC filters in the setting of heparin-induced thrombocytopenia. *Journal of Thrombosis and Haemostasis*. 2011;9:334.

Characteristics of included studies

Author/Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on--- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A,	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Hong 2003	Reviewed consecutive cases	HIT patients with central venous catheter (CVC)	CVC use	145 had a CVC placed during the 2-week period prior to the episode of HIT. The remaining 115 patients with HIT did not receive a CVC.	260	Platelet count	14C-serotonin release assay	NR	serologically confirmed HIT	upper- and lower-extremity DVTs
Jung 2011	case report and data chart review	A 69-year-old woman with breast cancer and HIT, A 48-year-old woman with HIT	IVC filter and Warfarin, Lepirudin	NA	2 cases had IVC filter, 9/56 HIT patients had IVC filter	Platelet count	immunoassay test (ELISA, PaGIA, PAT, etc.)	NR	Acute HIT	Limb gangrene, subsequent thromboses: caval thrombosis up to the filter (1), recurrent PE (1), or both (1).

3.5 Oral anticoagulation (VKA) be initiated before platelet recovery

1. Warkentin TE, Elavathil LJ, Hayward CP, Johnston MA, Russett JI, Kelton JG. The pathogenesis of venous limb gangrene associated with heparin-induced thrombocytopenia. *Annals of internal medicine*. 1997;127(9):804-812.
2. Warkentin TE, Kelton JG. A 14-year study of heparin-induced thrombocytopenia. *The American journal of medicine*. 1996;101(5):502-507.
3. Srinivasan AF, Rice L, Bartholomew JR, et al. Warfarin-induced skin necrosis and venous limb gangrene in the setting of heparin-induced thrombocytopenia. *Archives of internal medicine*. 2004;164(1):66-70.

Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A,	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Srinivasan 2004	Case reports	HIT patients	Warfarin, Lepirudin, Vitamin K	NA	6	Platelet count	Enzyme- linked immunosor bent assay	NR	Acute HIT	Skin necrosis, Venous Limb Gangrene, Leg and breast amputations, Death
Warkentin 1996	Single arm observ ational study	Isolated HIT	Warfarin	Discontin ue heparin and replacing with warfarin	57	Platelet count	C serotonin release assay	NA	Isolated HIT	DVT, PE, Arterial thrombosis, Sudden death,
Warkentin 1997	case control studies	patients with venous limb gangrene (<i>n</i> = 8), limb arterial thrombosis (<i>n</i> = 10), and	vitamin K, Warfarin	Discontin ue heparin and replacing with warfarin	158	Platelet count	Enzyme- linked immunosor bent assay	NR	serologically confirmed HIT patients	Limb amputation

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A,	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		uncomplicated deep venous thrombosis (<i>n</i> = 58).								

3.6 Platelet vs no platelet

1. Goel R, Ness PM, Takemoto CM, Krishnamurti L, King KE, Tobian AA. Platelet transfusions in platelet consumptive disorders are associated with arterial thrombosis and in-hospital mortality. *Blood*. 2015;125(9):1470-1476.
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Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A,	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Goel 2015	Hospital data review	Hospitalized patients	Platelet transfusions	plasma exchange or plasma infusion	6332	Hospital HIT record	NR	NR	HIT patients	Arterial/venous thrombosis, acute myocardial infarction (AMI), stroke, and in- hospital mortality
Refaai 2010	retrospe ctive review	Hospitalized surgery patients	Platelet transfusion	Platelet transfusions	37	4T, Positive anti-platelet factor 4 (PF4)	Polyvinyl sulfate enzyme- linked immunosor bent assay (ELISA)	OD median (range) 0.746 (0.43–3.15)	HIT patients	Thrombotic events, Bleeding, Mortality
Hopkins 2008	Case reports	Clinically indicated in patients with HIT.	Platelet transfusions	Platelet transfusions	4	clinical criteria and laboratory tests	The serotonin release assay (SRA).	NR	Not clear	A thrombotic complication, posttransfusion PLT increments, Bleeding
Senzel 2016	Case report	Emergency patient with acute	Massive transfusion	Cardiac bypass surgery	1	Platelet count	ELISA	NR	Acute HIT	SRA performed on the initial EIA specimen was

		myocardial infarction	(Plt and RBC)							strongly positive. A second EIA, drawn after a massive transfusion, was negative.
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3.7.a & 3.7.b. Ultrasonography and ultrasonography for persons with central venous catheter

1. Elalamy I, Tardy-Poncet B, Mulot A, et al. Risk factors for unfavorable clinical outcome in patients with documented heparin-induced thrombocytopenia. *Thrombosis research*. 2009;124(5):554-559.
2. Greinacher A, Farner B, Kroll H, Kohlmann T, Warkentin TE, Eichler P. Clinical features of heparin-induced thrombocytopenia including risk factors for thrombosis. *Thromb Haemost*. 2005;94(1):132-135.
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4. Tardy B, Tardy-Poncet B, Fournel P, Venet C, Jospe R, Dacosta A. Lower limb veins should be systematically explored in patients with isolated heparin-induced thrombocytopenia. *Thrombosis and haemostasis*. 1999;82(3):1199-1200.
5. Warkentin TE, Kelton JG. A 14-year study of heparin-induced thrombocytopenia. *The American journal of medicine*. 1996;101(5):502-507.

