ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ
ΙΠΠΟΚΡΑΤΕΙΟ

Αντιθρομβωτική αγωγή στις χειρουργημένες βαλβιδοπάθειες

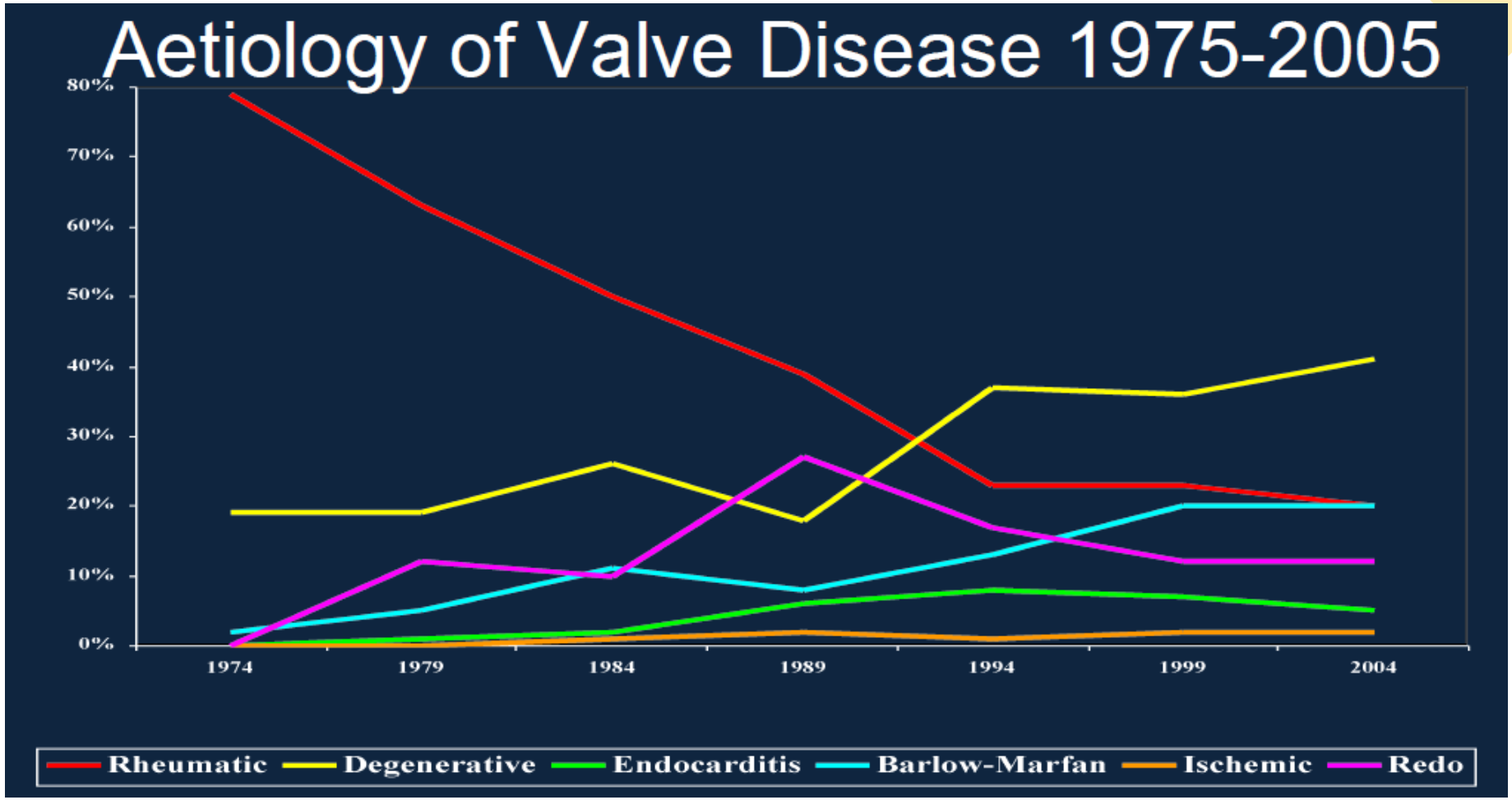
ΑΝΔΡΕΑΣ ΚΑΤΣΑΡΟΣ

ΚΑΡΔΙΟΛΟΓΟΣ

ΚΑΡΔΙΟΧΕΙΡΟΥΡΓΙΚΟ ΤΜΗΜΑ - Γ.Ν.Α. ΙΠΠΟΚΡΑΤΕΙΟ

1ο Ετήσιο Συνέδριο
Καρδιοχειρουργικού Τμήματος
Ιπποκρατείου Αθηνών
«ΣΥΓΧΡΟΝΗ ΚΑΡΔΙΟΧΕΙΡΟΥΡΓΙΚΗ 2025»

5-6 Δεκεμβρίου 2025
Αμφιθέατρο / Γ.Ν.Α. Ιπποκράτειο



Bernard Prendergast

THE PATIENT WITH COEXISTING VALVULAR AND CORONARY ARTERY DISEASE: A DIFFICULT, BUT COMMON, PROBLEM

Richard P. Anderson, M.D., Lawrence I. Bonchek, M.D.,
Shahbudin H. Rahimtoola, M.B., F.R.C.P., and Albert Starr, M.D.

The presence of coronary artery disease complicates the management of patients with valvular heart disease and increases the risk of valvular surgery.[1-3] Since the advent of coronary bypass grafting for obstructed coronary artery lesions, many groups,[4,10] including our own,[11] have attempted to reduce this risk by combining valvular and coronary surgery in the same operative procedure.

Cardiovascular Diseases, Bulletin of the Texas Heart Institute, Vol. 2, No. 1. 1975

Table 5. Baseline Characteristics of the 2150 Patients Who Underwent Valve Intervention During the Survey Period

	AS (n=866)	AR (n=93)	MS (n=109)	Primary MR (n=277)	Secondary MR (n=90)	Multiple Left-Sided (n=470)	Isolated Right-Sided (n=24)	Previous Valve Intervention (n-221)
Percutaneous coronary intervention	48 (5.5)	0 (0.0)	1 (0.9)	8 (2.9)	6 (6.7)	15 (3.2)	0 (0.0)	7 (3.2)
Coronary artery bypass grafting	133 (15.4)	11 (11.8)	5 (4.6)	29 (10.5)	25 (27.8)	71 (15.1)	4 (16.7)	10 (4.5)

European Survey on Management of Valvular Disease

Circulation. 2019;140:1156–1169.

Interface between valve disease and ischaemic heart disease

- Degenerative lesions are now the most frequent cause of valve disease in western countries and they frequently occur in old patients, who are also at higher risk for atherosclerotic disease

- The association of calcified aortic stenosis and coronary heart disease is the main problem, because it is the most frequently encountered association

B. Iung. Heart 2000; 84:347-52

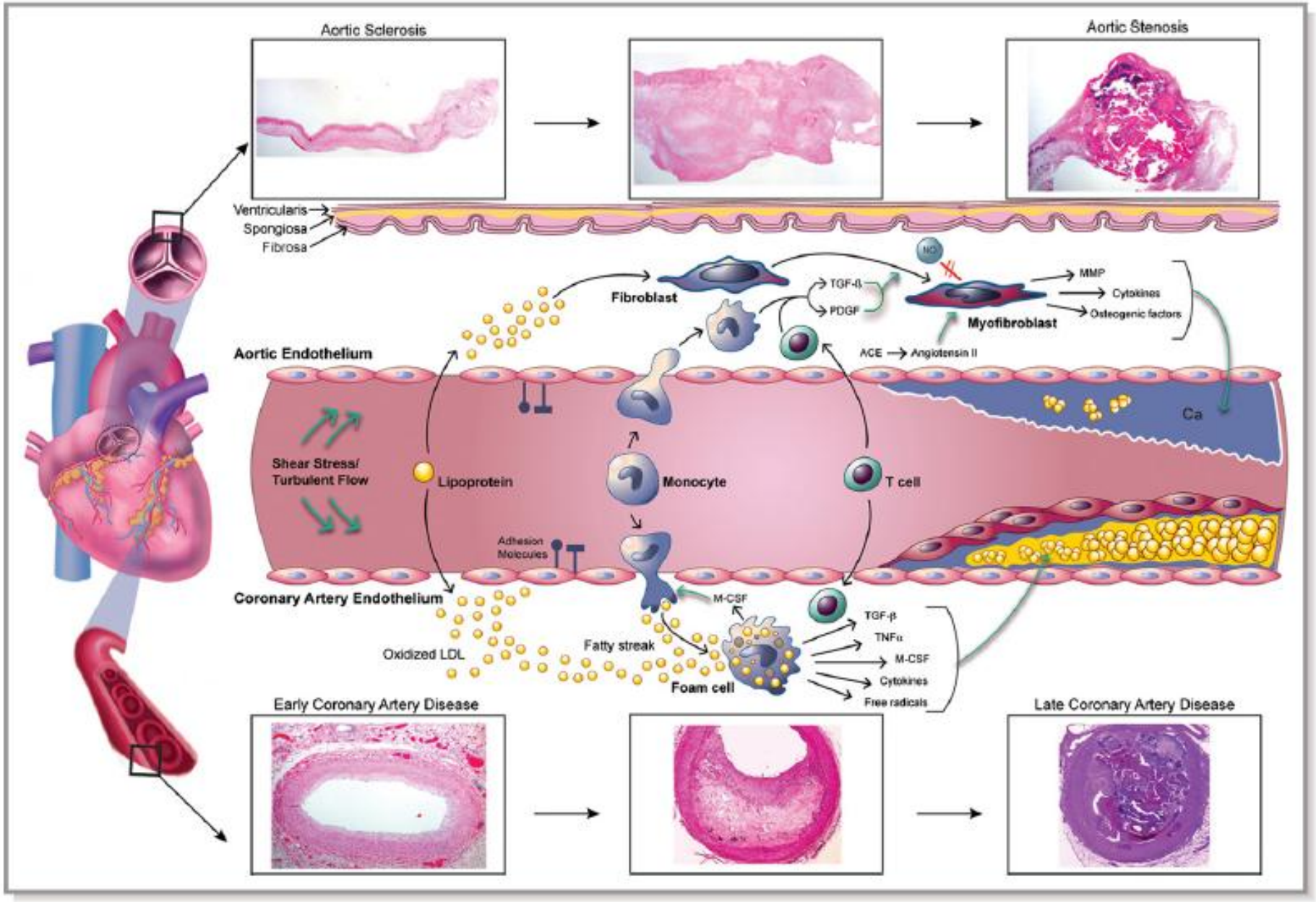


Figure 1. Pathophysiology of aortic sclerosis, aortic stenosis, and coronary artery disease.

