

## Summary of the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy

CHEST 2004; 126:163S-696S

Grade of Recommendation	Clarity of Risk vs. Benefit	Methodological Strength of Supporting Evidence	Implications
1A	Clear	Randomized Clinical Trials (RCT) without important limitations	Strong recommendation; can apply to most patients in most circumstances without reservation
1C+	Clear	No RCTs but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Strong recommendation; can apply to most patients in most circumstances
1B	Clear	RCTs with important limitations (inconsistent results, methodological flaws ♦)	Strong recommendation; likely to apply to most patients
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	RCTs without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values
2C+	Unclear	No RCTs but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Weak recommendation; best action may differ depending on circumstances or patients' or societal values
2B	Unclear	RCTs with important limitations (inconsistent results, methodological flaws)	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendations; other alternatives might be equally reasonable

Since studies in category B and C are flawed, it is likely that most recommendations in these classes will be level 2. The following considerations will bear on whether the recommendation is Grade 1 or Grade 2: the magnitude and precision of the treatment effect; patients' risk of the target event being prevented; the nature of the benefit and the magnitude of the risk associated with treatment; variability in patient preferences; variability in regional resource availability and health-care delivery practice; and cost considerations. Inevitably, weighing these considerations involves subjective judgment.

♦ These situations include RCTs with both lack of blinding and subjective outcomes, where the risk of bias in measurement of outcomes is high, or RCTs with large loss to follow-up.

**Antithrombotic Therapy for Coronary Artery Disease**

CHEST 2004; 126:513S-548S

<b>Acute Management of Non-ST-Elevation Acute Coronary Syndromes (NSTEMI ACS)</b>			
<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Antiplatelet Therapies	Without clear allergy to Aspirin	Aspirin (Immediate) 75 – 325 mg PO Aspirin (Daily) 75 – 162 mg	1A
	With Aspirin allergy	Clopidogrel (Immediate) 300 mg Clopidogrel (Daily) 75 mg	1A
	Diagnostic catheterization will be delayed or CABG will not occur until > 5 days following coronary angiography	Clopidogrel (Immediate) 300 mg Clopidogrel (Daily) 75 mg x 9 – 12 months + Aspirin (Daily) 75 – 162 mg	1A
	Angiography will take place rapidly (≤ 24 hours)	Clopidogrel (after coronary artery has been determined)	2A
	Patients having received Clopidogrel and are scheduled to undergo CABG	Discontinue Clopidogrel 5 days prior to scheduled surgery	2A
Glycoprotein IIb/IIIa Inhibitors	Moderate-to high-risk patients presenting with NSTEMI ACS	Eptifibatid or Tirofiban (initial treatment) + Aspirin + Heparin	1A
	Moderate-to high-risk patients presenting with NSTEMI ACS who are also receiving Clopidogrel	Eptifibatid or Tirofiban (additional initial treatment)	2A
	All patients presenting with NSTEMI ACS	<b>Against</b> Abciximab as initial treatment except when coronary anatomy is known and PCI planned within 24 hours	1A

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Antithrombin Therapies	All patients presenting with NSTEMI ACS	Unfractionated heparin (UFH) recommended over no Heparin for short term use with antiplatelet therapies	1A
	All patients presenting with NSTEMI ACS who are then prescribed IV Heparin	Weight based dosing of UFH and maintenance of aPTT between 50s and 75s	1C+
	Acute treatment of NSTEMI ACS	Low Molecular Weight Heparins (LMWH) recommended over UFH	1B
	Patients receiving LMWHs with NSTEMI ACS	<i>Against</i> routine monitoring of anticoagulant effect of LMWHs	1C
		Continue LMWH during PCI treatment	2C
	Patients receiving GP IIb/IIIa inhibitors as upstream treatment of NSTEMI ACS	LMWH recommended over UFH as the anticoagulant of choice	2B
Patients presenting with NSTEMI ACS	<i>Against</i> Direct Thrombin Inhibitors (DTIs) as routine initial antithrombin therapy	1B	

### Post-Myocardial Infarction and Post-ACS

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Antiplatelet Therapies	ACS with and without ST-segment elevation	Aspirin (Initial) 160 – 325 mg Aspirin (Indefinite) 75 – 162 mg daily	1A
	Patients with a history of Aspirin –induced bleeding or with risk factors for bleeding	Aspirin ≤ 100 mg daily	1C+
	Aspirin is contraindicated or not tolerated	Clopidogrel (Long-term) 75 mg daily	1A
Comparison of Antiplatelet and Anticoagulant Therapy and/or Combinations of Aspirin and Warfarin Trials	Most health-care settings, for moderate- and low-risk patients with a myocardial infarction	Aspirin alone recommended over Oral Vitamin K Antagonists (VKA) <i>plus</i> Aspirin	2B
	In health-care settings in which meticulous INR monitoring is standard and routinely accessible, for both high- and low-risk patients after MI	Long-term (up to 4 years) high-intensity oral VKAs (target INR 3.5; range 3.0 – 4.0) without concomitant Aspirin <i>or</i> Moderate-intensity oral VKAs (target INR 2.5; range 2.0 – 3.0) <i>plus</i> Aspirin	2B
	High-risk patients with MI, including those with large anterior MI, those with significant heart failure, those with intracardiac thrombus visible on echocardiography, and those with a history of a thromboembolic event	Combined use of moderate-intensity oral VKAs (INR 2.0 – 3.0) <i>plus</i> low dose Aspirin (≤ 100 mg daily) for 3 months after the MI	2A

### Chronic, Stable CAD

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Antiplatelet Therapies	All patients with chronic, stable CAD	Aspirin 75 – 162 mg daily	1A
		Continue Aspirin indefinitely	2C
	Stable, chronic coronary disease with a risk profile indicating a high likelihood of development of AMI	Clopidogrel (Long-term) <i>plus</i> Aspirin	2C
Vitamin K Antagonists	Patients with chronic, stable CAD without prior MI	<i>Against</i> long-term oral VKAs	2C

### Congestive Heart Failure With and Without CAD

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
VKA, Aspirin	CHF due to nonischemic etiology	<i>Against</i> routine use of Aspirin or oral VKAs	1B
	Patients with CHF requiring Aspirin	Aspirin, regardless of whether the patient is receiving an ACE-Inhibitor	1C+

### Primary Prevention

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Aspirin, VKA, or Both	Patients with at least moderate risk for a coronary event (based on age and cardiac risk factor profile with a 10-year risk of a cardiac event of > 10%)	Aspirin 75 – 162 mg daily recommended over no antithrombotic therapy	2A
		Aspirin 75 – 162 mg daily recommended over VKAs	2A
	Patients at particularly high risk of events in whom the INR can be monitored without difficulty	Low-dose VKAs with target INR of approximately 1.5	2A

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**Thrombolysis and Adjunctive Therapy in Acute Myocardial Infarction**

CHEST 2004;126:549S-575S

**Patients with Acute Myocardial Infarction: Thrombolysis**

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Thrombolysis with Streptokinase, t-PA, Anistreplase, Reteplase, and Tenecteplase	Patients with ischemic symptoms characteristic of acute MI $\leq$ 12 hours in duration, and ST-segment elevation or left bundle-branch block (of unknown duration) on ECG	Any approved fibrinolytic agent	1A
		Recommended: Streptokinase, Anistreplase, Reteplase, Alteplase, Tenecteplase	1A
	Patients with symptom duration $\leq$ 6 hours	Administration of Alteplase or Tenecteplase recommended <i>over</i> Streptokinase	1A
	Patients with known allergy or sensitivity to Streptokinase	Alteplase, Reteplase, Tenecteplase	1A
	Patients with recurrent acute myocardial infarction	<b>Do not</b> use repeat administration of Streptokinase	2C
	Patients with ischemic symptoms characteristic of acute MI of $\leq$ 12 hours in duration and 12-lead ECG findings consistent with a true posterior MI	Fibrinolytic therapy	2C
	High-risk patients with ongoing symptoms characteristic of acute MI or hemodynamic compromise and duration of 12 – 24 hours who have ST elevation or left bundle-branch block	Administration of IV fibrinolytic therapy	2B
	Health-care settings where prehospital administration of fibrinolytic therapy is feasible and primary angioplasty is not available	Prehospital administration of fibrinolytic therapy only	1A
	Patients with acute MI who are candidates for fibrinolytic therapy	Administration within 30 minutes of arrival to the hospital or first contact with the health-care system	1A
Patients with any history of intracranial hemorrhage, closed head trauma, or ischemic stroke within the past 3 months	<b>Against</b> administration of fibrinolytic therapy	1C+	

**Adjunctive Treatment with Antithrombotic Agents in Patients Receiving Fibrinolysis for Acute Myocardial Infarction**

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Adjunctive Treatment with Aspirin	Patients with acute ST elevation MI, whether or not they receive fibrinolytic therapy	Aspirin 160 – 325 mg PO at initial evaluation, then indefinite therapy (75 – 162 mg PO daily)	1A
Adjunctive Treatment with Clopidogrel	Patients with allergy to Aspirin	Clopidogrel—loading dose (300 mg PO), maintenance dose (75 mg PO daily)	2C
Adjunctive Treatment with Unfractionated Heparin	Patients receiving Streptokinase	IV UFH 5000 unit bolus 1000 units/hr (patients > 80 kg) 800 units/hr (patients < 80 kg) Target aPTT of 50 – 75 seconds	2C
		SC UFH 12,500 units Q12H for 48 hours	2A
	All patients with high risk of systemic or venous thromboembolism (anterior MI, pump failure, previous embolus, atrial fibrillation, or left ventricular thrombus)	Administration of IV UFH while receiving streptokinase	1C+
	Patients receiving Alteplase, Tenecteplase, Reteplase for fibrinolysis in acute MI	Administration of weight-adjusted heparin (60 units/kg bolus—maximum 4000 units) followed by 12 units/kg/hour (1000 units/hour maximum) adjusted to maintain aPTT 50 – 75 seconds for 48 hours	1C
Adjunctive Treatment with LMWH	Patients aged $\leq$ 75 years with preserved renal function (creatinine $\leq$ 2.5 mg/dL in males and $\leq$ 2.0 mg/dL in females)	Enoxaparin (30 mg bolus IV followed by 1 mg/kg SC Q12H) with Tenecteplase up to 7 days	2B

