

Arterial complications, venous thromboembolism and deep venous thrombosis prophylaxis after anterior cruciate ligament reconstruction: A systematic review

Rob Paulus Augustinus Janssen, Max Reijman, Daan Martijn Janssen, Jan Bernardus Antonius van Mourik

Rob Paulus Augustinus Janssen, Max Reijman, Daan Martijn Janssen, Jan Bernardus Antonius van Mourik, Department of Sports Medicine and Orthopaedic Surgery, Máxima Medical Center, 5600PD, Eindhoven, The Netherlands

Rob Paulus Augustinus Janssen, Max Reijman, Daan Martijn Janssen, Jan Bernardus Antonius van Mourik, Department of Orthopaedics and Trauma, Máxima Medical Center, 5500 Veldhoven, The Netherlands

Max Reijman, Department of Orthopaedic Surgery Erasmus MC, University Medical Center Rotterdam, 3100 Rotterdam, The Netherlands

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Correspondence to: Rob Paulus Augustinus Janssen, MD, PhD, Department of Sports Medicine and Orthopaedic Surgery, Máxima Medical Center, Postbus 90052, 5600PD, Eindhoven, The Netherlands. r.janssen@mmc.nl
 Telephone: +31-40-8885936
 Fax: +31-40-8885938

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Abstract

AIM

To summarize the current knowledge on vascular complications and deep venous thrombosis (DVT) prophylaxis after anterior cruciate ligament (ACL) reconstruction.

METHODS

A systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement. MEDLINE, EMBASE, Cochrane, Web of Science, CINAHL, PubMed publisher, and Google scholar medical literature databases were searched up to November 10, 2015. Any arthroscopic surgical method of primary or revision intra-articular ACL reconstruction of all graft types in humans was included. A risk of bias assessment was determined.

RESULTS

Forty-seven studies were included in the review. Pseudaneurysms were the most frequently reported arterial complication after ACL reconstruction, irrespective of graft type or method of graft fixation with an incidence of 0.3%. The time to diagnosis of arterial complications after ACL reconstruction varied from days to mostly weeks but even years. After ACL reconstruction without thromboprophylaxis, the incidence of DVT was 9.7%, of which 2.1% was symptomatic. The incidence of pulmonary embolism was 0.1%. Tourniquet time

> 2 h was related to venous thromboembolism. Thromboprophylaxis is indicated in patients with risk factors for venous thromboembolism.

CONCLUSION

After ACL reconstruction, the incidence of arterial complications, symptomatic DVT and pulmonary embolism was 0.3%, 2.1% and 0.1% respectively. Arterial complications may occur with all types of arthroscopic ACL reconstruction, methods of graft fixation as well as any type of graft. Patients considered to be at moderate or high risk of venous thromboembolism should routinely receive thromboprophylaxis after ACL reconstruction.

Key words: Anterior cruciate ligament reconstruction; Arterial complication; Pseudoaneurysm; Venous thromboembolism; Pulmonary embolism; Thromboprophylaxis

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Core tip: Vascular complications after anterior cruciate ligament (ACL) reconstruction of the knee may present serious morbidity and even mortality. Although rare, it is necessary to understand the main risks and symptoms of these devastating lesions. This systematic review presents the current knowledge on arterial injuries, venous thromboembolism and thromboprophylaxis after ACL reconstruction.

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INTRODUCTION

Vascular complications after anterior cruciate ligament (ACL) reconstructions cause serious morbidity and potential mortality^[1]. They can be categorized in arterial and venous thromboembolic complications. The incidence of arterial complications after ACL reconstruction is unknown^[1]. Case reports have been published using various techniques of ACL reconstruction^[1].

Venous thromboembolism (VTE) after ACL reconstruction may present clinically as symptomatic or asymptomatic deep venous thrombosis (DVT), pulmonary embolism (PE) and postthrombotic syndrome^[1-3]. The incidence of VTE after ACL reconstruction varies from 0.2%-14%^[1,2,4-11]. The variable incidence of VTE after ACL reconstruction depends on the diagnostic methods of DVT (clinical parameters, venography, ultrasound or magnetic resonance venography), the heterogeneity of patient demographics (age, risk factors, surgical time, concomitant surgery, tourniquet time and

postoperative mobilisation) and DVT prophylaxis^[1,12]. Deep venous thrombosis may cause pulmonary embolism which may be fatal in its immediate course or may result in pulmonary hypertension in the long term^[1,13]. The postthrombotic syndrome may cause serious morbidity and affects 23% of limbs 2 years after DVT, 35%-69% and 49%-100% at 3 and at 5-10 years respectively^[1,4,14]. ACL reconstruction ranks number 6 of most performed orthopedic operations^[15]. However uniform evidence-based clinical practice guidelines for DVT prophylaxis after ACL reconstruction are lacking^[1,2,16].

A thorough understanding of the incidence, risk factors and potential methods for prevention of vascular complications after ACL reconstruction is critical to optimize patient safety^[17]. This systematic review presents the current knowledge of arterial complications, VTE and thromboprophylaxis after arthroscopic ACL reconstruction. The review will highlight the incidence, types and risk factors of arterial complications and VTE after ACL reconstruction as well as the current recommendations for DVT prophylaxis.

MATERIALS AND METHODS

The reporting in this systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement^[18].

Eligibility criteria

Inclusion criteria were all study designs evaluating arterial complications and VTE after ACL reconstruction. Any arthroscopic surgical method of primary or revision intra-articular ACL reconstruction of all graft types was included. Only human *in vivo* studies were eligible for inclusion in the systematic review. The full inclusion and exclusion criteria are presented in Table 1.

Electronic search

MEDLINE, EMBASE, Cochrane, Web of Science, CINAHL, PubMed publisher, and Google scholar medical literature databases were searched up to November 10, 2015. Search terms included synonyms for anterior cruciate ligament reconstruction, and synonyms for vascular complications. Additionally, the reference lists of all eligible studies were manually screened.