Aortic valve calcification and prevalence of coronary artery disease

- The prevalence of CAD in patients undergoing surgical aortic valve replacement has been shown to increase with both age and the presence of valve calcification

- The presence of aortic valve calcification, like mitral annular calcification, almost certainly arises from the same systemic vascular atherosclerotic process that leads to CAD

European Heart Journal (2014) **35**, 2069–2082

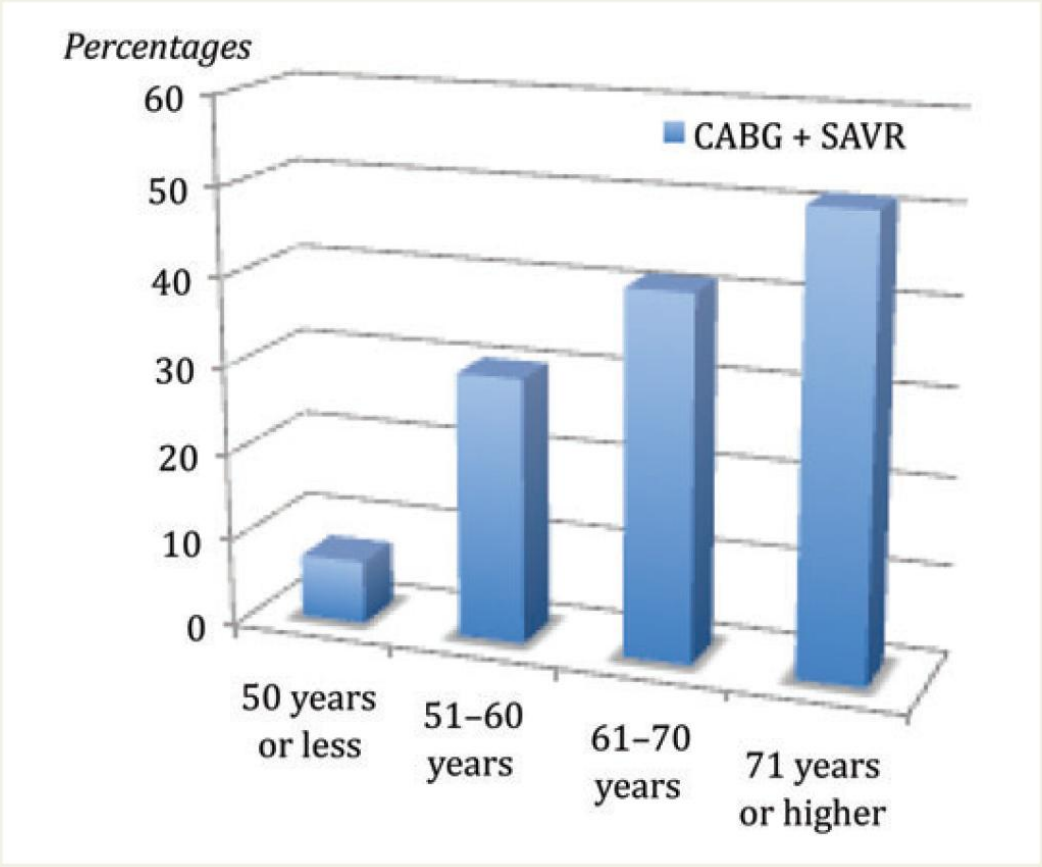
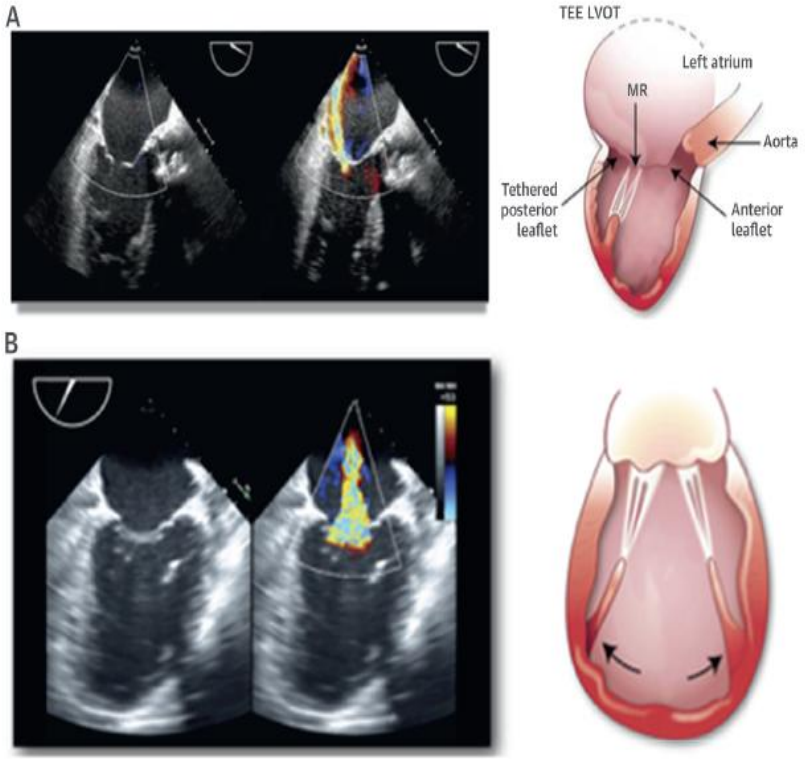


Figure 1 Percentages of simultaneous coronary artery bypass grafting surgery and surgical aortic valve replacement according to the Swedish registry.[7] CABG, coronary artery bypass graft surgery; SAVR, surgical aortic valve replacement.

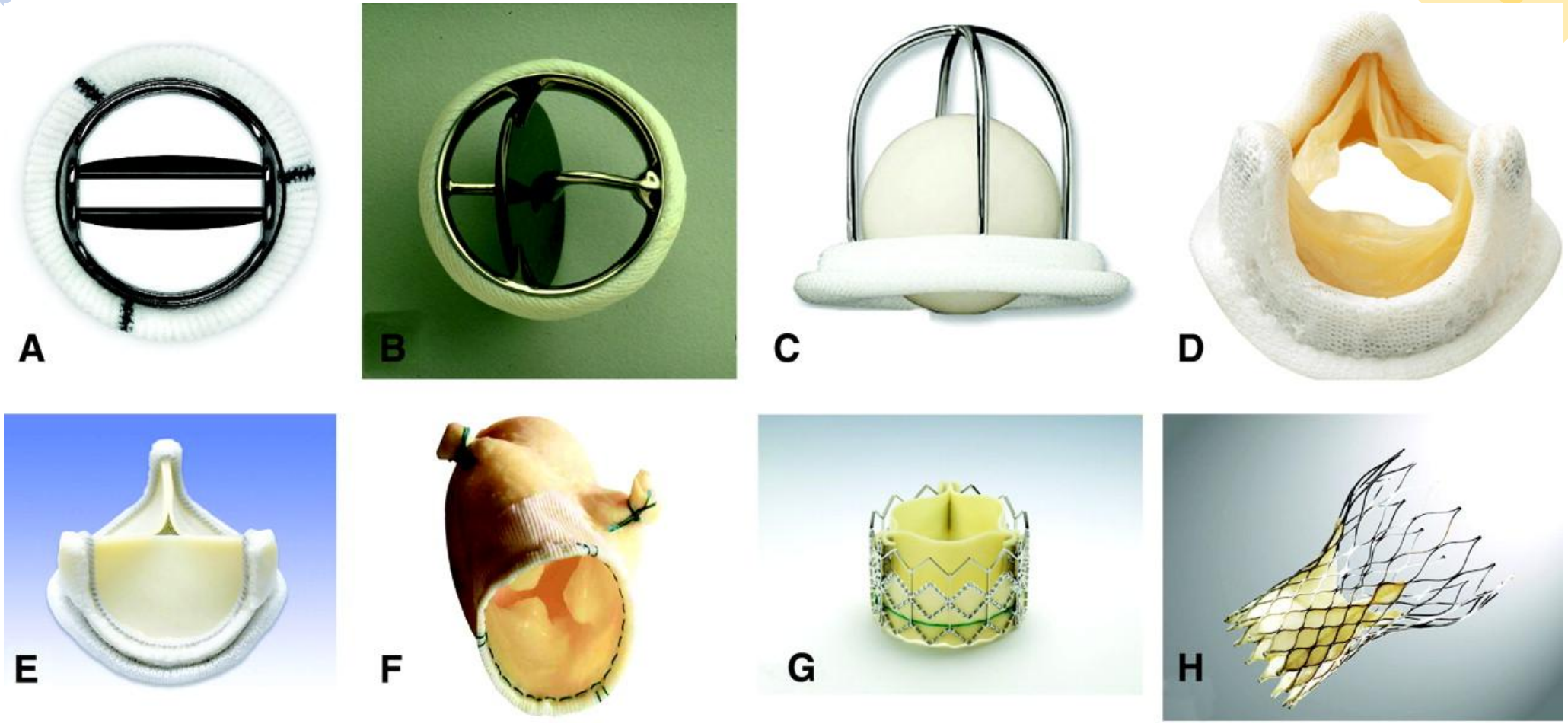
J Am Coll Cardiol 2000;**35**:747–756.

