7.2. Data extraction

Table 31 Randomized studies: VKA in the prevention of catheter-related thrombosis (CRT)

References Study design Inclusion period	Number of patients included/evaluated Follow-up	Features of included patients	Intervention	Catheter flushing	Endpoint	Arm A	Arm B	p value 95%CI
[BERN1990] Randomized controlled trial Not specified	121/82 patients 90 days	Solid tumors Lymphomas CVC ("port-a-cath", subclavian) Chemotherapy Inclusion 3 days before catheter insertion	Arm A (n=42): Warfarin 1 mg/day (3 days before CVC insertion and until Day 90 after insertion) PT measured weekly for 1 month, then at least monthly. If PT ≥15 seconds, then warfarin stopped, Vitamin K given and warfarin resumed when PT normal Arm B (n=40): no warfarin (no placebo)	UFH up to 500 IU / week	Rate of CRT Phlebography at Day 90 orif symptoms occurred	4/42 (9.5%) (4 symptomatic)	All CRT: 15/40 (37.5%) Symptomatic CRT: 13/40 (32.5%)	p <0.001
[COUBAN2005] Randomized controlled trial Mar 1999 - Jul 2002	255/255 patients Median: 25 (1-184) weeks	Solid tumors: 20% Most tumors: hematological malignancies	Arm A (n=130): Warfarin 1 mg/day (72h after catheter insertion), median duration: 8 weeks Arm B (n=125): Placebo, median duration: 9 weeks	Not specified	Rate of symptomatic CRT	6/130 (4.6%)	5/125 (4.0%)	HR=1.20 95% CI: [0.37-3.94]
					Death	22/130 (17%)	21/125 (17%)	p=0.98
					Major bleeding	0/130 (0%)	3 /125 (2%)	p=0.07 95% CI: [-5.1-0.3]
[RUUD2006] Randomized controlled trial Jan 2002 - Oct 2003	73/62 patients 6 months	Children with cancer Catheter inserted in the jugular vein	Arm A (n=29): Warfarin 0.1 mg/kg started on the day of catheter insertion (1.3 < INR < 1.9) Arm B (n=33): no warfarin Frequency of INR in target range: 64%	Not specified	Asymptomatic CRT Doppler US performed at Months 1, 3, 6	Arm A: 14/29 (48%) (intent-to-treat analysis: 15/31; 48%) Arm B: 12/33 (36%) (intent-to-treat analysis: 17/42; 40%) p=0.44 (intent-to-treat analysis of the 73 patients: p=0.63)		
					Major bleeding	Arm A: 2 events Arm B: 0 events (p not specified)		
					Symptomatic events (CRT / PE)	Arm A: 1 patient / 0 patient Arm B: 1 patient / 0 patient (p not specified)		
[HEATON2002] Randomized controlled trial Not specified	102 CVC placed in 88 patients 88 first CVC in the 88 patients studied 90 days	Hematological malignancies Subclavian catheter Hickman + Groshong®	Arm A (45/51): Warfarin 1 mg/day started on the day of catheter insertion Arm B (43/51): No anticoagulation	Hickman: UFH 50 mg x2/day Groshong®: NaCl	Number of patients with CRT confirmed by phlebography	Thrombosis: 8/45 (17.8%) Vein Thrombosis: 2/45 (4.4%) Intra luminal catheter thrombus: 6/45 (13.3%)	Thrombosis: 5/43 (11.6%) Vein thrombosis: 1/43 (2.3%) Intraluminal catheter thrombus: 4/43 (9.3%)	p=0.42

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Table 31 Randomized studies: VKA in the prevention of catheter-related thrombosis (CRT) - (continued)

