Common Consultation in Cardiology

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Scope of my talk

- Acute heart failure
- Acute pulmonary embolism
- Infective endocarditis

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Universal Definition for HF

Symptoms and/or signs of HF caused by a structural and/or functional cardiac abnormality

Plus at least one of following

Elevated NPs OR **Evidence of cardiogenic pulmonary or systemic congestion**

Bozkurt, et al. Universal Definition and Classification of Heart Failure. Journal of Cardiac Failure. 2021.

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Symptoms and Signs

Symptom (Typical)	Signs (Typical)
Breathlessness	Elevated JVP
Orthopnea	Hepatojugular reflux
Paroxysmal nocturnal dyspnea	S3 gallop
Fatigue	Laterally displace PMI
Ankle swelling	Cheyne Stokes respiration
Bendopnea	
Exercise intolerance	
Inability to exercise	

Bozkurt, et al. Universal Definition and Classification of Heart Failure, Journal of Cardiac Failure, 2021

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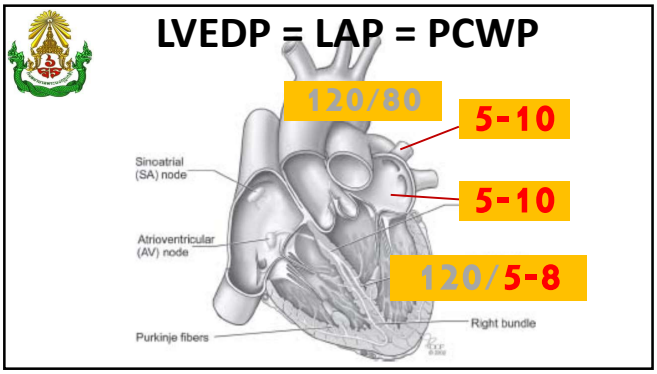
LVEDP = LAP = PCWP



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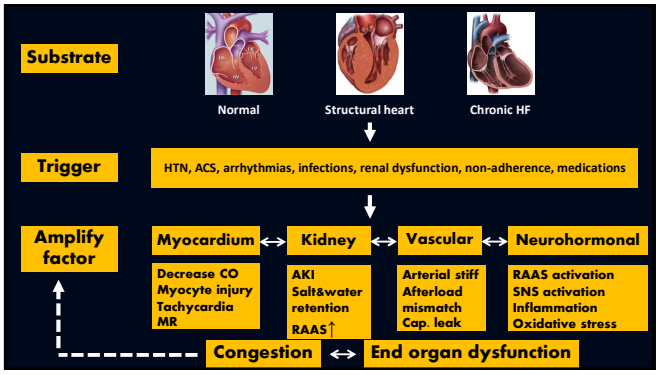

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Bedside assessment

Adequate perfusion Estimated CI ≥ 2.2 LPM/m²	Congestion Estimated PCWP ≥ 22 mmHg: -	Congestion Estimated PCWP ≥ 22 mmHg: +
-	Warm and Dry	Warm and Wet
+	Cold and Dry	Cold and Wet

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Bedside assessment(2)

Elevated PCWP	Elevated RAP: - (HJR, Orthopnea, Bendopnea, Square wave response)	Elevated RAP: + (JVD, Bilateral pedal edema, Ascites)
-	Normal LV and RV filling pressure	Isolated elevated RV filling pressure
+	Isolated elevated LV filling pressure	Elevated LV and RV filling pressure

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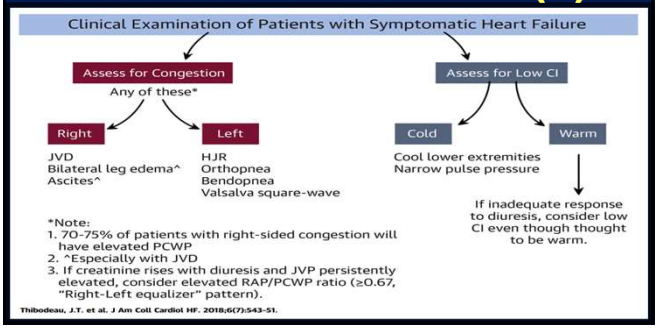
Bedside assessment(3)



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Diagnostic measurement

Recommendations	Class	Level
At admission in all patients presenting with suspected AHF, the following diagnostic tests are recommended: a. ***12-lead ECG***; b. ***CXR*** to assess signs of pulmonary congestion and detect other cardiac or non-cardiac diseases c. the following laboratory assessments in the blood: ***cardiac troponins, BUN, creatinine, sodium, potassium, glucose, CBC, LFT and TSH***	I	C

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Diagnostic measurement

Recommendations	Class	Level
Echocardiography is recommended ***immediately in haemodynamically unstable AHF*** patients and within 48 hours when cardiac structure and function are either not known or may have changed since previous studies.	I	C

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2023

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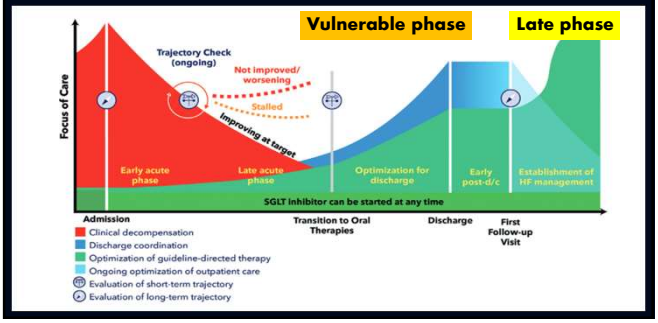
Phase of acute HF management



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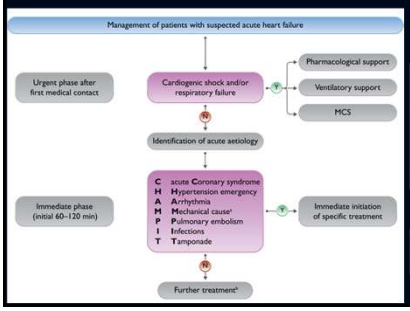
Initial management of AHF



Inotropes and/or vasopressors used to treat AHF

Drug	Infusion rate
Dobutamine	2–20 μg/kg/min (beta+)
Dopamine	3–5 μg/kg/min; inotropic (beta+) >5 μg/kg/min: inotropic (beta+), vasopressor (alpha+)
Milrinone	0.375–0.75 μg/kg/min
Enoximone	5–20 μg/kg/min
Levosimendan	0.1 μg/kg/min, which can be decreased to 0.05 or increased to 0.2 μg/kg/min
Norepinephrine	0.2–1.0 μg/kg/min
Epinephrine	0.05–0.5 μg/kg/min

Vasodilator used to treat AHF

Vasodilator	Dosing
Nitroglycerine	Start with 10–20 μg/min, increase up to 200 μg/min
Isosorbide dinitrate	Start with 1 mg/h, increase up to 10 mg/h
Nitroprusside	Start with 0.3 μg/kg/min and increase up to 5 μg/kg/min

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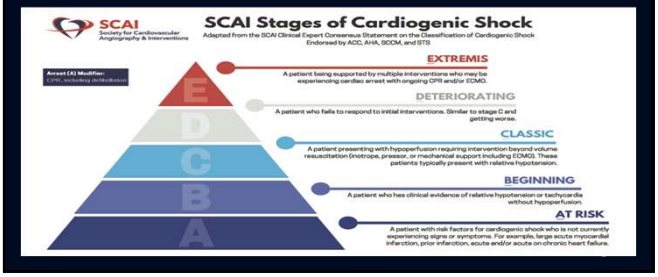
Cardiogenic shock



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Common hemodynamic in Cardiogenic Shock