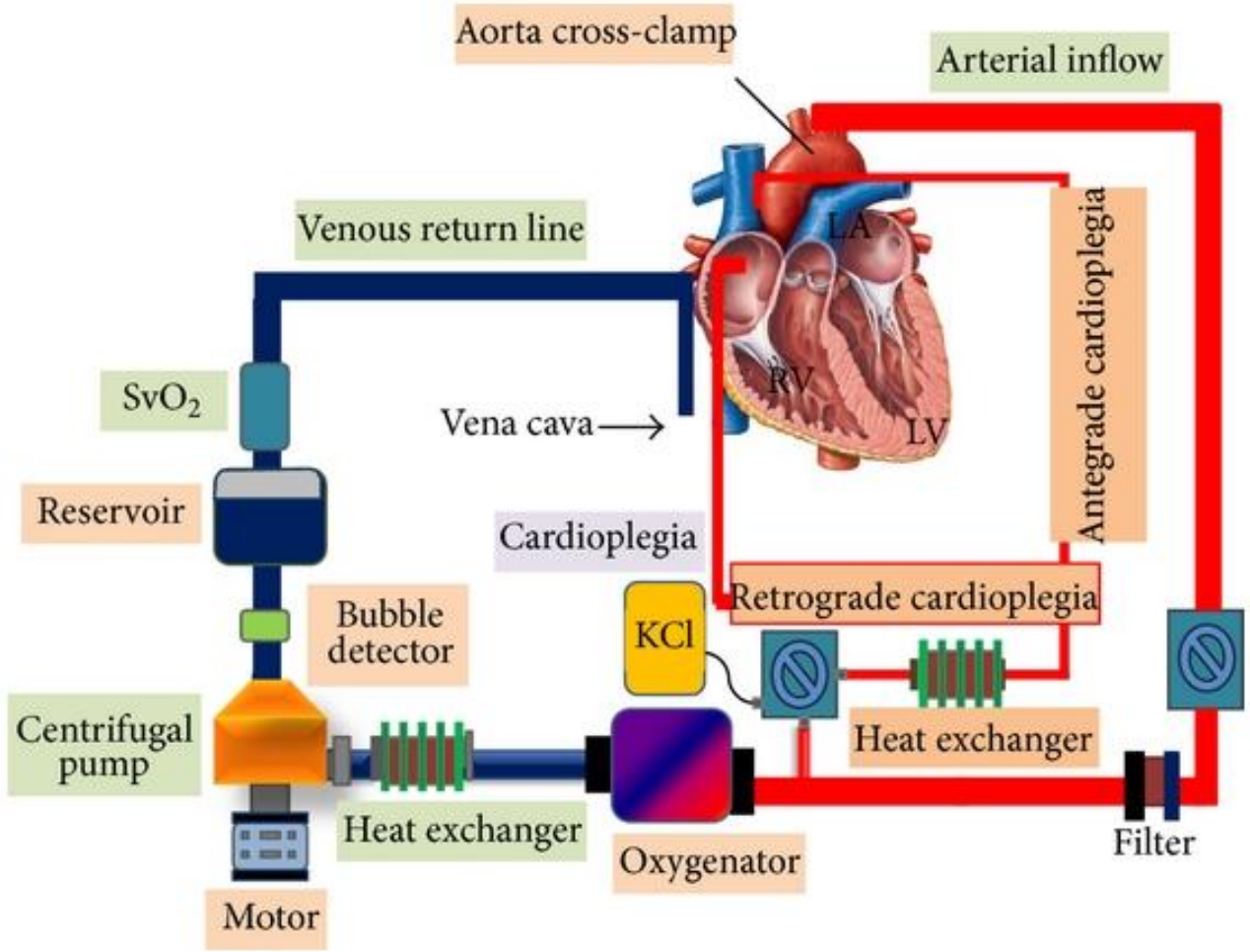


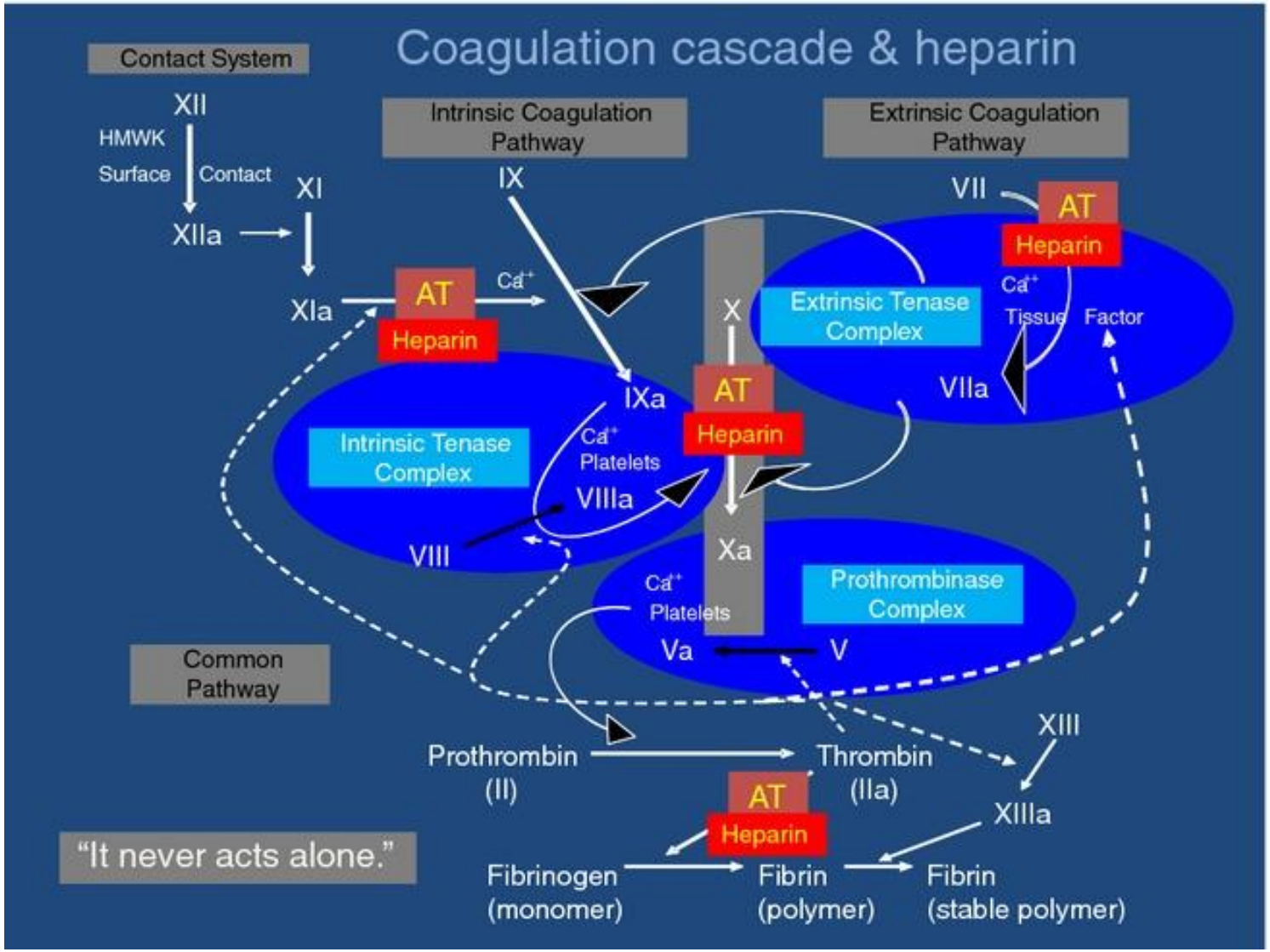
A

IMR		FMR
Inferior MI	Anterior MI	End Stage CMP
Preserved EF	Ischemic CMP	Severe Reduced EF
Local LV remodeling	Increased LV size	Spherical LV
Leaflet tethering	Annular dilation	Very dilated annulus
Type IIIb leaflet motion		Type I leaflet motion

Asgar et al. JACC 2015; 65:1231-48 / Punnoose et al. J Cardiac Fail 20014; 20:252-67


A
B
C
D
E
F
G
H


Aorta cross-clamp
Arterial inflow
Venous return line
LA
Antegrade cardioplegia
SvO_2
Vena cava
RV
LV
Reservoir
Cardioplegia
Retrograde cardioplegia
Bubble detector
KCl
Centrifugal pump
Heat exchanger
Heat exchanger
Oxygenator
Filter
Motor



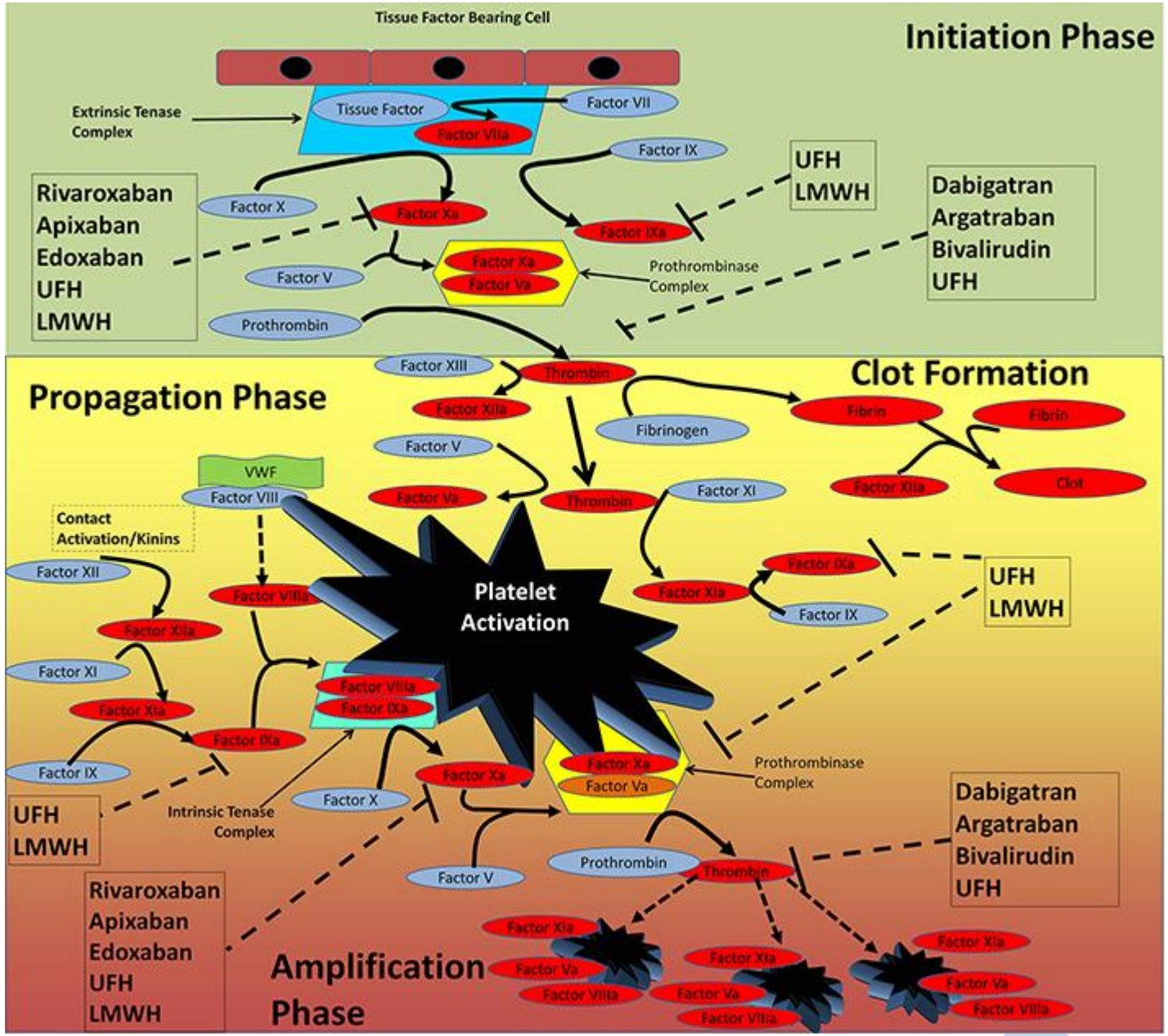
June 2015
Pages S336-S342

jth journal of thrombosis and haemostasis™

Drug	Clearance	Dose (mg/kg/hr)		Monitoring		Bleeding
		Child	Adult	Child	Adult	Child & Adult
UFH	Renal	15–28 IU/kg/hr	10–18 IU/kg/hr	aPTT 1.5–2X (<100 sec) ACT 180–220 sec Anti-Xa 0.3-0.6 IU/mL	PTT 40–60 ACT 180–220 sec	Protamine 1.5 mg/100 IU UFH (reversal)
LMWH	Renal	1.2 subcutaneous q 12hrs	1mg/kg subcutaneous q 12hrs	Anti-Xa 0.5–1 IU/mL		Protamine 1.5 mg/100 IU LMWH (partial reversal)
Argatroban	Hepatic	Infusion: 0.045 Adjust 0.06–0.015 Hepatic compromise 0.012 In HIT: 0.006-0.6;	Infusion: 0.12 In HIT: 0.012	PTT 1.5–3X (<100 sec) ACT 160–200	PTT 40–120 ACT 170–200	FVIIa** 30–90 µg/kg
Bivalirudin	Proteolysis: 75% Renal: 25%	Bolus 0.125–0.25 Infusion Primary: 0.125–0.2 Tx UFH: 0.1–0.8	Infusion:0.08–0.2 Adjust 0.03	PTT 50-70 ACT160–200	PTT 40–120 ACT 200–220	
Aspirin	Liver	1–5 mg/kg/d Max 91 mg		TEG MA and depression TEG AA Inhibition 70%		Platelet Transfusion
Clopidogrel	Liver	0.2 mg/kg/d	1 mg/kg/d	TEG MA and α depression		Platelet Transfusion
Dypyridamole	Liver	1.5 mg/kg/d		TEG MA and α depression TEG ADP net G 4–8		Platelet Transfusion

Table 2.
Dosing guides for anticoagulants for mechanical circulatory support.

https://www.intechopen.com/books/extracorporeal-membrane-oxygenation-advances-in-therapy/ecmo-biocompatibility-surface-coatings-anticoagulation-and-coagulation-monitoring