References Study design Inclusion period	Number of patients included/evaluated Follow-up	Features of included patients	Intervention	Catheter flushing	Endpoint	Arm A	Arm B	p value 95%CI
[YOUNG2009] Randomized controlled trial Not specified	1590/1570 patients Not specified	Solid or hematological tumors Age >16 years High frequency of colorectal tumor (52%) CVC Chemotherapy	A: warfarin 1 mg/day B: warfarin (INR 1.5 to 2) C: control (no warfarin) 812 assigned to uncertain warfarin benefit randomized to A or B or C 778 assigned to certain warfarin benefit randomized to A or B Analysis 1 Warfarin (408 patients: 322 in A + 84 in B) *vs*. no warfarin (404 patients) Analysis 2 Fixed dose A: 471 patients *vs*. adjusted dose B: 473 patients	Not specified	Symptomatic CRT radiologicaly confirmed	Any dose of warfarin: 24/404 (5.9%)	No warfarin: 24/408 (5.9%)	OR=0,99 95%CI: [0.57-1.72] p=0,98
						Fixed dose of warfarin: 34/471 (7.2%)	Adjusted dose of warfarin: 13/473 (2.7%)	OR=0.38 95%CI: [0.20-0.71] p=0.002
					Major bleeding	Any dose of warfarin: 7/408 (1.7%)	No warfarin: 1/404 (0.25%)	OR=6.93 95%CI: [0.86-56.00] p=0.07
						Fixed dose of warfarin: 7/471 (1.5%)	Adjusted dose of warfarin: 16/473 (3.4%)	OR=2,28 95%CI: [0.95-5.48] p=0.04

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Table 32 Randomized studies: heparins in the prevention of catheter-related thrombosis (CRT)

References Study design Inclusion period	Number of patients included/evaluated Follow-up	Features of included patients	Intervention	Catheter flushing	Endpoint	Arm A	Arm B	p value 95%CI
[ABDELKEFI2004] Randomized controlled trial May 2002 - Sep 2003	108/108 patients 128 CVC patients/128 17 months	Adults <60 years Children >4 years Bone marrow transplant	Arm A (patients: 55, CVC: 65): UFH (continuous IV perfusion 100 IU/kg/day), maximum: 10 000 IU/day) Arm B (patients: 53, CVC: 63): saline 50 mL/day	Catheter obstruction urokinase (2500 IU in 9.5 mL)	Symptomatic CRT+ asymptomatic CRT (Doppler US at catheter removal)	1/65 (1.5%)	8/63 (12.6%)	p=0.03
					Major bleeding	2/65 (3%)	3/63 (4.7%)	RR=0.95 95%CI: [0.06-14.6] p >0.05
[KARTHAUS2006] Randomized double-blind study Aug 1999 - Jun 2001	439/425 patients 16 weeks	Cancer Chemotherapy CVC inserted 5 to 7 days before randomization A/B: 2/1 Solid tumors: 271/125 Hematological tumors: 23/20	Arm A (294 included / 285 treated): dalteparin 5000 IU SC x1/day for 16 weeks Arm B (145 included / 140 treated) : placebo SC x1/day for 16 weeks	UFH 500 IU	Symptomatic CRT	11/285 (3.7%)	5/140 (3.4%)	RR=1.08; 95%CI: [0.37-3.19] p=0.88
					Asymptomatic CRT (phlebography or Doppler US for patients under 35 years)	11/285 (3.7%)	6/140 (4.1%)	OR=0.81 95%CI: [0.29-2.29] p >0.05
					Major bleeding Major and minor bleeding	1/285 (0.35%) 50/285 (17.5%)	1/140 (0.7%) 21/140 (15.0%)	RR=1.20 95%CI: [0.69-2.10] p=NS
[MISMETTI2003] Randomized controlled trial May 1998 - Mar 2000	59 /45 patients 6 months	Adults Solid tumors CVC	Arm A (29 included / 21 evaluated): nadroparin SC 2850 IU x1/day, started 2h before catheter insertion Arm B (30 included / 24 evaluated) : warfarin 1 mg/day, started 3 days before catheter insertion for 90±5 days or up to symptomatic CRT	Saline (10 mL) and heparinized saline (500 IU, 5 mL)	Asymptomatic and symptomatic CRT (venography) at 90 days	6/21 (28.6 %)	4/24 (16.7%)	p=0.48
					All VTE events at 6 months	8/22 (36.4%)	4/24 (16.7%)	p=0.13
					Major bleeding	1 patient	0 patient	p not specified
[MONREAL1996] Prospective open study Mar 1993 - Mar 1995	32/29 patients 90 days	Solid tumors CVC (Port-a-cath) platelet count >100 G/L no previous DVT	Arm A (n=16): dalteparin 2500 IU x1/day, started 2h before catheter insertion Arm B (n=13): no treatment For 90 days or up to symptomatic CRTconfirmed by phlebography	Heparinized saline (10 mL, once a week)	Asymptomatic CRT (venography)	1/16 (6.2%)	8/13 (61.5%)	RR=6.75 95%CI: [1.05-43.58] p=0.002
					Major bleeding	1 patient	0 patient	p not specified