Characteristics of included studies

Author/Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on---- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Elalamy 2009	Cohort	Inpatients hospitalized with HIT	No specified	NA	117	NR	PAT positive	NR	Not specified	Death, length of stay in hospital, DVT
Greinacher 2005	Retrospective analysis	HIT patients and post-cardiovascular surgery patients	NR	Trauma/orthopedic surgery	408	Platelet counts	HIPA	NR	Acute HIT	Thromboembolic complications (TECs)
Hong 2003	Observational study	HIT patients with central	CVC use	145 had a CVC placed during the 2-week period prior to the episode of HIT. The	260	Platelet count	14C-serotonin release assay	NR	serologically confirmed HIT	upper- and lower-extremity DVTs

		venous catheter (CVC)		remaining 115 patients with HIT did not receive a CVC.						
Tardy 1999	Retrospective review	Critically ill Patients	Danaparoid sodium	Different types of surgery such as Urologic surgery, Gynecologic surgery, Visceral surgery, Cardiac surgery etc.	42	Platelet count	Platelet aggregation test or by heparin-induced platelet antibodies assay	NR	Acute HIT or past HIT	Thrombotic complications nor thrombosis extension, Major bleeding, Mortality
Warkentin 1996	Case series, retrospective, multicenter	General HIT	Heparin discontinued	NR	127	Platelet count	Immune assay test	NR	With Thrombosis 65; with Isolated with Thrombosis Thrombocytopenia 62	Death all cause, Death due to thrombosis, New Thrombosis

3.8 Continue anticoagulation until platelet recovery or for 4-6 weeks or for 3 months in patients with isolated HIT

1. Warkentin TE, Kelton JG. A 14-year study of heparin-induced thrombocytopenia. *The American journal of medicine*. 1996;101(5):502-507.

Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment N (%)	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A,	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT N (%)
Warkentin 1996	Case series, retrospective, multicenter	General HIT	Heparin discontinued	NR	127	Platelet count	Immune assay test	NR	with Thrombosis 65; with isolated with Thrombosis Thrombocytopenia 62	Death all cause, Death due to thrombosis, New Thrombosis

3.9 VKA vs DOAC

1. Warkentin TE, Pai M, Linkins LA. Direct oral anticoagulants for treatment of HIT: update of Hamilton experience and literature review. *Blood*. 2017;130(9):1104-1113.

Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment N (%)	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A,	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT N (%)
Warkentin 2017	prospe ctive study	General HIT	DOACs (rivaroxaba n, apixaban, dabigatran, edoxaban)	NR	46	4Ts score >=4 points; positive platelet factor 4 [PF4]	heparin immunoass ay, positive serotonin- release assay	NR	confirmed HIT; acute HIT	New progressive, or recurrent thrombosis, major hemorrhage,

4.1 Anticoagulation with a non-heparin anticoagulant or preoperative plasma exchange with heparin or heparin with an antiplatelet agent for patients with acute HIT or subacute HIT who require urgent cardiovascular surgery

1. Aouifi A, Blanc P, Piriou V, Bastien OH, Ffrench P, Hanss M, et al. Cardiac surgery with cardiopulmonary bypass in patients with type II heparin-induced thrombocytopenia. *The Annals of thoracic surgery*. 2001;71(2):678-83.
2. Czosnowski QA, Finks SW, Rogers KC. Bivalirudin for patients with heparin-induced thrombocytopenia undergoing cardiovascular surgery. *Annals of Pharmacotherapy*. 2008;42(9):1304-9.
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6. Jaben EA, Torloni AS, Pruthi RK, Winters JL. Use of plasma exchange in patients with heparin-induced thrombocytopenia: A report of two cases and a review of the literature. *Journal of clinical apheresis*. 2011;26(4):219-24.
7. Koster A, Dyke CM, Aldea G, Smedira NG, McCarthy IHL, Aronson S, et al. Bivalirudin During Cardiopulmonary Bypass in Patients With Previous or Acute Heparin-Induced Thrombocytopenia and Heparin Antibodies: Results of the CHOOSE-ON Trial. *Annals of Thoracic Surgery*. 2007;83(2):572-7.
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9. Koster A, Kukucka M Fau - Bach F, Bach F Fau - Meyer O, Meyer O Fau - Fischer T, Fischer T Fau - Mertzlufft F, Mertzlufft F Fau - Loebe M, et al. Anticoagulation during cardiopulmonary bypass in patients with heparin-induced thrombocytopenia type II and renal impairment using heparin and the platelet glycoprotein IIb/IIIa antagonist tirofiban. *Anesthesiology*. 2001;94(2):245-51.
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12. Makhoul RG, McCann RL, Austin EH. Management of patients with heparin-associated thrombocytopenia and thrombosis requiring cardiac surgery. *Annals of Thoracic Surgery*. 1987;43(6):617-21.