Study selection

All eligible articles were screened by title and abstract by 2 teams of reviewers. One author screened all abstracts and 2 co-authors scored both half of the abstracts independently of the first author. After this first inclusion, the full-text articles were assessed. Disagreements on inclusions were resolved by discussion and, if necessary, a final decision was made by a fourth reviewer. Furthermore, all references of both excluded and included articles were analyzed for eligible articles. The consequences of the search strategy (screening

Table 1 Inclusion and exclusion criteria

<p>Inclusion criteria</p> <p>Studies (randomized, non-randomized, case series, prospective or retrospective design, case reports) evaluating vascular and thromboembolic complications after ACL reconstruction</p> <p>All types of ACL reconstruction surgery related arterial and venous complications</p> <p>All types of ACL reconstruction surgery related thromboembolic complications</p> <p>Any arthroscopic surgical method of primary or revision intra-articular ACL reconstruction</p> <p>All graft types for ACL reconstruction</p> <p>Multiligament reconstructions including ACL</p> <p>Combined ACL reconstruction and meniscal surgery</p> <p>Human <i>in vivo</i> studies with reported outcome</p> <p>English language</p> <p>Full text available</p> <p>Exclusion criteria</p> <p>Animal studies</p> <p>Cadaveric studies</p> <p>Nonsurgical related vascular or thromboembolic complications</p>

ACL: Anterior cruciate ligament.

of title and abstract) are that only those studies will be eligible for inclusion if arterial complications, VTE or DVT prophylaxis after ACL reconstruction are reported in the abstracts. Studies that did not report these findings in their abstract were consequently not included in the current review.

Data collection process

Two reviewers extracted the study characteristics, type of vascular complications, and if available the incidence of vascular complications in the study population.

Data items

The data included study type, patient demographics, type and incidence of vascular or thromboembolic complication (arterial, pulmonary embolism, symptomatic or asymptomatic DVT), surgical technique, graft type, graft fixation method, thromboprophylaxis, tourniquet time and pressure and comorbidity for vascular and thromboembolic complications.

Synthesis of results

Incidence of DVT (separated for all and symptomatic) and PE was pooled of the studies reporting data of isolated ACL reconstruction without thromboprophylaxis. Additionally, the incidence numbers of those studies with low risk of bias on the items patient selection and classification were pooled.

Assessment of risk of bias

Risk of bias was assessed in the studies used for the determination of the incidence of vascular and/or venous complications following an ACL reconstruction procedure. Risk of bias was not assessed for case reports. Two reviewers independently assessed the risk of bias of the studies. In case of disagreement, the

two reviewers tried to achieve consensus. If consensus was not achieved, a third reviewer was asked for final judgment. Those items of the checklist of the Dutch Cochrane Centre of risk of bias of studies reporting the incidence of adverse events, suitable for the current study objectives, were used for the risk of bias assessment^[19]. All items could be rated "positive" (+), "negative" (-) or "not clear" (?).

Studies were classified as low risk of selection bias when they scored "positive" on the item: "The authors reported inclusion of 'all' or 'consecutive' patients". Studies were classified as low risk of information bias when they scored "positive" on the items: "Follow-up period was minimally 1 year" and "if all included patients were evaluated for complications".

Research questions

The following research questions were formulated.

Arterial complications: (1) What is the incidence of arterial complications after ACL reconstruction? (2) What types of arterial complications occur after ACL reconstruction? (3) Is there a correlation between arterial complications and fixation methods for ACL reconstruction? (4) What is the time to diagnosis of arterial complications after ACL reconstruction?

Venous complications: (1) What is the incidence of VTE after ACL reconstruction without thromboprophylaxis? (2) Is tourniquet time related to VTE after ACL reconstruction? (3) Is thromboprophylaxis indicated after ACL reconstruction?

RESULTS

Study selection

The PRISMA flow chart of the systematic review is presented in Figure 1. A total of 47 studies were included: 2 randomized controlled trials (RCT)^[20,21], 8 prospective cohort studies^[5,6,10,11,22-25], 9 retrospective cohort studies^[2,4,7,8,26-30] and 28 case reports^[13,31-57].

Risk of bias assessment

The results of the risk of bias assessment for the included studies are presented in Table 2. Case reports were not eligible for risk of bias assessment.

Details of arterial complications and thromboprophylaxis

The results of the arterial complications are specified in Table 3. The details of VTE and thromboprophylaxis are detailed in Table 4. Table 5 presents the incidence of DVT and PE after pooling the data for isolated ACL reconstructions without thromboprophylaxis.

Results of individual studies and answers to research questions

Arterial complications: (1) What is the incidence of arterial complications after ACL reconstruction?

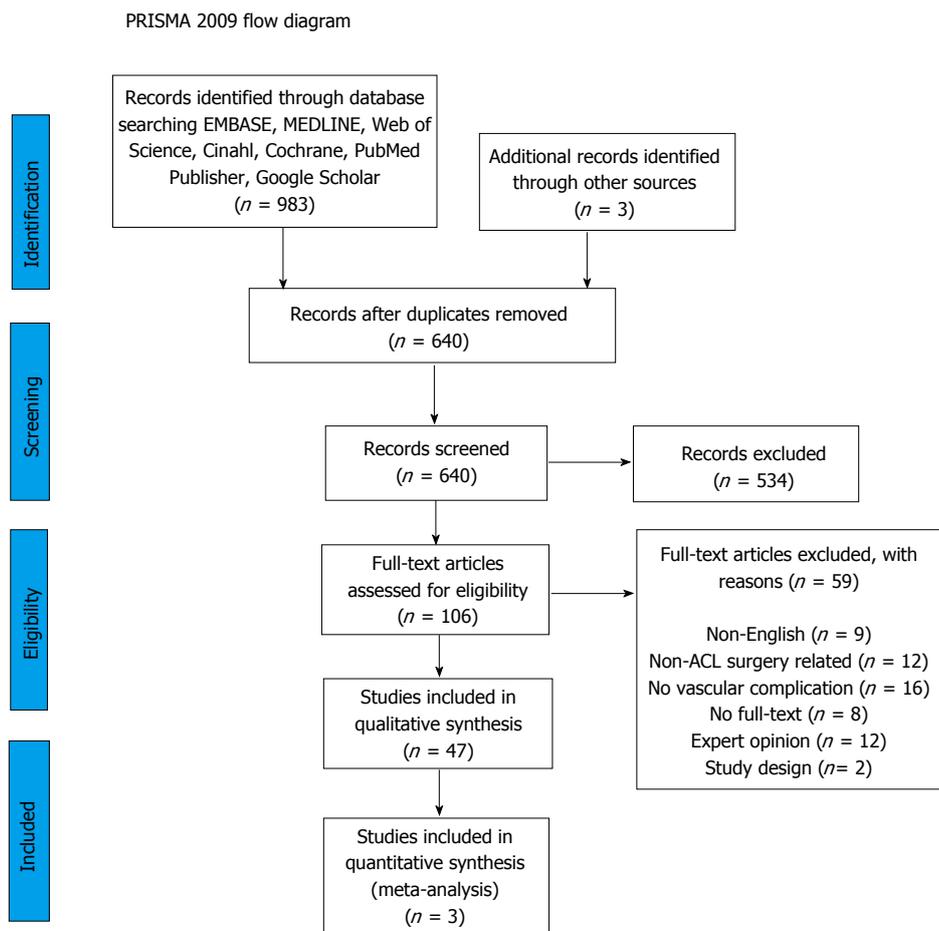


Figure 1 Prisma flow chart. ACL: Anterior cruciate ligament.