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Table 32 Randomized studies: heparins in the prevention of catheter-related thrombosis (CRT) - (continued)

References Study design Inclusion period	Number of patients included/evaluated Follow-up	Features of included patients	Intervention	Catheter flushing	Endpoint	Arm A	Arm B	p value 95%CI
[VERSO2005] Randomized double-blind study Mar 2000 - Mar 2003	385/310 patients 3 months	Cancer CVC	Arm A (n=191 included / 155 evaluated): enoxaparin 40 mg SC x1/day started 2h before catheter insertion Arm B (n=194 included / 155 evaluated): placebo 6 weeks	Not specified	Composite of asymptomatic or symptomatic CRT (venography at Day 42) or symptomatic PE	22/155 (14.1 %)	28/155 (18.0 %)	RR=0,78 95%CI: [0.4-1.31] p=0.35
					Symptomatic catheter thrombosis	2/155 (1 %)	6/155 (3.1 %)	RR=0.32 95%CI: [0.07-1.66] p=NS
					Major bleeding	No event		p not specified
					Death	2 5/155 (2.6 %)	2/155 (1.0 %)	p not specified
[DECICCO2009] Randomized controlled trial Not specified	450/348 patients Not specified	Cancer CVC	Arm A (n=120 evaluated/150): Acenocoumarol 1 mg/day started 3 days before CVC insertion for 8 days Arm B (n=114 evaluated/150): Dalteparin 5000 IU/day, 2h before CVC insertion for 8 days Arm C (n=114 evaluated/150): observation 8 days	Not specified	Asymptomatic CRT (venography Days 2, 8, 30 and every 2 months)	A *vs*. C 25/120 (21.9 %)(A) *vs*. 60/114 (55.3 %) (C); OR=4.35; 95%CI: [2.43-7.69]; p<0.001 B *vs*. C 48/114 (40 %) (B) *vs*. 60/114 (55.3 %) (C), OR=1.85; 95%CI: [1.10-3.13]; p=0.02 A *vs*. B 25/120 (21.9%) *vs*. 48/114 (40%) OR=2.37; 95%CI: [1.34-4.22]; p=0.003		
					Major bleeding PE	no major bleeding no PE		
[NIERS2007] Randomized controlled trial Not specified	113/87 patients	Hematologic malignancies; CVC (chemotherapy and stem-cell transplantation)	Arm A: (41 evaluated/56) nadroparin (2850 IU/day) Arm B: (46 evaluated/57) placebo 3 weeks	Not specified	Asymptomatic CRT (venography Day 21)	7/41 (17%)	4/46 (9%)	p=0.49
					Major bleeding Minor bleeding	0 5/56 (9%)	0 2/57 (4%)	p not specified

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Table 33 Meta-analysis: anticoagulation (VKA, UFH, and LMWH) in the prevention of catheter-related thrombosis (CRT)