Parameter	Pre-shock state Normotension hypoperfusion	Pre-shock state Hypotension Normoperfusion	LV dominant	RV dominant	BiV
Systolic BP (mmHg)	> 90	< 90	< 90	< 90	< 90
CVP (mmHg)	Variable	Variable	< 14	> 14	> 14
PCWP (mmHg)	Variable	Variable	> 18	< 18	Variable
CVP/PCWP	Variable	Variable	< 0.86	> 0.86	> 0.86
PAPi	Variable	Variable	> 1.5	< 1.5	< 1.5
Cardiac index	< 2.2	≥ 2.2	< 2.2	< 2.2	< 2.2
SVR (dyne-s/cm^{-5})	> 1600	800-1,600	800-1,600	800-1,600	800-1,600
CPO (W)	Variable	Variable	< 0.6	< 0.6	< 0.6

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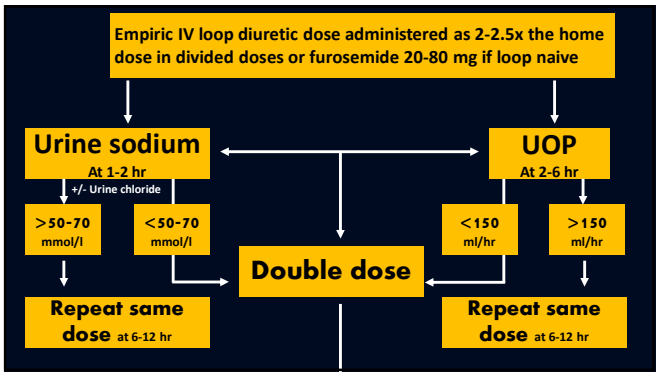

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Diuretic resistance
After R/O cold phenotype

Bolus+IV drip 20mg/hr

IV loop diuretic dose of 120-240 mg furosemide equivalents in 6 hr

Failure to achieved UOP or Una goal

Combination diuretic blockade with loop diuretic:
Upfront: SGLT2i regardless of LVEF and
Metabolic alkalosis: CAI or K-sparing
Hyponatremia: Vaptan
Hypomagnesemia: K-sparing or Vaptan

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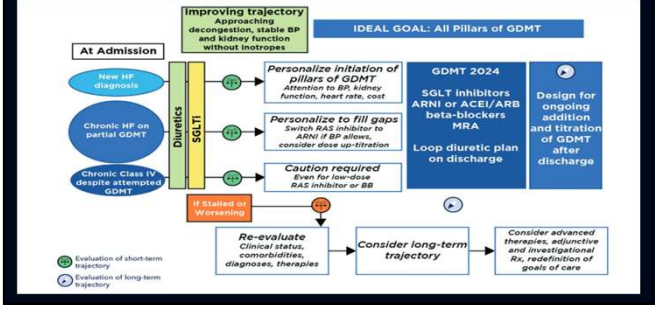
Titration



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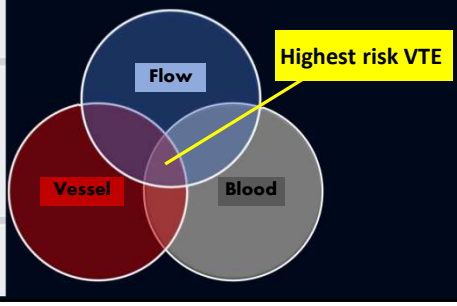
Acute Pulmonary Embolism



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The RV same as The LV

Preload

Afterload

Contractility

RV

LV

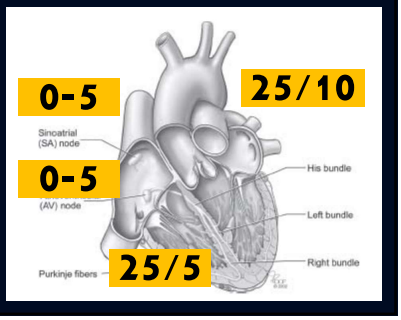
20

The RV same as The LV

Preload

Afterload

Contractility



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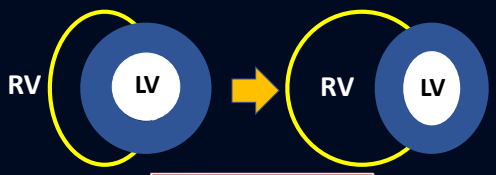
Acute Pulmonary Embolism

Acute loading event



High compliance

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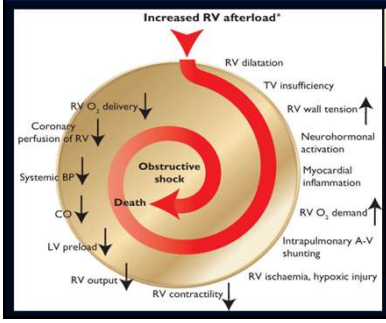
Acute Pulmonary Embolism



Loop of Death

Afterload Beget Afterload

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Symptoms and Signs

Symptom	Signs
Dyspnoea	Tachypnea
Chest pain, especially pleuritic	Tachycardia
Cough	JVD
Leg swelling and pain	Low grade fever
Hemoptysis	Accentuated P2
Anxiety	Leg edema, erythema, tenderness

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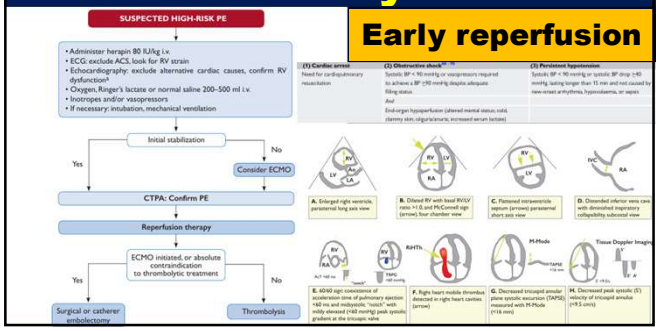
Acute Pulmonary Embolism

Early reperfusion



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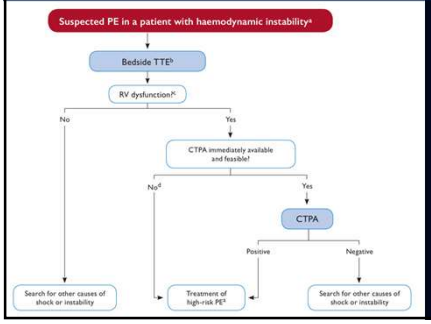
Acute Pulmonary Embolism



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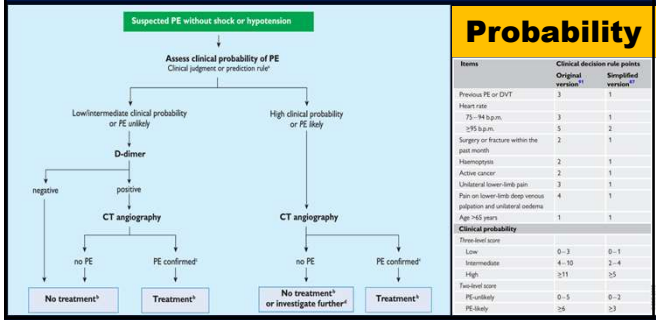
Acute Pulmonary Embolism

Probability



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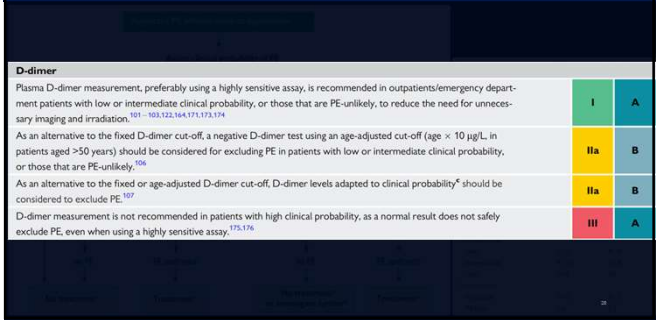
Acute Pulmonary Embolism



