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FOOT AND ANKLE (SG PAREKH, SECTION EDITOR)

Thrombembolic complications after total ankle replacement

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Abstract The literature addressing functional outcome and survivorship of prosthesis components is constantly growing. However, the data on thromboprophylaxis and thrombembolic complications in patients who underwent TAR are scarce. A total of 31 studies were included in the systemic literature review. The incidence of thrombembolic complications varied between 0.0 % and 9.8 %. Most commonly, low molecular weight heparin was used as thromboprophylaxis for 6 weeks postoperatively. The incidence of thrombembolic complications was comparable with that of symptomatic deep vein thrombosis in patients with total knee or hip replacement.

Keywords Total ankle replacement · Thromboprophylaxis · Thrombembolic complications · Thrombosis · Deep vein thrombosis · Pulmonary embolism

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Introduction

Total ankle replacement (TAR) is gaining acceptance as a viable treatment option in patients with end-stage ankle osteoarthritis [1•, 2, 3•]. In 2009, Saltzman et al. [4] published findings from a prospective controlled trial of the Scandinavian Total Ankle Replacement System (STAR) vs ankle fusion and reported TAR led to better functional outcome and similar postoperative pain relief compared with ankles that were fused. Several prosthesis designs are available on the market. While the STAR prosthesis is the only 3-component total ankle design with FDA approval in the United States [4–6], the most common ankle prostheses in Europe are 3-component designs [5, 7–9]. A recent review by Valderrabano et al. [10•] revealed no obvious differences in clinical outcomes between prosthesis types, yet biomechanical and kinematic studies show advantages of 3-component designs [11–14].

A review by Glazebrook et al. [15] provided a summary of TAR implant survival and complications in second or third generation ankle prostheses, and established a complication classification system. In total, 9 main complications were identified but thromboembolic complications were not among them. Thromboembolic complications are often mentioned as a possibility postoperatively [16–21], however, the exact incidence of postoperative thromboembolism is unknown. Furthermore, the use of thromboprophylaxis in patients who undergo TAR remains controversial [20, 22–25]. Conti and Wong [26] stated that thromboembolic prophylaxis should be at the surgeon's discretion. The same authors concluded that deep vein thrombosis is an uncommon complication after TAR, where careful surgical technique and standard deep vein thrombosis prophylaxis can help minimize the risk [16]. Gadgil et al. [27] performed an email-based survey of American and British foot and ankle surgeons. Only 19 % of surgeons routinely used thromboprophylaxis in both elective and trauma foot and ankle surgery. The most common indication

for use of thromboprophylaxis was postoperative immobilization and non-weight-bearing rehabilitation [27].

We performed a systematic literature review of relevant clinical studies targeting the following criteria: postoperative thromboembolic complications including deep vein thrombosis and/or pulmonary embolism, and the method and duration of thrombosis prophylaxis.

Systematic literature search

We reviewed the literature using PubMed, MEDLINE, Embase, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), ScienceDirect, and SpringerLink. All searches were unlimited, including publications in all languages and at all dates. All types of publications including prospective and retrospective studies, case reports, and review articles that explored the clinical outcome after primary and revision TAR were included. We also searched the electronic contents of several orthopedic and specifically foot and ankle journals including Foot and Ankle International, Journal of Bone and Joint Surgery (American Volume), Journal of Bone and Joint Surgery (British Volume, currently known as The Bone and Joint Journal), Clinical Orthopaedics and Related Research, Foot Ankle Clinics of North America, Journal of Foot and Ankle Surgery, and Orthopäde. We supplemented our search strategy by a manual search of the bibliographies of all identified studies. All online searches were done in duplicate.

We searched the databases for the following keywords: "total ankle replacement", "total ankle arthroplasty", "ankle replacement", "ankle arthroplasty", "ankle prosthesis". Secondary keywords used in the search strategy were: "thrombosis", "deep vein thrombosis", "pulmonary embolism", "thromboprophylaxis." The last search was performed on July 1, 2013.

Identification of relevant studies

Study eligibility was assessed independently and in duplicate, and the assessments were then crosschecked. The following data were identified as relevant and extracted for further review: method of thromboprophylaxis, duration of thromboprophylaxis, and documented postoperative thromboembolic complications.

All included studies have been described using following criteria: type of study (multi-center, single-center, case report), type of data collection (prospective, retrospective, retrospective review of prospectively collected data), level of evidence (assessment using the Journal of Bone and Joint Surgery ranking system) [28], patient cohort (number of patients who underwent TAR, number of replaced ankles), and ankle prosthesis type.