References	Bibliographic search Number of studies analyzed Period of study selection	Number of patients Treatment	Thrombosis	Bleeding	Other outcomes
[CARRIER2007]	Medline® (1950 - 2007) Embase® (1980 - 2007) CCTR (first semester 2007) 7 studies; 1950 - 2007	2131 patients VKA (warfarin 1 mg) or LMWH	Symptomatic CRT (defined as upper extremity DVT or CVC occlusion) VKA *vs*. control: RR=0.82; 95%CI: [0.46-1.47] LMWH *vs*. control: RR=0.473; 95%CI: [0.120-1.560] VKA or LMWH *vs*. control: RR=0.71; 95%CI: [0.42-1.20]	Major Bleeding VKA *vs*. control: 0 *vs*. 3 (2%) RR=0.14; 95%CI: [0.001-2.63] LMWH *vs*. control: RR=0.49; 95%CI: [0.03-7.83] Minor Bleeding VKA *vs*. control: RR=0.93; 95%CI: [0.31-2.77] LMWH *vs*. Control: RR=1.32; 95%CI: [0.87-2.02]	Mortality VKA *vs*. control RR=0.95; 95%CI: [0.62-1.46] LMWH *vs*. control RR=1.51; 95%CI: [0.49-4.70]
[RAWSON2007]	Medline® (1966 - 2007) Embase® (1988 - 2007) Cancerlit (1975 - 2007) Cinahl (1982 - 2007) ASCO abstracts (1999 - 2007) ASH abstracts (2001 - 2007) 4 studies 1966 - 2007	1236 patients Warfarin 1 mg or INR >1.5	Symptomatic or asymptomatic CRT VKA *vs*. control: 40/625 (6.4%) *vs*. 46/611 (7.5%) Risk difference: 5.0% ; 95%CI: [-9.0%-5.0%]; p=0.56		
[KIRKPATRICK2007]	Medline® (1964 - 2006) Embase® (2002 - 2005) ASCO, abstracts (1999 - 2006) ISTH, abstracts (2001 - 2005) 15 studies (10 studies on only cancer patients)	1714 patients VKA (fixed low dose) or LMWH	CRT (symptomatic or asymptomatic) VKA *vs*. control: 30/162 (18.5%) *vs*. 78/154 (50.6%) RR=0.37; 95%CI: [0.26-0.52]; p <0.001 LMWH *vs*. control: 93/617 (15.1%) *vs*. 113/447 (25.3%) RR=0.72; 95%CI: [0.57-0.90]; p=0.045 LMWH *vs*. VKA: 46/114 (40.4%) *vs*. 26/120 (21.7%) RR=1.88; 95%CI: [1.28-2.75] CRT (symptomatic) VKA *vs*. control: 12/217 (5.5%) *vs*. 19/208 (9.1%) RR=0.60; 95%CI: [0.30-1.20] LMWH *vs*. control: 12/500 (2.4%) *vs*. 11/352 (3.1%) RR=0.69; 95%CI: [0.30-1.59]	Major bleeding VKA *vs*. control: 0/175 (0%) *vs*. 3/168 (1.8%) RR=0.24; 95%CI: [0.03-2.13] LMWH *vs*. control: 1/529 (0.2%) *vs*. 1/368 (0.3%) RR=0.66; 95%CI: [0.12-3.68]	All-cause mortality VKA *vs*. control RR=0.95; 95%CI: [0.62-1.46] LMWH *vs*. control: RR=1.57; 95%CI: [0.54-4.58]

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Table 33 Meta-analysis: anticoagulation (VKA, UFH, and LMWH) in the prevention of catheter-related thrombosis (CRT) - (continued)

