



# Contents

<b>Foreword</b>	<b>XI</b>
<i>Fiorenzo Gaita</i>	
<b>Preface</b>	<b>XII</b>
<i>Giuseppe Patti</i>	
<b>1 Coagulative patterns in atrial fibrillation</b>	<b>1</b>
<i>Martina Berteotti, Domenico Prisco, Rossella Marcucci</i>	
Introduction	1
Atrial cardiomyopathy and the role of comorbidities	1
Blood stasis	2
Endothelial dysfunction	3
Hypercoagulability	3
Conclusions	4
<b>2 Thromboembolic risk stratification in patients with atrial fibrillation</b>	<b>7</b>
<i>Felice Gragnano, Vincenzo De Sio, Antonio Capolongo, Fabrizia Terracciano, Paolo Calabrò</i>	
Introduction	7
Scores for thromboembolic risk stratification	7
Other parameters potentially able to stratify the thromboembolic risk in the individual patient	9
Special populations	10
Conclusions	10
<b>3 Antithrombotic agents to prevent thromboembolism in atrial fibrillation</b>	<b>12</b>
<b>3.1 Antiplatelet therapy</b>	<b>12</b>
<i>Marco Palmieri, Stefano Benenati, Italo Porto</i>	
Introduction	12
Evidence with antiplatelet agents to prevent atrial fibrillation-related thromboembolism	12
Current recommendations	14
Conclusions	14
<b>3.2 Vitamin K antagonist anticoagulants</b>	<b>16</b>
<i>Giulia Renda, Francesca Ciliberti</i>	
Introduction	16
Mechanisms of action	16
Vitamin K antagonist anticoagulants and atrial fibrillation	18
Conclusions	19
<b>3.3 Non-vitamin K antagonist oral anticoagulants or direct oral anticoagulants</b>	<b>21</b>
<i>Paolo Ciacci, Ilaria Cavallari</i>	
Introduction	21
Doses of different direct oral anticoagulants in atrial fibrillation and overall results of these agents vs. vitamin K antagonist anticoagulants	22
To do list before prescribing a DOAC	23
Specific features related to various direct oral anticoagulants	25
Conclusions	31

<b>4</b>	<b>Monitoring of oral anticoagulation in atrial fibrillation</b>	<b>33</b>
	<i>Corrado Lodigiani, Luca Librè</i>	
	Introduction	33
	Vitamin K antagonist anticoagulants	33
	Direct oral anticoagulants	35
	Conclusive recommendations	37
<b>5</b>	<b>Oral anticoagulation in specific settings of patients with atrial fibrillation</b>	<b>40</b>
	<b>5.1 Patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score 0/CHA<sub>2</sub>DS<sub>2</sub>-VA score 0</b>	<b>40</b>
	<i>Domenico D'Amario, Giuseppe Patti</i>	
	Introduction	40
	Burden of atrial fibrillation	41
	Parameters of left atrium anatomy and function	42
	Biomarkers	44
	Specific conditions at higher thromboembolic risk	45
	Conclusions and future perspectives	46
	<b>5.2 Patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score 1/CHA<sub>2</sub>DS<sub>2</sub>-VA score 1</b>	<b>50</b>
	<i>Gabriele Dell'Era, Giuseppe Patti</i>	
	Introduction	50
	Evidence on CHA <sub>2</sub> DS <sub>2</sub> -VASc 1 patients in registration trials of direct anticoagulants	50
	Current recommendations for oral anticoagulation in atrial fibrillation patients with CHA <sub>2</sub> DS <sub>2</sub> -VASc score 1	51
	Empirical, tailored approach to oral anticoagulation in patients with CHA <sub>2</sub> DS <sub>2</sub> -VASc 1	52
	Conclusions	53
	<b>5.3 Patients undergoing cardioversion</b>	<b>54</b>
	<i>Vincenzo Russo, Michele Iavarone, Antonello D'Andrea</i>	
	Introduction	54
	Thromboembolic risk associated to cardioversion	55
	Cardioversion in patients with AF lasting >48 hours	55
	Cardioversion in patients with atrial fibrillation lasting ≤48 hours	57
	Anticoagulation after cardioversion	58
	Conclusions	59
	<b>5.4 Patients with concomitant coronary artery disease</b>	<b>61</b>
	<i>Andrea Rubboli, Matteo Lisi</i>	
	Introduction	61
	Early antithrombotic therapy	61
	Later antithrombotic therapy	64
	Debated issues and conclusions	65
	<b>5.5 Patients undergoing elective surgery</b>	<b>68</b>
	<i>Giuseppe Patti, Chiara Ghiglieno</i>	
	Introduction	68
	Stratification of the bleeding risk	68
	Stratification of the thromboembolic risk	70
	Timing of interruption and restart of direct oral anticoagulants	70
	Special populations	73
	<b>5.6 Patients with bleeding, trauma or urgent, unplanned surgery</b>	<b>75</b>
	<i>Vittorio Pengo</i>	
	Introduction	75
	Atrial fibrillation patients with trauma	75
	Atrial fibrillation patients candidate to urgent, unplanned surgery	78
	Conclusions	79