Included studies

In total, 30 clinical studies have been examined based on the inclusion criteria (Table 1). All studies were published between 1999 and 2013 with 13 (43.3 %) prospective (2 of them retrospective reviews of prospectively collected data) and 17 (56.7 %) retrospective studies. Two of the 30 studies (6.7 %) were case reports with 1 patient each. Only 1 study was multicenter in design. For the included articles, the levels of evidence ranged from II to V. There were 4 (13.3 %) level II studies, 24 (80.0 %) level IV studies, and 2 (6.7 %) kevel V studies (2 case reports).

Total ankle replacement

Disregarding the 2 case reports the number of total ankle arthroplasties varied between 10 and 722 (median 58 ankle arthroplasties) (Table 1). Eight different prosthesis designs were used: Scandinavian Total Ankle Replacement (STAR) [60] (10 studies, 32.3 %), HINTEGRA [34] (11 studies, 35.5 %), Ankle Evolutive System (AES) [61] (2 studies, 6.5 %), Agility [62] (2 studies, 6.5 %), Buechel-Pappas [63] (1 study, 3.2 %), INBONE [64] (1 study, 3.2 %), and Mobility [65] (1 study, 3.2 %). In 2 studies different prosthesis types (STAR/Buechel-Pappas prosthesis and STAR/Salto/INBONE prosthesis) were used. In 1 study custom made prosthesis components (based on the STAR) were used in a patient with traumatic loss of the talus. In most studies (26 studies, 83.9 %) a 3-component prosthesis design was used. In 23 studies (74.2 %) an intraoperative use of tourniquet was documented (Table 2). In 24 studies (77.4 %) postoperative rehabilitation was described in detail (Table 2). Most commonly full weight-bearing was allowed after surgery (12 studies, 38.7 %). In 5 studies (16.1 %) non-weight-bearing was chosen for postoperative rehabilitation. In 7 studies (22.6 %) both rehabilitation styles were used (first non-weight-bearing, then full or partial weight-bearing) in the first 6 week postoperative course. In total, 3 different types of immobilization were used: stable walker, cast, or posterior splint.

Thromboprophylaxis

In 23 of 31 studies (74.2 %) the method of thromboprophylaxis was described. In all but 2 studies low-molecular-weight heparin (LMWH) was used. In 1 study (case report with bilateral knee and ankle replacement) LMWH was used for the first 2 weeks, then oral medication with phenprocoumon was continued for 5 months. In another study oral medication with aspirin twice daily was used. In 18 of 31 studies (58.1 %) the duration of thromboprophylaxis was indicated, most commonly for 6 weeks (15 studies, 51.6 %).

Table 1 Included clinical studies reporting the postoperative incidence of deep-vein thrombosis and/or type of thromboprophylaxis in patients after total ankle replacement