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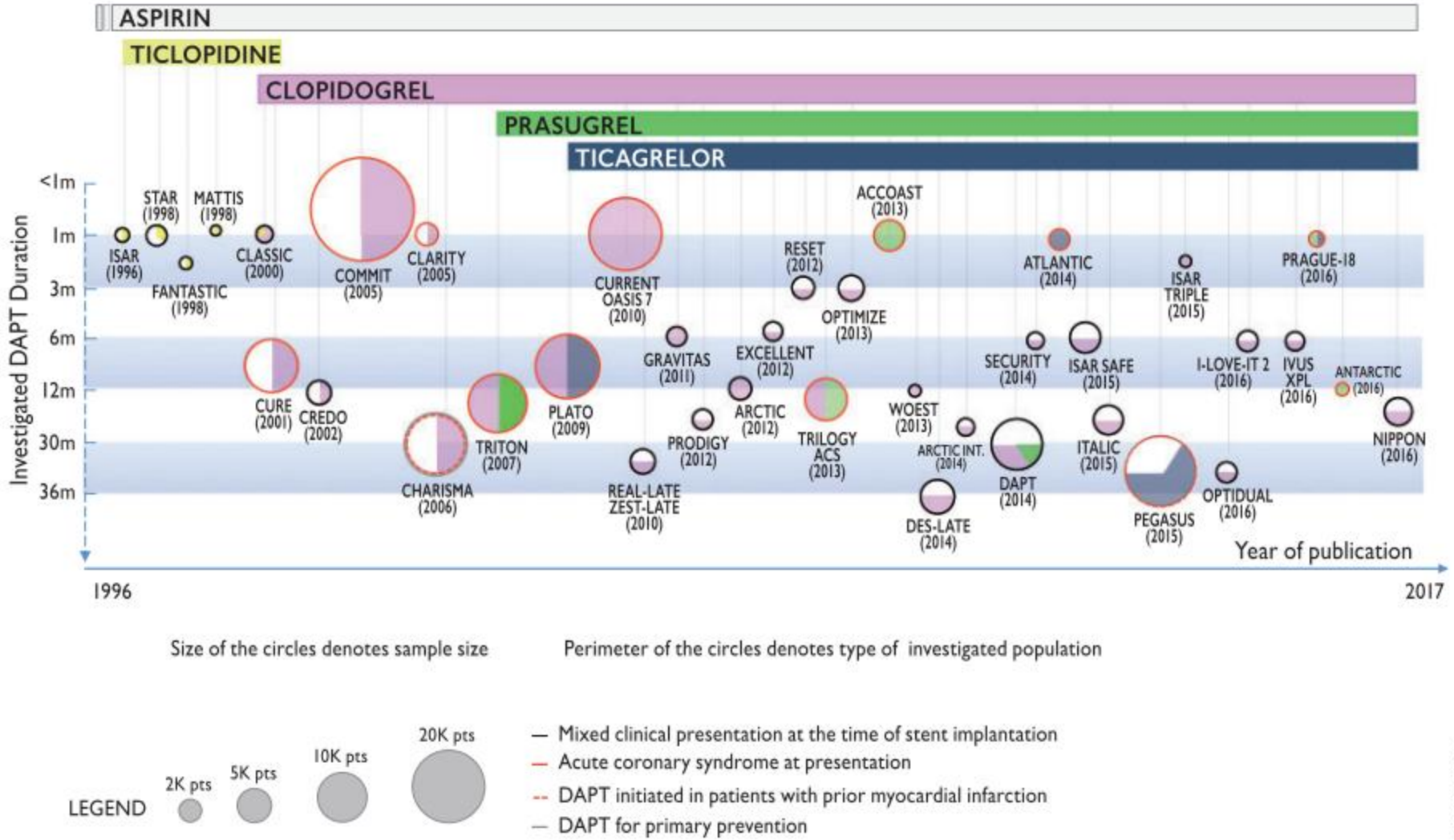
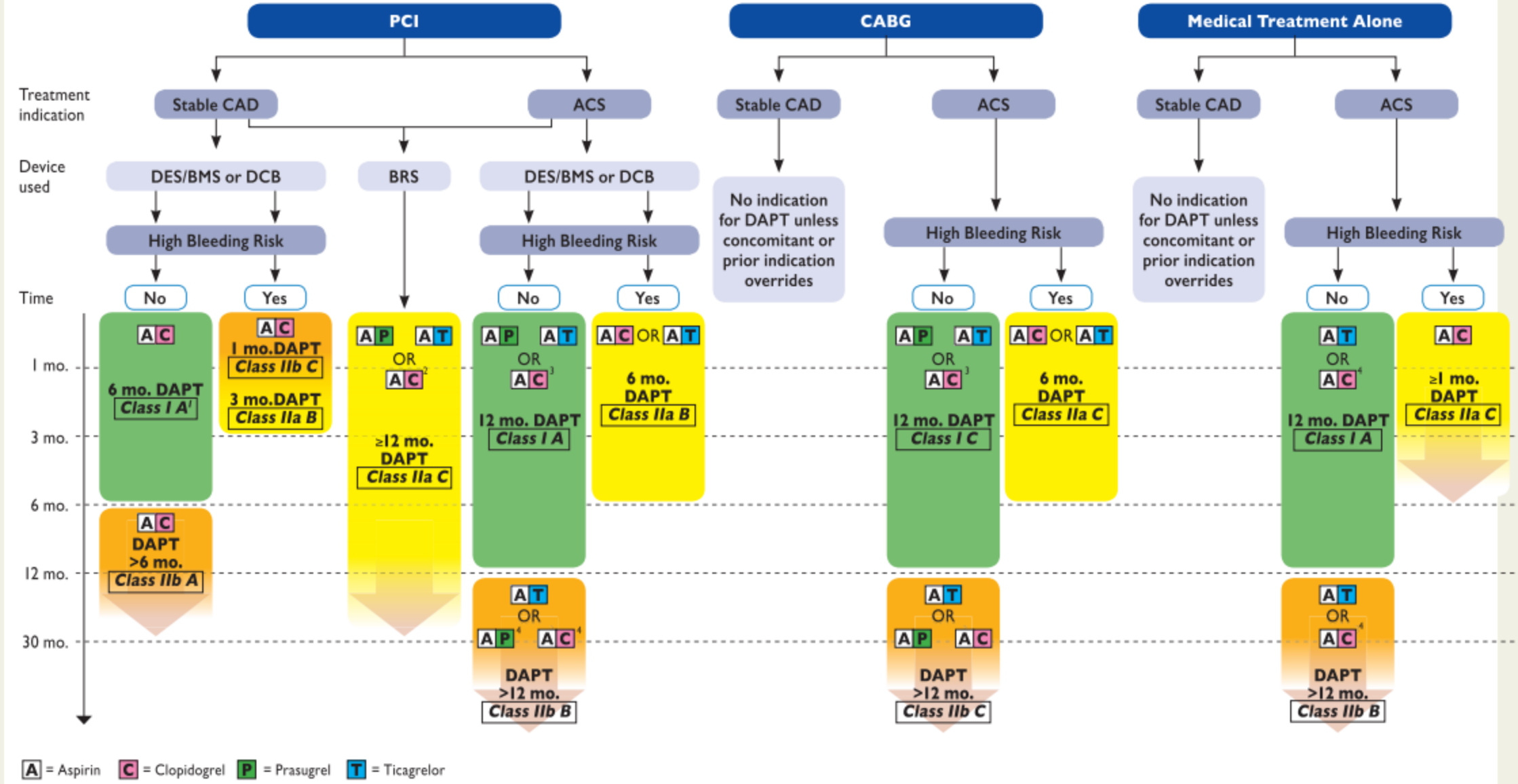
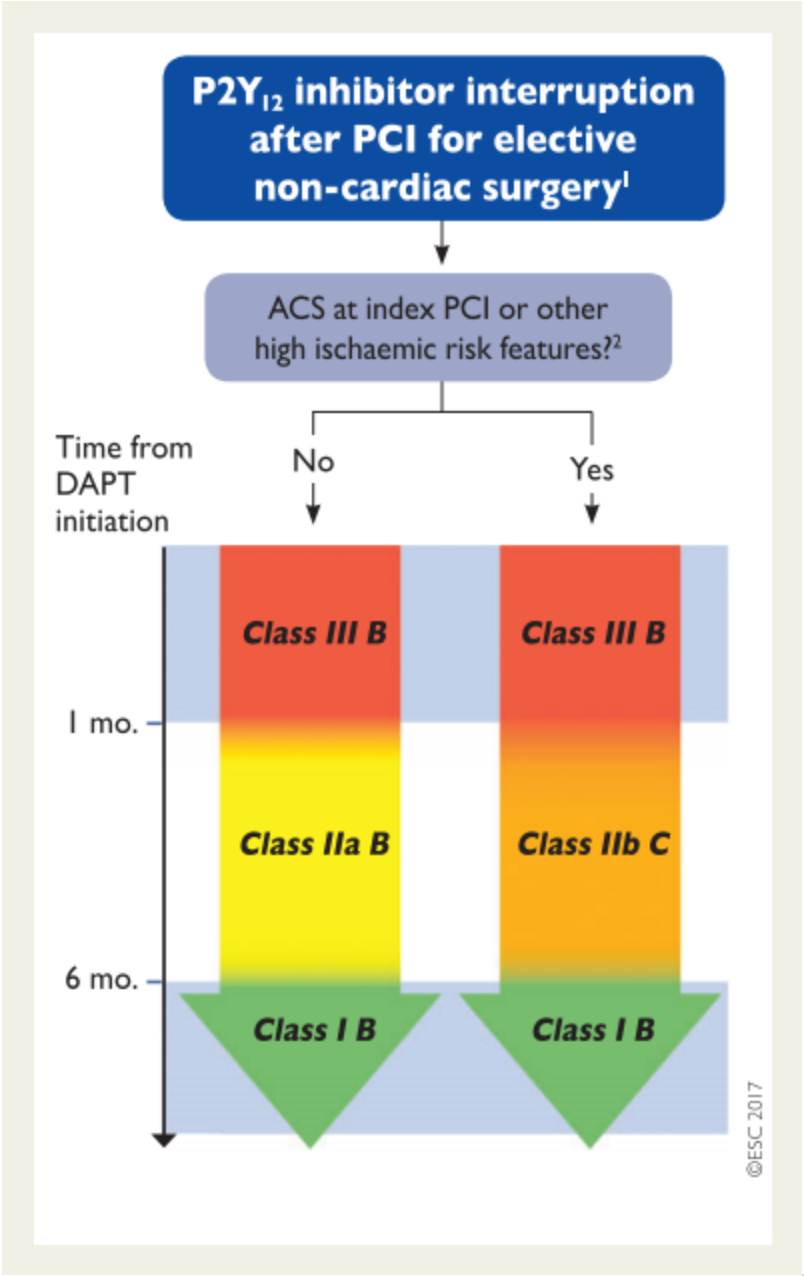
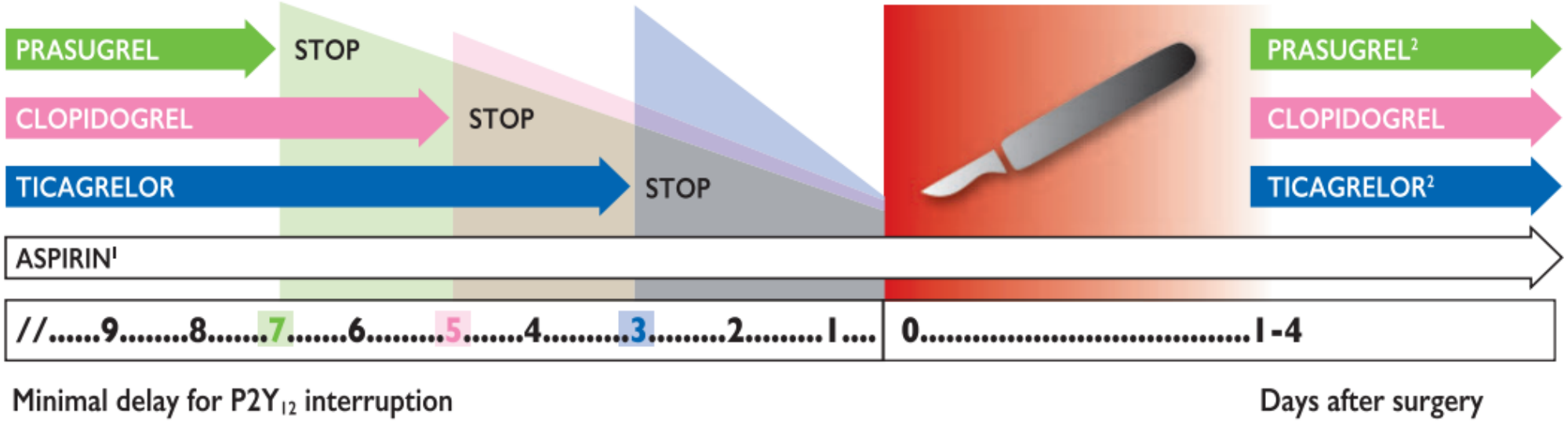

ASPIRIN
TICLOPIDINE
CLOPIDOGREL
PRASUGREL
TICAGRELOR
Investigated DAPT Duration
<1m
1m
3m
6m
12m
30m
36m
STAR (1998)
MATTIS (1998)
ISAR (1996)
CLASSIC (2000)
FANTASTIC (1998)
COMMIT (2005)
CLARITY (2005)
CURRENT OASIS 7 (2010)
ACCOAST (2013)
RESET (2012)
OPTIMIZE (2013)
ATLANTIC (2014)
ISAR TRIPLE (2015)
PRAGUE-18 (2016)
GRAVITAS (2011)
EXCELLENT (2012)
SECURITY (2014)
ISAR SAFE (2015)
I-LOVE-IT 2 (2016)
IVUS XPL (2016)
ANTARCTIC (2016)
CURE (2001)
CREDO (2002)
PLATO (2009)
ARCTIC (2012)
WOEST (2013)
NIPPON (2016)
TRITON (2007)
PRODIGY (2012)
TRILOGY ACS (2013)
ARCTIC INT. (2014)
ITALIC (2015)
CHARISMA (2006)
REAL-LATE ZEST-LATE (2010)
DAPT (2014)
OPTIDUAL (2016)
DES-LATE (2014)
PEGASUS (2015)
Year of publication
1996
2017
Size of the circles denotes sample size
Perimeter of the circles denotes type of investigated population
LEGEND
2K pts
5K pts
10K pts
20K pts
Mixed clinical presentation at the time of stent implantation
Acute coronary syndrome at presentation
DAPT initiated in patients with prior myocardial infarction
DAPT for primary prevention
©ESC 2017


PCI
CABG
Medical Treatment Alone
Treatment indication
Stable CAD
ACS
Stable CAD
ACS
Stable CAD
ACS
Device used
DES/BMS or DCB
BRS
DES/BMS or DCB
No indication for DAPT unless concomitant or prior indication overrides
No indication for DAPT unless concomitant or prior indication overrides
High Bleeding Risk
High Bleeding Risk
High Bleeding Risk
High Bleeding Risk
Time
No
Yes
No
Yes
No
Yes
No
Yes
No
Yes
1 mo.
3 mo.
6 mo.
12 mo.
30 mo.
A C
6 mo. DAPT
Class I A1
A C
1 mo.DAPT
Class IIb C
3 mo.DAPT
Class IIa B
A C
DAPT
>6 mo.
Class IIb A
A P A T
OR
A C2
≥12 mo.
DAPT
Class IIa C
A P A T
OR
A C3
12 mo. DAPT
Class I A
A C OR A T
6 mo.
DAPT
Class IIa B
A T
OR
A P4 A C4
DAPT
>12 mo.
Class IIb B
A P A T
OR
A C3
12 mo. DAPT
Class I C
A C OR A T
6 mo.
DAPT
Class IIa C
A T
OR
A P A C
DAPT
>12 mo.
Class IIb C
A T
OR
A C4
12 mo. DAPT
Class I A
A C
≥1 mo.
DAPT
Class IIa C
A T
OR
A C4
DAPT
>12 mo.
Class IIb B
A = Aspirin
C = Clopidogrel
P = Prasugrel
T = Ticagrelor



European Heart Journal (2018) **39**, 213–254



= *Expected average platelet function recovery*

1 Decision to stop aspirin throughout surgery should be made on a single case basis taking into account the surgical bleeding risk.