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Adjunctive Therapy with Glycoprotein IIb/IIIa Receptor Blockers	Patients with acute ST elevation MI	Recommend <b>against</b> the combinations: Standard-dose Abciximab + ½-dose Reteplase OR ½-dose Tenecteplase + low-dose IV UFH OVER Standard-dose Reteplase or Tenecteplase	1B
		Suggest clinicians <i>not</i> use the combination: Streptokinase + <i>any</i> GP IIb/IIIa inhibitor	2B
Adjunctive Therapy with Direct Thrombin Inhibitors	Patients with acute ST-elevation MI treated with Streptokinase	<b>Do not</b> use Bivalirudin routinely	2A
	Patients with known or suspected heparin-induced thrombocytopenia (HIT) who are receiving fibrinolytic therapy	Administration of Hirudin with tPA Administration of Bivalirudin with Streptokinase	1A 2A

### Antithrombotic Therapy During Percutaneous Coronary Intervention (PCI)

CHEST 2004;126:576S-599S

#### Patients Undergoing PCI: Oral Antiplatelet Therapy

Therapy	Details	Recommendation	Grade
Aspirin	Patients undergoing PCI	Pretreatment with Aspirin, 75 – 325 mg	1A
	Long-term treatment after PCI	Aspirin 75 – 162 mg daily	1A
	Long-term treatment after PCI in patients who receive antithrombotic agents such as Clopidogrel or Warfarin	Lower-dose Aspirin (75 – 100 mg daily)	1C+
Ticlopidine Versus Clopidogrel After Stent Placement	Patients who underwent stent placement	Combination of Aspirin and a thienopyridine derivative (Clopidogrel or Ticlopidine) over systemic anticoagulation	1A
		Clopidogrel recommended over Ticlopidine	1A
		Clopidogrel loading dose (300 mg) 6 hours prior to planned PCI	1B
	If Clopidogrel started < 6 hours prior to PCI If Ticlopidine is administered	Clopidogrel loading dose of 600 mg Loading dose of 500 mg at least 6 hours before planned PCI	2C 2C
Aspirin Intolerant Patients	PCI patients who cannot tolerate aspirin	Loading dose of Clopidogrel (300 mg) or Ticlopidine (500 mg) be administered at least 24 hours prior to planned PCI	2C
Duration of Thienopyridine Therapy After Stent Placement	After PCI, in addition to Aspirin	Clopidogrel (75 mg daily) for at least 9 – 12 months	1A
	If Ticlopidine is used in place of Clopidogrel after PCI	Ticlopidine for 2 weeks after placement of a bare metal stent in addition to Aspirin	1B
	Patients with low atherosclerotic risk, such as those with isolated coronary lesions	Clopidogrel for at least 2 weeks after placement of a bare metal stent	1A
		Clopidogrel for 2 – 3 months after placement of a Sirolimus-eluting stent	1C+
	Clopidogrel for 6 months after placement of a Paclitaxel-eluting stent	1C	
Other Oral Antiplatelet Agents	Patients after stent placement	Ticlopidine over Cilostazol	1B
		Clopidogrel over Cilostazol	1C
	Aspirin-intolerant patients undergoing PCI	<b>Do not</b> use Dipyridamole as an alternative to thienopyridine therapy	2C

#### Patients Undergoing PCI: GP IIb/IIIa Inhibitors

Therapy	Details	Recommendation	Grade
GP IIb/IIIa Inhibitors	All patients undergoing PCI, particularly for those undergoing primary PCI, or those with refractory unstable angina or other high-risk features	Use of a GP IIb/IIIa antagonist (Abciximab or Eptifibatide)	1A

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GP IIb/IIIa Inhibitors	Patients undergoing PCI for STEMI	Abciximab recommended over Eptifibatide ( <i>Remark: whenever possible, Abciximab should be started prior to balloon inflation</i> )	1B
	All patients undergoing PCI (Abciximab dosing)	Abciximab as a 0.25 mg/kg bolus followed by a 12-hour infusion at a rate of 10 mcg/min	1A
	All patients undergoing PCI (Eptifibatide dosing)	Eptifibatide as a double bolus (each 180 mcg/kg administered 10 minutes apart) followed by an 18-hour infusion of 2.0 mcg/kg/min	1A
	Patients undergoing PCI	<b>Against</b> use of Tirofiban as an alternative to Abciximab	1A
	Patients with NSTEMI/UA who are designated as moderate-to-high risk based on TIMI score	Upstream use of a GP IIb/IIIa antagonist (either Eptifibatide or Tirofiban) started as soon as possible prior to PCI	1A
	Patients with NSTEMI/UA who receive upstream treatment with Tirofiban	PCI be deferred for at least 4 hours after initiating Tirofiban infusion	2C
	Patients with planned PCI in NSTEMI/UA patients with an elevated troponin level	Abciximab be started within 24 hours prior to the intervention	1A

**Patients Undergoing PCI: Unfractionated Heparin**

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Unfractionated Heparin	Patients receiving a GP IIb/IIIa inhibitor	Heparin bolus (50 – 70 units/kg) to achieve target ACT > 200 s	1C
	Patients not receiving GP IIb/IIIa inhibitor	Heparin be administered in doses sufficient to produce an ACT 250 – 350 s	1C+
		Weight-adjusted Heparin bolus of 60 – 100 units/kg	2C
	Patients after uncomplicated PCI	<b>Against</b> routine postprocedural infusion of Heparin	1A

**Patients Undergoing PCI: LMWH**

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Low Molecular Weight Heparin	Patients who have received LMWH prior to PCI	Administration of additional anticoagulant therapy is dependent on the timing of the last dose of LMWH	1C
	If the last dose of Enoxaparin was administered ≤ 8 hours prior to PCI	No additional anticoagulant therapy	2C
	If the last dose of Enoxaparin was administered between 8 and 12 hours before PCI	0.3 mg/kg bolus of IV Enoxaparin at the time of PCI	2C
	If the last dose of Enoxaparin was administered > 12 hours before PCI	Conventional anticoagulation therapy during PCI	2C

**Patients Undergoing PCI: Direct Thrombin Inhibitors**

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Direct Thrombin Inhibitors	Patients undergoing PCI who are not treated with a GP IIb/IIIa antagonist	Bivalirudin (0.75 mg/kg bolus followed by an infusion of 1.75 mg/kg/hour for the duration of PCI) over Heparin during PCI	1A
	In PCI patients who are at low risk for complications	Bivalirudin as an alternative to Heparin as an adjunct to GP IIb/IIIa antagonists	1B
	In PCI patients who are at high risk for bleeding	Bivalirudin over Heparin as an adjunct to GP IIb/IIIa antagonists	1B

**Patients Undergoing PCI: Vitamin K Antagonists**

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Vitamin K Antagonists	Patients undergoing PCI with no other indication for systemic anticoagulation therapy	<b>Against</b> routine use of Warfarin (or other Vitamin K antagonist) after PCI	1A

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**Antithrombotic Therapy in Atrial Fibrillation**

CHEST 2004; 126:429S-456S

**Long-Term Antithrombotic Therapy for Chronic Atrial Fibrillation (AF) or Atrial Flutter, Anticoagulants and Antiplatelet Agents**

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Atrial Fibrillation	Patients with persistent (“sustained” or “permanent”) or paroxysmal (intermittent) AF at high risk of stroke (having any of the following features: prior ischemic stroke, TIA, systemic embolism, age > 75 years, moderately or severely impaired left ventricular systolic function and/or congestive heart failure, history of hypertension, or diabetes mellitus)	Anticoagulation with an oral VKA, such as Warfarin  (Target INR 2.5; Range 2.0 – 3.0)	1A
	Patients with persistent AF or PAF, age 65 – 75 years, in the absence of other risk factors	Antithrombotic therapy: Oral VKA, such as Warfarin (Target INR 2.5; Range 2.0 – 3.0) OR Aspirin 325 mg daily	1A
	Patients with persistent AF or PAF < 65 years old and with no other risk factors	Aspirin 325 mg daily	1B
Atrial Flutter	Patients with atrial flutter	Antithrombotic therapy decisions follow the same risk-based recommendations as for AF	2C
Valvular Heart Disease and Atrial Flutter	Patients with AF and mitral stenosis	Anticoagulation with an oral VKA, such as Warfarin (Target INR 2.5; Range 2.0 – 3.0)	1C+
	Patients with AF and prosthetic heart valves	Anticoagulation with an oral VKA, such as Warfarin	1C+
Atrial Fibrillation Following Cardiac Surgery	AF occurring shortly after open-heart surgery and lasting > 48 hours	Anticoagulation with an oral VKA, such as Warfarin, if bleeding risks are acceptable  Target INR 2.5 (Range 2.0 – 3.0)	2C
		Continue anticoagulation for several weeks following reversion to NSR, particularly if patients have risk factors for thromboembolism	2C

**Anticoagulation for Elective Cardioversion of Atrial Fibrillation or Atrial Flutter Patients**

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Atrial Fibrillation  *Comment: For all, continuation of anticoagulation beyond 4 weeks is based on whether the patient has experienced more than one episode of AF and on their risk factor status. Patients experiencing more than one episode of AF should be considered as having PAF.	AF of ≥ 48 hours or of unknown duration for whom pharmacologic or electrical cardioversion is planned	Anticoagulation with an oral VKA, such as Warfarin (Target INR 2.5; Range 2.0 – 3.0), for 3 weeks before elective cardioversion and for at least 4 weeks after successful cardioversion	1C+
		Immediate UFH with target PTT of 60 s (range 50 – 70 s) or at least 5 days of Warfarin with target INR of 2.5 (2.0 – 3.0) and a screening multiplane TEE. If no thrombus seen and cardioversion successful, anticoagulation with Warfarin (Target 2.5; Range 2.0 – 3.0) for at least 4 weeks	1B
	Multiplane TEE performed and thrombus visualized	Cardioversion should be postponed and anticoagulation should be continued indefinitely; Obtain repeat TEE before attempting later cardioversion	1B
	Patients with AF of known duration < 48 hours	Cardioversion can be performed without anticoagulation	2C
	Patients with AF of known duration < 48 hours and no known contraindication to anticoagulation	IV Heparin (Target PTT 60 s; range 50 – 70 s), or LMWH (at full DVT treatment doses) at presentation	2C