Table 2 Risk of bias of studies reporting venous complications

Ref.	Study design	Patient selection ¹	Follow-up ²	Classification ³
Adala <i>et al</i> ^[6]	PC	+	-	+
Born <i>et al</i> ^[26]	RS	+	-	-
Cullison <i>et al</i> ^[10]	PC	?	-	+
Dong <i>et al</i> ^[8]	RS	?	-	+
Ettema <i>et al</i> ^[27]	RS	-	?	-
Gaskill <i>et al</i> ^[2]	RS	+	-	-
Hetsroni <i>et al</i> ^[30]	RS	?	?	-
Hirota <i>et al</i> ^[22]	PC	-	-	+
Hirota <i>et al</i> ^[25]	PC	-	-	+
Jameson <i>et al</i> ^[28]	RS	?	-	-
Jaureguito <i>et al</i> ^[7]	RS	+	-	+
Lind <i>et al</i> ^[23]	PC	+	?	-
Maletis <i>et al</i> ^[11]	PC	?	?	-
Marlovits <i>et al</i> ^[20]	RCT	-	-	+
Mohtadi <i>et al</i> ^[21]	RCT	+	+	-
Struijk-Mulder <i>et al</i> ^[5]	PC	+	-	+
Sun <i>et al</i> ^[29]	RS	+	-	+
Williams <i>et al</i> ^[24]	PC	-	-	+
Ye <i>et al</i> ^[4]	RS	?	-	+

¹Inclusion of consecutive patients; ²Was follow-up period adequate (minimum 1 year) for exposure of adverse event? ³Was the used classification shown to be valid and reliable? +: Yes; -: No; ?: Not clear; RCT: Randomized controlled trial; PC: Prospective cohort study; RS: Retrospective study.

Twenty-two studies reported arterial complications after ACL reconstruction. These papers described a total of 23 case reports. Arterial complications after ACL reconstruction are rare. The incidence of arterial lesions after ACL reconstruction is only described in 1 study. Janssen *et al*^[45] have analysed their consecutive series retrospectively and found an incidence of 0.3% for arterial pseudoaneurysm in a series of 299 arthroscopic ACL reconstructions.

The incidence of arterial complications after ACL reconstruction is very low. The incidence of 0.3% presented in a retrospective series may be overestimated considering the fact that only case reports have been published in the literature. Long-term studies are necessary for analysis of the incidence of arterial complications after ACL reconstruction.

(2) What types of arterial complications occur after ACL reconstruction? Table 3 presents the details of the 23 published arterial complications after ACL reconstruction. The described complications were arterial-occlusions, avulsions, penetrating injuries, arteriovenous fistulae or pseudoaneurysms. Pseudoaneurysm was the most frequently reported arterial complication (13 cases). Various arteries around the knee were injured: Popliteal artery, posterior tibial

Table 3 Results arterial injuries (case reports)

Ref.	ACLR	Graft type	Fixation femur	Fixation tibia	Vascular injury	Diagnosis after ACLR	Treatment	Cause vascular complication
Spalding <i>et al</i> ^[31]	Primary	Gore-Tex	?	?	Compression popliteal artery	8 yr	Cyst removal	Compression by cyst containing ruptured Gore-tex graft
Aldridge <i>et al</i> ^[32]	Primary	BPTB	Interference screw	Interference screw	Avulsion middle gen. artery	4 wk	Direct repair avulsion	Lesion artery by shaver
Evans <i>et al</i> ^[33]	Primary	BPTB	Interference screw	Interference screw	Pseudoaneurysm med. inf. gen. artery	5 wk	Ligation pseudoaneurysm	Elevation periosteum medial tibia (tunnel preparation)
Friederich <i>et al</i> ^[34]	Primary	BPTB	Staples	Staples	Lesion sup. lat. gen. artery	5 mo	Removal staples	Hardware femur
Kanko <i>et al</i> ^[35]	Primary	BPTB	Interference screw	Bicortical screw	Pseudoaneurysm popliteal artery	2 yr	Ligation pseudoaneurysm	Drill bit for bicortical tibia fixation?
Keçeci <i>et al</i> ^[36]	Primary	BPTB	Interference screw	Interference screw	Popliteal arteriovenous fistula	18 mo	Venous re-anastomosis	Break-out posterior femoral cortex
Lamo-Espinosa <i>et al</i> ^[37]	Primary	BPTB	Interference screw	Interference screw	Lesion lat. inf. gen. artery	1 d	Embolization	Simultaneous lateral meniscectomy
Mello <i>et al</i> ^[38]	Primary	BPTB	Interference screw	Interference screw	Pseudoaneurysm med. inf. gen. artery	6 wk	Embolization	Direct lesion artery by shaver
Pereira <i>et al</i> ^[39]	Primary	BPTB	Interference screw	Interference screw	Pseudoaneurysm sup. lat. gen. artery	11 d	Ligation pseudoaneurysm	Hardware femur
Roth <i>et al</i> ^[40]	Primary	BTPB + augmentation	Staple	?	Occlusion popliteal artery	6 wk	Venous bypass	Entrapment between graft and femur
Tam Kelvin <i>et al</i> ^[41]	Primary	BPTB	Endobutton	Interference screw	Pseudoaneurysm popliteal artery	8 d	Repair by venous graft	Direct trauma by guide pin femoral canal
Lee <i>et al</i> ^[42]	Rerevision	?	Rigidfix cross pin	?	2 lesions sup. to level of med. and lat. gen. artery	6 wk	Venous re-anastomosis	Drill tip for Rigidfix cross pin
Ambrosia <i>et al</i> ^[57]	Primary	Hamstring	TightRope	Interference screw	Pseudoaneurysm popliteal artery	7 wk	Venous bypass	Hamstring harvest/previous catheterization-angioplasty?
Buda <i>et al</i> ^[43]	Primary	Hamstring ACL + allograft PCL	Staples	Staples	Pseudoaneurysm post. tibial artery	1 wk	Embolization	Surgical approach PCL or hamstring harvest?
Galanakis <i>et al</i> ^[44]	Primary	Hamstring + extra-artic. rec.	Staples	Pes anserinus	Pseudoaneurysm popliteal artery	Day of surgery	Venous re-anastomosis	Lesion artery by shaver and popliteal entrapment syndrome
Janssen <i>et al</i> ^[45]	Primary	Hamstring	Bone Mulch Screw	WasherLoc	Pseudoaneurysm popliteal artery	12 d	Venous repair	Drill tip for bicortical tibial fixation
Janssen <i>et al</i> ^[47]	Primary	Hamstring	Bone Mulch Screw	WasherLoc	Subtotal occlusion popliteal artery	19 d	Embolectomy	Preexistent intimal lesion after knee dislocation
Janssen <i>et al</i> ^[47]	Primary	Hamstring	Bone Mulch Screw	WasherLoc	Pseudoaneurysm and occlusion popliteal artery	9 d	Venous re-anastomosis	Drill tip for bicortical tibial fixation
Milankov <i>et al</i> ^[48]	Primary	Hamstring	Interference screw	Interference screw	Pseudoaneurysm med. inf. gen. artery	1 d	Ligation pseudoaneurysm	Hamstring harvest?
Panigrahi <i>et al</i> ^[56]	Primary	Hamstring ACL + PCL	?	?	Occlusion popliteal artery	Day of surgery	Embolectomy	Preexistent thrombotic occlusion after knee dislocation
Tsubosaka <i>et al</i> ^[54]	Primary	Hamstring	Cortical buttons	Screw post	Pseudoaneurysm med. inf. gen. artery	2 d	Embolization	Anteromedial portal
Pereira <i>et al</i> ^[39]	Revision	Hamstring	Transverse screw	Interference screw	Pseudoaneurysm sup. lat. gen. artery	2 d	Ligation pseudoaneurysm	Hardware femur
Carr <i>et al</i> ^[49]	Primary	Achilles tendon allograft	Interference screw	Suture+ washer bone plug	Traumatic arteriovenous fistula	7 wk	Ligation fistula	Injury at medial superior portal site