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16. Welsby IJ, Um J, Milano CA, Ortel TL, Arepally G. Plasmapheresis and heparin reexposure as a management strategy for cardiac surgical patients with heparin-induced thrombocytopenia. Anesthesia & Analgesia. 2010;110(1):30-5.

Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, what was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Aouifi 2001	Cross-sectional study	patients who underwent cardiac surgery and patients presented with preoperative type II HIT	danaparoid sodium n=4, heparin sodium n=6; transfusion of blood products, Fresh frozen plasma	Cardiac Surgery with Cardiopulmonary Bypass	10	Platelet count	NA	NA	Type II HIT	Intraoperative thrombotic complication,
Czosnowski 2008	Prospective and retrospective studies	HIT undergoing any cardiovascular surgical procedure other than percutaneous coronary intervention	Bivalirudin	Coronary Artery Bypass	93	Platelet count, Anti-PF4/H antibodies	Not clear	NR	on-pump CPB n=46; off-pump CPB n=47	Valve repair and replacement, right ventricular assist device implantation, and heart transplantation
Durand 2008	Case Report	Patient with MI need CABG and	Danaproid-Tirofiban + UFH, rFVIIa	CABG + Mitral valve	1	Platelet count	ELIZA, Plt aggregation test	NR	HIT I	No thrombosis, Major hemorrhage

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on--- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, what was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		mitral valve replacement		replacement+ CPB						
Dyke 2007	Prospective, open-label, multicenter study	least 18 years of age and scheduled for off-pump coronary artery bypass	Bivalirudin	Coronary Artery Bypass	51	Platelet count, Anti-PF4/H antibodies	Serologic and clinical evidence	NR	HIT/TS	thrombocytopenia or thrombosis, death, Bleeding, transfusion
Fernandes 2019	Case Report	Patient with LV failure candidate for heart transplantation undergo left ventricle assist device (LVAD)	Argatroban discharged with ASA and warfarin	left ventricle assist device (LVAD)	1	Reduced Platelet count,	ELISA, SRA	(OD) was >2, which indicated a very strong HIT correlation	HIT II	Discharged waiting for Cardiac transplant
Huang 2014	Case reports	patient requires cardiac pulmonary bypass surgery (CPB)	Therapeutic plasma exchange (TPE)	Cardiac Surgery	3	NR	serotonin release assay positivity	O.D. value >0.547	HIT	Duskinness, Reduce HIT ELISA Titer (HET)
Jaben 2011	Case Reports	Case 1 is a 46-year-old male with cardiac amyloidosis who needed urgent placement of a left ventricular assist device. Case 2 is a 34-year-old woman with acute myocarditis who needed placement of a biventricular assist device.	Plasma Exchange	Cardiopulmonary bypass surgery (CPB)	2	platelet count, Heparin/PF4 antibodies and clinical evidence	Enzyme-linked immunosorbent assay	NR	Acute HIT	Reduction in the thrombus, no complications

Koster 2000	Retrospective cohort	Patients with cardiac surgery require cardiopulmonary bypass	Recombinant hirudin	cardiac surgery	57	Platelet count	heparin-induced platelet aggregation assay	NR	HIT II	Thromboses or embolisms
Koster 2000	Case Report	Patients with cardiac surgery require cardiopulmonary bypass and impaired renal function	Recombinant hirudin, Tirofiban	Cardiopulmonary bypass surgery (CPB)	1	Platelet count	HIPA	NR	HIT II	No Thromboses or embolisms, No death
Koster 2000	Case Report	Patient need redo mitral valve replacement	Recombinant hirudin, Tirofiban	Cardiopulmonary bypass surgery (CPB)	1	Platelet count	HIPA	NR	HIT II	No clot in CPB system, No thrombosis, No emboli,
Koster 2001	Case series	Renal impairment, and CPB	Heparin and tirofiban	Cardiopulmonary bypass surgery (CPB)	10	Platelet count	HIPA	NR	HITII	No intra- post-operative thrombosis and emboli, no death
Koster 2001	One-arm prospective Cohort	Patients need cardiac surgery and CPB	UFH + Tirofiban	Cardiopulmonary Bypass	47	NR	HIPA	NR	HIT II	No Thrombosis, No Emboli, Minor Hemorrhage, Death,
Koster 2007	Open-label, multicenter trial	First time or redo-CABG, single valve surgery, or CABG plus single-valve surgery, and had a diagnosis of confirmed or suspected HIT	Bivalirudin	Cardiopulmonary Bypass	50	serologic and clinical evidence	serologic and clinical evidence	NR	HITT n=43, Remote HIT=6	Absence of death, Q-wave myocardial infarction (MI), repeat operation for coronary revascularization, and stroke, major bleeding
Makhoul 1987	Case reports	Patients with HATT require reexposure to heparin for emergency cardiac operations requiring cardiopulmonary bypass while still	Platelet aggregation to heparin in vitro; therefore, aspirin and dipyridamole were administered	Cardiopulmonary bypass	2	Platelet count	Platelet aggregation to heparin in vitro	NR	Heparin - associated thrombocytopenia and	recurrent chest pain, discharged home