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Atrial Fibrillation	Emergency cardioversion where a TEE-guided approach is not possible	IV UFH (target PTT 60 s; range 50 – 70 s) started as soon as possible, followed by 4 weeks of anticoagulation with an oral VKA, such as Warfarin (target INR 2.5; range 2.0 – 3.0) if NSR persists after cardioversion	2C
Atrial Flutter	Patients with atrial flutter	Use of anticoagulants in the same way as for cardioversion of patients with Atrial Fibrillation	2C

### Antithrombotic Therapy in Valvular Heart Disease—Native and Prosthetic

CHEST 2004; 126:457S-482S

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Rheumatic Mitral Valve Disease with AF or a History of Systemic Embolism	Rheumatic mitral valve disease and AF, or a history of previous systemic embolism	Long term oral anticoagulant therapy Target INR 2.5; Range 2.0 – 3.0	1C+
		<b>Do not</b> use concomitant therapy with oral anticoagulants and antiplatelet agents	2C
	Rheumatic mitral valve disease with AF or a history of systemic embolism who suffer systemic embolism while receiving oral anticoagulants at a therapeutic INR	Add Aspirin, 75 – 100 mg daily	1C
		Patients unable to take Aspirin, add Dipyridamole 400 mg daily, or Clopidogrel	1C
Mitral Valve Disease in Sinus Rhythm	Rheumatic mitral valve disease and normal sinus rhythm with a left atrial diameter > 5.5 cm	Long-term VKA Target INR 2.5; Range 2.0 – 3.0	2C
	Rheumatic mitral valve disease and normal sinus rhythm with a left atrial diameter < 5.5 cm	<b>Do not</b> use antithrombotic therapy	2C
Mitral Valvuloplasty	Patients undergoing mitral valvuloplasty	Anticoagulation with VKA with a target INR of 2.5 (range 2.0 – 3.0) for 3 weeks prior to the procedure and 4 weeks after the procedure	2C

### Mitral Valve Prolapse (MVP)

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Mitral Valve Prolapse	Patients who have not experienced systemic embolism, unexplained TIAs, or AF	Against any antithrombotic therapy	1C
	Documented but unexplained TIAs	Long-term Aspirin therapy, 50 – 162 mg daily	1A
	Documented systemic embolism or recurrent TIAs despite aspirin therapy	Long-term VKA therapy (target INR 2.5; range 2.0 – 3.0)	2C

### Mitral Annular Calcification (MAC)

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Mitral Annular Calcification	Complicated by systemic embolism, not documented to be calcific embolism	Long-term VKA therapy (target INR 2.5; range 2.0 – 3.0)	2C

### Aortic Valve and Aortic Arch Disorders

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Aortic Valve Disease	Patients with aortic valve disease	<b>Do not</b> use long-term Vitamin K antagonist therapy unless there is another indication for anticoagulation	2C
	Mobile aortic atheromas and aortic plaques > 4mm as measured by TEE	Oral anticoagulant therapy	2C

### Prosthetic Heart Valves—Mechanical Prosthetic Heart Valves

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Mechanical Prosthetic Heart Valves	All patients with mechanical prosthetic heart valves	Vitamin K Antagonists	1C+
		Administration of UFH or LMWH until the INR is stable at a therapeutic level for 2 consecutive days	2C
	St. Jude Medical bileaflet valve in the aortic position	Target INR of 2.5 (2.0 – 3.0)	1A

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Mechanical Prosthetic Heart Valves	Tilting disk valves and bileaflet mechanical valves in the mitral position	Target INR of 3.0 (2.5 – 3.5)	1C+
	CarboMedics bileaflet valve or Medtronic Hall tilting disk mechanical valves in the aortic position, normal left atrium size and sinus rhythm	Target INR of 2.5 (2.0 – 3.0)	1C+
	Mechanical valves and additional risk factors such as AF, myocardial infarction, left atrial enlargement, endocardial damage, and low ejection fraction	Target INR of 3.0 (2.5 – 3.5) combined with low doses of Aspirin (75 – 100 mg daily)	1C+
	Patients with caged ball or caged disk valves	Target INR 3.0 (2.5 – 3.5) in combination with Aspirin (75 – 100 mg daily)	2A
	Mechanical prosthetic heart valves who suffer systemic embolism despite a therapeutic INR	Maintenance of INR 3.0 (2.5 – 3.5) plus addition of Aspirin (75 – 100 mg daily)	1C+
	Prosthetic heart valves in whom VKA must be discontinued	LMWH or Aspirin 80 – 100 mg daily	1C

**Prosthetic Heart Valves—Bioprosthetic Valves**

<i>Time Frame</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
First 3 Months After Valve Insertion	Bioprosthetic valve in the mitral position	VKAs; Target INR 2.5 (range 2.0 – 3.0) for the first 3 months after valve insertion	1C+
	Bioprosthetic valve in the aortic position	VKAs; Target INR 2.5 (2.0 – 3.0) for the first 3 months after valve insertion	2C
		Aspirin 80 – 100 mg daily	1C
	Patients who have undergone valve replacement	Heparin (LMWH or UFH) until the INR is stable at therapeutic levels for 2 consecutive days	2C
	Patients with bioprosthetic valves who have a history or systemic embolism	VKAs for 3 – 12 months	1C
Long-Term Treatment	Patients with bioprosthetic valves who have evidence of a left atrial thrombus at surgery	VKAs with a dose sufficient to prolong the INR to a target of 2.5 (range 2.0 – 3.0)	1C
	Patients with bioprosthetic valves who have AF	Long-term treatment with VKAs with a target INR of 2.5 (range 2.0 – 3.0)	1C+
	Patients with bioprosthetic valves who are in sinus rhythm and do not have AF	Long-term therapy with Aspirin, 75 – 100 mg daily	1C+

**Infective Endocarditis and Nonbacterial Thrombotic Endocarditis**

<i>Disease State</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Endocarditis	Mechanical prosthetic valve and endocarditis who have no contraindications	Continuation of long-term Vitamin K Antagonists	2C
	Patients with nonbacterial thrombotic endocarditis and systemic or pulmonary emboli	Full-dose IV UFH or SQ Heparin	1C
	Disseminated cancer or debilitating disease with aseptic vegetations	Full-dose UFH	2C

**Prevention of Venous Thromboembolism**

CHEST 2004;126:338S-400S

**General Recommendations**

<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Mechanical Prophylaxis	Mechanical methods of prophylaxis including graduated compression stockings (GCS), the use of intermittent pneumatic compression (IPC) devices and the venous foot pump (VFP)	Used primarily in patients who are at high risk of bleeding	1C+
		Used as an adjunct to anticoagulant-based prophylaxis	2A
		Careful attention be directed toward ensuring the proper use of, and optimal compliance with, the mechanical device	1C+
Aspirin for Prophylaxis	Any patient group	<b>Against</b> the use of Aspirin alone as prophylaxis against VTE	1A
Dosing	For each of the antithrombotic agents	Clinicians consider the manufacturer's suggested dosing guidelines	1C

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Renal Impairment	All patients, particularly elderly patients and those who are at high risk for bleeding	Consider renal impairment when deciding on doses of LMWH, Fondaparinux, the direct thrombin inhibitors and other antithrombotic drugs that are cleared by the kidneys	1C+
Neuraxial Anesthesia	All patients undergoing neuraxial anesthesia or analgesia	Special caution when using anticoagulant prophylaxis	1C+

**General, Vascular, Gynecologic and Urologic Surgery**

<i>Surgery Type</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
General Surgery	Low risk general surgery patients  <i>Low risk—minor surgery in patients &lt; 40 yr with no additional risk factors</i>	<b>Against</b> use of specific prophylaxis other than early and persistent mobilization	1C+
	Moderate risk general surgery patients  <i>Moderate risk—nonmajor procedure in patients 40 – 60 yrs or &lt; 40 yrs with additional risk factors or patients undergoing major operations and are &lt; 40 yrs of age with no additional risk factors</i>	Prophylaxis with LDUH 5000 units BID or LMWH ≤ 3400 units once daily	1A
	Higher risk general surgery patients  <i>Higher risk—nonmajor surgery and &gt; 60 years of age or additional risk factors or patients undergoing major surgery who are &gt; 40 year of age or have additional risk factors</i>	Prophylaxis with LDUH 5000 units TID or LMWH > 3400 units daily	1A
	High risk general surgery patients with multiple risk factors	Pharmacologic methods (LDUH TID or LMWH > 3400 units daily) be combined with use of GCS and/or IPC	1C+
	General surgery patients with high risk of bleeding	Mechanical prophylaxis with properly fitted GCS or IPC, at least initially until the bleeding risk decreases	1A
	Selected high risk general surgery patients, including those who have undergone major cancer surgery	Post-hospital discharge prophylaxis with LMWH	2A
	Vascular Surgery	Patients undergoing vascular surgery who do not have additional thromboembolic risk factors	<b>Do not</b> use thromboprophylaxis routinely
Patients undergoing major vascular surgical procedures who have additional thromboembolic risk factors		Prophylaxis with LDUH or LMWH	1C+
Gynecologic Surgery	Patients undergoing brief procedures of ≤ 30 min for benign disease	<b>Against</b> use of specific prophylaxis other than early and persistent mobilization	1C+
	Patients undergoing laparoscopic gynecologic procedures in whom additional VTE risk factors are present	Use of thromboprophylaxis with one or more of the following: LDUH, LMWH, IPC, GCS	1C
	Major gynecologic surgery	Thromboprophylaxis should be used	1A
	Patients undergoing major gynecologic surgery for benign disease without additional risk factors	LDUH 5000 units BID	1A
		Once-daily prophylaxis with LMWH ≤ 3400 units daily	1C+
		IPC started just before surgery and used continuously while the patient is not ambulating	1B
	Patients undergoing extensive surgery for malignancy and for patients with additional VTE risk factors	Routine prophylaxis with LDUH 5000 units TID	1A
		Higher doses of LMWH (i.e. > 3400 units daily)	1A
		IPC alone continued until hospital discharge	1A
		Combination of LDUH or LMWH plus mechanical prophylaxis with GCS or IPC	1C
	Patients undergoing major gynecologic procedures	Prophylaxis continue until discharge from the hospital	1C
Patients who are at particularly high risk including those who have undergone cancer surgery and who are > 60 years of age or have previously experienced a VTE	Continue prophylaxis for 2 – 4 weeks after hospital discharge	2C	