D-dimer		
Plasma D-dimer measurement, preferably using a highly sensitive assay, is recommended in outpatients/emergency department patients with low or intermediate clinical probability, or those that are PE-unlikely, to reduce the need for unnecessary imaging and irradiation.[101–103,122,164,171,173,174]	I	A
As an alternative to the fixed D-dimer cut-off, a negative D-dimer test using an age-adjusted cut-off (age × 10 µg/L, in patients aged >50 years) should be considered for excluding PE in patients with low or intermediate clinical probability, or those that are PE-unlikely.[106]	IIa	B
As an alternative to the fixed or age-adjusted D-dimer cut-off, D-dimer levels adapted to clinical probability[c] should be considered to exclude PE.[107]	IIa	B
D-dimer measurement is not recommended in patients with high clinical probability, as a normal result does not safely exclude PE, even when using a highly sensitive assay.[175,176]	III	A

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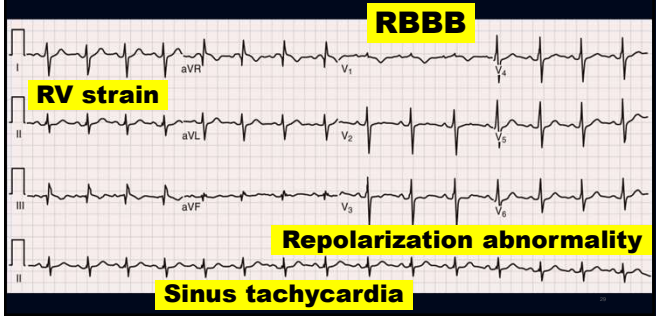
Acute Pulmonary Embolism

RBBB

RV strain

Repolarization abnormality

Sinus tachycardia



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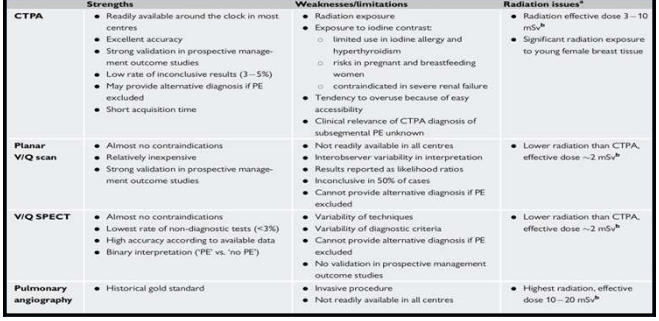
Acute Pulmonary Embolism



	Strengths	Weaknesses/limitations	Radiation issues[a]
CTPA	• Readily available around the clock in most centres • Excellent accuracy • Strong validation in prospective management outcome studies • Low rate of inconclusive results (3–5%) • May provide alternative diagnosis if PE excluded • Short acquisition time	• Radiation exposure • Exposure to iodine contrast: ○ limited use in iodine allergy and hyperthyroidism ○ risks in pregnant and breastfeeding women ○ contraindicated in severe renal failure • Tendency to overuse because of easy accessibility • Clinical relevance of CTPA diagnosis of subsegmental PE unknown	• Radiation effective dose 3–10 mSv[b] • Significant radiation exposure to young female breast tissue
Planar V/Q scan	• Almost no contraindications • Relatively inexpensive • Strong validation in prospective management outcome studies	• Not readily available in all centres • Interobserver variability in interpretation • Results reported as likelihood ratios • Inconclusive in 50% of cases • Cannot provide alternative diagnosis if PE excluded	• Lower radiation than CTPA, effective dose ~2 mSv[b]
V/Q SPECT	• Almost no contraindications • Lowest rate of non-diagnostic tests (<3%) • High accuracy according to available data • Binary interpretation ('PE' vs. 'no PE')	• Variability of techniques • Variability of diagnostic criteria • Cannot provide alternative diagnosis if PE excluded • No validation in prospective management outcome studies	• Lower radiation than CTPA, effective dose ~2 mSv[b]
Pulmonary angiography	• Historical gold standard	• Invasive procedure • Not readily available in all centres	• Highest radiation, effective dose 10–20 mSv[b]

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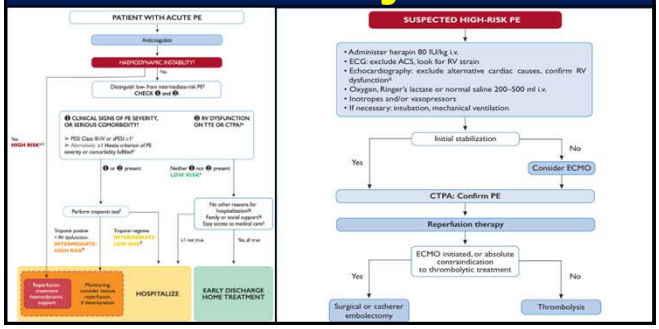
Acute Pulmonary Embolism



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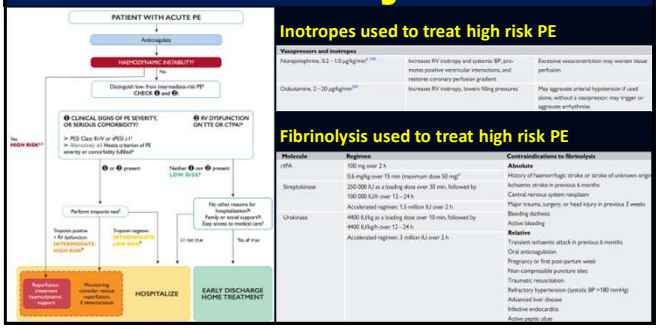
Acute Pulmonary Embolism



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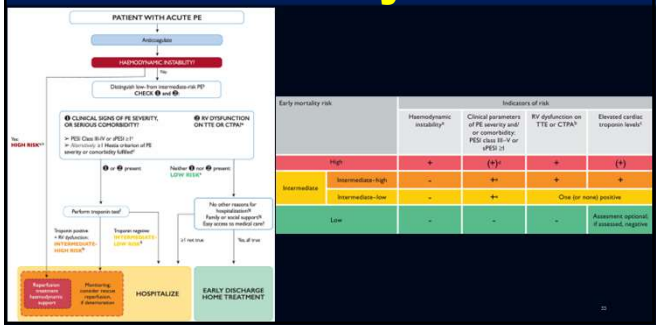
Acute Pulmonary Embolism



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Acute Pulmonary Embolism

Pulmonary Embolism Severity Index

Parameter	Original version	Simplified version
	Class I: ≤65 points very low 30 day mortality risk (0–1.6%)	**0 points** = 30 day mortality risk 1.0% (95% CI 0.0–2.1%)
	Class II: 66–85 points low mortality risk (1.7–3.5%)	
	Class III: 86–105 points moderate mortality risk (3.2–7.1%)	**≥1 point(s)** = 30 day mortality risk 10.9% (95% CI 8.5–13.2%)
	Class IV: 106–125 points high mortality risk (4.0–11.4%)	
	Class V: >125 points very high mortality risk (10.0–24.5%)	

Age	Age in years	1 point (if age >80 years)
Cancer	+30 points	1 point
Systolic BP <100 mmHg	+30 points	1 point
Respiratory rate >30 breaths per min	+20 points	–
Altered mental status	+60 points	–

High risk

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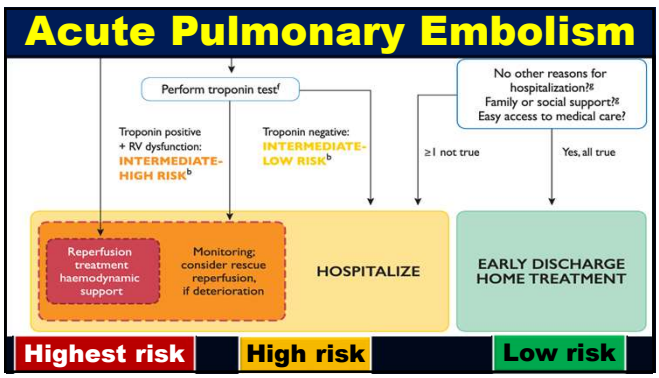
Acute Pulmonary Embolism