References	Bibliographic search Number of studies analyzed Period of study selection	Number of patients Treatment	Thrombosis	Bleeding	Other outcomes
[AKL2007]	Medline® (1966 - NS) Embase® (1980 - NS) ASCO abstracts (1982 - NS) ASH abstracts (2003 - NS) Nine studies	852 patients asymptomatic CRT 1859 patients symptomatic CRT VKA or heparin (UFH or LMWH)	Asymptomatic DVT VKA *vs.* control: RR=0.56; 95%CI: [0.10-2.99] LMWH *vs.* control: 30/465 (6.5%) *vs*. 31/313 (9.9%) RR=0.84; 95%CI: [0.52-1.36] Heparin *vs.* control: 0/38 (0%) *vs*. 1/36 (2.8%) RR=0.82; 95%CI: [0.51-1.32] VKA or heparin *vs.* control: 30/503 (6%) *vs*. 32/349 (9.2%) RR=0.82; 95%CI: [0.73-1.68] Symptomatic DVT VKA *vs.* control: 31/507 (6.1%) *vs*. 47/500 (9.4%) RR=0.62; 95%CI: [0.30-1.27] LMWH *vs.* control: 13/465 (2.8%) *vs*. 16/313 (5.1%) RR = 0.49; 95% CI [0.17-1.39] Heparin *vs.* control: 1/38 (2.6%) *vs*. 5/36 (13.9%) RR=0.43; 95%CI: [0.18-1.06] VKA or heparin *vs.* control: 45/1010 (4.5%) vs. 89/849 (10.5%) RR=0.56; 95%CI: [0.34-0.92]; p=0.02	Major bleeding Heparin *vs.* control: 2/323 (0.62%) *vs*. 2/176 (1.1%) RR=0.68; 95%CI: [0.10-4.78] VKA or heparin *vs.* control: 9/731 (1.2%) *vs*. 3/579 (0.52%) RR=1.83; 95%CI: [0.34-9.87]	Death LMWH *vs.* control: 18/492 (3.7%) *vs*. 22/347 (6.3%) RR=0.73; 95%CI: [0.39-1.36] Heparin *vs.* control: 1/38 (2.6%) *vs*. 1/36 (2.8%) RR=0.74; 95%CI: [0.40-1.36] VKA or heparin *vs.* control: 19/530 (3.6%) *vs*. 23/383 (6%) RR=0.74; 95%CI: [0.40-1.36]
[CHAUKIYAL2008]	Medline® (1966 - 2006) CCTR (June 2006) Eight studies	1428 patients VKA (warfarin 1 mg) or heparin (UFH or LMWH)	CRT (symptomatic or asymptomatic) VKA *vs.* control: 18/217 (8.3%) *vs*. 25/208 (12%) RR = 0.75 ; 95% CI: [0.24-2.35] ; p=0.63 Heparin *vs.* control: 34/520 (6.5%) *vs*. 49/366 (13.4%) RR=0.46; 95%CI: [0.18-1.20]; p=0.06 VKA or heparin *vs.* control: 52/737 (7.1%) *vs*. 74/574 (12.9%) RR=0.59; 95%CI: [0.31-1.13]; p=0.11 VKA *vs.* LMWH: 6/21 (28,6%) *vs*. 4/24 (16.7%) RR=1.71; 95%CI: [0.56-5.26]	Major bleeding VKA *vs*. control: 6/175 (3.4%) *vs*. 6/168 (3.6%) RR=0.14; 95%CI: [0.01-2.63] Heparin *vs*. control: 63/499 (12.6%) *vs*. 28/351 (8%) RR=0.41; 95%CI: [0.05-3.30] ; VKA or heparin *vs*. control: 69/674 (10.2%) *vs*. 34/519 (6.6%) RR=0.44; 95%CI: [0.12-1.67]	
[AKL2008]	Same results as [AKL2007] but study addressed only symptomatic CRT	Same results as [AKL2007] but study addressed only symptomatic CRT	Same results as [AKL2007], but study addressed only symptomatic CRT	Same results as [AKL2007], but study addressed only symptomatic CRT	Same results as [AKL2007], but study addressed only symptomatic CRT

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Table 34 Fibrinolytics in the prophylaxis of catheter-related thrombosis (CRT)

References Study design Inclusion period	Number of patients included/evaluated Follow-up	Features of included patients	Intervention	Catheter flushing	Endpoint	Arm A	Arm B	p value 95%CI
[KALMANTI2002] Non-randomized prospective study Mar 1998 - Dec 2000	30/26 patients 210 days (30-780)	Children Solid and hematologic tumors CVC	Arm A (15 patients/16 CVC): Urokinase 10,000 IU over 4h, x1/week Arm B (15 patients/19 CVC) control	Every 3 days or after each CVC use with Hep-Lock, 10 IU/mL	CRT (systematic Doppler US with venography or MRI if symptomatic)	7/15 (43%) 7 IJV	9/11 (81%) 5 distal tip of CVC 4 IJV	p=0.047
					Bleeding	No bleeding		p=NS
[VANROODEN2008] Randomized double-blind study Jan 1996 - Feb 1999	161/160 patients Not specified	Adult patients Intensive chemotherapy or BMT Tunneled CVC	Arm A: Urokinase 5 mL of 5000 IU/mL x3/week Arm B: Placebo 5 mL x3/week	Not specified	Primary: CVC-related infection	15/82 (18.3%)	19/78 (24.4%)	RR=0.75; 95%CI: [0.41-1.36]
					Secondary: 1. Infections not related to CVC 2. Premature CVC removal 3. Symptomatic CRT (Doppler US or venography)	1. 7/82 (8.5%) 2. 17/82 (20.7%) 3. 1/82 (1.2%)	1. 7/78 (9%) 2. 21/78 (26.9%) 3. 5/78 (6.4%)	p=NS RR=2.22 95%CI: [0.65-7.76] Not specified
					Bleeding	1 fatal bleed	0 bleed	p=NS