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Urologic Surgery	Patients undergoing transurethral or other low-risk urologic procedures	<b>Against</b> the use of specific prophylaxis other than early and persistent mobilization	1C+
	Patients undergoing major, open urologic procedures	Routine prophylaxis with LDUH twice daily or three times daily	1A
		Prophylaxis with IPC and/or GCS	1B
		Prophylaxis with LMWH	1C+
	Urologic surgery patients who are actively bleeding or are at very high risk for bleeding	Mechanical prophylaxis with GCS and/or IPC at least until the bleeding risk decreases	1C+
Patients with multiple risk factors	Combine GCS and/or IPC with LDUH or LMWH	1C+	
Laparoscopic Surgery	Most patients	Against routine thromboprophylaxis other than aggressive mobilization	1A
	Patients undergoing laparoscopic procedures who have additional thromboembolic risk factors	Use of thromboprophylaxis with one or more of the following: LDUH, LMWH, IPC or GCS	1C+

### Orthopedic Surgery

<i>Surgery Type</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Elective Hip Arthroplasty (THR)	Patients undergoing elective THR	Routine use of one of the following: LMWH (at a usual high-risk dose, started 12 h before surgery, or 12 – 24 h after surgery, or 4 – 6 h after surgery at half the usual high-risk dose and then increasing to the usual high-risk dose the following day) Fondaparinux (2.5 mg started 6 – 8 h after surgery) Adjusted-dose VKA started preoperatively or the evening after surgery (INR target 2.5; range 2.0 – 3.0)	1A
		<b>Against</b> the use of Aspirin, Dextran, LDUH, GCS, IPC or VFP as the only method of thromboprophylaxis in these patients	1A
Elective Knee Arthroplasty (TKA)	Patients undergoing elective TKA	Routine thromboprophylaxis using LMWH (at the usual high-risk dose), Fondaparinux, or adjusted dose VKA (target INR 2.5; range 2.0 – 3.0)	1A
		The optimal use of IPC is an alternative option to anticoagulant prophylaxis	1B
		<b>Against</b> the use of the following as sole methods of thromboprophylaxis: Aspirin, or LDUH	1A
		<b>Against</b> the use of VFP as the sole method of thromboprophylaxis	1B
Knee Arthroscopy	Most patients	<b>Do not</b> use routine thromboprophylaxis in these patients, other than early mobilization	2B
	Patients undergoing arthroscopic knee surgery who are at a higher than usual risk based on preexisting VTE risk factors or following a prolonged or complicated procedure	Thromboprophylaxis with LMWH	2B
Hip Fracture Surgery (HFS)	Patients undergoing HFS	Routine use of Fondaparinux	1A
		Routine use of LMWH at the usual high-risk dose	1C+
		Routine use of adjusted-dose VKA (target INR 2.5; range 2.0 – 3.0)	2B
		Routine use of LDUH	1B
		<b>Against</b> use of Aspirin alone	1A

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Hip Fracture Surgery (HFS)	Surgery will likely be delayed	Prophylaxis with either LDUH or LMWH be initiated during the time between hospital admission and surgery	1C+	
	Anticoagulant prophylaxis contraindicated because of high bleeding risk	Mechanical prophylaxis	1C+	
Other Prophylaxis Issues in Major Orthopedic Surgery	Major orthopedic surgical procedures	Decision about the timing of the initiation of pharmacologic prophylaxis be based on efficacy-to-bleeding tradeoffs for that particular agent	1A	
		For LMWH there are only small differences between starting preoperatively or postoperatively, and both options are acceptable.	1A	
	Following major orthopedic surgery	<b>Against</b> the routine use of Doppler Ultrasonography (DUS) screening at the time of hospital discharge in asymptomatic patients	1A	
	Patients undergoing THR, TKA, or HFS	Thromboprophylaxis with LMWH (using a high-risk dose), Fondaparinux (2.5 mg daily) or a VKA (target INR 2.5; range 2.0 – 3.0) for at least 10 days	1A	
	Patients undergoing THR or HFS	Give extended prophylaxis for up to 28 – 35 days after surgery	1A	
	Extended prophylaxis		Options for THR: LMWH, VKA	1A
			Option for THR: Fondaparinux	1C+
		Option for HFS: Fondaparinux	1A	
	Options for HFS: LMWH, VKA	1C+		
Elective Spine Surgery	Spinal surgery patients with no additional risk factors	<b>Against</b> routine use of any thromboprophylaxis modality, apart from early and persistent mobilization	1C	
	Patients undergoing spinal surgery who exhibit additional risk factors such as advanced age, known malignancy, presence of a neurologic deficit, previous VTE, or an anterior surgical approach	Some form of prophylaxis be used	1B	
	Patients with additional risk factors		Postoperative LDUH alone	1C+
			Postoperative LMWH alone	1B
			Perioperative IPC alone	1B
		Perioperative GCS alone	2B	
	Perioperative IPC combined with GCS	2C		
Patients with multiple risk factors for VTE	Combine LDUH or LMWH with GCS and/or IPC	1C+		
Isolated Lower Extremity Injuries	Patients with isolated lower extremity injuries	<b>Do not</b> routinely use thromboprophylaxis	2A	

### Neurosurgery

<i>Surgery Type</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Neurosurgery	Patients undergoing major neurosurgery	Thromboprophylaxis be used routinely	1A
	Patients undergoing intracranial neurosurgery	Use of IPC with or without GCS	1A
		Prophylaxis with LDUH	2B
		Postoperative LMWH	2A
	High-risk neurosurgery patients	Combination of mechanical prophylaxis (i.e. GCS and/or IPC) and pharmacologic prophylaxis (i.e. LDUH or LMWH)	2B

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**Trauma, Spinal Cord Injury, Burns**

<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>	
Trauma	All trauma patients with at least one risk factor for VTE	Receive thromboprophylaxis, if possible	1A	
	In the absence a of major contraindication	Clinicians use LMWH prophylaxis starting as soon as it is considered safe to do so	1A	
	If LMWH prophylaxis is delayed, or currently contraindicated due to active bleeding, or patient is at a high risk for hemorrhage	Mechanical prophylaxis with IPC, or possibly with GCS alone, be used	1B	
	Patients who are at high risk for VTE (e.g. presence of a SCI, lower extremity or pelvic fracture, major head injury, or an indwelling femoral venous line) and who have received suboptimal prophylaxis or no prophylaxis	DUS screening	1C	
	Trauma patients		<b>Against</b> use of inferior vena cava filter (IVCF) as primary prophylaxis	1C
			Continue thromboprophylaxis until hospital discharge, including the period of inpatient rehabilitation	1C+
	Patients with major impaired mobility	Continue prophylaxis after discharge with LMWH or a VKA (target INR 2.5; range 2.0 – 3.0)	2C	
Acute Spinal Cord Injury (SCI)	All patients with acute SCI	Thromboprophylaxis be provided	1A	
		<b>Against</b> the use of LDUH, GCS, or IPC as single prophylaxis modalities	1A	
		Prophylaxis with LMWH should be commenced once primary hemostasis is evident	1B	
		Combined use of IPC and LDUH as an alternative to LMWH	2B	
		Combined use of IPC and LMWH as an alternative to LMWH	2C	
	When anticoagulant prophylaxis is contraindicated early after injury	Use of IPC and/or GCS	1C+	
	All patients with acute SCI	<b>Against</b> the use of IVCF as primary prophylaxis against PE	1C	
	During the rehabilitation phase following acute SCI	Continuation of LMWH prophylaxis or conversion to an oral VKA (INR target 2.5; range 2.0 – 3.0)	1C	
Burns	Burn patients with additional risk factors for VTE, including one or more of the following: advanced age, morbid obesity, extensive or lower extremity burns, concomitant lower extremity trauma, use of a femoral venous catheter and/or prolonged immobility	Give thromboprophylaxis, if possible	1C+	
	If there are no contraindications	Use either LDUH or LMWH starting as soon as it is considered safe to do so	1C+	

**Medical Conditions**

<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Medical Patients	Acutely ill medical patients who have been admitted to the hospital with congestive heart failure or severe respiratory disease, or who are confined to bed and have one or more additional risk factors, including active cancer, previous VTE, sepsis, acute neurologic disease or inflammatory bowel disease	Prophylaxis with LDUH or LMWH	1A
	Medical patients with risk factors for VTE and in whom there is a contraindication to anticoagulant prophylaxis	Mechanical prophylaxis with GCS or IPC	1C+

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<b>Cancer Patients</b>			
<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Patients with Cancer	Cancer patients undergoing surgical procedures	Use prophylaxis that is appropriate for their current risk state	1A
	Hospitalized cancer patients who are bedridden with an acute medical illness	Use prophylaxis that is appropriate for their current risk state	1A
	Patients with long-term indwelling central venous catheters (CVCs)	<i>Do not</i> routinely use prophylaxis to try to prevent thrombosis	2B
		<i>Do not</i> use LMWH for this indication	2B
	<i>Against</i> the use of fixed-dose Warfarin for this indication	1B	
<b>Critical Care</b>			
<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Critical Care Patients	On admission to a critical care unit	All patients be assessed for their risk of VTE. Accordingly, most patients should receive thromboprophylaxis	1A
	Patients who are at a high risk for bleeding	Mechanical prophylaxis with GCS and/or IPC until the bleeding risk decreases	1C+
	ICU patients who are at a moderate risk for VTE (e.g. medically ill or postoperative patients)	LDUH or LMWH prophylaxis	1A
	Patients who are at higher risk, such as that following major trauma or orthopedic surgery	LMWH prophylaxis	1A
<b>Long Distance Travel</b>			
<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Patients Traveling Long-Distance	Long-distance travelers (i.e. flights of > 6 h duration)	Avoid constrictive clothing around the lower extremities or waist; avoid dehydration; frequent calf muscle stretching	1C
	Long-distance travelers with additional risk factors for VTE	General strategies listed above	
	If active prophylaxis is considered because of the perceived increased risk of venous thrombosis	Use of properly fitted, below-knee GCS providing 15 – 30 mmHg of pressure at the ankle	2B
		Single prophylactic dose of LMWH injected prior to departure	2B
	Long-distance travelers (i.e. flights of > 6 h duration)	<i>Against</i> the use of Aspirin for VTE prevention associated with travel	1B

