

Appendix 5: Anticoagulation intensity and risk of hemorrhagic and thromboembolic events (part 1 of 2)

International normalized ratio	Hemorrhagic event		Thromboembolic event		Combined events	
	n / N	Relative risk (95% CI)	n / N	Relative risk (95% CI)	n / N	Relative risk (95% CI)
Rosove et al. ¹	NR		6 / 55		NR	
< 2		NR		7.2 (1.9–539.3)		NR
3–5		NR		0.0 (0.0–0.0)		NR
> 5		NR		NR		NR
Hutten et al. ²	4 / 1 303		15 / 1 303		19 / 1 303	
< 2		2.4 (0.4–13.3)		2.6 (1.2–5.6)		2.5 (1.3–5.0)
3–5		2.0 (0.2–10.2)		0.9 (0.2–2.3)		1.2 (0.8–1.3)
> 5		NR		NR		NR
Yasaka et al. ³	0 / 203		14 / 203		14 / 203	
< 2		0.0 (0.0–0.0)		2.6 (1.0–23.4)		0.9 (0.4–2.2)
3–5		5.7 (0.0–19.5)		0.0 (0.0–0.0)		3.6 (0.0–10.8)
> 5		NR		NR		NR
EAFT ⁴	0 / 214		7 / 214		7 / 214	
< 2		0.0 (0.0–0.0)		10.9 (3.3–286.5)		6.5 (2.0–29.1)
3–5		2.6 (0.5–31.4)		4.4 (1.5–759.3)		3.7 (1.5–18.9)
> 5		46.5 (11.4–398.6)		6.2 (0.0–11.0)		22.3 (6.2–97.4)
Chimowitz et al. ⁵	1 / 289		23 / 289		24 / 289	
< 2		0.3 (0.0–1.1)		4.9 (2.6–10.8)		3.0 (1.7–5.5)
3–5		4.3 (2.0–16.0)		1.1 (0.0–3.0)		2.4 (1.0–4.8)
> 5		35.0 (9.4–96.5)		4.0 (0.0–13.6)		16.7 (4.9–34.5)
Andersen et al. ⁶	0 / 204		0 / 204		0 / 204	
< 2		0.0 (0.0–0.0)		0.0 (0.0–0.0)		0.0 (0.0–0.0)
3–5		1.8 (1.1–2.9)		0.4 (0.0–2.2)		1.0 (0.2–3.3)
> 5		161.3 (94.0–332.5)		0.0 (0.0–0.0)		69.1 (23.6–222.0)
Torn et al. ⁷	0 / 356		3 / 356		3 / 356	
< 2		0.0 (0.0–0.0)		7.3 (0.5–30.0)		5.2 (0.2–17.1)
3–5		2.4 (0.8–9.6)		0.5 (0.2–2.5)		1.1 (0.5–3.6)
> 5		20.5 (5.6–143.4)		4.1 (0.3–16.8)		8.8 (3.2–28.3)
Cheung et al. ⁸	3 / 555		28 / 555		31 / 555	
< 2		0.3 (0.0–1.1)		3.2 (1.6–10.9)		1.8 (1.0–3.7)
3–5		10.6 (3.6–34.0)		0.0 (0.0–0.0)		5.3 (1.8–12.0)
> 5		NR		NR		NR
ESPRIT ⁹	4 / 536		5 / 536		9 / 536	
< 2		4.4 (0.7–15.6)		2.2 (0.4–5.2)		2.8 (1.0–5.7)
3–5		5.4 (3.4–9.3)		1.0 (0.1–2.4)		2.3 (1.0–4.4)
> 5		66.6 (39.3–127.1)		2.2 (0.0–4.9)		20.6 (9.3–40.0)
Poli et al. ¹⁰	12 / 903		20 / 903		32 / 903	
< 2		2.2 (1.0–3.9)		4.9 (2.6–8.3)		3.3 (2.1–4.9)
3–5		1.2 (0.7–2.0)		0.8 (0.3–1.4)		1.0 (0.7–1.5)
> 5		4.0 (0.6–8.2)		0.0 (0.0–0.0)		2.3 (0.3–4.5)
Tangelder et al. ¹¹	9 / 1 326		23 / 1 326		32 / 1 326	
< 2		2.3 (0.9–5.4)		3.0 (1.7–5.2)		2.8 (1.7–4.4)
3–5		1.6 (0.9–3.4)		0.2 (0.1–0.4)		0.7 (0.4–1.0)
> 5		7.8 (4.0–17.3)		3.1 (1.6–5.7)		4.7 (3.0–7.4)

Appendix 5: Anticoagulation intensity and risk of hemorrhagic and thromboembolic events (part 2 of 2)

International normalized ratio	Hemorrhagic event		Thromboembolic event		Combined events	
	n / N	Relative risk (95% CI)	n / N	Relative risk (95% CI)	n / N	Relative risk (95% CI)
Kearon et al.¹²	3 / 738		8 / 738		11 / 738	
< 2		0.7 (0.1–3.4)		3.5 (1.1–19.2)		0.5 (0.2–1.7)
3–5		11.1 (3.7–77.7)		2.8 (0.0–36.1)		42.0 (15.2–156.0)
> 5		NR		NR		NR
Casais et al.¹³	2 / 811		NR		NR	
< 2		1.0 (0.0–3.2)		NR		NR
3–5		0.5 (0.1–1.5)		NR		NR
> 5		4.2 (1.6–12.1)		NR		NR
Palareti et al.^{14,15}	6 / 2 745		27 / 2 745		33 / 2 745	
< 2		2.0 (1.0–2.4)		3.1 (1.8–5.4)		NR
3–5		1.4 (1.3–2.9)		0.9 (0.3–1.7)		NR
> 5		13.8 (6.1–16.6)		NR		NR
Van Walraven et al.¹⁶	31 / 10 020		46 / 10 020		77 / 10 020	
< 2		0.9 (0.6–1.3)		2.0 (1.4–3.1)		1.3 (1.0–1.7)
3–5		3.0 (1.4–3.9)		2.1 (0.8–3.3)		2.7 (2.0–3.5)
> 5		33.8 (12.9–54.4)		9.0 (0.0–19.0)		26.1 (16.0–37.8)
Azar et al.¹⁷	8 / 1 700		282 / 1 700		290 / 1 700	
< 2		0.4 (0.1–1.7)		2.5 (1.7–4.0)		2.1 (1.5–3.3)
3–5		2.1 (1.0–12.9)		0.8 (0.6–1.4)		1.1 (0.7–1.7)
> 5		11.1 (4.4–54.8)		0.3 (0.0–0.9)		2.0 (1.0–3.6)
Hylek et al.¹⁸	12 / 13 559		97 / 13 559		109 / 13 559	
< 2		1.0 (0.4–1.8)		5.1 (3.7–7.6)		3.5 (2.6–4.8)
3–5		2.3 (0.9–4.3)		1.3 (0.5–2.4)		1.7 (0.9–2.6)
> 5		26.0 (10.8–48.6)		4.6 (0.0–10.5)		13.1 (6.2–21.3)
Oden et al.¹⁹	28 / 42 451		NR		NR	
< 2		1.0 (0.6–1.5)		NR		NR
3–5		2.5 (1.9–3.3)		NR		NR
> 5		11.7 (3.7–20.4)		NR		NR

Note: CI = confidence interval, EAFT = European Atrial Fibrillation Trial Study Group, ESPRIT = European and Australian Stroke Prevention in Reversible Ischaemia Trial.

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