		demonstrating positive in vitro platelet aggregation with heparin.							thrombosis (HATT)	
Palatianos 2004	Longitudinal data	Patients with immune heparin-induced thrombocytopenia undergoing cardiac surgery	Iloprost	cardiac surgery	10	Platelet count	EIA and HIPA	NR	HITT	Mortality, Major Bleeding,
Palatianos 2015	Longitudinal data for 11 years	cardiac surgery patients with HIT	Iloprost (n=110) Controls (n=118)	cardiac surgery	46	Platelet count	EIA and HIPAG	OD <0.300	Acute HIT	Adverse events, 30-Day mortality, Thromboembolism, Bleeding
Wadia 2008	Case report	A Patient with Heparin-Induced Thrombocytopenia and a Left Ventricular Assist Device	Plasmapheresis (3 L of the patient's plasma replaced with donor plasma).	Cardiac Transplantation	1	Platelet count	Immune assay test	NR	Acute HIT	No evidence of thrombosis in the bypass circuit or elsewhere, no complications, Alive
Welsby 2010	A retrospective chart review	Cardiac Surgical Patients with Heparin-Induced Thrombocytopenia	Plasmapheresis and Heparin Re-exposure	Cardiac Surgery	11	Positive antiheparin/platelet factor 4 (anti-HPF4) antibody titer	NR	NR	acute or subacute HIT	Developed an ischemic foot, in the setting of cardiogenic shock, reduced titers

4.2 Anticoagulation with a non-heparin anticoagulant or preoperative plasma exchange with heparin or heparin with an antiplatelet agent for patients with subacute HIT B or remote HIT who require urgent cardiovascular surgery

1. Olinger G, Hussey C, Olive J, Malik M. Cardiopulmonary bypass for patients with previously documented heparin-induced platelet aggregation. *The Journal of thoracic and cardiovascular surgery*. 1984;87(5):673-677.
2. Pötzsch B, Klövekorn W-P, Madlener K. Use of heparin during cardiopulmonary bypass in patients with a history of heparin-induced thrombocytopenia. *New England Journal of Medicine*. 2000;343(7):515-515.
3. Selleng S, Haneya A, Hirt S, Selleng K, Schmid C, Greinacher A. Management of anticoagulation in patients with subacute heparin-induced thrombocytopenia scheduled for heart transplantation. *Blood*. 2008;112(10):4024-4027.
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11. Warkentin TE, Sheppard J-AI, Chu FV, Kapoor A, Crowther MA, Gangji A. Plasma exchange to remove HIT antibodies: dissociation between enzyme-immunoassay and platelet activation test reactivities. *Blood*. 2015;125(1):195-198.

Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Davis 2003	Case report	case with previous syncopal episodes, progressive shortness of breath, pulmonary edema, severe calcific aortic stenosis, and a history of HIT required aortic valve replacement.	Bivalirudin	Cardiopulm onary Bypass	1	Anti- PF4	A repeat enzyme- linked immunosor bent assay (ELISA) was -ve		a previous positive assay for anti-PF4 patient	No blood clot, discharged home
Grocott 1997	Case report	A 65-year-old man presented for coronary artery bypass graft surgery (CABG) after developing class IV angina	Heparinoid, Danaparoid Sodium	Cardiopulm onary Bypass	1	Anti- PF4	A repeat enzyme- linked immunosor bent assay (ELISA) was -ve	NR	past clinical history of HIT	Surgery and CPB proceeded without incident, Blood clot, Discharged home
Kappa 1987	Case reports	Patients with confirmed heparin- induced platelet activation	Aspirin, Iloprost	carotid endarterect omy	2	Platelet count, PF4	Not clear	Not clear	Not clear	No thrombotic complications
Nuttall 2003	Prospectiv e study	Cardiac surgical patients undergoing CPB	Porcine heparin, r- hirudin or Lepirudin	CPB	12	Platelet count, PF4	Enzyme- linked immunosor bent assay (ELISA)	NR	Previous clinical diagnosis of HITT type II	Patients survived the surgery, and thrombotic or embolic complications
Olinger 1984	Case reports	Patients with prior heparin-dependent intravascular coagulation who	Cardiac catheterizat ion	Cardiopulm onary bypass	3	Platelet count	Not clear	NR	Patients with previously documented heparin-	Mortality, Intravascular thrombosis or bleeding diathesis,

