

Effectiveness and security of anticoagulation in Japanese patients having laparoscopic surgery for colorectal cancer to prevent venous thromboembolism

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Aim: To examine the effectiveness and security of anticoagulation for preventing venous thromboembolism (VTE) with having laparoscopic surgery for colorectal cancer (CRC), which is unknown in Japanese patients.

Methods: This randomized controlled trial at nine institutions in Japan were conducted from 2011 to 2015. Three hundred and two eligible patients aged 20 years or older having elective laparoscopic surgery for CRC were included in the trial. Random assignment for the patients was allocated either to an intermittent pneumatic compression (IPC) therapy group or to an IPC + anticoagulation therapy group. Anticoagulation therapy consisted of fondaparinux or enoxaparin for preventing VTE after surgery. VTE after surgery was diagnosed by enhanced multi-detector helical computed tomography. The primary endpoint was incidence of VTE, including asymptomatic cases, the secondary endpoint was incidence of major bleeding, and an intention-to-treat analysis was conducted. This study is registered in UMINCTR (UMIN000008435).

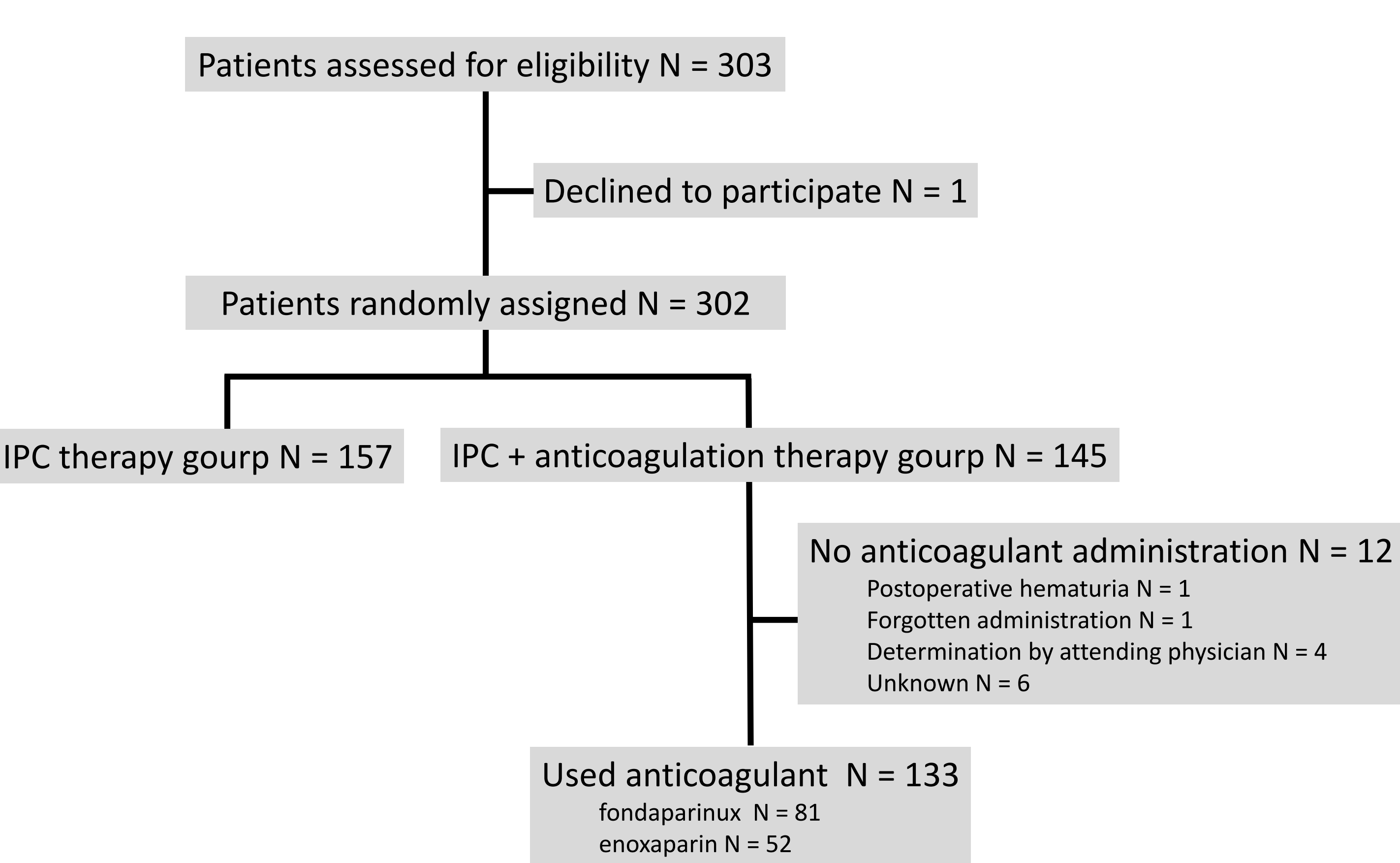


Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flowchart of the study

	VTE (-)	VTE (+)	Location (n)	Frequency (%)	P	
IPC therapy group	149	8	PE (3)	1.91	5.10%	0.382
			Pulmonary artery (1)			
			Pulmonary artery + posterior tibial vein (2)			
			Proximal VTE (3)	2.01		
			External iliac vein/popliteal vein (1)			
			External iliac vein (1)			
IPC + anticoagulation therapy group	141	4	Superficial femoral vein + deep femoral vein (1)		2.76%	
			Distal VTE (2)	1.34		
			Soleal vein (2)			
			PE (1)	0.69		
			Pulmonary artery (1)			
			Proximal VTE (3)	2.13		
			Deep femoral vein (2)			
			Popliteal vein (2)			
			Distal VTE (0)	0		

Abbreviations: IPC, intermittent pneumatic compression; PE, pulmonary embolism; VTE, venous thromboembolism

Table 2 Incidence of VTE in the patients in this study

Characteristic	IPC therapy group (n = 157)	IPC + anticoagulation therapy group (n = 145)	P value
Male/female	84:72; 54%:46%	84:61; 58%:42%	.476
Mean age	64.9 ± 10.3	65.4 ± 9.5	.691
Weight	58.3 ± 9.75	58.7 ± 11.4	.731
BMI	22.5 ± 3.21	22.6 ± 3.60	.848
Cancer location (colon/rectum)	130/27	130/15	.09
Stage (adenoma/0/I/II/III/IV/unknown)	1/2/57/39/52/0/6	0/5/44/36/49/3/8	.322
Risk factor for VTE (%)			