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Table 35 Influence of type, position and method of insertion of catheter in the primary prevention of CVC-associated thrombosis: non-randomized prospective trials and retrospective studies

References Study design Inclusion period	Number of patients included/evaluated Follow-up	Features of included patients	Intervention	Endpoint	Results
[NIGHTINGALE1997] Non-randomized prospective study 1993 -1994	949/832 patients Not specified	Gastrointestinal cancer Tunneled CVC in: - right subclavian vein (727) - left subclavian vein (81) - right femoral vein (2) - jugular vein (1)	Warfarin (1 mg/day) Flushing: heparinized saline	1. Thrombotic complications leading to CVC removal 2. Predictive factor for CVC removal (multivariate analysis)	1. 4.7% (38/817); p=NS If distal CVC tip in SVC: 3.5% (20/569) If distal CVC tip in right atrium: 2.5%, (4/160), 2. CVC in SVC: HR=2.57; 95%CI: [1.29-5.11]
[LUCIANI2001] Non-randomized prospective study 1995 - 1998	145 patientsts/not specified 113 CVC/not specified >3 years	Oropharyngeal tract cancer Totally implantable CVC	Flushing: saline (10 mL), then heparinized saline (5 mL at 50 UI/mL)	Asymptomatic or symptomatic CVC-associated DVT (Doppler US)	11.7% (17/145), 76% asymptomatic 1. Distal CVC tip location SVC or junction SVC-right atrium: 6% (5/87) Above junction SVC-right atrium: 46% (12/26); p <0.001 2. Left-sided CVC: 65% (11/17) Right-sided CVC: 35% (6/17), p=NS
[LABOUREY2004] Non-randomized prospective study One year but not specified	246 patients/not specified 249 CVC/not specified 332 days (1-725)	Solid tumors CVC not specified	Flushing: 3-5 mL heparinized saline (100 UI/mL) after insertion Occlusion: urokinase (5000 to 10000 units)	Catheter occlusion Catheter-related thrombosis	1. Catheter occlusion: CVC >T4: 4/5 (80%) *vs*. CVC <T4: 9/244 (3.6%); p <0.001 2. CRT as mediastinal and/or cervical mass: >6 cm: 5/12 (41%) *vs*. <6 cm: 6/237 (2.5%); p <0.001
[LEE2006] Non-randomized prospective study 2002 - 2003	444 patients/not specified 555 CVC/not specified CVC removal + 4 weeks or up to 52 weeks after CVC insertion	Solid tumors (66%) Hematologic malignancies (34%) All types of CVC in the upper limb vasculature	Flushing: - Implanted ports: heparinized saline (100 U/mL), - Other CVC: saline	Predictive factors for symptomatic CVC-associated DVT (Doppler US, venography, contrast-computed tomography, or MRI) by multivariate analysis	1. >1 insertion attempts: OR=5.5; 95%CI: [1.2-24.6]; p=0.03 2. Previous CVC insertion: OR=3.8;95%CI: [1.4-10.4]; p=0.01 3. CVC blockage: OR=14.7; 95%CI: [5.5-40]; p <0.001
[EASTRIDGE1995] Non-randomized retrospective study 1989 - 1992	274 patients/not specified 332 CVC/not specified Not specified	Solid tumors (51%) Hematologic malignancies (49%) Tunneled CVC (65%) Implantable CVC (35%)	Flushing: heparinized saline (3 mL/day at 100 UI/mL)	Predictive factors for symptomatic CVC-associated DVT (venography or clinical follow-up)	1. Position of CVC tip and CRT: >T3 CRT: 78% *vs.* <T3 CRT: 37%; p<0.05 2. Triple-lumen CVC CRT: 21% (10/48) *vs*. Double-lumen CVC CRT: 7% (11/160); p<0.05 3. Implantable CVC CRT: 6% (7/113) *vs*. Tunneled CVC CRT; 10% (21/209); p=NS
[CRAFT1996] Non-randomized retrospective study Not specified	122/120 patients 153/150 CVC 55 days (1-650)	Solid tumors (48%) Hematologic malignancies (41%) Tunneled CVC (Hickman®)	Flushing: heparinized saline	CVC-associated DVT Predictive factors for symptomatic CVC-associated DVT (venography)	8% (12/150) 1. Position of CVC tip: - Junction SVC-right atrium or lower third of SVC CRT: 6/73 (8.2%) - Upper third of SVC CRT 3/40 (7.5%); RR=0.9; 95%CI: [0.2-3.4]; p=NS 2. Side of CVC: Right-sided: CRT 4/92 (5%) *vs*. Left-sided: CRT 4/21 (19%) RR=4.4; 95%CI: [1.2-16]; p=0.04