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		require cardiopulmonary bypass							induced platelet aggregation	
Pötzsch 2000		Cardiopulmonary Bypass in Patients with a History of Heparin- Induced Thrombocytopenia	Heparin(unfractionat ed heparin)	Cardiopulm onary Bypass	10	Had heparin- induced platelet- aggregatio n assay positive	At the time of surgery, all patients were negative to an antigenic assay	NR	Patients with a History acute HIT	No prolonged thrombocytopenia, Excellent recovery
Selleng 2001	Case report	Patient with a history of bilateral nephrectomy and HIT who needed emergency coronary artery bypass grafting.	heparin	Coronary artery bypass Surgery; Renal replacemen t therapy	1	Clinically suspected	serologically proved by the heparin- induced platelet activation assay (HIPA)	NR	Patient with a history	No HIT-related complications, Platelet counts continuously Increased, Major bleeding
Selleng 2008	Case report	Patients scheduled for heart transplantation with end-stage heart failure complicated by subacute heparin- induced thrombocytopenia (HIT).	unfractionat ed heparin (UFH)	Heart transplantat ion	3	Platelet count, anti- PF4/hepar in IgG antibodies	EIA, but HIPA negative	OD 0.627 OD; cut-off 0.500	Acute HIT, previous HIT	Major bleeding, Thromboembolic complications, Thrombotic events
Warkentin 2001	Reviewed the medical and	Patients with serologically confirmed heparin induced thrombocytopenia	heparin	Not clear	243	Platelet count	platelet serotonin- release assay	NR	Typical onset HIT (n=170); Rapid onset HIT (n=73)	New thrombosis, Fatal hemorrhage, Mortality within 30days after onset of HIT

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
	laboratory records									
Warkentin 2014	Case reports	Cases presenting with thrombotic stroke/thrombocytopenia: one following shoulder hemiarthroplasty (performed without heparin) and the other presenting to the emergency room without prior hospitalization, heparin exposure, or preceding infection.	Aspirin, fondaparinux, argatroban warfarin; heparin, argatroban, fondaparinux	Internal carotid artery terminus,	2	Platelet count	EIAs and in the SRA	< 0.40	spontaneous HIT syndrome (for acute thrombosis and thrombocytopenia)	Recovered,
Warkentin 2015	Case report	A 76-year-old female with renal carcinoma invading the inferior vena cava (IVC)/right atrium developed HIT without thrombosis	Repeated therapeutic plasma exchange (TPE)	coronary artery bypass grafting (CABG) and removal of IVC/intracardiac tumor thrombus	1	Serologically confirmed	SRA and EIA remained strongly positive	2.58 optical density [OD] units	Acute or subacute HIT	Discharged on postoperative day 34. Tumor removal was incomplete.

5.1 Anticoagulation with a non-heparin anticoagulant for patients with acute HIT or subacute HIT A who require urgent percutaneous cardiovascular interventions

1. Jang I-K, Lewis BE, Matthai WH, Kleiman NS. Argatroban anticoagulation in conjunction with glycoprotein IIb/IIIa inhibition in patients undergoing percutaneous coronary intervention: an open-label, nonrandomized pilot study. *Journal of thrombosis and thrombolysis*. 2004;18(1):31-37.
2. Lee MS, Liao H, Yang T, et al. Comparison of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitors in patients undergoing an invasive strategy: a meta-analysis of randomized clinical trials. *Int J Cardiol*. 2011;152(3):369-374.
3. Lewis BE, Matthai Jr WH, Cohen M, Moses JW, Hursting MJ, Leya F. Argatroban anticoagulation during percutaneous coronary intervention in patients with heparin-induced thrombocytopenia. *Catheterization and Cardiovascular Interventions*. 2002;57(2):177-184.
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Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, what was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Jang 2004	multicenter, prospective pilot study	patients undergoing percutaneous coronary intervention.	Argatroban	PCI	152	NR	NR	NR	NR	Mortality, Myocardial infarction, or urgent revascularization, Major bleeding

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on--- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, what was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Lee 2011	Systematic Review	Patients undergoing PCI	9785 bivalirudin and 9987 heparin plus GP IIb/IIIa inhibitors	Percutaneous coronary intervention (PCI)	19,772	NR	NR	NR	NR	Mortality, Urgent revascularization, Major bleeding
Lewis 2002	Prospective study	patients were males or nonpregnant females >18 years old	Argatroban	Percutaneous coronary intervention (PCI)	Initial group (n =91) Repeat group (n =21)	Platelet count	Antibody test for HIT	NR	Patient with history of HIT or a previous or current clinical diagnosis of HIT	Adequate, anticoagulation, Mortality, Myocardial infarction, or Revascularization, hospitalization, Major bleeding
Magnani 2006	Cross sectional study	General HIT, Renal failure patients	danaparoid	Dialysis	1,291 /1,478	Platelet count	Immune assay test, platelet aggregation test (PAT, or HIPA	NR	isolated HIT, Past HIT, Current HIT	Death all cause, New thromboses, Adverse events, Major bleeding, Amputation
Mahaffey 2003	Prospective, open-label study	Patients aged 18 years or older with a new diagnosis of or previous clinically suspected or objectively recorded HIT/HITS were eligible for inclusion if the decision to perform PCI had been made.	Bivalirudin	Percutaneous Coronary Intervention	52	Platelet count	heparin-induced platelet aggregation or other functional assay for HIT or immunoassay for HIT antibodies,	NR	HIT 19 (37%) or HIT with thrombotic syndrome (HITS) 22 (43%) patients	Mortality, Major bleeding, Major cardiac events