ACL: Anterior cruciate ligament; ACLR: ACL reconstruction; BPTB: Bone-patellar tendon-bone; PCL: Posterior cruciate ligament.

Table 4 Data venous thromboembolism and thromboprophylaxis

Ref.	Study design	Number ACLR	Mean age (yr)	Male (M) Female (F)	Graft type	Mean duration surgery (min)	Mean tourniquet time (min)	BMI (kg/m ²)	Thromboprophylaxis	Hospital stay (d)
Marlovits <i>et al</i> ^[20]	RCT	140 (87 vs 88 placebo)	29.9 ± 7.4 vs 30.2 ± 6.9	M 63% F 60%	BTPB	Mean > 120	?	Comparable between groups	Yes (enoxaparin 3-8 d + 20 d enoxaparin vs enoxaparin 3-8 d + placebo)	3-8
Mohtadi <i>et al</i> ^[21]	RCT	330	28.5 (14-50)	M 183 F 147	BPTB, hamstring	?	?	?	?	?
Adala <i>et al</i> ^[6]	PC	112	31.6	M 61 F 51	Hamstring	64.9 ± 7.8	?	?	None	2
Cullison <i>et al</i> ^[10]	PC	67	26.5 (19-39)	All men	BPTB	?	83 (0-115)	?	None	?
Hirota <i>et al</i> ^[25]	PC	30	24.1 ± 8.3	M 14 F 16	?	?	?	?	None	?
Hirota <i>et al</i> ^[22]	PC	40 (20 ACLR vs 20 TKA)	26.7 ± 13.4 vs 71.3 ± 6.8	M:F ACLR 10:10 vs TKA 6:14	?		87.1 ± 24.4 vs 87.2 ± 18.4	?	None	?
Lind <i>et al</i> ^[23]	PC	5818	?	M approximately 57%	BPTB and hamstring	Prim. ACLR 69.4 ± 21.1; rev. ACLR 90.0 ± 32.3	?	?	18.5% (prim. ACLR 15.7%; rev. ACLR 20.8%)	?
Maletis <i>et al</i> ^[11]	PC	Prim. ACLR 15101	Prim. ACLR 29.5 ± 11.5	M 9604 F 5497	Autograft 57.6%, allografts 42.4%	?	?	≥ 30 = 23.3%	?	?
		Rev. ACLR 1091	Rev. ACLR 29.8 ± 10.7	M 693 F 398	Autograft 20.9%, allografts 78.8%	?	?	≥ 30 = 20.8%	?	?
Struijk-Mulder <i>et al</i> ^[5]	PC	100	30.0 ± 10.0	M 77 F 23	Autograft HS 84, BPTB 14 allograft 2	68.0 ± 22.0	76.0 ± 23.0	25.0 ± 4.0	None	1 to 2
Williams <i>et al</i> ^[24]	PC	23	31 (19-42)	M 17 F 6	BPTB	?	103 (89-136)	?	None	2-3
Born <i>et al</i> ^[26]	RC	136 ACLR + multiligament rec.	VTE group 42 (24-43); Non-VTE group 31 (SD 11)	DVT group M: F 3:0; Non-VTE group 103:28	?	VTE group 152.0; Non-VTE group 233 ± 76	VIE group 78.0; Non-VIE group 102 ± 54	VTE group 35 (28-42); Non-VTE group 30 (SD 7)	Yes (before 2007, 3 wk aspirin. After 2007, LMWH 3 wk)	?
Dong <i>et al</i> ^[8]	RC	152 ACLR	34.9	M 91 F 61	Hamstring/allograft	?	3 groups < 90, 90-120, > 120	22.6	None	?
Ettema <i>et al</i> ^[27]	RC	?	?	?	?	?	?	?	50% prescribed LMWH or coumarin during hospital stay; 5% for 1-2 wk; 2% for 3-4 wk and 35% for 6 wk	?
Gaskill <i>et al</i> ^[2]	RC	15767 ACLR + HTO/PCL non specified	28.9 (SD 7.6)	M 13794	?	?	?	27.8	?	?
Hetsroni <i>et al</i> ^[30]	RC	58863 ACLR, total 418323 arthroscopies	PE group 50.3 (15-79) vs non-PE group 45.5 (0-100)	F 2764 PE group 57.3% vs non-PE group 46.8%	?	?	?	(SD 4.0) ?	?	?
Jameson <i>et al</i> ^[28]	RC	13941	29.3 (8-83)	F 46.8% M 79.5%	?	?	?	?	?	1-4

Jaureguito <i>et al</i> ^[7]	RC	131 group 1 (knee arthroscopy)	?	F 20.5% M 73	-	?	?	?	Aspirin (325 mg) daily for 3 wk postsurgery if age > 45 yr Idem	?
		108 group 2 (ACL, osteotomy)		F 58 M 60	?	?	?	?		?
Sun <i>et al</i> ^[29]	RC	231	23.6	F 48 M 69.3%	?	88.4	67.5	24.5	None	?
Ye <i>et al</i> ^[4]	RC	171	30.1 ± 10.0	F 30.7% M 123 F 48	Hamstring	86.9 ± 26.4	69.9 ± 15.9	24.4 ± 3.2	None	4
Ackerman <i>et al</i> ^[55]	CR	1	45	F 1	BPTB	?	0	?	Aspirin 325 mg daily none	Outpatient ?
Chien <i>et al</i> ^[50]	CR	1	34	M 1	?	110	?	30	LMWH during hospital stay	3
Janssen <i>et al</i> ^[13]	CR	1	19	F 1	Hamstring	96	110	27.5	None	?
Kang <i>et al</i> ^[51]	CR	1 (+MCL rec.)	48	F 1	Hamstring	?	90	?	None	?
Liu <i>et al</i> ^[52]	CR	1	34	M 1	Hamstring	110	119	30.1	None	5
Theron <i>et al</i> ^[53]	CR	1	30	F 1	?	?	?	?	?	Occurred day after surgery