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Table 35 Influence of type, position and method of insertion of catheter in the primary prevention of CVC-associated thrombosis: non-randomized prospective trials and retrospective studies (continued)

References Study design Inclusion period	Number of patients included/evaluated Follow-up	Features of included patients	Intervention	Endpoint	Results
[CADMAN2004] Randomly sampled retrospective study 1996 - 2001	334 patients/not specified 448 CVC/not specified 72 (1-720) days	Solid tumors (69%) Hematologic malignancies (31%) Tunneled CVC	Not specified	CVC-associated DVT Predictive factors for symptomatic CVC-associated DVT (venography, Doppler US)	9% (30/334) 1. Position of CVC tip: - Right atrium: 0% - Lower third of SVC: 2.6% - Middle third of SVC: 5.3% - Upper third of SVC: 41.7%; p <0.005 2. Side of CVC placement: - Right-sided: 6.8% - Left-sided: 25.6%; p <0.001
[CAERS2005] Non-randomized Retrospective study 1993 - 1998	437 patients/not specified 448 CVC/not specified	Solid tumors (84%) Hematologic malignancies (13%)	Flushing: saline (10 mL), then heparinized saline (5 mL at 100 UI/mL)	Predictive factors for symptomatic CVC-associated DVT (venography, Doppler US) (multivariate analysis)	8.5% (37/437) CVC tip *vs*. right atrium or inferior vena cava: Brachiocephalic vein: OR=64.7; 95%CI: [7.6-553.8] Cranial part of the SVC: OR=17.4; 95%CI: [2.0-148.8]
[MORAZIN2005] Non-randomized prospective study 1995 - 1999	5447 CVC/not specified Up to CVC removal	Solid tumors (50% breast cancer) Tunneled CVC (silicone)	Not specified	CVC-associated DVT Predictive factors for symptomatic CVC-associated DVT (venography, Doppler US, contrast computed tomography) (multivariate analysis)	2.5% (135/5447) 1. Left subclavian vein + jugular vein *vs*. right subclavian vein: RR=2.6; 95% CI not provided; p <0.001 2. Femoral vein *vs*. right subclavian vein: RR=6.5; p <0.001 3. Placement duration >25 min *vs*. ≤25 min: RR=1.52; p=0.02
[MCLEAN2005] Retrospective analysis of 2 phase III studies Jun 1992 - Nov 1999	374/362 patients 362/308 CVC	Children + ALL Internal CVC: 245 External CVC: 63	Chemotherapy induction for ALL Not specified for CVC	Predictive factors for CRT, CVC removal and CVC infection (multivariate analysis)	External *vs*. internal CVC: 1. Infection: OR=3.1; 95%CI: [1.3-7.5]; p=0.01 2. Thrombosis: OR=3.9; 95%CI: [1.5-10.3]; p=0.006 3. Removal: OR=5.6; 95%CI: [2.7-11.6]; p=0.001