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Acute Pulmonary Embolism

Treatment in non-high risk PE

Recommendations	Class	Level
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE, while diagnostic workup is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.	I	A
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.	I	A
When patients are treated with a VKA, overlapping with parenteral anticoagulation is recommended until an INR of 2.5 (range 2.0–3.0) is reached.	I	A
NOACs are not recommended in patients with severe renal impairment, during pregnancy and lactation, and in patients with antiphospholipid antibody syndrome.	III	C

Parenteral anticoagulant in non-high risk PE

	Dosage	Interval
Enoxaparin	1.0 mg/kg	Every 12 h
	or	
	1.5 mg/kg	Once daily
Tinzaparin	175 U/kg	Once daily
Dalteparin	100 IU/kg	Every 12 h
	or	
	200 IU/kg	Once daily
Nadroparin	86 IU/kg	Every 12 h
	or	
	171 IU/kg	Once daily
Fondaparinux	5 mg (body weight <50 kg);	Once daily
	7.5 mg (body weight 50–100 kg);	
	10 mg (body weight >100 kg)	

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Acute Pulmonary Embolism

Treatment in non-high risk PE

Recommendations	Class[a]	Level[b]
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE,[c] while diagnostic workup is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.[262,309–311]	I	A
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.[260,261,312–314]	I	A
When patients are treated with a VKA, overlapping with parenteral anticoagulation is recommended until an INR of 2.5 (range 2.0–3.0) is reached.[315,316]	I	A
NOACs are not recommended in patients with severe renal impairment,[d] during pregnancy and lactation, and in patients with antiphospholipid antibody syndrome.[260,261,312–314]	III	C

NOAC in acute phase non-high risk PE

Characteristics[a]	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Target	Factor Xa	Factor IIa	Factor Xa	Factor Xa
Time to peak effect	1–2 h	1–3 h	1–2 h	2–4 h
Half-life	8–14 h	14–17 h	5–11 h	7–11 h
Renal elimination	27%	80%	50%	33%
Caveats due to interactions with concomitant medication[b]	Not recommended in patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp (azole antimycotics, HIV protease inhibitors). Concomitant use with strong CYP3A4 and P-gp inducers (rifampicin, phenytoin, carbamazepine, phenobarbital, or St John's Wort) may lead to an ~50% reduction in apixaban exposure.	Strong P-gp inhibitors (systemic ketoconazole, cyclosporine, tirasiconate, and dronedarone) are contraindicated. Concomitant treatment with tacrolimus is not recommended. Concomitant administration of P-gp inducers (rifampicin, St John's wort, carbamazepine, and phenytoin) is expected to result in decreased dabigatran plasma concentrations and should be avoided.	In patients concomitantly taking edoxaban and the P-gp inhibitors cyclosporine, dronedarone, erythromycin, or ketoconazole, the recommended dose is 30 mg edoxaban o.d.	Not recommended in patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp (azole antimycotics, HIV protease inhibitors).
Further conditions in which NOACs are contraindicated or not recommended[c]	CrCl <15 mL/min. Severe hepatic impairment (Child–Pugh C) or hepatic disease associated with coagulopathy.	CrCl <30 mL/min. Concomitant treatment with P-gp inhibitors in patients with CrCl <50 mL/min.	CrCl <15 mL/min. Moderate or severe hepatic impairment. (Child–Pugh B and C) or hepatic disease associated with coagulopathy.	CrCl <30 mL/min (FDA). CrCl <15 mL/min (EMA). Moderate or severe hepatic impairment. (Child–Pugh B and C) or hepatic disease associated with coagulopathy.

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Acute Pulmonary Embolism

Treatment in non-high risk PE

Recommendations	Class[a]	Level[b]
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE,[c] while diagnostic workup is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.[262,309–311]	I	A
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.[260,261,312–314]	I	A
When patients are treated with a VKA, overlapping with parenteral anticoagulation is recommended until an INR of 2.5 (range 2.0–3.0) is reached.[315,316]	I	A
NOACs are not recommended in patients with severe renal impairment,[d] during pregnancy and lactation, and in patients with antiphospholipid antibody syndrome.[260,261,312–314]	III	C

Reperfusion therapy in non-high risk PE

Reperfusion treatment		
Rescue thrombolytic therapy is recommended for patients with haemodynamic deterioration on anticoagulation treatment.[282]	I	B
As an alternative to rescue thrombolytic therapy, surgical embolectomy[e] or percutaneous catheter-directed treatment[e] should be considered for patients with haemodynamic deterioration on anticoagulation treatment.	IIa	C

IVC filters in pulmonary embolism

Recommendations	Class[a]	Level[b]
IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation.	IIa	C
IVC filters should be considered in cases of PE recurrence despite therapeutic anticoagulation.	IIa	C

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Acute Pulmonary Embolism

Estimated risk for long-term recurrence[a]	Risk factor category for index PE[b]	Examples[b]
Low (<3% per year)	Major transient or reversible factors associated with >10-fold increased risk for the index VTE event (compared to patients without the risk factor)	• Surgery with general anaesthesia for >30 min • Confined to bed in hospital (only "bathroom privileges") for ≥3 days due to an acute illness, or acute exacerbation of a chronic illness • Trauma with fractures
Intermediate (3–8% per year)	Transient or reversible factors associated with ≤10-fold increased risk for first (index) VTE	• Minor surgery (general anaesthesia for <30 min) • Admission to hospital for <3 days with an acute illness • Oestrogen therapy/contraception • Pregnancy or puerperium • Confined to bed out of hospital for ≥3 days with an acute illness • Leg injury (without fracture) associated with reduced mobility for ≥3 days • Long-haul flight
	Non-malignant persistent risk factors	• Inflammatory bowel disease • Active autoimmune disease
	No identifiable risk factor	
High (>8% per year)		• Active cancer • One or more previous episodes of VTE in the absence of a major transient or reversible factor • Antiphospholipid antibody syndrome

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Acute Pulmonary Embolism

Patients in whom extension of anticoagulation beyond 3 months should be considered[c,d]		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor.[330,331,347,351–353]	IIa	A
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a persistent risk factor other than antiphospholipid antibody syndrome.[330,352,353]	IIa	C
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a minor transient or reversible risk factor.[330,331,352]	IIa	C
Patients in whom extension of anticoagulation beyond 3 months is recommended		
Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor.[358]	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with antiphospholipid antibody syndrome.[359]	I	B