2 In patients not requiring OAC.

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Dual antiplatelet therapy in patients treated with cardiac surgery with stable or unstable coronary artery disease

Recommendations	Class[a]	Level[b]
It is recommended that the heart team estimates the individual bleeding and ischaemic risks, and guides the timing of CABG as well as the antithrombotic management.	I	C
In patients on aspirin who need to undergo non-emergent cardiac surgery, it is recommended to continue aspirin at a low daily regimen throughout the perioperative period.	I	C
In patients treated with DAPT after coronary stent implantation who subsequently undergo cardiac surgery, it is recommended to resume $P2Y_{12}$ inhibitor therapy post-operatively as soon as is deemed safe so that DAPT continues until the recommended duration of therapy is completed.	I	C
In patients with ACS (NSTE-ACS or STEMI) treated with DAPT, undergoing CABG, and not requiring long-term OAC therapy, resumption of $P2Y_{12}$ inhibitor therapy as soon as is deemed safe after surgery and continuation up to 12 months is recommended.	I	C

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Dual antiplatelet therapy in patients treated with cardiac surgery with stable or unstable coronary artery disease

In patients on $P2Y_{12}$ inhibitors who need to undergo non-emergent cardiac surgery, postponing surgery for at least 3 days after discontinuation of ticagrelor, at least 5 days after clopidogrel, and at least 7 days after prasugrel should be considered.[152,153,160]	IIa	B
In CABG patients with prior MI who are at high risk of severe bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.	IIa	C
Platelet function testing may be considered to guide decisions on timing of cardiac surgery in patients who have recently received $P2Y_{12}$ inhibitors.[169,172–174]	IIb	B
In patients perceived to be at high ischaemic risk with prior MI and CABG, who have tolerated DAPT without a bleeding complication, treatment with DAPT for longer than 12 and up to 36 months may be considered.	IIb	C

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Table 4 Strategies to avoid bleeding complications in patients treated with oral anticoagulant

• Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA_2DS_2-VASc, ABC, HAS-BLED) with a focus on modifiable risk factors.
• Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.
• Consider the use of NOACs instead of VKA.
• Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65–70%) when VKA is used.
• Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation.[a]
• Clopidogrel is the $P2Y_{12}$ inhibitor of choice.
• Use low-dose (≤ 100 mg daily) aspirin.
• Routine use of PPIs.

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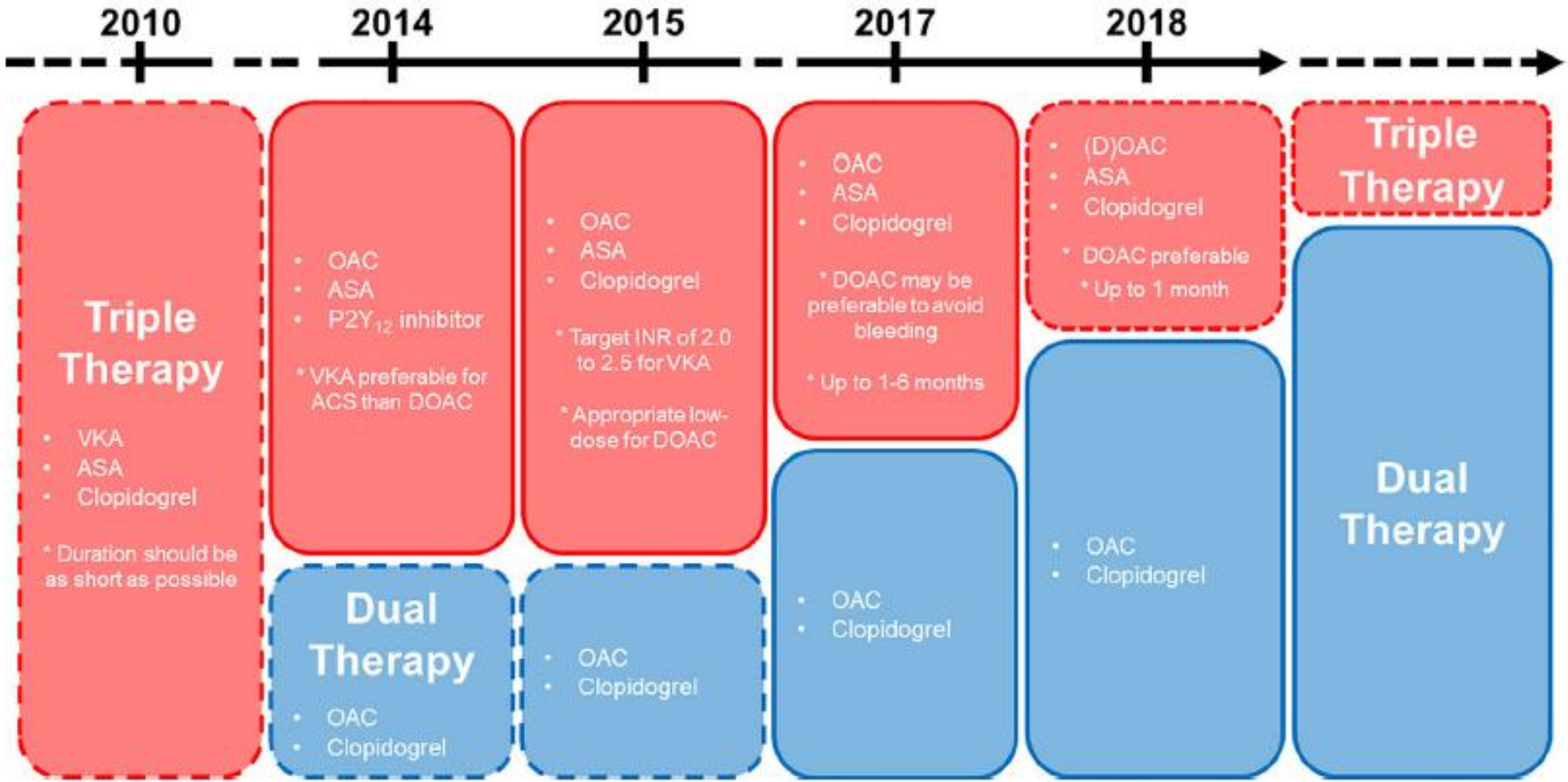

2010
2014
2015
2017
2018
Triple Therapy
• VKA
• ASA
• Clopidogrel
* Duration should be as short as possible
• OAC
• ASA
• P2Y12 inhibitor
* VKA preferable for ACS than DOAC
Dual Therapy
• OAC
• Clopidogrel
• OAC
• ASA
• Clopidogrel
* Target INR of 2.0 to 2.5 for VKA
* Appropriate low-dose for DOAC
• OAC
• Clopidogrel
• OAC
• ASA
• Clopidogrel
* DOAC may be preferable to avoid bleeding
* Up to 1-6 months
• OAC
• Clopidogrel
• (D)OAC
• ASA
• Clopidogrel
* DOAC preferable
* Up to 1 month
• OAC
• Clopidogrel
Triple Therapy
Dual Therapy

FIGURE 3 Periprocedural Antithrombotic Strategies

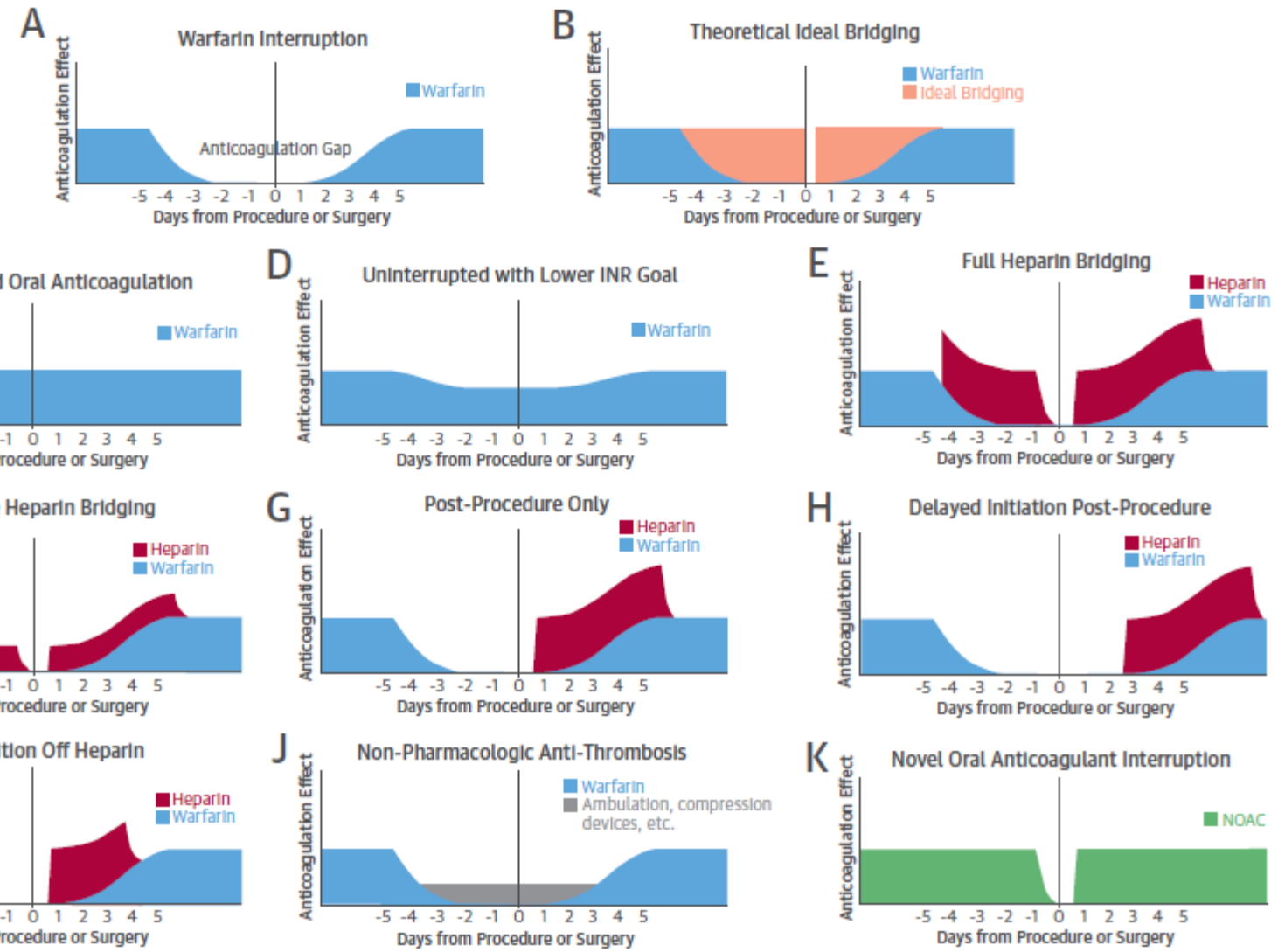
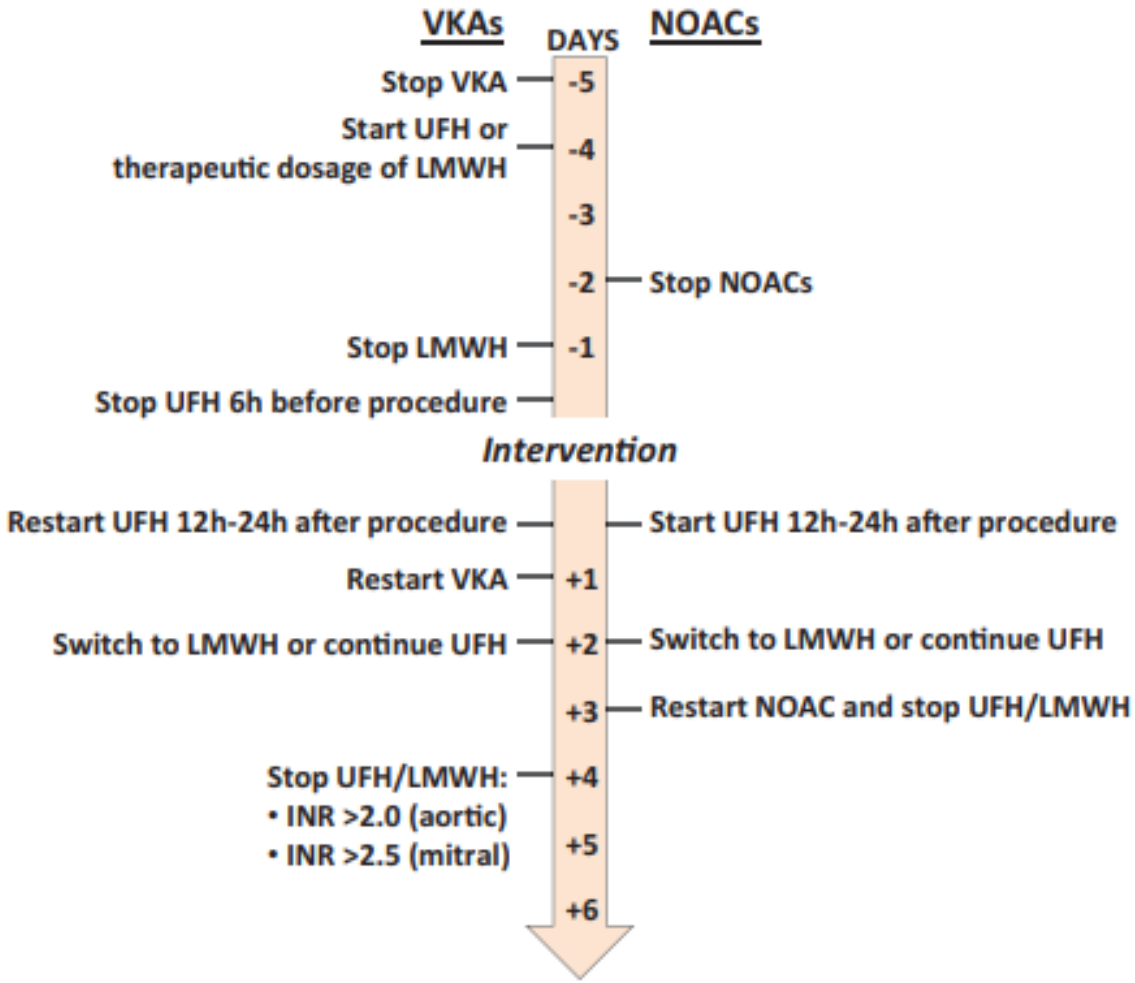