### Antithrombotic Therapy for Venous Thromboembolic Disease

CHEST 2004;126:401S-428S

<b>Treatment of Deep Venous Thrombosis</b>			
<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Initial Treatment of Acute DVT of the Leg	Objectively confirmed DVT	Short-term treatment with SC LMWH or IV UFH or SC UFH	1A
	High clinical suspicion of DVT	Treatment with anticoagulants while awaiting the outcome of diagnostic tests	1C+
	Acute DVT	Initial treatment with LMWH or UFH for at least 5 days	1C
	All patients with DVT	Initiation of VKA together with LMWH or UFH on the first treatment day and discontinuation of heparin when INR is stable and > 2.0	1A

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IV UFH for the Initial Treatment of DVT	If IV UFH chosen as initial therapy for DVT	Administer by continuous IV infusion with dose adjustment to achieve and maintain an aPTT prolongation corresponding to plasma heparin levels form 0.3 – 0.7 IU/mL anti-Xa activity by the amidolytic assay	1C+
	Patients requiring large therapeutic doses of UFH without achieving a therapeutic aPTT	Measurement of anti-Xa level for dose guidance	1B
SC UFH for the Initial Treatment of DVT	Patients with acute DVT	SC administered UFH can be used as an adequate alternative to IV UFH	1A
	Patients who receive SC UFH	Initial dose of 35,000 units/24 hrs SC with subsequent dosing to maintain the aPTT in the therapeutic range	1C+
LMWH for the Initial Treatment of DVT	Patients with acute DVT	Initial treatment with LMWH SC once or twice daily over UFH as an outpatient, if possible	1C
		Initial treatment with LMWH SC once or twice daily over UFH as an inpatient if necessary	1A
	Patients with severe renal failure	IV UFH recommended over LMWH	2C
Systematically Administered Thrombolysis in Initial Treatment of DVT	Patients with DVT	<b>Against</b> routine use of IV thrombolytic treatment	1A
	Selected patients, such as those with massive iliofemoral DVT at risk of limb gangrene secondary to venous occlusion	IV thrombolysis	2C
Catheter-Directed Thrombolysis in the Initial Treatment of DVT	Patients with DVT	<b>Against</b> routine use of catheter-directed thrombolysis	1C
		Catheter-directed thrombolysis should be confined to selected patients such as those requiring limb salvage	2C
Catheter Extraction or Fragmentation and Surgical Thrombectomy for Initial Treatment of DVT	Patients with DVT	<b>Against</b> routine use of venous thrombectomy	1C
	Selected patients, such as those with massive iliofemoral DVT at risk of limb gangrene secondary to venous occlusion	Venous thrombectomy	2C
Vena Caval Interruption for the Initial Treatment of DVT	Most patients with DVT	<b>Against</b> routine use of a vena cava filter in addition to anticoagulants	1A
	Patients with a contraindication for, or a complication of anticoagulant treatment	Placement of inferior vena caval filter	2C
	Patients with recurrent thromboembolism despite adequate anticoagulation	Placement of inferior vena caval filter	2C
Nonsteroidal Anti-inflammatory Agents for the Initial Treatment of DVT	Initial treatment of DVT	<b>Against</b> use of nonsteroidal anti-inflammatory agents	2B
Immobilization	Patients with DVT	Ambulation as tolerated	1B

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<b>Long-Term Treatment of Acute DVT of the Leg</b>			
<b>Therapy</b>	<b>Details</b>	<b>Recommendation</b>	<b>Grade</b>
Vitamin K Antagonists for the Long-Term Treatment of DVT	Patients with a first episode of DVT secondary to a transient (reversible) risk factor <i>(applies both to patients with proximal vein thrombosis and to patients with symptomatic DVT confined to the calf veins)</i>	Long-term treatment with VKA for 3 months over treatment for shorter periods	1A
	Patients with first-episode idiopathic DVT	VKA at least 6 – 12 months	1A
		Consider indefinite anticoagulant therapy	2A
	Patients with DVT and cancer	LMWH for first 3 – 6 months of long-term anticoagulant therapy	1A
		Anticoagulant therapy continued indefinitely or until the cancer is resolved	1C
	Patients with a first episode of DVT who have documented antiphospholipid antibodies or who have two or more thrombophilic conditions (e.g. combined Factor V Leiden and prothrombin 20210 gene mutations)	Treatment for 12 months	1C+
		Indefinite anticoagulant therapy	2C
	Patients with a first episode of DVT who have documented deficiency of antithrombin, deficiency of protein C or protein S, or the Factor V Leiden or prothrombin 20210 gene mutation, homocysteinemia or high factor VIII levels (>90 <sup>th</sup> percentile of normal)	Treatment for 6 – 12 months	1A
		Consider indefinite anticoagulant therapy	2C
	Patients with 2 or more episodes of objectively documented DVT	Indefinite anticoagulant therapy	2A
	For all treatment durations	Dose of VKA be adjusted to maintain a target INR of 2.5 (2.0 – 3.0)	1A
		Recommend <b>against</b> high-intensity VKA therapy (INR range 3.1 – 4.0) compared to INR range of 2.0 – 3.0	1A
		Recommend against low-intensity therapy (INR 1.5 – 1.9) compared to INR range of 2.0 – 3.0	1A
Patients receiving indefinite anticoagulant treatment	Risk-benefit of continuing such treatment should be reassessed in the individual patient at periodic intervals	1C	
	Repeat testing with compression ultrasonography for the presence or absence of residual thrombosis or measurement of plasma D-dimer	2C	
Low Molecular Weight Heparin for Long-Term Treatment of DVT	Most patients with DVT and cancer  <i>*The LMWH regimens that have been established to be effective for long-term treatment in randomized trials are Dalteparin 200 IU/kg QD for 1 month followed by 150 IU/kg QD thereafter, and Tinzaparin at 175 IU/kg body weight SC QD</i>	Treatment with LMWH for at least the first 3 – 6 months of long-term treatment	1A

**The Post-Thrombotic Syndrome**

<b>Situation</b>	<b>Details</b>	<b>Recommendation</b>	<b>Grade</b>
Elastic Stockings for the Prevention of the Post-Thrombotic Syndrome	After an episode of DVT	Use of elastic compression stockings with a pressure of 30 – 40 mmHg at the ankle for a duration of 2 years	1A

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Physical Treatment of the Post-Thrombotic Syndrome	Severe edema of the legs due to PTS	Course of intermittent pneumatic compression	2B
	Mild edema of the leg due to PTS	Use of elastic compression stockings	2C
Drug Treatment for the Post-Thrombotic Syndrome	Mild edema due to PTS	Administration of rutosides	2B

### Initial Treatment of Acute Pulmonary Embolism

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>	
IV UFH or LMWH for the Initial Treatment of Pulmonary Embolism	Patients with objectively confirmed non-massive PE	Short-term treatment with SC LMWH, or IV UFH	1A	
	Patients with high clinical suspicion of PE	Treatment with anticoagulants while awaiting the outcome of diagnostic tests	1C+	
	Patients with acute non-massive PE		LMWH recommended over IV UFH	1A
			Initial treatment with LMWH or UFH for at least 5 days	1C
	Patients with acute non-massive PE treated with LMWH	<b>Against</b> routine monitoring with anti-Xa levels	1A	
	Patients with severe renal failure	IV UFH suggested over LMWH	2C	
	If IV UFH chosen as therapy	Administration by continuous infusion with dose adjustment to achieve and maintain an aPTT prolongation corresponding to plasma heparin levels from 0.3 – 0.7 IU/mL anti-Xa activity by the amidolytic assay	1C+	
	In patients requiring large daily doses of UFH without achieving a therapeutic aPTT	Measurement of the anti-Xa level for dose guidance	1B	
For all patients with PE	Initiation of VKA together with LMWH or UFH on the first treatment day and discontinuation of heparin when the INR is stable and > 2.0	1A		
Systemically and Locally Administered Thrombolytic Drugs for the Initial Treatment of PE	Most patients with PE	<b>Do not</b> use systemic thrombolytic therapy	1A	
	Selected patients with PE	Systemic administration of thrombolytic therapy	2B	
	Patients who are hemodynamically unstable	Suggest use of thrombolytic therapy	2B	
	For all patients with PE	Suggest clinicians not use local administration of thrombolytic therapy via a catheter	1C	
	For patients with PE who receive thrombolytic regimens	Use of thrombolytic regimens with a short infusion time over those with prolonged infusion times	2C	
Catheter Extraction or Fragmentation for the Initial Treatment of PE	Most patients with PE	<b>Against</b> use of mechanical approaches	1C	
	Selected highly compromised patients who are unable to receive thrombolytic therapy or whose critical status does not allow sufficient time to infuse thrombolytic therapy	Suggest use of mechanical approaches	2C	
Pulmonary Embolectomy for the Initial Treatment of PE	Most patients with PE	<b>Against</b> pulmonary embolectomy	1C	
	Selected highly compromised patients who are unable to receive thrombolytic therapy or whose critical status does not allow sufficient time to infuse thrombolytic therapy	Suggest pulmonary embolectomy	2C	

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Vena Caval Interruption for the Initial Treatment of PE	PE patients with a contraindication for, or a complication of anticoagulant treatment	Placement of an inferior vena caval filter	2C
	PE patients with recurrent thromboembolism despite adequate anticoagulation		