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Acute Pulmonary Embolism

Active[a]	Study	Comparison	Design	No. patients enrolled	Patients with index PE	Treatment duration	VTE rate in control group	Risk reduction for recurrent VTE (HR; 95% CI)	Major or CRNM bleeding in active[a] group (HR; 95% CI)
Dabigatran	RE-SONATE[55]	Placebo vs. D 150 mg b.i.d.	Superiority	1343	33%	6 months	5.6%	92% (0.08; 0.02–0.25)	5.3% (2.92; 1.52–5.60)
	RE-MEDY[55]	Warfarin (INR 2–3) D 150 mg b.i.d.	Non-inferiority	2856	35%	18–36 months	1.3%	Risk difference, 0.38% vs. VKA (1.44; 0.78–2.64)	5.6% (0.54; 0.41–0.71)
Rivaroxaban	EINSTEIN Extension[57]	Placebo R 20 mg o.d.	Superiority	1196	38%	6–12 months	7.1%	82% (0.18; 0.09–0.39)	6.0% (5.19; 2.3–11.7)
	EINSTEIN Choice[53]	Aspirin 100 mg o.d. R 20 mg o.d. R 10 mg o.d.	Superiority	3365	49%	12 months	4.4%	66% (0.34; 0.20–0.59; R 20 mg vs. aspirin)	3.3% (1.59; 0.94–2.69)
								74% (0.26; 0.14–0.47; R 10 mg vs. aspirin)	2.4% (1.16; 0.67–2.03)
Apixaban[b]	AMPLIFY Extension[54]	Placebo vs. A 5 mg b.i.d. vs. A 2.5 mg b.i.d.[b]	Superiority	2486	35%	12 months	8.8%	80%[d] (0.36; 0.25–0.53; A 5 mg vs. placebo)	4.3% (1.62; 0.96–2.73)
								81% (0.33; 0.22–0.48; A 2.5 mg vs. placebo)	3.2% (1.20; 0.69–2.10)
Aspirin	WARFASA[55]	Placebo vs. ASA 100 mg daily	Superiority	402	40%	≥24 months	11.2%[c]	40% (0.58; 0.36–0.93)	1.0% (0.98; 0.24–3.96)
	ASPIRE[56]	Placebo vs. ASA 100 mg daily	Superiority	822	30%	Between 2 and 4 years (actual, 27 months)	6.5%[c]	26% (0.74; 0.52–1.05)	1.1%
Sulodexide	SURVET[57]	Placebo vs. S 2 cp 250 mg b.i.d.	Superiority	617	8%	24 months	9.7%	51% (0.49; 0.27–0.92)	0.6% (0.97; 0.14–6.88)

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Acute Pulmonary Embolism

Clinical setting	Suggested management[a]
Subsegmental PE	Single subsegmental PE in an outpatient without cancer and without proximal DVT: • Clinical surveillance. Single subsegmental PE in a hospitalized patient, a patient with cancer, or if associated with confirmed proximal DVT: • Anticoagulant treatment. Multiple subsegmental PE: • Anticoagulant treatment.
Incidental PE	If single subsegmental PE: • Proceed as above. In all other cases: • Anticoagulant treatment.
Management of acute PE in a patient with active bleeding	• Insert inferior vena cava filter (preferably retrievable). • Reassess the possibility of anticoagulation as soon as the bleeding has ceased and the patient is stabilized, and remove the filter as soon as anticoagulant treatment is resumed.

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Acute Pulmonary Embolism

Treatment in elderly and frailty

PE diagnosis and anticoagulation in the elderly, frail patients, and patients with polypharmacy	• Assess clinical probability of PE as in the non-frail patient, but caution needed in the nursing home setting as clinical prediction rules may be unreliable.[27] • Generally prefer NOACs over VKAs in elderly and frail patients, but observe the following: a. Avoid NOACs in patients with severe renal impairment.[b] b. Consult the drugs' summary of product characteristics and the updated European Heart Rhythm Association guide[19] for possible interactions between NOACs and the patient's concomitant medication. • Reassess, at regular intervals, drug tolerance and adherence, hepatic and renal function, and the patient's bleeding risk

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Acute Pulmonary Embolism

Treatment in oral contraceptives

Duration of anticoagulation in a young female patient suffering acute PE while on oral contraceptives	If patient was taking an oestrogen-containing contraceptive, and especially if PE occurred in the first 3 months of initiation of contraception: • Discontinue hormonal contraceptives after discussing alternative methods of contraception; consider discontinuing anticoagulation after 3 months.

Treatment in pregnancy

Long-term management of a patient who suffered PE during pregnancy	• Anticoagulant treatment with LMWH throughout pregnancy and >6 weeks post-partum. • No NOACs during pregnancy or lactation! • Advise patient on the need for prophylaxis with LMWH in case of future pregnancies.

44

Acute Pulmonary Embolism

Treatment in cancer

Anticoagulation in the patient with PE and cancer, after the first 6 months	If cancer still active:[e] • Continue anticoagulation LMWH or, alternatively, edoxaban or rivaroxaban, as recommended in *section 8.4* If cancer in remission: • Continue oral anticoagulation (NOAC or VKA); alternatively, consider discontinuing if the bleeding risk is high. • In either case, periodically reassess the risk—benefit ratio of continuing/resuming anticoagulation.

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Acute Pulmonary Embolism

Treatment in cancer

Recommendations	Class[a]	Level[b]
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs.[360–363]	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[366]	IIa	B
Rivaroxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[367]	IIa	C
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months)[c] should be considered for an indefinite period or until the cancer is cured.[378]	IIa	B
In patients with cancer, management of incidental PE in the same manner as symptomatic PE should be considered, if it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with proven DVT.[376,377]	IIa	B

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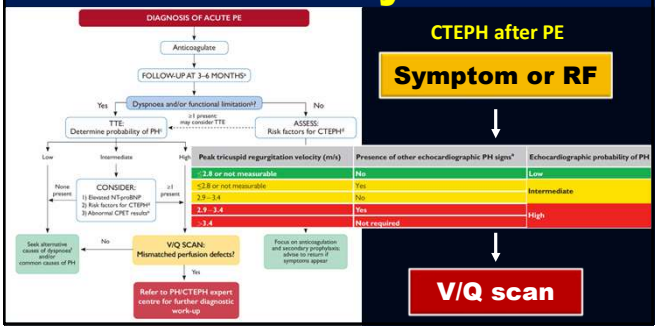
Acute Pulmonary Embolism



CTEPH after PE

Symptom or RF

V/Q scan

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What is IE

Infections involving the heart valves

48

What is the

Prevalence of IE in clinical practice?

A. Less than 1 %

B. 1-5 %

C. 5-10 %

D. Above 10%

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Pathogenesis

Host

Pathogen ⇌ Environment

50

Pathogenesis

Abnormal endocardial structure

Virulence factor

51

Pathogenesis

Abnormal endocardial structure

Non-bacterial thrombotic endocarditis

Virulence factor

52

Pathogenesis

Abnormal endocardial structure

Virulence factor: Adhesin

S.aureus , Streptococci and enterococci

53

Predisposing factor

	Total Cohort	Patients Admitted Directly to Study Sites Only[b]	Region				*P* Value for the Difference in Regions
			North America	South America	Europe	Other	
Baseline characteristics							
Age, median (IQR), y	57.9 (43.2-71.8)	59.8 (44.2-73.1)	52.9 (44.1-66.4)	56.8 (40.3-70.4)	61.4 (45.1-72.7)	58.0 (40.5-72.9)	<.001
Male	1889/2777 (68)	1045/1556 (67)	388/596 (65)	179/254 (70)	873/1212 (72)	449/715 (63)	<.001
First sign to admission <1 mo	2088/2711 (77)	1201/1529 (79)	496/582 (85)	166/244 (68)	896/1174 (76)	530/711 (75)	<.001
Hemodialysis	220/2777 (8)	130/1556 (8)	124/596 (21)	20/254 (8)	49/1210 (4)	27/717 (4)	<.001
Diabetes mellitus	447/2764 (16)	261/1550 (17)	158/592 (27)	25/253 (10)	169/1207 (14)	95/712 (13)	<.001
HIV positive	58/2748 (2)	41/1540 (3)	16/594 (3)	4/236 (2)	33/1211 (3)	5/707 (0.7)	.02
Cancer	230/2772 (8)	160/1553 (10)	52/596 (9)	15/251 (6)	101/1210 (8)	62/715 (9)	.56
IE type							.05
Native valve	1901/2636 (72)	1048/1471 (71)	411/573 (72)	167/246 (68)	860/1166 (74)	463/651 (71)	
Prosthetic valve	563/2636 (21)	321/1471 (22)	116/573 (20)	66/246 (27)	227/1166 (20)	154/651 (24)	
Pacemaker/ICD	172/2636 (7)	102/1471 (7)	46/573 (8)	13/246 (5)	79/1166 (7)	34/651 (5)	
Predisposing conditions							
Current IV drug use	268/2746 (10)	157/1540 (10)	93/587 (16)	1/249 (0.4)	113/1203 (9)	61/707 (9)	<.001
Previous IE	222/2780 (8)	138/1557 (9)	66/596 (11)	26/254 (10)	84/1213 (7)	46/717 (6)	.003
Invasive procedure within 60 d	690/2581 (27)	392/1463 (27)	162/508 (32)	64/247 (26)	289/1145 (25)	175/681 (26)	.03
Chronic IV access	244/2763 (9)	142/1548 (9)	148/595 (25)	12/251 (5)	56/1205 (5)	28/712 (4)	<.001
Endocavitary device							
Pacemaker	262/2752 (10)	146/1540 (9)	55/595 (9)	23/252 (9)	137/1191 (12)	47/714 (7)	.005
ICD	27/2720 (1)	15/1521 (1)	16/593 (3)	0/249 (0)	8/1172 (0.7)	3/706 (0.4)	<.001
Congenital heart disease	311/2656 (12)	167/1481 (11)	62/582 (11)	53/244 (22)	111/1156 (10)	85/674 (13)	<.001
Native valve predisposition	884/2761 (32)	538/1547 (35)	147/596 (25)	93/252 (37)	370/1201 (31)	274/712 (38)	<.001