ACL: ACL reconstruction; BPTB: Bone-patellar tendon-bone; TKA: Total knee arthroplasty; LMWH: Low molecular weight heparin; HTO: High tibial osteotomy; VTE: Venous thromboembolism; PCL: Posterior cruciate ligament; prim: Primary; MCL: Medial collateral ligament; rev: Revision; RCT: Randomized controlled trial; PC: Prospective cohort study; RS: Retrospective study; CR: Case report; SD: Standard deviation; DVT: Deep venous thrombosis; rec.: Reconstruction.

artery, medial and lateral inferior genicular arteries and lateral superior genicular artery. Clinical presentations were repeated hemarthrosis, pain and a pulsatile mass after ACL reconstruction.

The types of arterial complications after ACL reconstruction may be categorized in arterial- occlusions, avulsions, penetrating injuries, arteriovenous fistulae or pseudoaneurysms. Pseudoaneurysm is the most common arterial complication (13/23 cases).

(3) Is there a correlation between arterial complications and fixation methods for ACL reconstruction? Twenty-three case reports on arterial complications have been published using various techniques of ACL reconstruction, detailed in Table 3. There was no correlation between arterial complications and ACL reconstruction technique, methods of graft fixation or graft type. Eighteen studies reported that the vascular injury was caused by instruments during the ACL reconstruction (shaver, a drill bit for graft fixation, portal incision, previous catheterization and graft harvest). Pseudoaneurysm was the most frequently reported arterial complication after ACL reconstruction, irrespective of graft type or method of graft fixation. Four studies related their vascular complications to concurrent lateral meniscectomy, PCL reconstruction and preexistent intimal popliteal artery injury due to a previous knee dislocation.

No correlation was found between arterial complications and ACL reconstruction technique, methods of graft fixation or graft type.

(4) What is the time to diagnosis of arterial com-

plications after ACL reconstruction? Six studies reported a time to diagnosis of 0-2 d after ACL reconstruction (Table 3). All other studies showed a certain delay in diagnosis (1-7 wk postsurgery up to 8 years). Contrast-, CT- or MRI- angiographies are the diagnostic tools of choice^[46]. Remarkably, most case reports described palpable dorsalis pedis and posterior tibial arterial pulses at time of clinical presentation with swelling and pain around the popliteal area. These findings have misled surgeons to underestimate vascular complications after ACL reconstruction. Prolonged follow-up and a high level of suspicion, with clinical symptoms of painful pulsating mass and sensory deficits in lower leg and foot, is mandatory in detecting these potentially devastating lesions. An immediate surgical exploration is imperative in limiting neurological damage^[45]. Other than the Gore-Tex rupture ligament case^[31], all patients maintained adequate ACL stability after vascular surgery. The neurological deficits however may be permanent.

The time to diagnosis of arterial complications after ACL reconstruction varies from days to mostly weeks but even years.

Venous complications: (1) What is the incidence of venous thrombo-embolism after ACL reconstruction without thromboprophylaxis? The incidence of VTE after ACL reconstruction without thromboprophylaxis varied from 1.5%-17.9%^[1,58]. The variable incidence of VTE after ACL reconstruction depended on the diagnostic methods of DVT (clinical parameters, venography, ultrasound or magnetic resonance venography) and

Table 5 Incidence venous thromboembolism, risk factors and thromboprophylaxis recommendations

Ref.	Study design	Incidence DVT (symptomatic if specified)	Incidence PE (symptomatic if specified)	Detection method VTE	Risk factors DVT	Thromboprophylaxis recommendations
Marlovits <i>et al</i> ^[20]	RCT	2 = 2.8% with extended prophylaxis; 28 = 41.2% without extended prophylaxis	0%	MRI venography	Comparable between groups	Age > 30, prolonged immobilisation and complex procedures
Mohtadi <i>et al</i> ^[21]	RCT	1 (0.3%) symptomatic	1 (0.3%) symptomatic	Clinical, additional exam in suspected cases	None	-
Adala <i>et al</i> ^[6]	PC	2 = 1.78% (1 pt symptomatic)	0%	Ultrasound preop and day 2-3	None	None if absent high risk factors DVT or age < 45 yr
Cullison <i>et al</i> ^[10]	PC	1 = 1.5%	0%	Ultrasound preop, day 3 and 4 wk	None	None in male patients < 40 yr and absence of risk factors
Hirota <i>et al</i> ^[25]	PC	0%	Peak emboli 50s after tourniquet release	Transoesophageal echocardiography	?	-
Hirota <i>et al</i> ^[22]	PC	0%	0%	Transoesophageal echocardiography	?	-
Lind <i>et al</i> ^[23]	PC	?	?	?	?	-
Maletis <i>et al</i> ^[11]	PC	26 = 0.2% in primary ACLR	15 = < 0.1% in primary ACLR	Various methods	?	?
		2 = 0.2% in revision ACLR	0% in revision ACLR	Idem	?	?
Struijk-Mulder <i>et al</i> ^[5]	PC	9 = 9.0% (symptomatic 4 = 4.0%)	1 = 1%	Bilateral ultrasound	Age, contraceptive use	Further research for DVT prophylaxis, especially when risk factors are present
Williams <i>et al</i> ^[24]	PC	0%	0%	Bilateral ultrasound preop and 7-14 d postop	In 3 patients, non-specified	Future studies needed
Born <i>et al</i> ^[26]	RC	3 = 2.0% symptomatic	?	Clinical, ultrasound in suspected cases	Multiligamentous injury, age, history DVT	In multiligament reconstruction. cf guidelines ACCP "major orthopaedic surgery"
Dong <i>et al</i> ^[8]	RC	17 = 8.5% (44.1% nonsymptomatic of all DVT cases = 12.1% of all patients)	?	Color doppler ultrasound < 24 h after admission and 3 and 7 d postsurgery	Multiligament reconstruction, tourniquet time > 2 h, age	In case of PCL reconstruction and tourniquet time > 2 h
Ettema <i>et al</i> ^[27]	RC	?	?	?	?	None
Gaskill <i>et al</i> ^[2]	RC	55 symptomatic	35	Clinical, additional exam in suspected cases	Age ≥ 35, smoking, cocomitant HTO/ PCL surgery	Further research for VTE prophylaxis
Hetsroni <i>et al</i> ^[30]	RC	?	117 = 0.0003% all symptomatic	Clinical, additional exam in suspected cases	Female gender, age, surgical time, previous cancer	Further research for thromboprophylaxis in high risk patients
Jameson <i>et al</i> ^[28]	RC	42 = 0.3% all symptomatic	25 = 0.8% all symptomatic	Clinical, additional exam in suspected cases	Age > 40	No advise due to lack of evidence
Jaureguito <i>et al</i> ^[7]	RC	Retrospectively clinically 0.24%	0%	Duplex ultrasonography pre-operatively and 5 and 10 d postsurgery	None	-
Sun <i>et al</i> ^[29]	RC	Prospectively 7 (2.9%, 5 asymptomatic = 2.1%) total 36 = 15.6% (4 prox DVT = 2.4%. Distal DVT 32 = 13.9%)	0%	Venography day 3 postsurgery	Age, multiligament surgery	None
Ye <i>et al</i> ^[4]	RC	24 = 14.0% (4 pts prox. DVT)	0%	Chest X-ray and venography day 3 post ACLR	Female gender, age > 35 yr	In female patients and age > 35 yr
Ackerman <i>et al</i> ^[55]	CR	1 = 100%	0%	Clinical, ultrasound, CT and venography	May-Thurner Syndrome	In case of high risk patient
Chien <i>et al</i> ^[50]	CR	?	1 = 100%	Clinical, CT scan	BMI, ACL surgery	Further investigation for thromboprophylaxis after knee arthroscopy needed