TABLE 4 Bridging Recommendations and Considerations for High-Risk Patients by OAC Indication

High-Risk OAC Indication	Thromboembolism Risk During OAC Interruption	Major Bleeding Risk	Guideline Recommendation (ACCP)	Guideline Recommendation (AHA/ACC/HRS)	Considerations Favoring *Not* Bridging
Atrial fibrillation ($CHADS_2$ ≥5)	+	+++	Bridging is favored (Grade 2C)	No specific recommendation to bridge. Individualize based on bleeding and TE risk.	• Short OAC interruption (<3-5 days) • Concurrent dual antiplatelet therapy • Active bleeding • High risk of major bleeding (BleedMAP score) • No prior TE • Sinus rhythm
Recent VTE	+	++	Bridging is favored (Grade 2C)	N/A	• Same as atrial fibrillation considerations • VTE >3 months prior
Recent or active arterial TE	++	++	Bridging is favored (Grade 2C)	No specific recommendation to bridge. Individualize on the basis of bleeding and TE risk.	• Same as atrial fibrillation considerations • TE >3 months prior
Mechanical heart valve(s)	++	+++	Bridging is favored (Grade 2C)	No specific recommendation to bridge. Individualize on the basis of bleeding and TE risk.	• Same as atrial fibrillation considerations • Aortic position only

ACC = American College of Cardiology; ACCP = American College of Chest Physicians; AHA = American Heart Association; HRS = Heart Rhythm Society; OAC = oral anticoagulation; TE = thromboembolism; other abbreviations as in Table 1.


VKAs
DAYS
NOACs
Stop VKA
-5
Start UFH or
therapeutic dosage of LMWH
-4
-3
-2
Stop NOACs
Stop LMWH
-1
Stop UFH 6h before procedure
Intervention
Restart UFH 12h-24h after procedure
Start UFH 12h-24h after procedure
Restart VKA
+1
Switch to LMWH or continue UFH
+2
Switch to LMWH or continue UFH
+3
Restart NOAC and stop UFH/LMWH
Stop UFH/LMWH:
• INR >2.0 (aortic)
• INR >2.5 (mitral)
+4
+5
+6

Recommendations for management of antithrombotic therapy after prosthetic valve implantation or valve repair in the perioperative and postoperative periods

Recommendations	Class[a]	Level[b]
Management of antithrombotic therapy in the perioperative period		
It is recommended that VKAs are timely discontinued prior to elective surgery to aim for an INR <1.5.[c]	I	C
Bridging of OAC, when interruption is needed, is recommended in patients with any of the following indications: • Mechanical prosthetic heart valve. • AF with significant mitral stenosis. • AF with a CHA_2DS_2-VASc score ≥3 for women or 2 for men.[d] • Acute thrombotic event within the previous 4 weeks. • High acute thromboembolic risk.[e]	I	C
Therapeutic doses of either UFH or subcutaneous LMWH are recommended for bridging.[476,504]	I	B
In patients with MHVs, it is recommended to (re)-initiate the VKA on the first postoperative day.	I	C
In patients who have undergone valve surgery with an indication for postoperative therapeutic bridging, it is recommended to start either UFH or LMWH 12–24 h after surgery.	I	C
In patients undergoing surgery, it is recommended that aspirin therapy, if indicated, is maintained during the periprocedural period.	I	C
In patients treated with DAPT after recent PCI (within 1 month) who need to undergo heart valve surgery in the absence of an indication for OAC, it is recommended to resume the $P2Y_{12}$ inhibitor postoperatively, as soon as there is no concern over bleeding.	I	C
In patients treated with DAPT after recent PCI (within 1 month) who need to undergo heart valve surgery in the absence of an indication for OAC, bridging $P2Y_{12}$ inhibitors with short-acting glycoprotein IIb/IIIa inhibitors or cangrelor may be considered.	IIb	C

Recommendations for management of antithrombotic therapy after prosthetic valve implantation or valve repair in the perioperative and postoperative periods

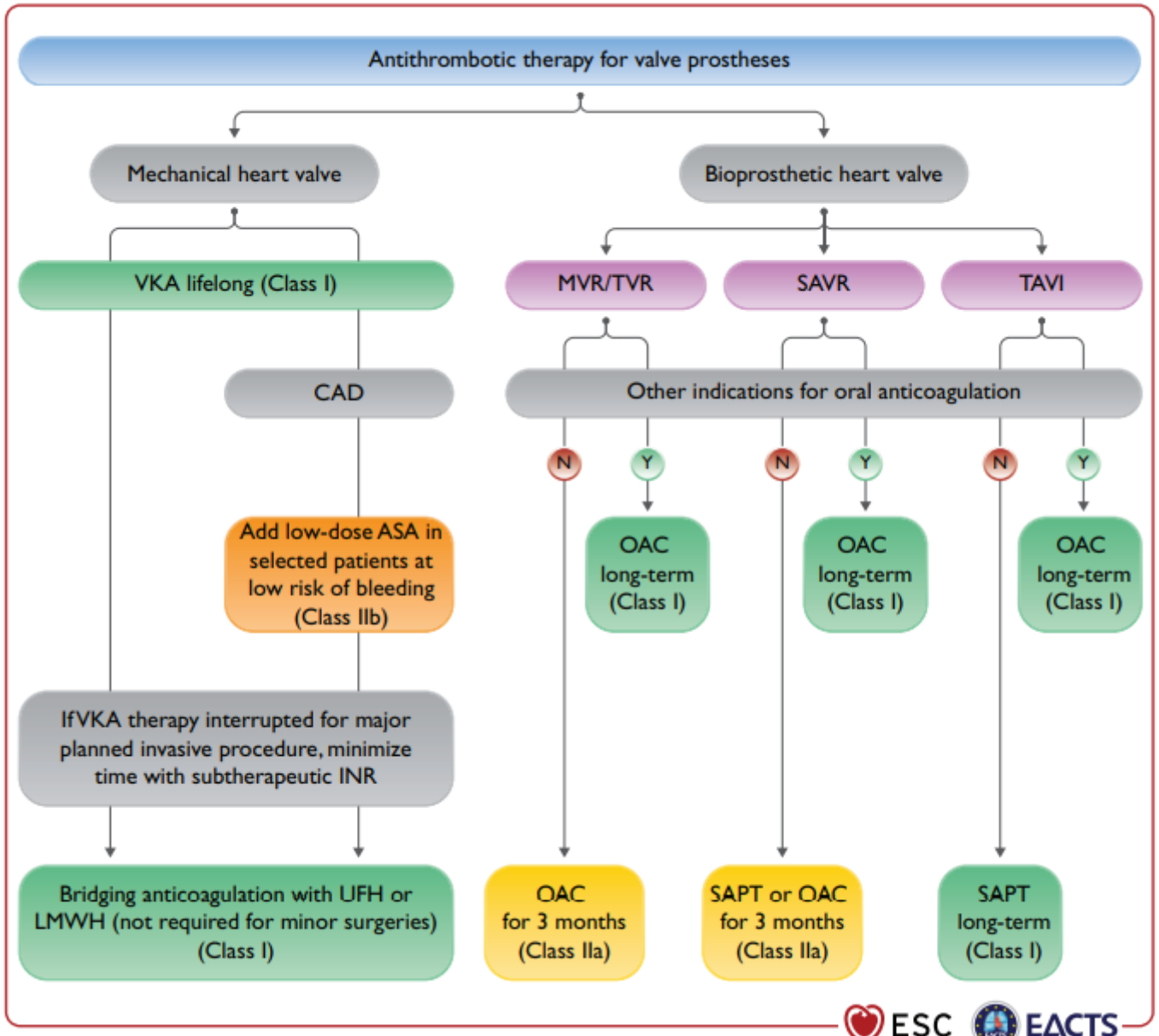
Patients with an indication to concomitant antiplatelet therapy		
After uncomplicated PCI or ACS in patients requiring long-term OAC, early cessation (≤1 week) of aspirin and continuation of dual therapy with OAC and a $P2Y_{12}$ inhibitor (preferably clopidogrel) for up to 6 months (or up to 12 months in ACS) is recommended if the risk of stent thrombosis is low or if concerns about bleeding risk prevail over concerns about risk of stent thrombosis, irrespective of the type of stent used.[505–509]	I	B
Discontinuation of antiplatelet treatment in patients treated with an OAC is recommended after 12 months.[74,510–512]	I	B
After uncomplicated PCI or ACS in patients requiring both OAC and antiplatelet therapy, triple therapy with aspirin, clopidogrel and OAC for longer than 1 week should be considered when the risk of stent thrombosis outweighs the risk of bleeding, with the total duration (≤1 month) decided according to assessment of these risks and clearly specified at hospital discharge.	IIa	C
In patients treated with a VKA (e.g. MHVs), clopidogrel alone should be considered in selected patients (e.g. HAS-BLED ≥3 or ARC-HBR met and low risk of stent thrombosis) for up to 12 months.[512,513]	IIa	B
In patients requiring aspirin and/or clopidogrel in addition to VKA, the dose intensity of VKA should be considered and carefully regulated with a target INR in the lower part of the recommended target range and a time in the therapeutic range >65–70%.[505,514]	IIa	B

Recommendations for management of antithrombotic therapy after prosthetic valve implantation or valve repair in the perioperative and postoperative periods