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Predisposing factor

	No. (%) of Patients[a]						
			Region				
	Total Cohort	Patients Admitted Directly to Study Sites Only[b]	North America	South America	Europe	Other	*P* Value for the Difference Between Regions
Vegetation present	2406/2764 (87)	1325/1545 (86)	530/594 (89)	223/254 (88)	1041/1201 (87)	612/715 (86)	.26
AV	1031/2741 (38)	524/1535 (34)	198/593 (33)	117/252 (46)	460/1189 (39)	256/707 (36)	.003
MV	1125/2740 (41)	640/1534 (42)	253/593 (43)	103/252 (41)	474/1188 (40)	295/707 (42)	.70
TV	323/2741 (12)	177/1534 (12)	107/593 (18)	18/252 (7)	129/1189 (11)	69/707 (10)	<.001
PV	29/2739 (1)	11/1534 (0.7)	8/593 (1)	5/252 (2)	7/1187 (0.6)	9/707 (1)	.15
Complications							
Stroke	462/2727 (17)	225/1528 (15)	118/595 (20)	37/252 (15)	199/1169 (17)	108/711 (15)	.11
Embolization, nonstroke	611/2709 (23)	324/1524 (21)	139/587 (24)	46/251 (18)	295/1163 (25)	131/708 (19)	.002
CHF	876/2713 (32)	414/1527 (27)	207/591 (35)	97/249 (39)	383/1162 (33)	189/711 (27)	<.001
Intracardiac abscess	389/2707 (14)	176/1522 (12)	101/590 (17)	48/250 (19)	156/1157 (13)	84/710 (12)	.005
Persistent positive blood culture	251/2699 (9)	131/1515 (9)	124/586 (21)	7/250 (3)	82/1153 (7)	38/710 (5)	<.001
New conduction abnormality	217/2695 (8)	100/1511 (7)	70/591 (12)	25/250 (10)	72/1152 (6)	50/702 (7)	<.001
Treatment/outcome							
Surgical therapy	1335/2769 (48)	574/1549 (37)	268/595 (45)	141/252 (56)	613/1210 (51)	313/712 (44)	.001
In-hospital mortality	490/2774 (18)	274/1555 (18)	108/596 (18)	43/254 (17)	231/1210 (19)	108/714 (15)	.17

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55

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AV	1031/2741 (38)	524/1535 (34)	198/593 (33)	117/252 (46)	460/1189 (39)	256/707 (36)	.003
MV ***Regurgitant > Stenosis***	1125/2740 (41)	640/1534 (42)	253/593 (43)	103/252 (41)	474/1188 (40)	295/707 (42)	.70
TV	323/2741 (12)	177/1534 (12)	107/593 (18)	18/252 (7)	129/1189 (11)	69/707 (10)	<.001
PV	29/2739 (1)	11/1534 (0.7)	8/593 (1)	5/252 (2)	7/1187 (0.6)	9/707 (1)	.15
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Pathogenesis

Abnormal endocardial structure

Non-bacterial thrombotic endocarditis

Virulence factor

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Organism in IE

Broundwald's textbook of cardiovascular disease	NATIVE VALVE			PROSTHETIC VALVE	
	HEALTH CARE–ASSOCIATED IE (%)			EARLY IE (%) (*n* = 140)	LATE IE (%) (*n* = 390)[h,i]
ORGANISM	COMMUNITY-ACQUIRED IE (%) (*n* = 1201)	NOSOCOMIAL (*n* = 370)	NON-NOSOCOMIAL (*n* = 254)	INTRAVENOUS DRUG USERS WITH IE (%) (*n* = 237)	
Staphylococcus aureus	21	45	42	68	34	19
Coagulase-negative staphylococci	6	12	15	3	28	20
Enterococcus species	10	14	16	5	10	13
Viridans group streptococci	26	10	6	10	1	11
Streptococcus gallolyticus[e]	10	3	3	1	1	7
HACEK	3	0	0	0	0	2
Fungi	0	2	2	1	6	3
Other	13	7	10	7	6	15
Negative blood culture	11	7	6	5	14	10

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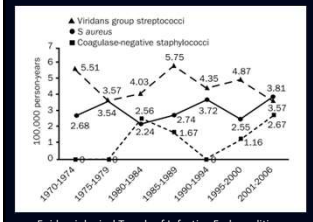
Organism in IE



Epidemiological Trends of Infective Endocarditis. Mayo Clin Proc. 2010;85(5):422-426

Cause of Endocarditis	Total Cohort (N=2781)
Staphylococcus aureus	**869** (31)
Coagulase-negative staphylococcus	**304** (11)
Viridans group streptococci	**483** (17)
Streptococcus bovis	**165** (6)
Other streptococci	**162** (6)
Enterococcus species	**283** (10)
HACEK	**44** (2)
Fungi/yeast	**45** (2)
Polymicrobial	**28** (1)
Negative culture findings	**277** (10)
Other	**121** (4)

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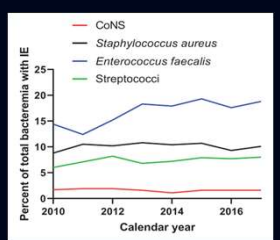
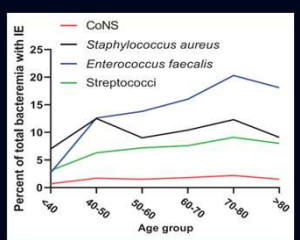
Organism in IE





Prevalence of infective endocarditis in patients with positive blood cultures: a Danish nationwide study. European heart journal 2019 (40), 3237-3244

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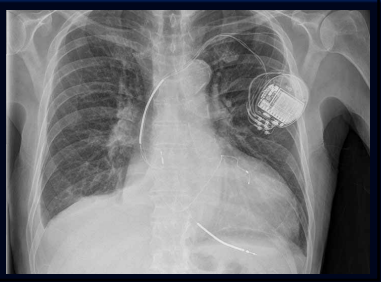
Organism in IE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Symptom in IE

Symptom	% Affect	Symptom	% Affect
Fever	80-95	Weight loss	20-30
Chill	40-70	Myalgia/arthralgia	10-30
Weakness	40-50	Stroke	10-20
Anorexia	20-40	Confusion	10-20
Headache	20-40	Edema	5-15
Dyspepsia	20-40	Chest pain	5-15
Cough	20-30	Abdominal pain	5-15

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Signs in IE

Sign	% Affect	Sign	% Affect
Fever	80-90	Petechiae	10-40
Heart murmur	75-85	Sphinter hemorrhage	5-15
New murmur	10-50	Janeway lesion	5-10
Changing murmur	5-20	Osler nodes	3-10
Neuro sign	20-40	Roth spot	2-10
Splenomegaly	10-40		