Janssen <i>et al</i> ^[47]	CR	1 = 100%	1 = 100%	Clinical, transoesophageal echocardiography	Misdiagnosis DVT, Protein S deficiency? ACL surgery, contraceptive use	Further investigation for thromboprophylaxis after knee arthroscopy needed
Kang <i>et al</i> ^[51]	CR	1 = 100%	0%	Clinical, ultrasound	Primary thrombocytopenia, Factor VIII, Proteine C and S	None
Liu <i>et al</i> ^[52]	CR	1 = 100%	1 = 100%	Clinical, cardiac sonography	BMI	Patients with increased risk and prolonged tourniquet time
Theron <i>et al</i> ^[53]	CR	?	1 = 100%	Clinical, CT	Contraceptive use	None

ACL: ACL reconstruction; BPTB: Bone-patellar tendon-bone; TKA: Total knee arthroplasty; LMWH: Low molecular weight heparin; HTO: High tibial osteotomy; VTE: Venous thromboembolism; PCL: Posterior cruciate ligament; prim: Primary; RCT: Randomized controlled trial; PC: Prospective cohort study; RS: Retrospective study; CR: Case report; CT-scan: Computerized tomography-scan; BMI: Body mass index; DVT: Deep venous thrombosis; ACL: Anterior cruciate ligament; rec.: Reconstruction; pts: Patients; prox.: Proximal.

Table 6 Incidence of venous thromboembolism

Ref.	ACL (n)	Incidence DVT (n)	Incidence sympt DVT (n)	Incidence PE (n)	Thromboprophylaxis	Risk of bias
Adala <i>et al</i> ^[6]	112	2	1	0	No	Low
Cullison <i>et al</i> ^[10]	67	1		0	No	-
Dong <i>et al</i> ^[8]	152	11		NA	No	-
Jameson <i>et al</i> ^[28]	13941	42	42	25	NA	-
Maletis <i>et al</i> ^[11]	15101	26		15	NA	-
Marlovits <i>et al</i> ^[20]	140 (72 vs 68)	2 vs 28		0	Yes	-
Mohtadi <i>et al</i> ^[21]	330	1	1	1	NA	-
Struijk-Mulder <i>et al</i> ^[5]	100	9	4	1	No	Low
Sun <i>et al</i> ^[29]	231	36		0	No	Low
Williams <i>et al</i> ^[24]	23	0	0	0	No	-
Ye <i>et al</i> ^[4]	171	24		0	No	-

Pooled incidence: All DVT: 79/14093 = 9.7%; symptomatic DVT: 5/235 = 2.1%; all DVT of low risk bias studies: 47/443 = 10.6%; PE = 1/704 = 0.1%. ACL: Anterior cruciate ligament reconstruction; DVT: Deep venous thrombosis; sympt: Symptomatic; PE: Pulmonary embolism; NA: Not applicable.

the heterogeneity of patient demographics (age, risk factors, surgical time, concomitant surgery, tourniquet time and postoperative mobilisation). Eleven studies reported data of isolated ACL reconstruction without thromboprophylaxis (Table 5). The pooled total incidence of DVT was 9.7%, of which 2.1% was symptomatic. The pooled incidence of DVT in only low-risk bias studies was 10.6%. The pooled incidence of PE was 0.1% (Table 6).

After ACL reconstruction without thromboprophylaxis, the incidence of DVT is 9.7%, of which 2.1% is symptomatic. The incidence of PE is 0.1%.

(2) Is tourniquet time related to VTE after ACL reconstruction? Eight studies that were evaluated by risk of bias analysis documented tourniquet time in ACL reconstruction. This varied from 67.5 min to > 2 h. Deep venous thrombosis was more frequent with tourniquet time > 2 h. Extended tourniquet time was associated with combined ACL reconstruction and concomitant surgery. The incidence of DVT among patients with tourniquet lasting > 2 h increased from 12.1% to 17.4%^[1,58]. In these cases, thromboprophylaxis was recommended with > 2 h tourniquet time.

Tourniquet time > 2 h is related to VTE after ACL reconstruction.

(3) Is thromboprophylaxis indicated after ACL recon-

struction? Eight studies made recommendations for thromboprophylaxis after knee ligament surgery. No thromboprophylaxis was deemed necessary in case of isolated ACL reconstruction in patients without risk factors. Risk factors for VTE were those reported in the ACCP guidelines^[59], female gender, > 30 years of age, complex or concomitant surgical procedures, prolonged immobilization and tourniquet time > 2 h. Further research on thromboprophylaxis is recommended by most authors.

Thromboprophylaxis is indicated in patients considered to be at moderate or high risk of VTE^[20].

DISCUSSION

The most important finding of the present study is that after ACL reconstruction, the incidence of arterial complications, symptomatic DVT and PE was 0.3%, 2.1% and 0.1% respectively. The incidence of 0.3% of arterial complications may be overestimated considering the fact that only case reports have been published in the literature. However, the pooled incidence of DVT after ACL reconstruction without thromboprophylaxis was 9.7%, of which 2.1% of patients was symptomatic.