### Long-Term Treatment of Acute Pulmonary Embolism

Therapy	Details	Recommendation	Grade
Vitamin K Antagonists for the Long-Term Treatment of Pulmonary Embolism	Patients with a first episode of PE secondary to a transient (reversible) risk factor	Long-term treatment with a VKA for at least 3 months	1A
	Patients with a first episode of idiopathic PE	Treatment with a VKA at least 6 – 12 months	1A
		Consider indefinite anticoagulation therapy	2A
	Patients with a PE and cancer	LMWH for the first 3 – 6 months of long-term anticoagulant therapy	1A
		Patients should receive anticoagulant therapy indefinitely or until the cancer is resolved	1C
	Patients with a first episode of PE who have documented antiphospholipid antibodies or who have 2 or more thrombophilic conditions (e.g. combined Factor V Leiden and prothrombin 20210 gene mutations)	Treatment for 12 months	1C+
		Indefinite anticoagulant therapy	2C
	Patients with a first episode of PE who have documented deficiency of antithrombin, deficiency of protein C or protein S, or the Factor V Leiden or prothrombin 20210 gene mutation, homocysteinemia, or high factor VIII levels (> 90 <sup>th</sup> percentile)	Anticoagulant treatment for 6 – 12 months	1A
	Patients with an idiopathic PE	Indefinite anticoagulant therapy	2C
	Patients with 2 or more episodes of objectively documented PE	Indefinite anticoagulant therapy	2A
For all treatment durations	In patients receiving indefinite anticoagulant therapy	The dose of VKA should be adjusted to maintain a target INR of 2.5 (range 2.0 – 3.0)	1A
		Recommend <i>against</i> high-intensity VKA therapy (INR range 3.1 – 4.0) compared to INR range of 2.0 – 3.0	1A
		Recommend <i>against</i> low-intensity therapy (INR range 1.5 – 1.9) compared to INR range of 2.0 – 3.0	1A
		The risk-benefit of continuing such treatment should be reassessed in the individual patient at periodic intervals	1C
LMWH for the Long-Term Treatment of PE	Most patients with PE and concurrent cancer  <i>*The LMWH regimens that have been established to be effective for long-term treatment are Dalteparin 200 IU/kg QD for 1 month followed by 150 IU/kg QD thereafter, and Tinzaparin at 175 IU/kg body weight SC QD</i>	Treatment with LMWH for at least the first 3 – 6 months of long-term treatment	1A

### Chronic Thromboembolic Pulmonary Hypertension (CTPH)

Therapy	Details	Recommendation	Grade
Pulmonary Thromboendarterectomy, VKA, and Caval Filter for the Treatment of Chronic Thromboembolic Pulmonary Hypertension	In selected patients with CTPH (i.e. patients with central disease under the care of an experienced surgical/medical team)	Pulmonary thromboendarterectomy	1C
	Following pulmonary thromboendarterectomy	Life-long treatment with VKA to an INR of 2.0 – 3.0	1C
	Patients with CTPH who are ineligible for pulmonary thromboendarterectomy		
	Before, or at the time of pulmonary thromboendarterectomy for CTPH	Placement of a vena caval filter	2C

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### Superficial Thrombophlebitis

<i>Therapy</i>	<i>Qualifying Details</i>	<i>Recommendation</i>	<i>Grade</i>
Treatment for Superficial Thrombophlebitis	Patients with superficial thrombophlebitis as a complication of an infusion	Topical Diclofenac gel	1B
		Oral Diclofenac	2B
	Patients affected by spontaneous superficial thrombophlebitis	Intermediate dosages of UFH or LMWH for at least 4 weeks	2B

### Acute Upper Extremity DVT

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
IV UFH or LMWH for the Initial Treatment of Upper Extremity DVT	Patients with acute upper-extremity DVT	Initial treatment with UFH	1C+
		Initial treatment with LMWH	1C+
Thrombolytic Therapy for the Initial Treatment of Upper Extremity DVT	In selected patients with acute upper-extremity DVT (e.g. those with a low risk of bleeding and symptoms of recent onset)	Short course of thrombolytic therapy for initial treatment	2C
Catheter Extraction, Surgical Thrombectomy, or Superior Vena Caval Filter for the Initial Treatment of Upper Extremity DVT	In selected patients with acute upper-extremity DVT (e.g. those with failure of anticoagulant or thrombolytic treatment and persistent symptoms)	Surgical embolectomy	2C
		Catheter extraction	2C
	In selected patients with acute upper-extremity DVT (e.g. those in whom anticoagulant treatment is contraindicated)	A superior vena caval filter could be considered for initial treatment	2C
Anticoagulants for the Long-Term Treatment of Upper Extremity DVT	Patients with acute upper-extremity DVT	Long-term treatment with VKA  <i>*As for acute DVT of the leg, a similar process should be used for determining the duration of VKA treatment</i>	1C+
Elastic Bandages for the Long-Term Treatment of Upper Extremity DVT	In patients with upper extremity DVT who have persistent edema and pain	Elastic bandages for symptomatic relief	2C

### The Pharmacology and Management of the Vitamin K Antagonists

CHEST 2004; 126:204S-233S

#### Initiation of Oral Anticoagulants

<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Appropriate Dose for Initiation of Oral Anticoagulants	Most individuals beginning therapy	Initiation with doses between 5mg and 10mg for the first 1 – 2 days with subsequent dosing based on the INR response	2B
	In the elderly, patients who are debilitated, malnourished, have CHF or have liver disease	Use of a starting dose ≤ 5 mg	2C

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### Monitoring of Oral Anticoagulants

Situation	Details	Recommendation	Grade
Frequency of Monitoring of Oral Anticoagulants	Patients starting therapy	Start INR monitoring after the initial 2 or 3 doses of oral anticoagulation therapy	2C
	Patients receiving a stable dose of oral anticoagulants	Monitor at an interval of no longer than every 4 weeks	2C

### Administration of Vitamin K & Dosing of Warfarin (or VKA) when the INR is Nontherapeutic

Situation	Details	Recommendation	Grade
Management of Dosing when the INR is Nontherapeutic	Patients with INR > therapeutic range, but < 5.0 who have no significant bleeding	Lower the dose of VKA or omit the next dose, monitor more frequently, and resume therapy at a lower dose when the INR is in the therapeutic range. <i>If only minimally above the therapeutic range, no dose reduction may be required.</i>	2C
	Patients with INRs $\geq$ 5.0 but < 9.0 who have no significant bleeding	Omit the next 1 or 2 doses of Warfarin, monitor more frequently, and resume therapy at a lower dose when the INR is in the therapeutic range.	2C
		Alternatively, omit a dose of Warfarin and administer Vitamin K1 (1 – 2.5 mg orally), particularly if the patient is at an increased risk of bleeding.	2C
	Patients with INRs $\geq$ 5.0 but < 9.0 who have no significant bleeding—More rapid reversal required because the patient requires urgent surgery	Vitamin K1 ( $\leq$ 5mg orally) can be given with the expectation that a reduction of the INR will occur in 24 hours.	2C
	If the INR is still high	Additional Vitamin K1 can be given (1 – 2 mg orally)	2C
	Patients with INRs $\geq$ 9.0 who have no significant bleeding	Hold Warfarin therapy. Administer Vitamin K1 (5 – 10 mg orally) with the expectation that the INR will be reduced substantially in 24 – 48 hours. Monitor the patient more frequently and use additional Vitamin K1 if necessary. Resume therapy at a lower dose when the INR is in the therapeutic range.	2C
	Patients with serious bleeding and elevated INRs	Hold Warfarin therapy. Administer Vitamin K1 (10 mg by slow IV infusion) supplemented with Fresh Plasma, Prothrombin Complex Concentrate, or Recombinant Factor VIIa, depending on the urgency of the situation. Vitamin K1 administration can be repeated every 12 hours.	1C
	Patients with life-threatening bleeding and elevated INRs	Hold Warfarin therapy. Administer Prothrombin Complex Concentrate or Recombinant Factor VIIa supplemented with Vitamin K1 (10 mg by slow IV infusion). Repeat the procedure if necessary, depending on the INR.	1C
	Patients with mild to moderately elevated INRs who have no major bleeding	Vitamin K should be administered orally rather than SC	1A

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<b>Bridging Warfarin (or VKA) Therapy for Invasive Procedures</b>																			
<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>																
Management of Dosing When an Invasive Procedure is Required	Patients with a low risk of thromboembolism*	Stop Warfarin approximately 4 days before surgery, allow the INR to return to near-normal values	2C																
	<table border="0"> <tr> <td><u>*Condition</u></td> <td><u>*Annualized Thrombosis Risk, %</u></td> </tr> <tr> <td>Lone atrial fibrillation</td> <td>1</td> </tr> <tr> <td>Average risk atrial fibrillation</td> <td>5</td> </tr> <tr> <td>High-risk atrial fibrillation</td> <td>12</td> </tr> <tr> <td>Dual-leaflet (St. Jude) aortic valve prosthesis</td> <td>10 – 12</td> </tr> <tr> <td>Single-leaflet (Bjork-Shiley) aortic valve prosthesis</td> <td>23</td> </tr> <tr> <td>Dual-leaflet (St. Jude) mitral valve prosthesis</td> <td>22</td> </tr> <tr> <td>Multiple St. Jude prostheses</td> <td>91</td> </tr> </table>	<u>*Condition</u>	<u>*Annualized Thrombosis Risk, %</u>	Lone atrial fibrillation	1	Average risk atrial fibrillation	5	High-risk atrial fibrillation	12	Dual-leaflet (St. Jude) aortic valve prosthesis	10 – 12	Single-leaflet (Bjork-Shiley) aortic valve prosthesis	23	Dual-leaflet (St. Jude) mitral valve prosthesis	22	Multiple St. Jude prostheses	91	Briefly use postoperative prophylaxis (if the intervention increases the risk of thrombosis) with a low dose of UFH (5000 units SC) or a prophylactic dose of LMWH and <b>simultaneously begin Warfarin therapy</b>	2C
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Low risk includes no recent (> 3 mo) VTE, Afib w/out h/o stroke or other risk factors, and bileaflet mechanical cardiac valve in aortic position.	Alternatively, a low dose of UFH or a prophylactic dose of LMWH also can be administered <b>preoperatively</b>	2C																	
Patients with an intermediate risk of thromboembolism*	Stop Warfarin therapy approximately 4 days before the surgery, allow the INR to fall, cover the patient beginning 2 days preoperatively with a low dose of UFH (5000 units SC) or a prophylactic dose of LMWH and then commence administration of a low dose of UFH (or LMWH) and Warfarin postoperatively	2C																	
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Patients with a high risk of thromboembolism*	Stop Warfarin therapy approximately 4 days before surgery to allow the INR to return to normal at the time of surgery, and begin therapy with a full dose of UFH or a full dose of LMWH as the INR falls (approximately 2 days preoperatively). UFH can be administered as a SC injection on an outpatient basis and as a continuous IV infusion after hospital admission in preparation for surgery and should be discontinued approximately 5 hours before surgery with the expectation that the anticoagulant effect will have worn off by the time of surgery.	2C																	
Examples of high risk of thromboembolism include recent (< 3mo) history of VTE, mechanical cardiac valve in mitral position, and old model of cardiac valve (ball/cage).	An alternative is to continue to use SC UFH or LMWH preoperatively and to stop therapy 12 – 24 hours before surgery with the expectation that the anticoagulant effect will be very low or have worn off by the time of surgery, then commence administering a low dose of UFH (or LMWH) and Warfarin postoperatively.	2C																	
Patients with a low risk of bleeding	Continue Warfarin therapy at a lower dose and operate at an INR of 1.3 – 1.5. The dose of Warfarin can be lowered 4 or 5 days before surgery. Warfarin therapy then can be restarted postoperatively, supplemented with a low dose of UFH (5000 units SC) or a prophylactic dose of LMWH, if necessary.	2C																	
Patients who are undergoing dental procedures with a need to control local bleeding	Use Tranexamic mouthwash without interrupting anticoagulant therapy	2B																	
	Use Epsilon Amino Caproic Acid mouthwash without interrupting anticoagulant therapy	2B																	