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Skin
Lung Heart
CNS **IE** Vascular
Spleen Kidney
Musculoskeletal

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Skin
Lung Heart
CNS **IE** Vascular
Spleen Kidney
Musculoskeletal

Heart
- Vegetation
- Local extension
- Myocardial abscess
- Myopericarditis

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Skin
Lung Heart
CNS **IE** Vascular → Mycotic aneurysm
Rupture?
Spleen Kidney
Musculoskeletal

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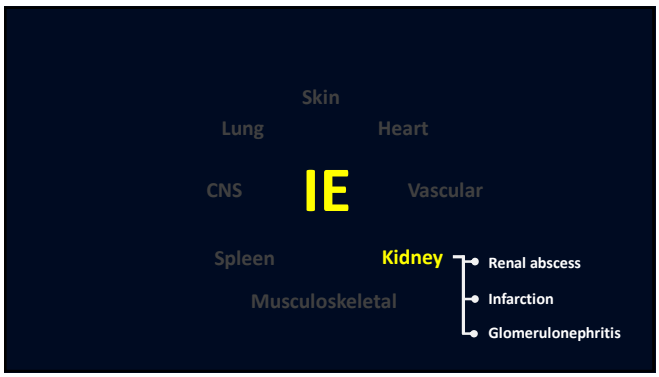

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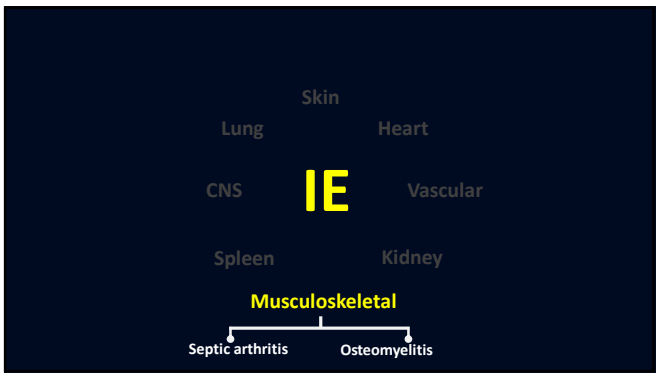

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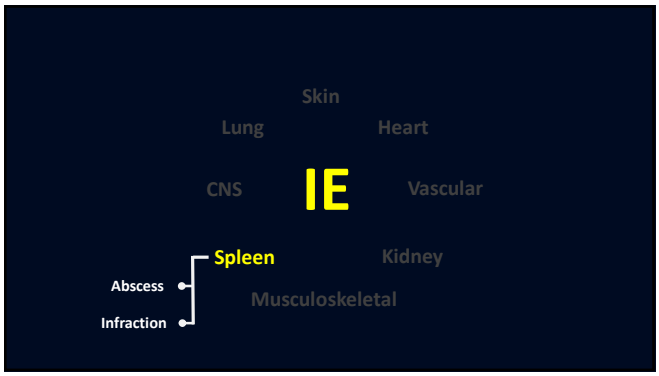

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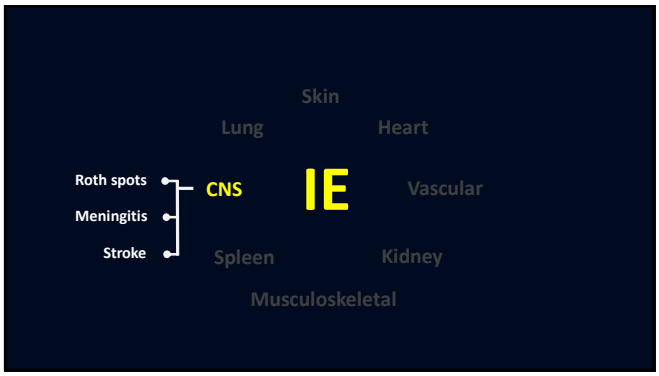

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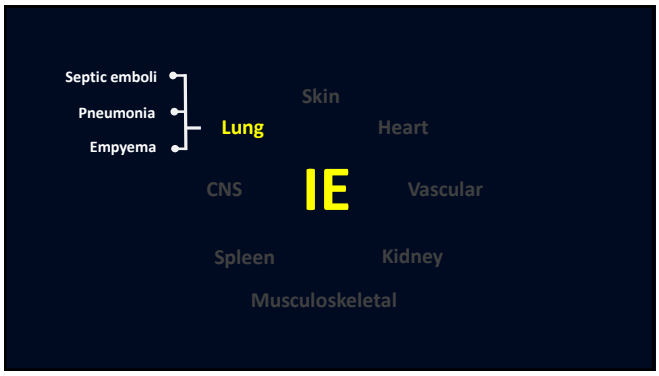

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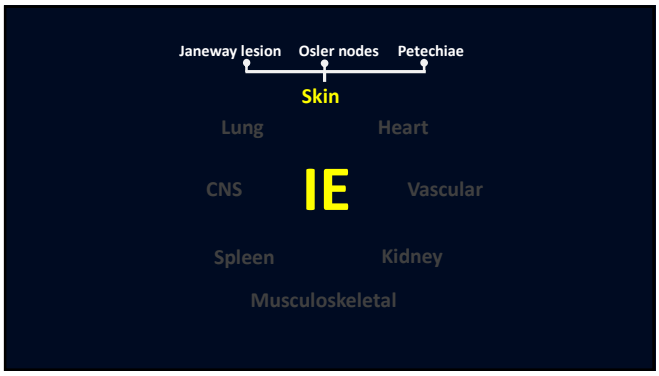

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Who should concern?

Following situation

1. New regurgitant heart murmur
2. Embolic event of unknown origin
3. Sepsis of unknown origin
4. Fever with something !!!

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How to diagnose?

Definite IE

Pathological criteria
- Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathological lesions; vegetation or intracardiac abscess by histological examination showing active endocarditis

Clinical criteria
- 2 major criteria; or 1 major criterion and 3 minor criteria; or 5 minor criteria

Possible IE
- 1 major criterion and 1 minor criterion; or 3 minor criteria

Rejected IE

Firm alternate diagnosis; or Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or
- No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or
- Does not meet criteria for possible IE, as above

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ESC 2023 criteria

Major criteria

Blood culture positive for IE
- Typical pathogen from 2 separate blood cultures
- Persistently positive blood culture
- Single positive blood culture for Coxiella burnetii or phase I IgG

Imaging positive
- Echocardiography
- Abnormal activities around site of prosthethic implantation
- Paravalvular leakage from CT

Minor criteria
- Predisposition such as predisposing heart condition, or injection drug use.
- Fever as temperature >38°C.
- Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
- Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
- Microbiological evidence: positive blood culture but does not meet a major criterion as noted above

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Imaging test in IE

Test	When to consider	Advantages	Limitations
FDG-PET	Suspected IE in patients with prosthetic valve or cardiac implanted electronic devices and negative or inconclusive echocardiography Patients with persistent bacteremia and negative CT to identify nidus of infection for source control	Increases sensitivity in patients with CIED Can identify source of bacteremia Better than echocardiography for intracardiac abscesses and pseudoaneurysms	False positives in ≤ 3 months after cardiac surgery False-negatives with antibiotics for several days Limited diagnostic precision in native valve IE Dietary carbohydrate restriction 12–24 hours before study Expensive, limited availability
Leukocyte scintigraphy	Same as FDG-PET	Same as FDG-PET	Long study duration Expensive, limited availability Radiation exposure

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Echocardiography in IE

Role of echocardiography

1. For Diagnosis
2. For follow up medical treatment
3. During intra-operative surgery
4. For follow up at treatment completion