5.2 Anticoagulation with a non-heparin anticoagulant or unfractionated heparin for patients with subacute HIT B or remote HIT who require urgent percutaneous cardiovascular interventions

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Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on---- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Davis 2003	Case report	case with previous syncopal episodes, progressive shortness of breath, pulmonary edema, severe calcific aortic stenosis, and a history of HIT required aortic valve replacement.	Bivalirudin	Cardiopulm onary Bypass	1	Anti- PF4	A repeat enzyme- linked immunosor bent assay (ELISA) was -ve		a previous positive assay for anti-PF4 patient	No blood clot, discharged home
Grocott 1997	Case report	A 65-year-old man presented for coronary artery bypass graft surgery (CABG) after developing class IV angina	Heparinoid, Danaparoid Sodium	Cardiopulm onary Bypass	1	Anti- PF4	A repeat enzyme- linked immunosor bent assay (ELISA) was -ve	NR	past clinical history of HIT	Surgery and CPB proceeded without incident, Blood clot, Discharged home
Hale 1998	Case report	A 54-year-old physician with the factor V	bolus of Orgaran, abciximab	catheter- based	1	NA	NA	NA	Not HIT	thrombotic or hemorrhagic complications

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on---- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		Leiden mutation and heparin exposure for treatment of PE		therapy of the RCA and possibly the Cx-OM						
Jang 2004	multicenter, prospective pilot study	patients undergoing percutaneous coronary intervention.	Argatroban	PCI	152	NA	NA	NA	Not HIT	Mortality, Myocardial infarction, or urgent revascularization, Major bleeding
Lee 2011	Systematic Review	Patients undergoing PCI	9785 bivalirudin and 9987 heparin plus GP IIb/IIIa inhibitors	Percutaneous coronary intervention (PCI)	19,772	NA	NA	NA	Not HIT	Mortality, Urgent revascularization, Major bleeding
Olinger 1984	Case reports	Patients with prior heparin- dependent intravascular coagulation who require cardiopulmonary bypass	Cardiac catheterization	Cardiopulmonary bypass	3	Platelet count	Not clear	NR	Patients with previously documented heparin- induced platelet aggregation	Mortality, Intravascular thrombosis or bleeding diathesis,
Pöttsch 2000		Cardiopulmonary Bypass in Patients with a History of Heparin- Induced	Heparin (unfractionated heparin)	Cardiopulmonary Bypass	10	Had heparin- induced platelet- aggregation assay positive	At the time of surgery, all patients were negative to an antigenic assay	NR	Patients with a History acute HIT	No prolonged thrombocytopenia, Excellent recovery

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on---- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		Thrombocytopenia								
Selleng 2001	Case report	Patient with a history of bilateral nephrectomy and HIT who needed emergency coronary artery bypass grafting.	heparin	Coronary artery bypass Surgery; Renal replacement therapy	1	Clinically suspected	serologically proved by the heparin induced platelet activation assay (HIPA)	NR	Patient with a history	No HIT-related complications, Platelet counts continuously increased, Major bleeding
Selleng 2008	Case report	Patients scheduled for heart transplantation with end-stage heart failure complicated by subacute heparin-induced thrombocytopenia (HIT).	unfractionated heparin (UFH)	Heart transplantation	3	Platelet count, anti-PF4/heparin IgG antibodies	EIA, but HIPA negative	OD 0.627 OD; cut-off 0.500	Acute HIT, previous HIT	Major bleeding, Thromboembolic complications Thrombotic events
Warkentin 2001	Reviewed the medical and laboratory records	Patients with serologically confirmed heparin induced thrombocytopenia	heparin	Not clear	243	Platelet count	platelet serotonin-release assay	NR	Typical onset HIT (n=170); Rapid onset HIT (n=73)	New thrombosis, Fatal hemorrhage, Mortality within 30days after onset of HIT
Warkentin 2014	Case reports	Cases presenting with	Aspirin, fondaparinux,	Internal carotid	2	Platelet count	EIAs and in the SRA	< 0.40	spontaneous HIT syndrome	Recovered

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on---- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		thrombotic stroke/thrombocytopenia: one following shoulder hemiarthroplasty (performed without heparin) and the other presenting to the emergency room without prior hospitalization, heparin exposure, or preceding infection.	argatroban warfarin; heparin, argatroban , fondaparinux	artery terminus,					(for acute thrombosis and thrombocytopenia)	

6.1 & 6.2 Renal replacement therapy for acute HIT, subacute HIT or remote HIT

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4. Yamamoto S, Koide M, Matsuo M, et al. Heparin-induced thrombocytopenia in hemodialysis patients. *American journal of kidney diseases*. 1996;28(1):82-85.
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11. De Pont A-CJ, Hofstra J-JH, Pik DR, Meijers JC, Schultz MJ. Pharmacokinetics and pharmacodynamics of danaparoid during continuous venovenous hemofiltration: a pilot study. *Critical Care*. 2007;11(5):R102.
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14. Zerbi S, Manfrini V, Castellano A, Pezzotta M, Ruggiero P, Pedrini LA. Use of fondaparinux for extracorporeal circuit anticoagulation in patients with heparin-induced thrombocytopenia type II (HIT II) on haemodiafiltration (HDF). *Nephrology Dialysis Transplantation*. 2015;30:iii236.
15. Haase M, Bellomo R, Rocktaeschel J, et al. Use of fondaparinux (ARIXTRA) in a dialysis patient with symptomatic heparin-induced thrombocytopenia type II. *Nephrology Dialysis Transplantation*. 2005;20(2):444-446.