Pseudaneurysms were the most frequently re-

ported arterial complication after ACL reconstruction, irrespective of graft type or method of graft fixation. Pseudoaneurysms differ from true aneurysms in that they do not contain all the layers of an artery. They resemble organized hematomas that have internal arterial flow^[1]. A direct arterial trauma by a drill bit, shaver, hardware or fixation device for ACL reconstruction may cause a pseudoaneurysm. This condition usually presents with repeated hemarthrosis and a pulsatile mass within days to weeks after ACL reconstruction. Their growth may lead to neuropraxia and DVT due to compression of nerves and nearby veins, respectively^[1]. Patients with poor collateral development may have severe ischemia and poor prognosis, even leading to amputation^[1,35,38].

Krupp *et al.*^[60] analysed the safety of femoral cross-pin in ACL reconstruction. They concluded that insertion angle, not tunnel drilling method, influenced saphenous nerve and femoral artery/vein injury at risk^[60]. Post *et al.*^[61] studied the relative position of the neurovascular structures at risk when drilling bicortical screws for tibial fixation in ACL reconstruction^[45]. Arthroscopic tibial tunnels were made in cadaver human knees using lateral X-rays for accurate positioning. A 4.5 mm bicortical drill hole was placed perpendicular to the tibial surface 1 cm distal to the tibial tunnel. The distances from the posterior tibial drill exit point to the nearby neurovascular structures were measured with a caliper. The closest structure to the exit point was the bifurcation of the popliteal artery/vein (11.4 ± 0.6 mm). The next closest was the anterior tibial vein (11.7 ± 1.6 mm). The closest any individual hole came to a neurovascular structure was 3.5 mm from the anterior tibial vein. They concluded that bicortical screw and spiked washer fixation of soft tissue ACL grafts appears to be relatively safe^[45,61]. Curran *et al.*^[58] performed an *in vitro* study comparing 2 techniques for ACL tibial fixation with a bicortical screw. They concluded that aiming the screw towards the fibula reduced the risk of vascular injury compared to screws drilled perpendicular to the cortex. Other possible recommendations to prevent neurovascular damage are the use of a drill bit stop for bicortical screws or a single cortex fixation on the tibia without compromising stability of fixation^[1]. The incidence of arterial complications in the present review (0.3%)^[45] was updated in a consecutive series of 1961 ACL reconstructions with hamstring autografts and bicortical tibia fixation by the same authors^[1]. The incidence was reduced from 0.3% to 0.15% after the safety measures were applied as suggested by Janssen *et al.*^[1] and Curran *et al.*^[58].

A high level of suspicion, with clinical symptoms of painful pulsating mass and sensory deficits in lower leg and foot, is mandatory in detecting these potentially devastating lesions. The differential diagnosis should include compartment syndrome and DVT^[47]. Doppler examination and intact dorsal pedal and posterior tibial pulses are unreliable in diagnosing arterial lesions after ACL reconstruction^[47]. Contrast-, CT- or MRI-angiographies are the diagnostic tools of choice^[45,46].

Surgical exploration and vascular repair (or ligation/embolization of the feeding vessel) remain standard management^[45,46]. An immediate surgical exploration is imperative in limiting neurological damage^[1,45,46].

A meta-analysis of DVT after knee arthroscopy without thromboprophylaxis found an overall DVT rate of 9.9% (3.1%-17.9%) when routine screening using ultrasound or contrast venography was used^[13]. Proximal DVT rate was 2.1% (0%-4.9%)^[13,62]. Proximal DVT may progress to PE, however the clinical significance of distal DVT remains questionable^[62-64]. Sun *et al.*^[29] found that the total incidence of VTE, diagnosed with venography on the third day after arthroscopic knee surgery, was 14.9%, of which only 3.7% were symptomatic. Delis *et al.*^[14] found 50% of the DVT patients to be completely asymptomatic. They also examined the history of DVT if treated (aspirin in calf DVT, heparin-warfarin in proximal DVT)^[13]. Following early diagnosis, total clot lysis was documented in 50% and partial clot lysis in the remaining 50%, within 118 d median follow-up. Segmental venous reflux developed in at least 75% of the legs sustaining thrombosis. A previous thrombosis or the presence of two or more risk factors for thromboembolism significantly increased the incidence of DVT. No symptoms or signs of PE were documented^[13,14].

The current review showed that after ACL reconstruction without thromboprophylaxis, the incidence of DVT was 9.7%, of which 2.1% was symptomatic. The incidence of PE was 0.1%. These findings are similar to the conclusions by Erickson *et al.*^[3]. They described an 8.4% rate of DVT after ACL reconstructions in patients without postoperative thromboprophylaxis (73% was asymptomatic), while the rate of symptomatic PE was 0.2%^[3]. Maletis *et al.*^[11] described symptomatic DVT in 0.2% of 16192 primary and revision ACL surgeries. However, the authors did not specify the use of thromboprophylaxis^[11]. Cullison *et al.*^[10] and Adala *et al.*^[6] found comparable rates of DVT of 1.5% and 1.8% respectively using prospective pre- and postoperative ultrasonography in patients without VTE risk factors. The authors recommended that thromboprophylaxis is not necessary in the absence of risk factors in patients younger than 45 years of age with early postoperative mobilization^[6]. In a study of 282 Chinese patients, the incidence of DVT was 12.1% after ACL reconstruction. Tourniquet time > 2 h and concomitant PCL reconstructions were risk factors for DVT^[8]. Ye *et al.*^[4] found that the incidence of DVT was 14%, diagnosed by unilateral venography on the third day after ACL reconstruction. Proximal DVT occurred in 16.7% of DVT patients. None of the DVT patients developed PE. The authors recommended thromboprophylaxis in female patients and patients older than 35 years^[4]. The described variable incidence of VTE after ACL reconstruction depends on the diagnostic methods of DVT (clinical parameters, venography, ultrasound or magnetic resonance venography) and the heterogeneity

of patient demographics (age, risk factors, surgical time, concomitant surgery, tourniquet time and postoperative immobilization).