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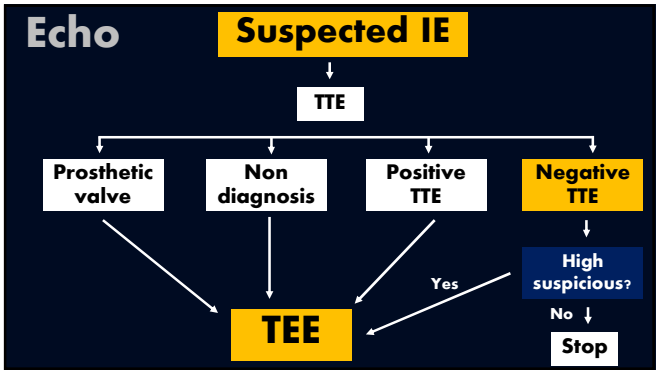

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Echocardiography in IE

Recommendations	Class	Level
TTE is recommended as the first-line imaging modality in suspected IE.	I	B
TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.	I	B
TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.	I	B
Echocardiography should be considered in S.aureus E. faecalis, and some Streptococcus spp.bacteraemia	IIa	B

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ATB Treatment in IE

Recommendations		Class	Level
Penicillin-susceptible oral streptococci and Streptococcus gallolyticus use 4 wks (in NVE) or 6 wks (in PVE)			
Penicillin G	12–18 millionc U/day i.v. either in 4–6 doses	I	B
Amoxicillin	100–200 mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	2 g/day i.v. in 1 dose		

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ATB Treatment in IE

Recommendations		Class	Level
Penicillin-susceptible oral streptococci and Streptococcus gallolyticus use 2 wks (in non-complicated NVE)			
Penicillin G	12–18 millionc U/day i.v. either in 4–6 doses	I	B
Amoxicillin	100–200 mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	2 g/day i.v. in 1 dose		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose		

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ATB Treatment in IE

Recommendations		Class	Level
IE caused by methicillin-susceptible staphylococci used ATB for 4–6 weeks			
Cloxacillin	12 g/day i.v. in 4–6 doses	I	B
Cefazolin	6 g/day i.v. in 3 doses		
In patients with PVE due to methicillin-susceptible staphylococci used ATB with rifampin for at least 6 wks and gentamicin for 2 wks			
Cloxacillin	12 g/day i.v. in 4–6 doses	I	B
Cefazolin	6 g/day i.v. in 3 doses		
Rifampicin	900 mg/day i.v. or orally in 3 equally divided doses		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		

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ATB Treatment in IE

Recommendations		Class	Level
NVE due to non-HLAR Enterococcus spp., the combination of ampicillin or amoxicillin with ceftriaxone for 6 weeks or with gentamicin for 2 weeks is recommended using the following doses:			
Amoxicillin	200 mg/kg/day i.v. in 4–6 doses	I	B
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. in 2 doses		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose		

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ATB Treatment in IE

Recommendations		Class	Level
In patients with PVE and patients with complicated NVE or >3 months of symptoms due to non-HLAR Enterococcus spp., the combination of ampicillin or amoxicillin with ceftriaxone for 6 weeks or with gentamicin for 2 weeks is recommended using the following doses:			
Amoxicillin	200 mg/kg/day i.v. in 4–6 doses	I	B
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. in 2 doses		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose		

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ATB Treatment in IE

Recommendations		Class	Level
In patients with community-acquired NVE or late PVE (≥12 months post-surgery), ampicillin in combination with ceftriaxone or with (flu)cloxacillin and gentamicin should be considered using the following doses:			
Cloxacillin	12 g/day i.v. in 4–6 doses	IIa	C
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. in 2 doses		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose		

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Treatment of IE

Phase	Guideline to use
Critical phase week 0-2	**Complications occur during this phase** • Preferred **inpatient treatment** during this phase • Consider OPAT if: oral streptococci or Streptococcus bovis with native valve with no complication
Continuation phase Beyond week 2	**Consider OPAT if medically stable** • **Do not consider OPAT** if: 1. Other than S. aureus, streptococci, CoNS, or E. faecalis 2. Signs of active infection 3. Need IV ATB from other cause 4. New TOE show any complications

Educate patient and staff
- Regular post-discharge evaluation (nurses 1/day, physician in charge 1 or 2/week)
- Prefer physician-directed programme, not home- infusion model

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Surgery in IE

Heart failure

- Refractory pulmonary edema or cardiogenic shock
- Symptoms or signs of poor hemodynamic tolerance

Emergency 24 hour

Uncontrolled infection

- Local uncontrolled infection
- Persistent blood culture positive despite adequate ATB and adequate control septic foci
- Highly resistant pathogen or high risk for ATB failure

Prevent emboli

- Depend on size and site

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Surgery in IE

Heart failure

- Refractory pulmonary edema or cardiogenic shock
- Symptoms or signs of poor hemodynamic tolerance

Urgency 3-5 days

Uncontrolled infection

- Local uncontrolled infection
- Persistent blood culture positive despite adequate ATB and adequate control septic foci
- Highly resistant pathogen or high risk for ATB failure

Prevent emboli

- Depend on size and site

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Surgery in IE

Heart failure

» Coma
» No meaningful recovery
» Severe comorbidities
» Stroke with severe damage

- Depend on size and site

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Prevention of IE

Undergoing oro-dental procedures

Recommendations	Class	Level
Antibiotic prophylaxis is recommended in patients with previous IE.	I	B
Antibiotic prophylaxis is recommended in patients with surgically implanted prosthetic valves and with any material used for surgical cardiac valve repair.	I	C
Antibiotic prophylaxis is recommended in patients with transcatheter implanted aortic and pulmonary valvular prostheses.	I	C
Antibiotic prophylaxis should be considered in patients with transcatheter mitral and tricuspid valve repair.	IIa	C

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Prevention of IE

Undergoing oro-dental procedures

Recommendations	Class	Level
Antibiotic prophylaxis is recommended in **untreated cyanotic CHD**, and patients treated with surgery or transcatheter procedures with **post-operative palliative shunts, conduits, or other prostheses.** **After surgical repair**, in the absence of residual defects or valve prostheses, antibiotic prophylaxis is recommended only for the **first 6 months**	I	C
Antibiotic prophylaxis is recommended in ventricular assist devices	IIa	C
Antibiotic prophylaxis may be considered in recipients of heart transplant	IIb	C

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Prevention of IE

Recommendations	Class	Level
Antibiotic prophylaxis is **not recommended** for **respiratory tract procedures**, including bronchoscopy or laryngoscopy, or transnasal or endotracheal intubation	III	C
Antibiotic prophylaxis is **not recommended** for **gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery or TOE**	III	C
Antibiotic prophylaxis is **not recommended** for any procedure of **skin and soft tissue**	III	C

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Prevention of IE

Situation	Antibiotic	Single-dose 30–60 min before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin	2 g orally	50 mg/kg orally
	Ampicillin	2 g i.m. or i.v.	50 mg/kg i.v. or i.m.
	Cefazolin or ceftriaxone	1 g i.m. or i.v.	50 mg/kg i.v. or i.m.
Allergy to penicillin or ampicillin	Cephalexin[a,b]	2 g orally	50 mg/kg orally
	Azithromycin or clarithromycin	500 mg orally	15 mg/kg orally
	Doxycycline	100 mg orally	<45 kg, 2.2 mg/kg orally >45 kg, 100 mg orally
	Cefazolin or ceftriaxone[b]	1 g i.m. or i.v.	50 mg/kg i.v. or i.m.

Generalize advise for reduce risk of IE

- Patients should be encouraged to maintain twice daily tooth cleaning and to seek professional dental cleaning and follow-up at least twice yearly for high-risk patients and yearly for others.
- Strict cutaneous hygiene, including optimized treatment of chronic skin conditions.
- Disinfection of wounds.
- Curative antibiotics for any focus of bacterial infection.
- No self-medication with antibiotics.
- Strict infection control measures for any at-risk procedure.
- Discouragement of piercing and tattooing.
- Limitation of infusion catheters and invasive procedures. when possible.
- Strict adherence to care bundles for central and peripheral cannulae should be performed.

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Thank you for your attention

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