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Characteristics of included studies

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolis m, Limb Amputation, Major Bleeding, recurrence of HIT
Al-Ali 2016	Case reports	Patients diagnosed with HIT	Bivalirudin	Ambulatory hemodialysi s	8	Platelet count	Immunological gel diffusion assay for HPF4 antibody	NR	Acute HIT	Recurrence of extracorporeal thrombosis (ECT) events
Alatri 2010	Case report	A 83-year- old woman with chronic renal failure started	Argatroban	Haemodialy sis	1	PF4	ELISA	OD 2.77; normal value< 0.40	HIT patient	thrombotic complication

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolis m, Limb Amputation, Major Bleeding, recurrence of HIT
		haemodialysis because of worsening of renal function								
Athar 2008	Case report	A 49-year-old female patient with systemic lupus erythematosus, antiphospholipid syndrome, end-stage renal disease maintained on peritoneal dialysis and on long-term anticoagulation with warfarin for a prosthetic	Argatroban	Renal replacement therapy	1	Platelet count	ELISA	NR	HIT Type II	Thrombotic complication , Discharge home
Barginear 2008	Case report	A 25-year-old female with a	Argatroban	Haemodialysis	1	Platelet count, PF4	ELISA	0.828	Acute HIT	Patient's platelets rose

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolis m, Limb Amputation, Major Bleeding, recurrence of HIT
		history of end-stage renal disease due to interstitial nephritis, tertiary hyperparath yroidism, and calciphylaxis was started on hemodialysis								
Brown 2013	Case report	88-year-old man newly initiated on high-flux hemodialysis who developed HIT and extracorpore al circuit thrombosis after 3 weeks of exposure to unfractionat ed heparin	Fondaparin ux	Hemodialysi s	1	Platelet count	ELISA, C-SRA	1.256	HIT II	Complications

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
De Pont 2007	A Mathema tical model/ a cohort of five patients with suspected HIT	Patients with acute renal failure, especially in patients' dependent on renal replacement therapy such as continuous venovenous hemofiltratio n (CVVH).	Danaparoid	Hemofiltrati on	5	NA	NA	NA	Suspected HIT	Bleeding, Thromboembolic events
Haase 2005	Case report	A 52-year- old renal transplant patient (80 kg) with pain in his left lower abdomen and groin, and a weakness of his left leg	Fondaparin ux	Dialysis	1	Platelet count	Serological tests for HIT II were repeatedly negative, clinically diagnosed HIT II syndrome	NR	Symptomatic heparin- induced thrombocytopa enia type II	Thromboembolis ms, Clotting of blood inside the haemodialysis membranes or bleeding occurred
Joseph 2014	Retrospec tive review	Consecutive patient who received bivalirudin	Bivalirudin	109 (23.6%) were dialysis- dependent	109	PF4	ELISA, HIPA or SRA	≥ 0.400	(11 Remote HIT, 69 suspected HIT, 29 Confirmed HIT)	Mortality , New thrombosis, Amputation, Major bleeding

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolis m, Limb Amputation, Major Bleeding, recurrence of HIT
		for a suspected, confirmed or previous history of HIT								
Koide 1995	Case report	A 74-year- old woman had diabetes mellitus had uraemia symptoms	Heparin and aspirin, Argatroban	Haemodialy sis	1	Platelet count, PF 4	Heparin- induced platelet aggregation test and ELISA	NR	Acute HIT	Bleeding complication, clot formation
Kommalap ati 2018	Case report	88-year-old man with sepsis clinical manifestatio n and hemodialysis for past three months for ESRD	Argatroban	Sepsis in the setting of hemodialysi s	1	Drop in Plt count, 4T,	heparin-platelet factor 4(PF4) antibodies, heparin inhibition, serotonin release assays ELISA	NR	Acute HIT	On day eight, venous duplex demonstrated normal compressibility and spontaneous flow in the vein of the right upper extremity. Platelet count recovery, no further thrombotic complications, second and third fingers amputated.