The use of a tourniquet improves operative visualization during arthroscopic ACL reconstruction^[65,66]. Various authors reported that tourniquet time in excess of 90 min increased the rates of VTE^[8,17,30,67]. Smith *et al.*^[65] published a meta-analysis of tourniquet assisted arthroscopic knee surgery. There was no difference in complication rate if tourniquet time exceeded 60 min. Hirota *et al.*^[22,25] quantified pulmonary emboli after tourniquet release in patients during ACL reconstruction (extramedullary) vs total knee arthroplasty (intramedullary procedure)^[13]. They chose these two groups for having more than 60 min tourniquet time and detected pulmonary emboli in all patients after release of the tourniquet using transesophageal echocardiography with a peak at 30-40 s postrelease^[13]. The amount of emboli was defined as percentage of total emboli formed in relation to the right atrial area. This percentage returned to baseline levels 2 min after tourniquet release in the ACL group. They found a significant linear correlation between the amount of emboli and duration of tourniquet inflation in the ACL group. In comparison, the total knee arthroplasty group had a significant larger amount of emboli (4-5 fold) with no return to baseline levels during the assessment period. No patient in either group showed signs of PE^[13,22,25]. In a recent systematic review, Papalia *et al.*^[66] concluded that a tourniquet can be used safely, provided that the inflation pressure is not excessive and tourniquet time is less than 2 h.

Asymptomatic pulmonary emboli occur in all patients with ACL reconstructions after tourniquet release^[1,13]. Furthermore, PE may occur as a result of proximal DVT^[13,24,50,52]. Hetsroni *et al.*^[30] analysed 418323 arthroscopic knee procedures and found an incidence of 0.03% for symptomatic PE. Risk factors were female sex, age, history of cancer and prolonged operating time (> 90 min). In spite of improved prevention and treatment of PE, the mortality is still estimated to be 20%-30%^[68]. It is the third most common cardiovascular cause of death, with 2/3 of the death occurring within the first few hours as a result of severe hemodynamic and respiratory disturbances^[53,68,69]. Janssen *et al.*^[1,13] found an incidence of fatal PE of 0.05% in a consecutive series of 1961 arthroscopic ACL reconstructions^[1]. Risk factors were preexistent coagulopathy, oral contraceptive medication and delay in DVT diagnosis.

Thromboprophylaxis after ACL reconstruction remains controversial^[1,9,16,27,50,52,59,70,71]. Geerts *et al.*^[59] reviewed the evidence-based literature for thromboprophylaxis in knee arthroscopy and only recommend prophylaxis with Low Molecular Weight Heparin in patients with risk factors for VTE (Grade 2B level of evidence). Risk factors in their study were history of DVT, age \geq 40 years, surgical time > 60 min. and a complicated/prolonged procedure^[59]. Additional risk factors for VTE after ACL reconstruction in other studies on VTE were smoking, oral contraceptive use

or hormone replacement, BMI > 30 kg/m², chronic venous insufficiency, cancer and thrombophilic conditions^[1,12,14,30,52,59,64,72]. In a randomized controlled trial, Marlovits *et al.*^[20] concluded that extended duration of thromboprophylaxis with enoxaparin by an additional 20 d significantly reduced venographically detected DVT after ACL reconstruction without an increase in major bleeding compared to enoxaparin limited to in-hospital thromboprophylaxis for 3-8 d. The authors found a 41.2% incidence of DVT for discharged patients who had a placebo as postdischarge thromboprophylaxis in contrast to 2.8% in the thromboprophylaxis group. Risk factors for DVT were age over 30 years, prolonged immobilization and surgical time^[20]. It should be noted that their mean surgical time as a teaching hospital (> 2 h) as well as their hospital stay of 3-8 d do not reflect most current ACL surgery practices with early discharge and mobilization. A Cochrane systematic review on interventions for preventing VTE in adults undergoing knee arthroscopy reported that no strong evidence was found to conclude that thromboprophylaxis is effective to prevent VTE in people with unknown risk factors for thrombosis^[20,68,70]. This is confirmed by other recent studies on DVT prophylaxis after ACL reconstruction and knee arthroscopic procedures^[2,17,64]. It is now common practice in a surgical setting to use a risk-assessment model, such as the one developed by Capriani *et al.*^[20]. Patients considered to be at moderate or high risk of VTE should routinely receive thromboprophylaxis^[1]. However, recommendations for the best type and duration of prophylaxis after ACL reconstruction still need to be defined^[5]. In spite of the scientific effort to date, no recommendations for routine thromboprophylaxis in ACL reconstruction can be provided in the absence of risk factors for VTE^[1,13]. Further investigation is required to analyse actual incidence and severity of venous thromboembolism as well as the efficacy-to-bleeding tradeoff for routine thromboprophylaxis after ACL reconstruction in patients without risk factors for VTE^[1,13].

This systematic review has several limitations. In the search for the available knowledge on vascular complications, studies of various level of evidence were included. Another weakness of this review is the inclusion of studies with small population size. Both the quality and limited amount of studies for specific research questions may limit the level of evidence for this review. Although strict and adapted for various study types, the risk of bias assessment of the Cochrane Library and the classifications of "low", "questionable" and "high" risk of bias for the studies may limit the strength of evidence. One might argue that a "low" risk of bias RCT study is of higher level of evidence than a "low" risk of bias prospective cohort study. Another weakness of this study is that only articles in English were included. Additional relevant articles published in languages other than English could contribute to the level of evidence presented in this review.

The clinical relevance of this review is that patients

undergoing ACL reconstruction may be informed that vascular complications can occur with any type of reconstruction and that thromboprophylaxis should be prescribed in patients with risk factors for VTE.

After ACL reconstruction, the incidence of arterial complications, symptomatic DVT and PE was 0.3%, 2.1% and 0.1% respectively. Arterial complications may occur with all types of arthroscopic ACL reconstruction, methods of graft fixation as well as any type of graft. Patients considered to be at moderate or high risk of VTE should routinely receive thromboprophylaxis after ACL reconstruction.

COMMENTS

Background

A thorough understanding of the incidence, risk factors and potential methods for prevention of vascular complications after anterior cruciate ligament (ACL) reconstruction is critical to optimize patient safety. This systematic review presents the current knowledge of arterial complications, venous thromboembolism (VTE) and thromboprophylaxis after arthroscopic ACL reconstruction. The review highlights the incidence, types and risk factors of arterial complications and VTE after ACL reconstruction as well as the current recommendations for deep venous thrombosis prophylaxis.

Research frontiers

This systematic review is related to research on thromboprophylaxis after ACL reconstruction.

Innovations and breakthroughs

This review presents a systematic overview of the incidence and type of arterial complications after ACL reconstruction. Such an overview has not been presented previously. Furthermore, an overview of the incidence, risk factors and indications for thromboprophylaxis after ACL reconstruction are presented. There is a need for this current knowledge due to the controversy in this field of research. Suggestions for further research are presented in the study.

Applications

Clinical implications are presented for adequate diagnosis and treatment of vascular complications after ACL reconstruction. Risk factors and indications for thromboprophylaxis are discussed.

Terminology

All terminology is explained in the manuscript.

Peer-review

This is an interesting systematic review that aims to evaluate the arterial and venous complications, by analyzing the relevant studies.

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