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<b>Management of INRs in the Antiphospholipid Syndrome</b>			
<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Therapeutic Range in the Presence of a Lupus Inhibitor	Patients who have a lupus inhibitor and who have no additional risk factors and have not failed to respond to therapy	Target INR of 2.5 (2.0 – 3.0)	2B
	Patients who have recurrent thromboembolic events with a therapeutic INR or other additional risk factors for thromboembolic events	Target INR of 3.0 (2.5 – 3.5)	2C
<b>Models of Anticoagulation Monitoring and Management</b>			
<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
	Physicians who manage oral anticoagulation	Therapy should be managed in a systematic and coordinated fashion, incorporating patients education, systematic INR testing, tracking and follow-up, and good patient communication of results and dosing decisions	1C+

### Antithrombotic and Thrombolytic Therapy for Ischemic Stroke

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<b>Acute Ischemic Stroke (AIS): Thrombolytic Therapy in Acute Stroke</b>			
<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
IV tPA for AIS Within 3 Hours of Symptom Onset  <i>ICH = Intracranial Hematoma</i>	For eligible patients (see inclusion and exclusion criteria)  <b>Inclusion Criteria:</b> <ul style="list-style-type: none"> <li>• Age ≥ 18 years</li> <li>• Clinical diagnosis of stroke with clinically meaningful neurologic deficit</li> <li>• Clearly defined time of onset of &lt; 180 min before treatment</li> <li>• Baseline CT showing no evidence of ICH</li> </ul> <b>Exclusion Criteria:</b> <ul style="list-style-type: none"> <li>• Minor or rapidly improving symptoms or signs</li> <li>• CT signs of ICH</li> <li>• A history of ICH</li> <li>• Seizure at stroke onset</li> <li>• Stroke or serious head injury within 3 months</li> <li>• Major surgery or serious trauma within 2 weeks</li> <li>• GI or urinary tract hemorrhage within 3 weeks</li> <li>• Systolic BP &gt; 185 mmHg</li> <li>• Diastolic BP &gt; 110 mmHg</li> <li>• Aggressive treatment required to lower BP</li> <li>• Glucose &lt; 50 mg/dL or &gt; 400 mg/dL</li> <li>• Symptoms of subarachnoid hemorrhage</li> <li>• Arterial puncture at a noncompressible site or lumbar puncture within 1 week</li> <li>• Platelet count &lt; 100,000/μL</li> <li>• Heparin therapy within 48 hours associated with elevated aPTT</li> <li>• Clinical presentation suggesting post-MI pericarditis</li> <li>• Pregnant or lactating Women</li> <li>• Current use of oral anticoagulants (PT &gt; 15 s; INR &gt; 1.7)</li> </ul>	Administration of IV tPA in a dose of 0.9 mg/kg (max 90 mg) with 10% of total dose administered as an initial bolus and the remainder infused over 60 min, provided that treatment is initiated within 3 h of clearly defined symptom onset	1A
		Patients with extensive (more than 1/3 of the MCA territory) and clearly identifiable hypodensity on CT	<b>Against</b> thrombolytic therapy
IV tPA for AIS Between 3 h to 6 h of Symptom Onset	For unselected patients with AIS of > 3 h but < 6 h	<b>Do not</b> use IV tPA	2A
IV Streptokinase For AIS Between 0 – 6 h Symptom Onset	For patients with AIS	<b>Against</b> streptokinase	1A

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Intra-Arterial Thrombolysis for AIS	Patients with angiographically demonstrated MCA occlusion and no signs of major early infarction on the baseline CT scan, who can be treated within 6 h of symptom onset	Use of intra-arterial thrombolytic therapy with tPA	2C
	Patients with acute basilar artery thrombosis and without major CT/MRI evidence of infarction	Intra-arterial thrombolysis with tPA	2C

### Acute Ischemic Stroke (AIS): Patients not Eligible for Thrombolysis

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Anticoagulants for Altering Outcomes Among Acute Stroke Patients not Eligible for Thrombolysis	Patients with AIS	<b>Do not</b> use full-dose anticoagulation with IV or SC Heparin, LMWH or Heparinoids	2B
Antiplatelet Agents for Altering Outcomes Among Acute Stroke Patients not Eligible for Thrombolysis	Patients with AIS who are not receiving thrombolysis	Early Aspirin therapy, 160 – 325 mg daily	1A
Antithrombotic Therapy for Prevention of DVT and PE in AIS	Acute stroke patients with restricted mobility	Prophylactic low-dose SC Heparin or LMWH or Heparinoids	1A
	Patients who have contraindications to anticoagulants	Use of intermittent pneumatic compression devices or elastic stockings	1C

### DVT/PE Prophylaxis in Patients with Intracerebral Hematoma (ICH)

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Heparin for DVT/PE Prophylaxis in Patients with ICH	Patients with acute ICH	Initial use of intermittent pneumatic compression	1C+
	Stable patients with acute ICH	Low-dose SC Heparin may be initiated as soon as the second day after the onset of the hemorrhage	2C

### Stroke Prevention

<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Prevention of Cerebral Ischemic Events in Patients with Non-cardioembolic TIA or Stroke: Anti-Platelet Drugs vs. Placebo or vs. an Alternative Anti-Platelet Drug	Patients who have experienced a noncardioembolic stroke or TIA (i.e. atherothrombotic, lacunar, or cryptogenic)	Treatment with an Anti-Platelet agent  <u>Acceptable options for initial therapy:</u> <ul style="list-style-type: none"> <li>Aspirin 50 – 325 mg daily</li> <li>Combination of Aspirin 25 mg and Extended-release Dipyridamole 200 mg twice daily (Aggrenox<sup>®</sup>)</li> <li>Clopidogrel 75 mg daily</li> </ul>	1A
	Patients receiving Aspirin who are at a moderate-to-high risk of bleeding complications	Low-dose Aspirin, 50 – 100 mg daily	1C+
	Patients who have experienced a noncardioembolic stroke or TIA	The combination of Aspirin and Extended-release Dipyridamole (Aggrenox <sup>®</sup> ) 25mg/200mg BID recommended <b>over</b> Aspirin	2A
		Clopidogrel recommended <b>over</b> Aspirin	2B
	Patients allergic to Aspirin	Clopidogrel	1C+
Prevention of Non-cardioembolic Cerebral Ischemic Events: Oral Anticoagulants	Most patients with noncardioembolic stroke or TIA	Anti-Platelet agents recommended <b>over</b> oral anticoagulation	1A
	Patients with well-documented prothrombotic disorders	Oral anticoagulation recommended <b>over</b> Anti-platelet agents	2C

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Prevention of Cerebral Ischemic Events in Patients Undergoing Carotid Endarterectomy: Anti-Platelet Agents	Patients undergoing carotid endarterectomy	Aspirin 81 – 325 mg prior to, and following, the procedure	1A
Prevention of Cardioembolic Cerebral Ischemic Events—Afib	Patients with atrial fibrillation who have had a recent stroke or TIA	Long-term oral anticoagulation (target INR 2.5; range 2.0 – 3.0)	1A
	Patients with cardioembolic stroke who have contraindications to anticoagulant therapy	Aspirin	1A
Patients with Aortic Atheromata	Patients with stroke associated with aortic atherosclerotic lesions	Anti-platelet therapy recommended over no therapy	1C+
	Patients with cryptogenic stroke associated with mobile aortic arch thrombi	Either oral anticoagulation or anti-platelet agents	2C
Patients with Patent Foramen Ovale (PFO)	In patients with cryptogenic ischemic stroke and a PFO	Anti-platelet therapy recommended over no therapy	1C+
		Anti-platelet agents suggested <i>over</i> anticoagulation	2A
Mitral Valve Strands and Prolapse	Patients with mitral valve strands or prolapse who have a history of TIA or stroke	Anti-platelet therapy	1C+

### Cerebral Venous Sinus Thrombosis

<i>Situation</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Anticoagulation for Cerebral Venous Sinus Thrombosis	Patients with venous sinus thrombosis	Unfractionated Heparin or LMWH over no anticoagulant therapy during the acute phase, even in the presence of hemorrhagic infarction	1B
		Oral anticoagulation for 3 – 6 months (target INR 2.5; range 2.0 – 3.0)	1C