Surgical valve replacement		
OAC using a VKA is recommended lifelong for all patients with an MHV prosthesis.[472,473]	I	B
For patients with a VKA, INR self-management is recommended provided appropriate training and quality control are performed.[482]	I	B
OAC is recommended for patients undergoing implantation of a surgical BHV who have other indications for anticoagulation.[f]	I	C
NOACs should be considered over VKA after 3 months following surgical implantation of a BHV in patients with AF.[74,499,500,515–518]	IIa	B
In patients with no baseline indications for OAC, low-dose aspirin (75–100 mg/day) or OAC using a VKA should be considered for the first 3 months after surgical implantation of an aortic BHV.[491,494]	IIa	B
In patients with no baseline indications for OAC, OAC using a VKA should be considered for the first 3 months after surgical implantation of a bio-prosthesis in the mitral or tricuspid position.[519,520]	IIa	B
The addition of low-dose aspirin (75–100 mg/day) to VKA may be considered in selected patients with MHVs in case of concomitant atherosclerotic disease and low risk of bleeding.	IIb	C
The addition of low-dose aspirin (75–100 mg/day) to VKA should be considered after thromboembolism despite an adequate INR.	IIa	C
NOACs may be considered over VKA within 3 months following surgical implantation of a BHV in mitral position in patients with AF.[499]	IIb	C
NOACs are not recommended in patients with a mechanical valve prosthesis.[474]	III	B

Recommendations for management of antithrombotic therapy after prosthetic valve implantation or valve repair in the perioperative and postoperative periods

Surgical valve repair		
OAC with VKA should be considered during the first 3 months after mitral and tricuspid repair.	IIa	C
SAPT with low-dose ASA (75–100 mg/day) should be considered for the first 3 months after valve-sparing aortic surgery when there are no other baseline indications to OAC.	IIa	C
Transcatheter aortic valve implantation		
OAC is recommended lifelong for TAVI patients who have other indications for OAC.[501 f]	I	B
Lifelong SAPT is recommended after TAVI in patients with no baseline indication for OAC.[495,496,521]	I	A
Routine use OAC is not recommended after TAVI in patients with no baseline indication for OAC.[497]	III	B


Antithrombotic therapy for valve prostheses
Mechanical heart valve
Bioprosthetic heart valve
VKA lifelong (Class I)
MVR/TVR
SAVR
TAVI
CAD
Other indications for oral anticoagulation
N
Y
N
Y
N
Y
Add low-dose ASA in selected patients at low risk of bleeding (Class IIb)
OAC long-term (Class I)
OAC long-term (Class I)
OAC long-term (Class I)
If VKA therapy interrupted for major planned invasive procedure, minimize time with subtherapeutic INR
Bridging anticoagulation with UFH or LMWH (not required for minor surgeries) (Class I)
OAC for 3 months (Class IIa)
SAPT or OAC for 3 months (Class IIa)
SAPT long-term (Class I)
ESC
EACTS

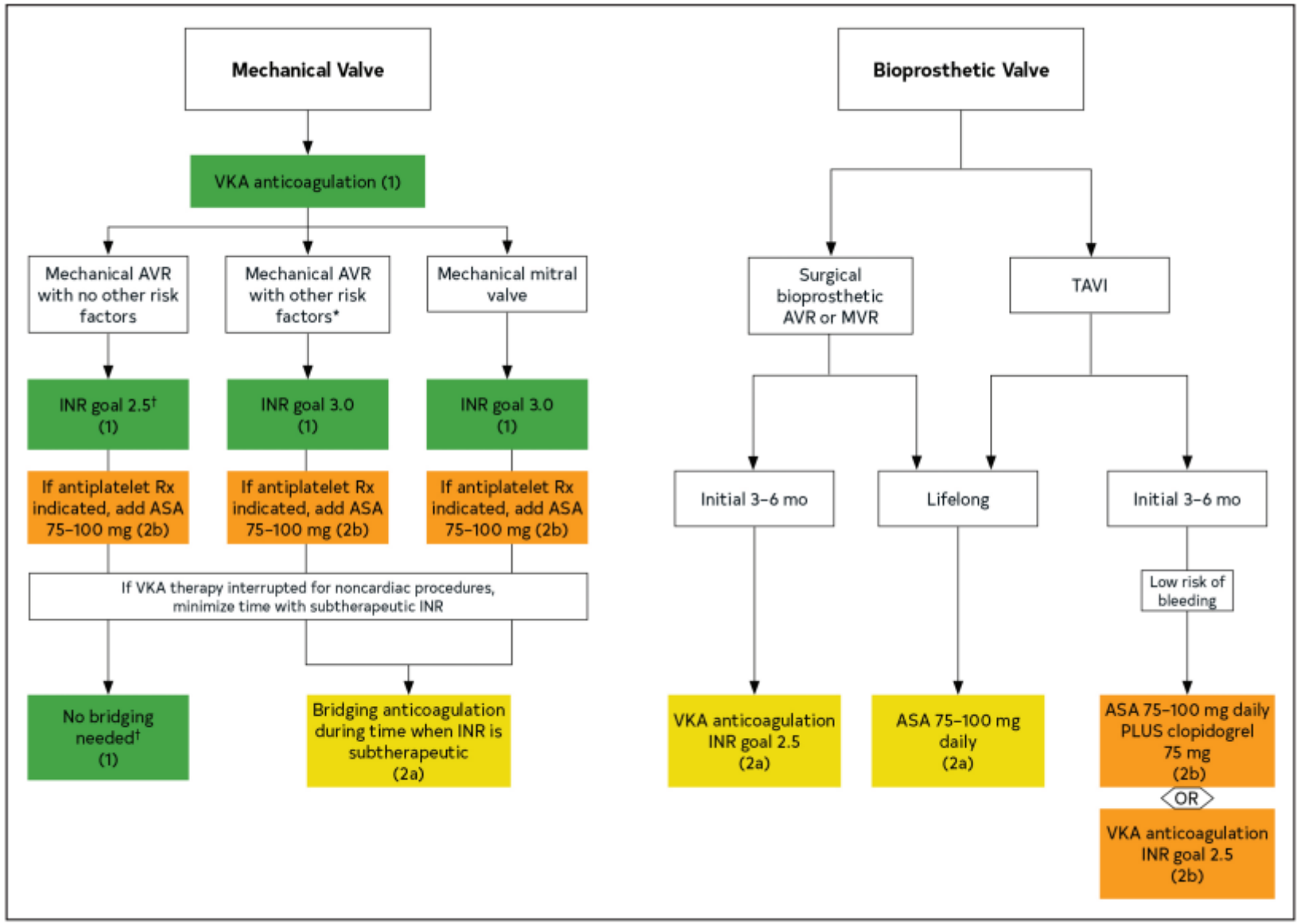


Figure 12. Antithrombotic therapy for prosthetic valves.

Table 10 Target INR for mechanical prostheses

Prosthesis thrombogenicity	Patient-related risk factors[a]	
	None	≥1 risk factor
Low[b]	2.5	3.0
Medium[c]	3.0	3.5
High[d]	3.5	4.0

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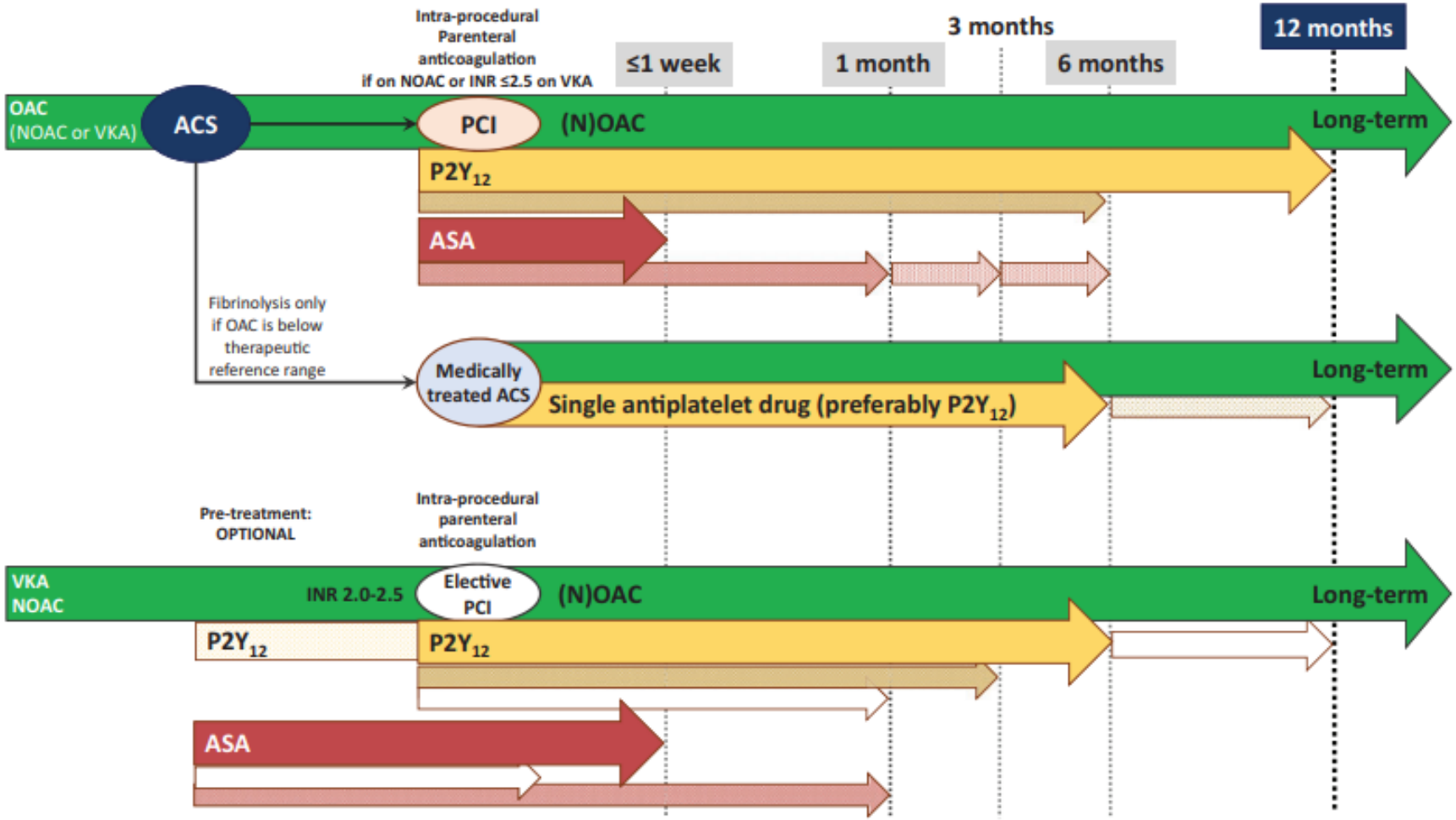
INR = international normalized ratio; LVEF = left ventricular ejection fraction.
[a]Mitral or tricuspid valve replacement; previous thromboembolism; atrial fibrillation; mitral stenosis of any degree; LVEF <35%.
[b]Carbomedics, Medtronic Hall, ATS, Medtronic Open-Pivot, St Jude Medical, On-X, Sorin Bicarbon.
[c]Other bileaflet valves with insufficient data.
[d]Lillehei-Kaster, Omniscience, Starr-Edwards (ball-cage), Bjork-Shiley and other tilting-disc valves.

Table 2. Randomized Controlled Trials Evaluating Higher vs. Lower INR Targets

	Design	Valve	INR Ranges	Mean Follow-Up	Thromboembolic Events	Bleeding Events
Acar et al, 1996[54]	Multicenter RCT	AVR or MVR with Omnicarbon or St Jude valve	Group 1 (n=192): 3.0–4.5	2.2 y	Group 1: 9	Group 1: 56
			Group 2 (n=188): 2.0–3.0		Group 2: 10	Group 2: 34
Hering et al, 2005[55]	Multicenter RCT	AVR, MVR, or DVR with St Jude valve	Group 1 (n=672): 3.0–4.5	2.5 y	Group 1: 16	Group 1: 627
					Group 2: 12	Group 2: 406
			Group 2 (n=677): 2.5–4.0		Group 3: 20	Group 2: 499
			Group 3 (n=675): 2.0–3.5			
Pengo et al, 2007[56]	Multicenter RCT	AVR, MVR, or DVR with various models	Group 1 (n=104): 3.7	1.6 y	Group 1: 2	Group 1: 2
			Group 2 (n=94): 2.5		Group 2: 0	Group 2: 4
Torella et al, 2010[57]	Single-center RCT	AVR with various models	Group 1 (n=199): 2.0–3.0	1.5 y	Group 1: 3	Group 1: 16
			Group 2 (n=197): 1.5–2.5		Group 2: 1	Group 2: 6
Puskas et al, 2014[16]	Multicenter RCT	AVR with On-X valve	Group 1 (n=190): 2.0–3.0	3.8 y	Group 1: 12	Group 1: 50
			Group 2 (n=185): 1.5–2.0		Group 2: 18	Group 2: 18
Koertke et al, 2015[58]	Multicenter RCT	AVR, MVR, or DVR with St Jude valve	Group 1 (n=526): 1.8–2.8 (AVR) or 2.5–3.5 (MVR or DVR)	5.6 y	Group 1: 4	Group 1: 21
			Group 2 (n=1045): 1.6–2.1 (AVR) or 2.0–2.5 (MVR or DVR)		Group 2: 6	Group 2: 9

The 6 trials detailed above were included in a meta-analysis by Gupta et al comparing thromboembolic events and bleeding in higher versus lower INR targets following mechanical valve replacement. This meta-analysis found no significant differences in TE between target ranges; however, a significant increase in bleeding with higher INR targets was discovered. ASA indicates acetylsalicylic acid; AVR, aortic valve replacement; DVR, double valve replacement; INR, international normalized ratio; MVR, mitral valve replacement; RCT, randomized controlled trial; TE, thromboembolic events; and y, years.