<b>5.7 Elderly/very elderly and fragile patients</b>	<b>81</b>
<i>Roberto Presta, Enrico Brunetti, Mario Bo</i>	
Introduction	81
Efficacy and safety of oral anticoagulant therapy in elderly patients	81
Appropriate dosing of direct oral anticoagulants	82
Clinical uncertainties in real-world older and frail atrial fibrillation patients	82
Practical conclusions	85
<b>5.8 Patients at the extremes of body weight</b>	<b>87</b>
<i>Federica De Vecchi, Giuseppe Patti</i>	
Introduction	87
General pharmacokinetic/pharmacodynamic principles for oral anticoagulant agents	88
Clinical data on direct oral anticoagulants	88
Current recommendations for oral anticoagulation	90
<b>5.9 Patients with chronic kidney disease</b>	<b>93</b>
<i>Carmen A. Spaccarotella, Andrea Mariani, Giovanni Esposito, Ciro Indolfi</i>	
Introduction	93
Current evidence with different oral anticoagulant agents	93
Conclusions	95
<b>5.10 Patients with cancer</b>	<b>98</b>
<i>Paola Gargiulo, Ermanno Nardi, Stefania Paolillo, Sara Fontanarosa, Pasquale Perrone Filardi</i>	
Introduction	98
Current recommendations and practice patterns	99
<b>5.11 Patients with different ethnicities</b>	<b>104</b>
<i>Rossella De Maria, Bianca Pellizzeri, Clelia Licata, Luca Lombardo, Marco Frazzetto, Bruno Francaviglia, Piera Capranzano</i>	
Introduction	104
Ethnic differences in warfarin dose requirements	104
Ethnic differences in clinical effects of warfarin	106
Doses and effects of direct oral anticoagulants across different ethnicities	106
Conclusions	112
<b>5.12 Patients in pregnancy</b>	<b>114</b>
<i>Marco G. Mennuni, Giuseppe Patti</i>	
Introduction	114
Pathophysiology and risk factors	115
Oral anticoagulant therapy	115
Parenteral anticoagulation	117
Practical approach	118
Breastfeeding	118
Conclusions	119
<b>5.13 Re-introduction of anticoagulation in patients after a major bleeding event</b>	<b>120</b>
<i>Giorgio Quadri, Giuseppe Musumeci, Roberta Rossini</i>	
Introduction	120
Intracranial bleeding	120
Gastrointestinal bleeding	122
Conclusions	123
<b>5.14 Patients receiving ablation</b>	<b>124</b>
<i>Massimo Grimaldi, Antonio Di Monaco</i>	
Introduction	124
Clinical trials and meta-analysis	125
ESC guidelines and real-life data	126

<b>5.15 Patients undergoing transcatheter aortic valve replacement</b>	<b>129</b>
<i>Pierluigi Merella, Gavino Casu</i>	
Introduction	129
Thromboembolic complications in TAVR recipients	130
Features of atrial fibrillation in TAVR patients	130
Management of atrial fibrillation patients undergoing TAVR	131
Conclusions	132
<b>5.16 Patients with secondary forms of atrial fibrillation</b>	<b>134</b>
<i>Letizia Riva, Giuseppe Di Pasquale</i>	
Introduction	134
Atrial fibrillation in the context of an acute coronary syndrome	135
Atrial fibrillation during sepsis	136
Atrial fibrillation and hyperthyroidism	136
<b>5.17 First episode of post-operative atrial fibrillation</b>	<b>138</b>
<i>Giuseppe Lanzillo, Rossana Totaro, Sergio Leonardi</i>	
Introduction	138
Epidemiology and prognosis	138
Pathophysiology	139
Pre- and intra-operative management	140
Post-operative management	141
Follow-up	143
<b>5.18 Patients with valvular heart disease</b>	<b>147</b>
<i>Greca Zanda, Ferdinando Varbella, Leonardo Grisafi</i>	
Introduction	147
Evidence with direct oral anticoagulants in patients with valvular heart disease	148
Patients with mechanical heart valves	149
Patients with moderate-severe/rheumatic mitral stenosis	150
Patients with surgical bioprosthetic valves	151
Patients undergoing mitral valve repair	152
<b>6 Oral anticoagulation in atrial fibrillation: a look to the future</b>	<b>154</b>
<i>Antonella Scala, Gianluca Campo, Giuseppe Patti</i>	
Brief history: from sweet, dried hay to factor XI inhibitors	154
Thrombosis and hemostasis	154
Factor XI: thrombosis and hemostasis	155
Factor XI inhibitors: rationale and use	155
Conclusions	160
<b>7 Alternative treatments to oral anticoagulation for preventing thromboembolism in atrial fibrillation</b>	<b>161</b>
<i>Antonio Rapacciuolo, Alfonsomaria Salucci</i>	
Introduction	161
Left atrial appendage: anatomy and pathophysiology	161
Surgical exclusion of the left atrial appendage	162
Percutaneous closure of the left atrial appendage	162
Epicardic and hybrid closure of the left atrial appendage	166
Alternatives to left atrial appendage occlusion	166