Study	Type of study	LoE	Patients (ankles)	Prosthesis type	Thromboprophylaxis	DVT (n, %)	Localization of DVT
Bardelli & Scoccianti, 2006 [29]	RS, SC	IV	24 (24)	STAR (24)	LMWH, duration not known	0 (0.0 %)	-
Barg et al. 2010 [30]	PS, SC	II	69 (92)	HINTEGRA (92)	LMWH for 6 wk	0 (0.0 %)	-
Barg et al. 2011 [31]	PS, SC	IV	26* (52)	HINTEGRA (52)	LMWH for 6 wk	0 (0.0 %)	-
Barg et al. 2011 [32•]	PS, SC	II	665 (701)	HINTEGRA (701)	LMWH for 6 wk	26 (3.7 %)	peroneal (18), posterior tibial (2), peroneal & posterior tibial (2), popliteal (2), superficial femoral (1), posterior tibial and superficial femoral (1)
Barg et al. 2011 [33]	RS, SC	IV	118 (123)	HINTEGRA (123)	LMWH for 6 wk	12 (9.8 %)	peroneal (12)
Barg et al. 2012 [34]	PS, SC	IV	301 (311)	HINTEGRA (311)	LMWH for 6 wk	n.a.	-
Barg et al. 2013 [35]	PS, SC	IV	684 (722)	HINTEGRA (722)	LMWH for 6 wk	n.a.	-
Besse et al. 2009 [36]	PS, SC	IV	47 (50)	AES (50)	n.a.	1 (2.0 %)	popliteal (1)
Bleazey et al. 2013 [37]	RS, SC	IV	57 (58)	INBONE (58)	n.a.	2 (3.4 %)	n.a.
Clement et al. 2013 [38]	RS, SC	IV	26 (26)	STAR (14), Salto (11), INBONE (1)	Aspirin (325 mg) twice daily for 6 wk	0 (0.0 %)	-
Dhawan et al. 2012 [39]	RS, SC	IV	29 (30)	Buechel-Pappas (30)	LMWH for 6 wk	n.a.	-
Gallardo et al. 2012 [40]	PS, SC	II	30 (30)	HINTEGRA (30)	LMWH, duration not known	n.a.	-
Haskell & Mann, 2004 [41]	RS, MC	IV	187 (187)	STAR (187)	n.a.	2 (1.1 %)	n.a.
Hintermann, 1999 [42]	PS, SC	IV	47 (50)	STAR (50)	LMWH for 6 wk	0 (0.0 %)	n.a.
Hintermann & Valderrabano, 2001 [43]	RS, SC	IV	76 (79)	STAR (79)	LMWH for 6 wk	n.a.	-
Hintermann et al. 2006 [44]	PS, SC	IV	261 (271)	HINTEGRA (271)	LMWH for 6 wk	n.a.	-
Hobson et al. 2009 [45]	RS, SC	II	111 (123)	STAR (123)	n.a.	0 (0.0 %)	-
Karantana et al. 2010 [46]	RS, SC	IV	45 (52)	STAR (52)	n.a.	0 (0.0 %)	-
Karantana et al. 2010 [47]	RS, SC	IV	5* (10)	STAR (10)	LMWH, duration not known	0 (0.0 %)	-
Knecht et al. 2004 [48]	RS, SC	IV	126 (132)	Agility (132)	n.a.	1 (0.8 %)	localization not known, DVT with documented pulmonary embolism without any long-term sequelae
Kokkonen et al. 2011[49]	RS, SC	IV	37 (38)	AES (38)	LMWH, duration not known	n.a.	-
Kumar & Dhar, 2007 [50]	RS, SC	IV	43 (50)	STAR (50)	LMWH, duration not known	0 (0.0 %)	-
Lee et al. 2008 [51]	RS, SC	IV	50 (50)	HINTEGRA (50)	n.a.	0 (0.0 %)	-
Magnan et al. 2004 [52]	CR	V	1 (1)	Custom made	LMWH for 4 wk	0 (0.0 %)	-
Pagenstert & Hintermann, 2011 [53]	CR	V	2† (1)	HINTEGRA (2)	LMWH for 2 wk, Phenprocoumon for 5 m	0 (0.0 %)	-
Rippstein et al. 2011 [54]	PS, SC	IV	233 (240)	Mobility (240)	LMWH for 6 wk	3 (1.3 %)	n.a.
Rzesacz & Gossé, 2007 [55]	RS, SC	IV	13 (13)	STAR (13)	LMWH for 6 wk	0 (0.0 %)	-
Saltzman et al. 2010 [56]	RS, SC	IV	42 (42)	STAR (42)	n.a.	2 (4.8 %)	-

Table 1 (continued)

Study	Type of study	LoE	Patients (ankles)	Prosthesis type	Thromboprophylaxis	DVT (n, %)	Localization of DVT
Valderrabano & Hintermann, 2004 [57]	PS, SC	IV	119 (125)	HINTEGRA (125)	LMWH for 6 wk daily	n.a.	-
van der Heide et al. 2009 [58]	RS, SC	IV	54 (58)	Agility (58)	LMWH for 6 wk	n.a.	-
Vienne, 2005 [59]	RS, SC	IV	85 (85)	Agility (85)	LMWH for 6 wk	n.a.	-

*all patients underwent simultaneous bilateral total ankle replacement

† patient underwent simultaneous bilateral total ankle replacement and bilateral total knee replacement

AES Ankle evolutive system, *CR* case report, *DVT* deep vein thrombosis, *LMWH* low molecular weight heparin, *LoE* level of evidence, *M* months, *MC* multicenter, *n.a.* not available, *RS* retrospective, *SC* single-center, *STAR* Scandinavian Total Ankle Replacement, *Wk* weeks

Incidence of thrombembolic complications

In 12 of 31 studies (35.5 %) the incidence of thromboembolic complications was not specified. In 13 of 31 studies (41.9 %) no thromboembolic complications were observed (Table 1). In 7 of 31 studies (22.6 %) the incidence of thromboembolic complications varied between 0.8 % and 9.8 % (median 2.0 %). In most cases, symptomatic deep vein thrombosis was observed. Only 1 patient presented with deep vein thrombosis and pulmonary embolism. In 3 studies exact localization of deep vein thrombosis was described, most commonly found in distal veins of the lower extremity.