11. Prosthetic valves



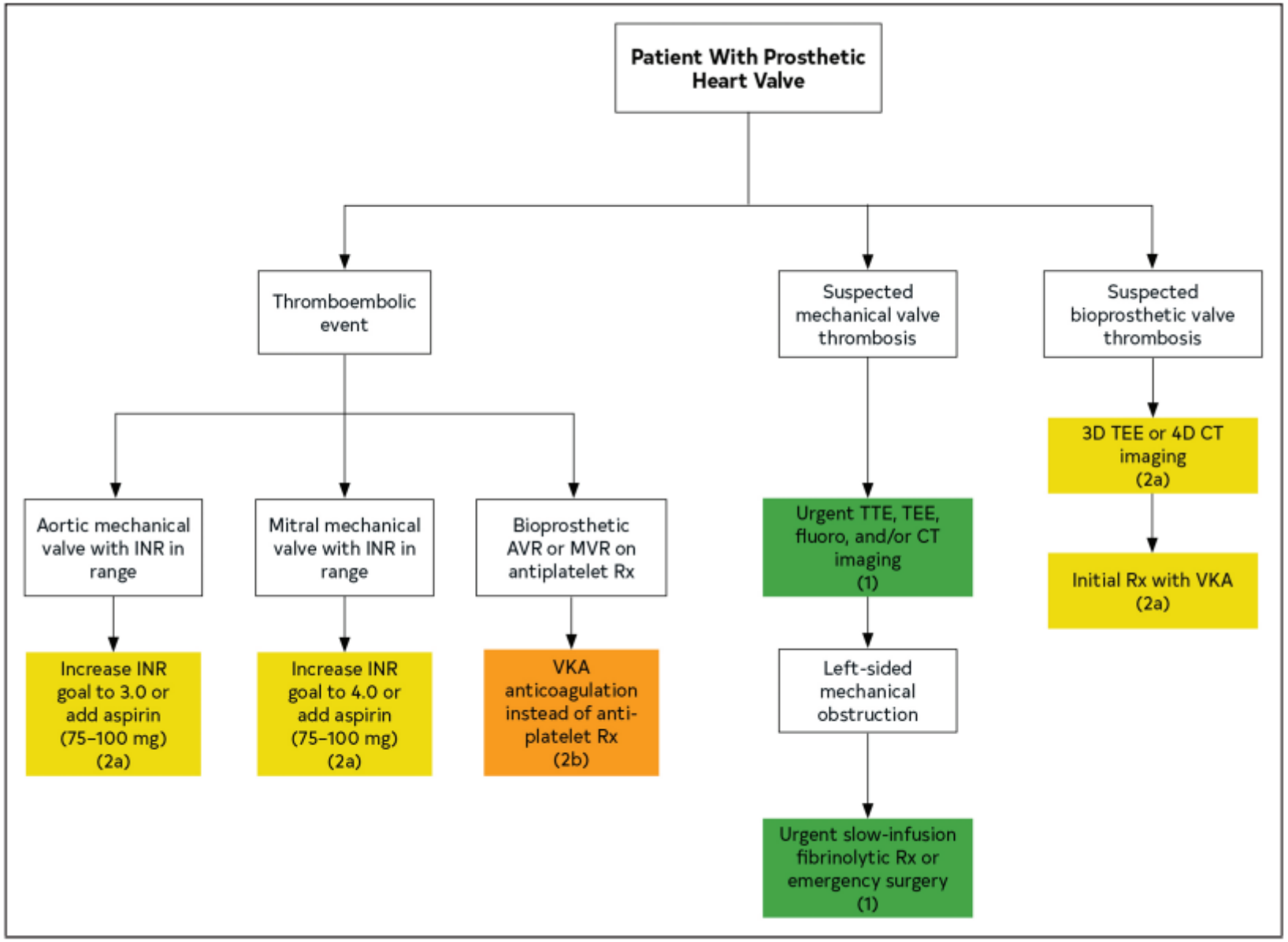
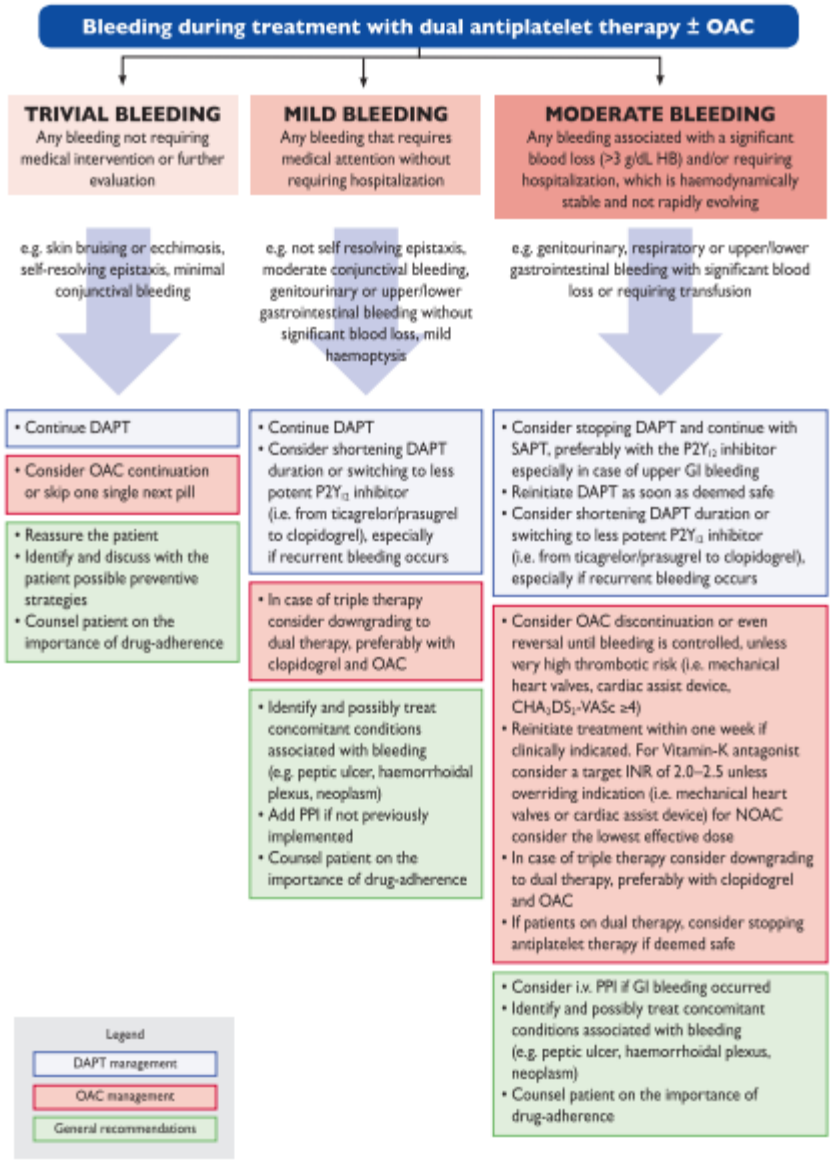
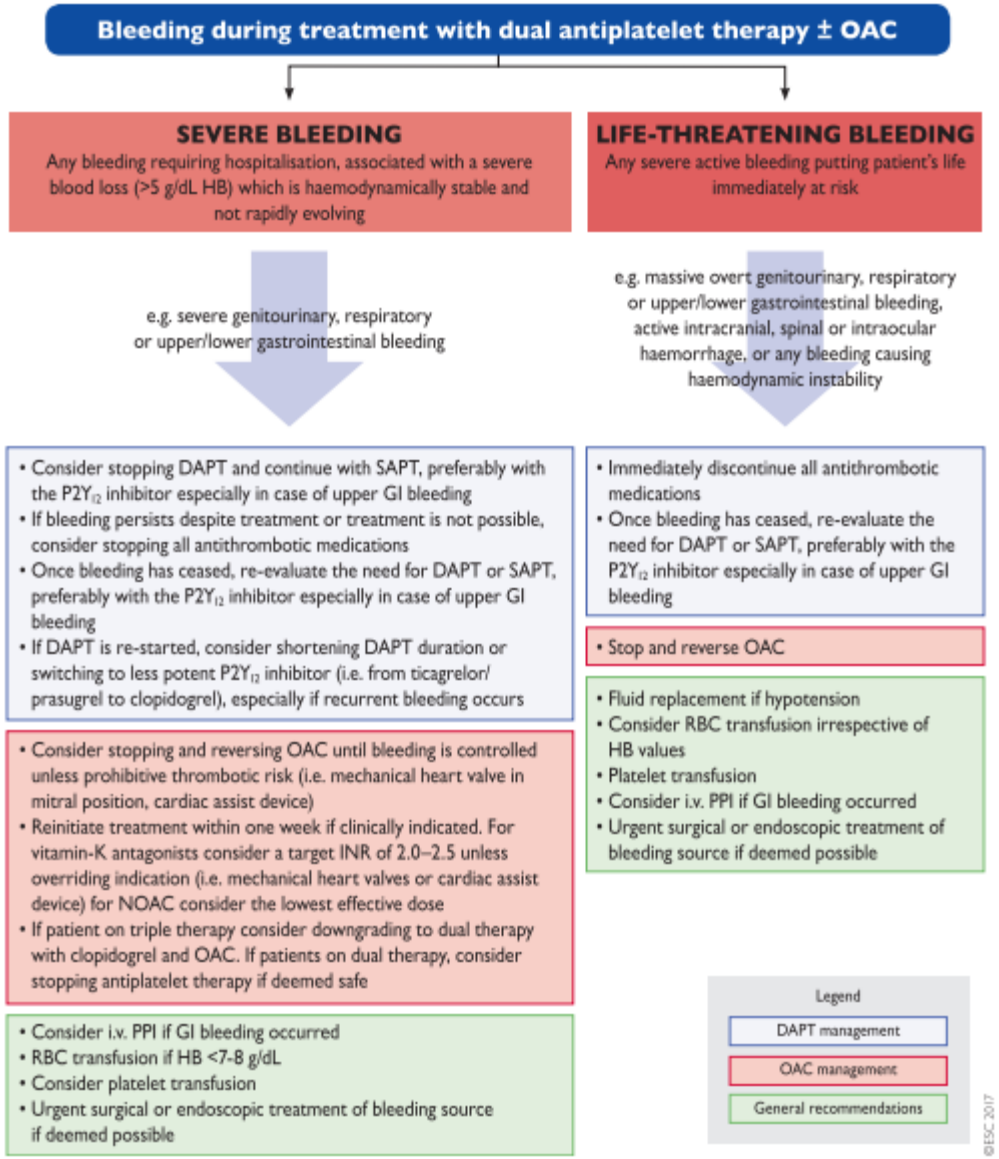


Figure 13. Management of embolic events and valve thrombosis.





European Heart Journal (2018) **39**, 213–254

Table 4 **Major gaps in evidence in anti-thrombotic therapy after valve replacement**

Combination of aspirin with VKA in patients with a mechanical prosthesis and contemporary target INRs
Optimal timing, doses, and type of heparin to be used early after mechanical valve replacement
Use of aspirin vs. VKA during the first three post-operative months following aortic valve replacement using a bioprosthesis
Use of DOACs in patients with a bioprosthesis
Use of anti-Xa DOACs in patients with a mechanical prosthesis
Anti-thrombotic therapy after TAVI in patients in sinus rhythm and in AF

European Heart Journal (2014) **35**, 2942–2949

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