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Table 36 Influence of type, position and method of insertion of catheter in the primary prevention of CVC-associated thrombosis: meta-analysis and prospective randomized trials

References Study design Inclusion period	Number of patients included / evaluated Follow-up	Features of included patients	Intervention	Endpoint	Results
[SABER2010] Meta-analysis of individual patient-level data 1995 - 2008	5636 patients included, but variable number of patients evaluated for each risk factor Mean: 133 days	Adult patients with cancer and CVC enrolled in randomized controlled trials	Not specified for each included study	Multivariate logistic regression analysis of risk factors of CRT during catheter insertion	Type of catheter: PICC (reference): OR=1 External CVC: OR=0.60; 95%CI: [0.33-1.10]; p=0.1 Implanted port OR=0.43; 95%CI: [0.23-0.80]; p=0.008 Insertion site: Upper arm vein (reference): OR=1 Subclavian veins: OR=2.16; 95%CI: [1.07-4.34]; p=0.029 Internal jugular vein OR=1.56; 95%CI: [0.71-3.40]; p=0.26 Catheter tip location, RA-SVC junction or RA Yes (reference): OR=1 No: OR=1.92; 95%CI: [1.22-3.02]; p=0.004
[BIFFI2001] Prospective randomized study Jul 1997 - Sep 1998	304/302 patients 237 days	Solid tumors Chemotherapy Implantable ports	Arm A: port with silastic 8.0-F and Groshong catheters Arm B: port with "open-ended" silastic 9.6-F catheter Flushing: saline (20 mL), then heparinized saline (5 mL at 50 UI/mL)	1. CRT (Doppler US at Months 1 and 4 confirmed by phlebography) 2. Catheter removal 3. Bleeding	1. CRT: p=NS Arm A: 6/152 (3.9%); 95%CI: [1.4-8.4] (symptomatic: 3) Arm B: 11/150 (7.3%); 95%CI: [3.7-12.7] (symptomatic: 3) 2. Removal: p=NS Arm A: 4/152 (2.7%); 95%CI: [0.7-6.6] Arm B: 16/150 (3.3 %); 95%CI [1.1-7.6] 3. Bleeding Arm A = Arm B = 0
[CARLO2004] Prospective randomized study Not specified	73/73 patients 180 days or up to CVC removal	Solid tumors Implantable ports	Arm A: valved implantable port + flushing with saline Arm B: non-valved implantable port with "open ended" tip + flushing with heparinized saline	Port-site cellulitis Catheter sepsis Catheter leakage CRT (diagnosis method not specified)	Cellulitis: Arm A: 2/37 (7.4%) *vs*. Arm B: 0/36; CVC sepsis: Arm A: 1/37 (2.7%) *vs*. Arm B: 1/36 (2.8%); p=NS CVC leakage: Arm A: 0/37 *vs*. Arm B: 1/36 (2.8%) CRT: Arm A: 1/37 (2.7%) *vs*. Arm B: 1/36 (2.8%)
[BIFFI2009] Prospective randomized study Jul 2003 - Dec 2006	403/360 patients 360 days	Adult patients Solid tumors >1 Chemotherapy 6F polyurethane catheter tubing (Bard Port)	Arm A: surgical insertion *via* the cephalic vein Arm B: percutaneous access to jugular vein without US guidance Arm C: percutaneous access to subclavian vein with US guidance	1. Early complications: pneumothorax or primary wrong position 2. Late complications: infections, wrong position, CRT (Doppler US at months 1 and 4) No real definition for each complication studied	1. Early complications Arm A = Arm B = Arm C = 0 2. Late complications: p=NS Infection: Arm A: 2/133, Arm B: 1/136, Arm C: 1/132 Wrong position: Arm A: 6/133, Arm B: 0/136, Arm C: 0/132 CRT: Arm A: 11/133 (9.2%), Arm B: 8/136 (6.5%), Arm C: 15/132 (12.8%); p=NS 21/34 symptomatic CRT (61.8%)

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