Authors' preferred treatment

In our clinic, all patients receive thromboprophylaxis with subcutaneous LMWH (Fragmin, 5000 IE or weight-adjusted, Pfizer AG, Zürich), starting 12 hours preoperatively and continuing daily for 6 weeks postoperatively. In the last 36 months an alternative oral application of rivaroxaban (Xarelto, 10 mg, Bayer AG, Zürich) has been used. Rivaroxaban has been shown to be superior to enoxaparin for thromboprophylaxis after total knee [66] and total hip replacement [67] with similar rates of bleeding. However, to date there is no literature addressing the efficacy and safety of rivaroxaban in patients who underwent foot and ankle surgery.

After surgery, a splint is used to keep the foot in a neutral position. When the wound is dry and no secretion is present, the foot is placed in a stabilizing walker or cast for 6 to 8 weeks. In patients with additional procedures (eg, fusion of adjacent joint or corrective osteotomies), the immobilization can be prolonged until osseous healing at the site of fusion and/or osteotomy is verified. Weight-bearing is allowed as tolerated with the exception of patients who underwent additional corrective osteotomies. Active and passive mobilization of the first metatarsophalangeal joint may increase venous blood flow of the lower extremity, which results in an anti-edema and thromboprophylactic effect [68].

In patients with suspicion of deep vein thrombosis, color duplex sonography is considered. This method is increasingly used as an alternative, noninvasive method for DVT diagnosis. The high sensitivity and specificity of both duplex compression ultrasonography and color-flow Doppler imaging has been shown previously [69, 70]. However, its efficacy as a screening tool in asymptomatic patients with proximal thrombi remains controversial [71]. Our sonography results are considered reliable since they are performed by experienced vascular radiologists [72]. The data on thromboprophylaxis and thrombembolic complications in patients who underwent TAR are scarce. To date, there is only 1 study specifically addressing the incidence of thrombembolic complications and risk factors for those in patients with TAR [32•].

Table 2 Included clinical studies reporting type postoperative mobilization and use of tourniquet in patients after total ankle replacement

Study	Postoperative Mobilization	Use of Tourniquet	DVT (n,%)
Bardelli & Scoccianti, 2006 [29]	Full weight-bearing in a cast for 6 wk	n.a.	0 (0.0 %)
Barg et al. 2010 [30]	Full weight-bearing in a stable walker for 6 wk	yes	0 (0.0 %)
Barg et al. 2011 [31]	Full weight-bearing in a stable walker for 6 wk	yes	0 (0.0 %)
Barg et al. 2011 [32]	Full weight-bearing in a cast or a stable walker for 6 wk (610 ankles), non-weight-bearing in a cast or a stable walker for 6 wk (91 ankles)	yes	26 (3.7 %)
Barg et al. 2012 [34]	Full or partial weight-bearing in a cast or a stable walker for 6 wk	yes	n.a.
Barg et al. 2013 [35]	Full or partial weight-bearing in a cast or a stable walker for 6 wk	yes	n.a.
Besse et al. 2009 [36]	Cast immobilization for 45 days in 92 % of cases, with a maximum of 75 days	n.a.	1 (2.0 %)
Bleazey et al. 2013 [37]	Non-weight-bearing in a posterior splint for 2 wk, then mobilization in a sneaker	yes	2 (3.4 %)
Dhawan et al. 2012 [39]	Non-weight-bearing in a cast for 6 wk	yes	n.a.
Gallardo et al. 2012 [40]	n.a.	yes	n.a.
Hintermann, 1999 [42]	Full weight-bearing in a cast or a walker for 6 wk	yes	0 (0.0 %)
Hintermann & Valderrabano, 2001 [43]	Full weight-bearing in a cast or a walker for 6 wk	n.a.	n.a.
Hintermann et al. 2006 [44]	Full weight-bearing in a cast or a walker for 6 wk	yes	n.a.
Hobson et al. 2009 [45]	Touch weight-bearing in a cast for 6 wk	n.a.	0 (0.0 %)
Karantana et al. 2010 [46]	Non-weight-bearing in a cast for 6 wk and fully weight-bearing in an Aircast walker for a further 6 wk	n.a.	0 (0.0 %)
Karantana et al. 2010 [47]	Full weight-bearing in a plaster walking cast for 2 wk, then below knee walking cast or Donjoy pneumatic walker for a further 4 wk	yes	0 (0.0 %)
Knecht et al. 2004 [48]	Non-weight-bearing in a posterior splint for 6 wk	yes	1 (0.8 %)
Kokkonen et al. 2011 [49]	Non-weight-bearing in a cast for 2 wk, partial weight-bearing in a cast for a further 2 wk, full weight-bearing in a cast for a further 2 wk	yes	n.a.
Kumar & Dhar, 2007 [50]	Full weight-bearing in a plaster cast for 6 wk	yes	0 (0.0 %)
Magnan et al. 2004 [52]	Non-weight-bearing for 1 week, full-weight-bearing in a below knee brace for a further 5 wk	n.a.	0 (0.0 %)
Pagenstert & Hintermann, 2011 [53]	Full weight-bearing in a cast for 8 wk	yes	0 (0.0 %)
Rippstein et al. 2011 [54]	Full weight-bearing in a removable walker for 6 wk	yes	3 (1.3 %)
Rzesacz & Gossé, 2007 [55]	Full weight-bearing in a walker for 6 wk	yes	0 (0.0 %)
Valderrabano & Hintermann, 2004 [57]	Full weight-bearing in a cast or a walker for 6 wk	yes	n.a.
van der Heide et al. 2009 [58]	Non-weight-bearing for 2 wk, full-weight-bearing in a cast for a further 2 wk	yes	n.a.
Vienne, 2005 [59]	Non-weight-bearing in a synthetic cast for 2 wk, 15 kg partial weight-bearing without cast for a further 4 wk	yes	n.a.