### Antithrombotic Therapy in Peripheral Arterial Occlusive Disease

CHEST 2004; 126:609S-626S

### Chronic Limb Ischemia

<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Antiplatelet Therapy	Patients with clinically manifest coronary or cerebrovascular disease	Lifelong Aspirin therapy, 75 – 325 mg daily recommended over no antiplatelet therapy	1A
	Patients without clinically manifest coronary or cerebrovascular disease	Lifelong Aspirin therapy, 75 – 325 mg daily recommended over no antiplatelet therapy	1C+
Ticlopidine	Patients with chronic limb ischemia	Clopidogrel recommended <i>over</i> Ticlopidine	1C+
Clopidogrel	Patients with chronic limb ischemia	Recommend Clopidogrel in comparison to no antiplatelet therapy	1C+
		Suggest Aspirin be used instead of Clopidogrel	2A
Cilostazol	Patients with disabling intermittent claudication who do not respond to conservative measures (risk factor modification and exercise therapy) and who are not candidates for surgical or catheter-based intervention	Cilostazol recommended	2A
	Patients with less-disabling claudication	<i>Do not</i> use Cilostazol	2A
Pentoxifylline	Patients with chronic limb ischemia	<i>Against</i> the use of Pentoxifylline	1B
Prostaglandins	For limb ischemia	<i>Do not</i> use Prostaglandins	2B
Other Agents	Patients with intermittent claudication	<i>Against</i> the use of Anticoagulants	1A

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<b>Acute Limb Ischemia</b>			
<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Heparin	Patients with acute arterial emboli or thrombosis	Treatment with immediate systemic anticoagulation with UFH to prevent thrombotic propagation	1C
		Systemic anticoagulation with UFH followed by long-term VKA to prevent recurrent embolism in patients undergoing embolectomy	1C
Thrombolysis	Patients with short-term (< 14 days) thrombotic or embolic disease with low risk of myonecrosis and ischemic nerve damage developing during the time to achieve revascularization by this method	Intra-arterial thrombolytic therapy	2B
<b>Vascular Grafts</b>			
<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Intraoperative Anticoagulation During Vascular Reconstructions	Patients undergoing major vascular reconstructive procedures	UFH at the time of application of vascular cross-clamps	1A
Prolonging the Patency of Grafts	Patients undergoing prosthetic infrainguinal bypass	Aspirin	1A
	Patients undergoing infrainguinal femoropopliteal or distal vein bypass	<b>Do not</b> routinely use VKA	2A
	Routine patients undergoing infrainguinal bypass without special risk factors for occlusion	<b>Against</b> VKA plus Aspirin	1A
	Those patients at high risk of bypass occlusion and limb loss	VKA plus Aspirin	2B
<b>Carotid Endarterectomy</b>			
<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Aspirin	Patients undergoing carotid endarterectomy	Aspirin 75 – 325 mg daily be give preoperatively and continued indefinitely	1A
<b>Asymptomatic and Recurrent Carotid Stenosis</b>			
<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Aspirin	Nonoperative patients with asymptomatic or recurrent carotid stenosis	Aspirin 75 – 162 mg daily, lifelong	1C+
<b>Lower Extremity Endovascular Procedures</b>			
<i>Therapy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Aspirin	All patients undergoing lower-extremity balloon angioplasty (with or without stenting)	Long-term Aspirin 75 – 162 mg daily	1C+

### Heparin-Induced Thrombocytopenia (HIT): Recognition, Treatment and Prevention

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<b>Recognition of HIT</b>			
<i>Monitoring</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Platelet Count Monitoring for HIT	Patients receiving Heparin in whom the risk of HIT is considered to be > 0.1%	Platelet count monitoring recommended over no platelet count monitoring	1C
	Patients who are starting UFH or LMWH treatment and who have received UFH within the past 100 days, or those patients in whom exposure history is uncertain	Obtain a baseline platelet count and then a repeat platelet count within 24 h of starting heparin	2C
	Patients who acquire acute inflammatory, cardiorespiratory, neurologic, or other unusual symptoms and signs within 30 minutes following an IV UFH bolus	Recommend performing an immediate platelet count measurement and comparing this value to recent prior platelet counts, compared to not performing a platelet count	1C

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Platelet Count Monitoring for HIT	Patients receiving therapeutic-dose UFH	At least every-other-day platelet count monitoring until day 14, or until UFH is stopped, whichever occurs first	2C
	Patients who are receiving postoperative antithrombotic prophylaxis with UFH (HIT risk > 1%)	At least every-other-day platelet count monitoring between postoperative days 4 – 14, or until UFH is stopped, whichever occurs first	2C
	Medical/obstetrical patients who are receiving prophylactic-dose UFH, postoperative patients receiving prophylactic dose LMWH, postoperative patients receiving intravascular catheter UFH “flushes” or medical/obstetric patients receiving LMWH after first receiving UFH (HIT risk 0.1 – 1%)	Platelet count monitoring every 2 or 3 days from day 4 – 14 (or until Heparin is stopped, whichever occurs first), when practical	2C
	Medical/obstetrical patients who are only receiving LMWH, or medical patients who are receiving only intravascular catheter UFH flushes (HIT risk < 0.1%)	<b>Do not</b> use routine platelet count monitoring	2C
Screening for Subclinical HIT Antibody Seroconversion	Patients who receive Heparin	<b>Against</b> routine HIT antibody testing in the absence of thrombocytopenia, thrombosis, Heparin-induced skin lesions, or other sequelae of HIT	1C
When Should HIT be Suspected?	Patient receiving Heparin or who have received Heparin within the previous 2 weeks	Recommend excluding a diagnosis of HIT if the platelet count falls by $\geq 50\%$ and/or a thrombotic event occurs between days 4 – 14 following initiation of Heparin, even if the patient is no longer receiving Heparin when thrombosis or thrombocytopenia have occurred	1C
Anticoagulant Prophylaxis and Platelet Count Monitoring After Cardiac Surgery	Postoperative cardiac surgery patients	Recommend excluding a diagnosis of HIT if the platelet count falls by $\geq 50\%$ and/or a thrombotic event occurs between postoperative days 4 to day 14 (day of cardiac surgery = day zero)	1C

### Treatment of HIT

Therapy	Details	Recommendation	Grade
Nonheparin Anticoagulants for HIT	Patients with strongly suspected (or confirmed) HIT, whether or not complicated by thrombosis	Alternative, nonheparin anticoagulant recommended <b>over</b> further UFH or LMWH therapy, and over no further anticoagulation (with or without vena caval filter)	
		Lepirudin	1C+
		Argatroban	1C
		Bivalirudin	2C
		Danaproid	1B
Routine Ultrasonography	Patients with strongly suspected (or confirmed) HIT, whether or not there is clinical evidence of lower-limb DVT	Recommend routine ultrasonography of the lower-limb veins for investigation of DVT, over not performing routine ultrasonography	1C
Vitamin K Antagonists	Patients with strongly suspected or confirmed HIT	<b>Against</b> the use of VKA therapy until after the platelet count has substantially recovered (e.g. to at least $100 \times 10^9/L$ and preferably $150 \times 10^9/L$ )	1C
		VKA should be administered only during overlapping alternative anticoagulation (minimum 5-day overlap)	
		Begin VKA with low, maintenance doses (maximum 5 mg Warfarin)	
		Alternative anticoagulant should not be stopped until the platelet count has reached a stable plateau and the INR has been within the target range for at least the last 2 days	

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VKA Therapy Reversal	Patients receiving VKA at the time of diagnosis of HIT	Use of Vitamin K recommended	2C
LMWH for HIT	Patients with strongly suspected HIT, whether or not complicated by thrombosis	<b>Against</b> the use of LMWH	1C+
Prophylactic Platelet Transfusions for HIT	Patients with strongly suspected or confirmed HIT who do not have active bleeding	<b>Do not</b> administer prophylactic platelet transfusions	2C

### Special Patient Populations

<i>Patient Type</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Previous HIT Undergoing Cardiac or Vascular Surgery	Patients with a history of HIT who are HIT antibody negative and require cardiac surgery	UFH recommended <b>over</b> nonheparin anticoagulant  <i>*Preoperative and postoperative anticoagulation, if indicated, should be administered with a nonheparin anticoagulant</i>	1C
Acute or Subacute HIT Undergoing Cardiac Surgery	Patients with acute HIT (thrombocytopenic, HIT antibody positive) who required cardiac surgery  <i>Use one of the following alternative anticoagulant approaches (descending order of preference)</i>	Delay surgery (if possible) until HIT antibodies are negative	1C
		Use Bivalirudin for intraoperative anticoagulation during cardiopulmonary bypass (if ecarin clotting time [ECT] available)	1C
		Use Bivalirudin for intraoperative anticoagulation during off-pump cardiac surgery (if ecarin clotting time [ECT] available)	1C+
		Use Lepirudin for intraoperative anticoagulation (if ecarin clotting time [ECT] available and patient has normal renal function)	1C
		Use UFH plus the antiplatelet agent, Epoprostenol (if ECT monitoring not available or renal insufficiency precludes Lepirudin use)	2C
		Use UFH plus the antiplatelet agent Tirofiban	2C
		Use Danaproid for intraoperative anticoagulation (if anti-factor Xa levels are available)	2C
Patient Requiring PCI	Patients with subacute HIT (platelet count recovery, but continuing HIT antibody-positive)	Delay surgery (if possible) until HIT antibodies are negative and then use Heparin	1C
		Use a Nonheparin anticoagulant	2C
Patient Requiring PCI	Patients with acute or previous HIT who require cardiac catheterization or PCI	Alternative anticoagulant recommended <b>over</b> Heparin	
		Argatroban	1C
		Bivalirudin	1C
		Lepirudin	1C
		Danaproid	2C

### Prevention of HIT

<i>Strategy</i>	<i>Details</i>	<i>Recommendation</i>	<i>Grade</i>
Reducing HIT Antibody Formation and Clinical HIT	Postoperative orthopedic surgery patients	LMWH recommended <b>over</b> UFH	1A
	Treatment of patients with thrombosis	<b>Against</b> the use of bovine UFH in comparison with porcine UFH or LMWH	1A
	Patients undergoing cardiac surgery	Use porcine UFH for intraoperative anticoagulation in comparison with bovine UFH	1B

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Sections of the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy *not* summarized above:

- Methodology for Guideline Development for the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy
- Heparin and Low-Molecular-Weight-Heparin
- Platelet-Active Drugs: The Relationships Among Dose, Effectiveness, and Side Effects
- New Anticoagulant Drugs
- Hemorrhagic Complications of Anticoagulant Treatment
- Antithrombotic Therapy in Patients with Saphenous Vein and Internal Mammary Artery Bypass Grafts
- Use of Antithrombotic Agents During Pregnancy
- Antithrombotic Therapy in Children
- Antithrombotic and Thrombolytic Therapy: From Evidence to Application