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolis m, Limb Amputation, Major Bleeding, recurrence of HIT
Lindhoff- Last 2001	Retrospec tive analysis of	Critically ill patients with acute renal failure and suspected heparin- induced thrombocyto penia (HIT) needing renal replacement therapy (RRT).	Danaparoid	Renal Replacemen t Therapy	13	Platelet count and	Positive heparin- induced antibodies	NR	HIT patients = 2; Non-HIT = 11	Mortality, Thromboembolic complications
Link 2009	Prospecti ve, dose finding study	Medical and surgical with acute or histories of heparin- induced thrombocyto penia type II and acute renal failure with necessity for CRRT.	CRRT with argatroban	Continuous renal replacement therapy (CRRT)	30	Platelet count	The enzyme- linked immunosorbent assay	NR	Acute or histories of heparin- induced thrombocyto penia type II	Minor bleeding, Severe bleeding episodes,
Magnani 2010	Systemati c review/	In severely ill patients with heparin	Danaparoid	Intermittent haemodialys is	122	4T pre- test scores	Functional serological test	NR	HIT patients	Mortality, Major bleeding, Serious adverse event:

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolis m, Limb Amputation, Major Bleeding, recurrence of HIT
	122 case reports	intolerance for intermittent haemodialysi s (HD)								
Matsuo 1988	Case reports	Patients with acute renal failure who were given continuous infusions of heparin during hemodialysis by use of a hollow fiber type dialyzer.	MD805 (Mitsubishi Chemical Co.)	Hemodialysi s	5	Platelet count	ELISA assay	NR	Acute HIT	PBIgG level, Preventing clot formation
Matsuo 1992	Case report	A 78-year- old woman had suffered from non- insulin dependent diabetes and admitted for the treatment of azotaemia by	UFH, LMWH, Argatroban	Haemodialy sis using hollow fibre dialyser	1	Platelet count	Not clear	NR	Not HIT	clotting or thrombocytopeni a occurred during haemodialysis

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		haemodialysis								
Ng 2015	Case reports	63-year-old woman with end stage renal failure, 2 Surgery patients	Rivaroxaban	Haemodialysis	3	platelet count	HPIA	OD reading – 3.20, positive cut-off value – 0.497	Acute HIT	recurrent thrombotic or bleeding complications
Reddy 2005	Retrospective records reviewed	Patients with HIT and renal failure requiring RRT who were identified from the prospective multicenter studies of argatroban in HIT	Argatroban	Renal replacement therapy (RRT)	47	Platelet count	NR	NR	Had HIT with or without thrombosis (or a history of HIT and required anticoagulation	Mortality, Amputation, New thrombosis, Major bleeding
Trujillo 2018	Case report	71- year- old former smoker with a previous history of hypertension , hypothyroidism, CKD,	Fondaparinux, Apixaban		1	Drop in Plt count, 4T,	4Ts score and 4 antiplatelet aAB	NR	Acute HITT	Amputation, multiple thrombotic events, After Apixaban no thrombotic episodes, kidney function improved

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		psoriasis, and primary myelofibrosis with arterial thrombosis								Hemodialysis was suspended. No hemorrhagic complications
Williamson 2004	Case reports	Consecutive patients with proven heparin- induced thrombocyto- penia (HIT), acute renal failure requiring continuous renal replacement therapy, and various levels of transient hepatic impairment	Argatroban	Continuous renal replacement therapy	4	Not clear	Not clear	NR	Suspected HIT, diagnosed HIT	Bleeding or thrombotic complications
Yamamoto 1996	Cross- sectional study	Consecutive patients were newly treated with hemodialysis	Heparin	Hemodialysis	154	PF4	Enzyme-linked immunosorbent assay	NR	6 HIT type II; 148 non-HIT	Clot Formation during hemodialysis

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on- --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut- off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
		due to chronic or acute renal failure.								
Zerbi 2015	Prospective observational dose finding study	Patients who developed HIT II after start of twice weekly chronic dialysis with mixed HDF	Fondaparinux	Haemodiafiltration (HDF)	7	Not clear	Not clear	NR	HIT type II	No clotting, Bleeding, Side effects

7. VTE prophylaxis in patients with Remote HIT

1. Warkentin, T. E. and J. G. Kelton (2001). "Temporal aspects of heparin-induced thrombocytopenia." New England Journal of Medicine **344**(17): 1286-1292.

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Warkentin 2001	Single arm observational study	Cardiac surgery and vascular surgery	Heparin for 8-19 days	N/A	3	Serologic confirmed remote HIT, No thrombocytopenia, or seroconversion	Not reported	Not reported	Remote HIT	No thrombosis, no thrombocytopenia,

8.1. & 8.2. Emergency identification for persons with HIT

1. Gorlin, J., et al. (2011). "Use of emergency medical identification in the paediatric haemophilia population: a national study." *Haemophilia* **17**(2): 215-222.

Author/ Year	Study Design	Study population	Treatment	Procedure	Number of eligible patients in the study	Patients have received a diagnosis of HIT based on --- ?	Laboratory test for diagnosis -	For ELISA test only, was Optical Density cut-off or individual OD reported? Y/N; if Y, What was the OD reported?	Type of HIT (acute HIT A etc)	Outcomes: Mortality, Thromboembolism, Limb Amputation, Major Bleeding, recurrence of HIT
Gorlin 2011	Single arm observational study	Pediatric hemophiliacs	emergency medical identification (EMI) such as MedicAlert	NA	97 nurses	NA	NA	NA	NA	Adverse reactions from wearing an emergency medical identification device