DVT deep vein thrombosis, *n.a.* not available

Conclusions

TAR is gaining increasing acceptance among orthopedic surgeons as a valuable treatment option in patients with end-stage ankle OA. The number of studies in the literature addressing outcomes after TAR is growing; however, many are only reporting functional outcomes or survivorship of prosthesis components.

In a previous study we identified the following statistically significant independent risk factors for symptomatic deep vein thrombosis: obesity, a previous venous thrombembolic event, and the absence of full postoperative weight-bearing [32•]. A previous venous thrombembolic event was the most important risk factor with the odds ratio of 7.07 (95 % confidence interval 2.99 to 16.73). Similar findings were observed in patients who underwent total knee or hip replacement [73, 74]. Another important risk factor for symptomatic deep vein thrombosis of the lower extremity in patients with TAR was obesity (BMI≥35 kg/m^2) with an odds ratio of 6.94 (95 % confidence interval 2.22 to 21.68). Obese patients who underwent total knee or hip replacement have also higher risk of thromboembolic complications [75–77]. Finally, postoperative non-weight-bearing was associated with an increased incidence of symptomatic deep vein thrombosis resulting in the odds ratio 4.53 (95 % confidence interval 1.86 to 11.00). In another clinical study of patients with Achilles tendon injury, prolonged immobilization in a cast without weight-bearing was also associated with increased incidence of thrombembolic complications [78]. Conversely, early mobilization after total knee replacement resulted in a 30-fold reduction in the risk of deep vein thrombosis [79]. Malignant tumor disease has been shown to be an important risk factor for development of deep vein thrombosis [80, 81]. However, we have not observed co-incidence between this comorbidity and increased incidence of thrombembolic complications. Other factors were not associated with increased incidence of deep vein thrombosis in our study: higher age (≥ 60 years), gender, preoperative American Society of Anesthesiologists classification, tobacco use, surgery duration (≥ 120 min), anesthesia method (spinal vs general), postoperative mobilization (stable walker vs cast), or additional surgical procedures (eg, arthrodesis of adjacent joints) [32•]. Furthermore, it has been shown that patients with bilateral ankle osteoarthritis can be safely treated as simultaneous bilateral procedures with the use of thromboprophylaxis [30, 31, 32•].

In our clinic all patients with TAR receive thromboprophylaxis with subcutaneous LMWH. In the literature the question of whether TAR patients need thromboprophylaxis or not remains unanswered. Jameson et al. [82] analyzed venous thrombembolic events following foot and ankle surgery in the English National Health Service between January 2005 and June 2008. In total, 1633 patients with TAR were included into this study. No deep vein thrombosis and only case of non-fatal pulmonary embolism (0.061 %) were observed [82]. However, in recent literature the incidence of thrombembolic complications should not be underestimated [23, 27]. Based on our experience we suggest thromboprophylaxis in patients who undergo TAR, especially those with the aforementioned risk factors.

Compliance with Ethics Guidelines

Conflict of Interest Alexej Barg declares that he has no conflict of interest. Katharina Barg declares that she has no conflict of interest. Stefan W. Schneider declares that he has no conflict of interest. Geert Pagenstert declares that he has no conflict of interest. Marcel Gloyer declares that he has no conflict of interest. Heath B. Henninger declares that he has no conflict of interest. Victor Valderrabano declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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