Diabetes mellitus	9.8	11.5	.700
Past VTE	0.6	0	1.000
Chronic renal failure	1.3	1.4	1.000
Past history of stroke	1.3	0.7	1.000
Past history of angina	3.2	2.1	.725
Past history of cardiac infarction	0	0	—
Varicose veins	3.2	4.1	.763
Dyslipidemia	15.3	16.6	.875
Leg paralysis	0	1.4	.230
Laboratory data			
PreOP D-dimer (µg/mL)	0.55 ± 0.40	0.53 ± 0.55	.710
APTT (s)	30.1 ± 3.66	30.2 ± 3.26	.726
Hemoglobin (g/L)	13.3 ± 0.60	14.3 ± 0.60	.216
Platelets (×10 ⁴ /L)	33.0 ± 3.41	32.3 ± 3.54	.872
Surgical data			
Open conversion rate	1.9%	4.8%	.153
OP times	297 ± 11.3	280 ± 311.8	.309
Blood loss (mL)	84.7 ± 17.6	97.9 ± 18.3	.606
VTE prophylaxis			
IPC duration (d)	1.19 ± 0.58	1.31 ± 0.96	.272
Anticoagulant duration (d)	—	6.0 ± 2.05	

Abbreviations: APTT, activated partial thromboplastin time; BMI, body mass index; IPC, intermittent pneumatic compression; VTE, venous thromboembolism.

Table 1 Baseline characteristics of the patients in the study

	IPC therapy group (%)	IPC + anticoagulation therapy group (%)	P
All bleeding	5/157 (3.18)	19/145 (13.1)	.002
Major bleeding	2/157 (1.27)	2/145 (1.38)	.936
Minor bleeding	3/157 (1.91)	17/145 (11.7)	.001

Abbreviation: IPC, intermittent pneumatic compression.

Table 3 Incidence of bleeding in the patients in this study

	IPC therapy group	IPC + anticoagulation therapy group		
		Fondaparinux	Enoxaparin	Without administration
Major bleeding	Anastomosis 1 Intrapelvic 1		Anastomosis 1	Anastomosis 1
Minor bleeding	Melena 2 Bloody drain discharge 1	Melena 3 Bloody drain discharge 2 Subcutaneous 5 Unknown 1	Melena 1 Subcutaneous 1 Unknown 1	Melena 1 Hematuria 1

Abbreviation: IPC, intermittent pneumatic compression.

Table 5 Location of bleeding

Results: Incidence of VTE after surgery was 5.10% with IPC therapy and 2.76% with IPC + anticoagulant therapy ($p = .293$). No symptomatic VTE was detected in any cases. The rates of major bleeding were 1.27% and 1.38% with IPC alone and with the combination ($p = .936$), respectively. The rates of overall bleeding were 7.69% for enoxaparin and 13.6% for fondaparinux ($p = .500$), and no bleeding-related deaths occurred.

Conclusion: Anticoagulation did not reduce the incidence of VTE and there was no significant difference as for the incidence of major bleeding between the two groups. Anticoagulation after laparoscopic surgery for CRC was not demonstrated to be useful in this study. In Japanese CRC patients with higher risk of VTE, pharmacological prophylaxis should be restricted after laparoscopic surgery.