FOOT AND ANKLE

Risk factors for symptomatic deep-vein thrombosis in patients after total ankle replacement who received routine chemical thromboprophylaxis

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The aim of this study was to identify the incidence of post-operative symptomatic deep-vein thrombosis (DVT), as well as the risk factors for and location of DVT, in 665 patients (701 ankles) who underwent primary total ankle replacement. All patients received low-molecular-weight heparin prophylaxis. A total of 26 patients (3.9%, 26 ankles) had a symptomatic DVT, diagnosed by experienced radiologists using colour Doppler ultrasound. Most thrombi (22 patients, 84.6%) were localised distally in the operated limb. Using a logistic multiple regression model we identified obesity, a previous venous thromboembolic event and the absence of full post-operative weight-bearing as independent risk factors for developing a symptomatic DVT.

The incidence of symptomatic DVT after total ankle replacement and use of low-molecular-weight heparin is comparable with that in patients undergoing total knee or hip replacement.

Total ankle replacement (TAR) is increasingly being used as an alternative to arthrodesis in patients with osteoarthritis of the ankle.1-4 We have previously reported the results of patients having simultaneous bilateral TAR5 and in patients undergoing TAR along with hindfoot fusion.6 In this study we studied the incidence of symptomatic deep-vein thrombosis (DVT) following TAR.

Although DVT is discussed as a complication following TAR,7 there are few reports on its incidence after surgery of the foot and ankle, particularly TAR (Table I).4,10-18 Our aim was to determine the post-operative incidence and site of symptomatic DVTs, and to identify the risk factors for DVT in patients undergoing TAR.

Patients and Methods

Between May 2000 and March 2009, 665 consecutive patients (701 ankles: 378 (53.9%) right, 323 (46.1%) left) underwent primary TAR (Fig. 1). There were 343 men (362 ankles) and 322 women (339 ankles) with a mean age of 60.6 years (19.8 to 90.0; Table II). A total of 36 patients underwent a bilateral procedure, 23 undergoing simultaneous bilateral TAR.5 The internal review board of the University of Basel approved the protocol of the study and informed consent was obtained from all patients.

The HINTEGRA total ankle prosthesis (Newdeal SA, Lyon, France/Integra, Plainsboro, New Jersey) was used throughout. All patients were treated following the same operative technique19 and any additional procedures were performed under the same anaesthetic (Table III). An anterior longitudinal incision 10 cm to 12 cm long was made to expose the retinaculum. Dissection of the retinaculum and a capsulotomy was performed and osteophytes on the tibia and the talar neck were removed. The tibial cutting block was introduced with its alignment rod using the tibial tuberosity. The tibial cut was introduced using a reciprocating saw. Talar resection was done using the talar resection block. Trial implants were inserted and fluoroscopy was used to check the position of implants while the foot was held in neutral position. After insertion of final implants the stability and movement was verified. The splints and dressings were removed two days post-operatively and a below-knee splint was applied. Once the wound was dry and stable, typically three to four days post-operatively, a stable walker (VACOpod; OPED AG, Cham, Switzerland) or below-knee walking cast (3M Scotchcast Plus; 3M (Schweiz) AG, Rüschlikon, Switzerland) was used for six weeks in most cases, and eight weeks in some cases. Full weight-bearing was allowed as tolerated, except in patients who underwent simultaneous supramalleolar osteotomies or those with reduced bone quality. All patients received...
thromboprophylaxis with subcutaneous low-molecular-weight heparin (LMWH) (Fragmin, 5000 IU; Pfizer AG, Zürich, Switzerland), starting 12 hours pre-operatively and continuing daily for six weeks post-operatively.

All patients with clinical evidence of DVT formation were assessed by duplex colour Doppler ultrasonography (Phillips IU22, 8/4 linear array probe; Philips Ultrasound, Bothell, Washington) of the affected limb incorporating the Valsalva manoeuvre.20 The clinical criteria suggestive of DVT were pain and tenderness in the calf, swelling of the whole limb or of the calf by ≥2 cm more than the circumference of the asymptomatic side (measured 10 cm below the tibial tuberosity), or increasing oedema confined to the asymptomatic leg. The ultrasound was considered negative if there was normal blood flow in the femoral, popliteal, tibial and peroneal veins, with the vessel lumen fully compressible and completely filled with colour flow. A DVT was diagnosed if the vessel wall was not compressible. Two experienced radiologists were present for the examination and, if there was difficulty interpreting the ultrasound, venography was performed using standard techniques.21

**Statistical analysis.** This was performed using SPSS v.16.0 software (SPSS Inc., Chicago, Illinois) and Sigmaplot 2004 (Systat Software Inc., San Jose, California). A Kolmogorov-Smirnov test was performed to verify whether the data were normally distributed. Independent-samples t-tests were used for continuous variables and chi-squared tests for categorical data. A univariate Cox’s regression test was performed to identify factors associated with an increased incidence of DVT. These included age ≥60 years, gender, body mass index (BMI) ≥35 kg/m², American Society of Anesthesiologists classification (ASA),22 use of tobacco, previous venous thromboembolism (VTE), operative time ≥120 minutes, type of anaesthesia used, additional procedures (e.g., realignment osteotomies), bilateral simultaneous TAR and the post-operative mobilisation regime. The odds ratios (OR) and 95% confidence intervals (CI) were calculated. Factors associated with an increased incidence of DVT (significance at p ≤0.1) were considered for inclusion in a logistic multiple-regression model with stepwise forward and backward variable selection. Those statistically significant (p ≤0.05) factors that remained in the model were considered to be independent predictors of DVT. The calibration of the model was assessed by comparing the observed and expected risk outcome using a Hosmer-Lemeshow goodness-of-fit test.24

### Results

Of the 665 patients undergoing TAR, 26 (3.9%) developed symptomatic DVT at a mean of 15.2 days (5 to 37; Fig. 2). This involved 11 men and 15 women, with a mean age of 61.4 years (28.4 to 83.9; Table II). Isolated distal DVT was confirmed by Doppler ultrasound in 22 patients, of whom 18 had thrombi in the peroneal vein, two in the posterior tibial vein, and two in both. Three patients had thrombi localised proximally, two popliteal and one in the superficial femoral vein. In one case a mixed DVT was diagnosed where thrombi were seen in both the posterior tibial and the superficial femoral veins. Thus, a total of 26 patients (3.9%) had a symptomatic DVT. In all but two cases (both with thrombi in the peroneal vein) the DVT was in the operated limb. No DVT was observed in patients who underwent bilateral TAR. In three cases venography was performed to confirm the sonographic findings. In 26 other

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**Table I.** Studies reporting the post-operative incidence of deep-vein thrombosis (DVT) in patients after total ankle replacement (TAR)

<table>
<thead>
<tr>
<th>Study</th>
<th>Type†</th>
<th>TAR (n)</th>
<th>Thromboprophylaxis‡</th>
<th>Post-operative mobilisation</th>
<th>DVT (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barg et al (current study)</td>
<td>PS, SC</td>
<td>665</td>
<td>LMWH for six weeks</td>
<td>Stable walker/below-knee walking cast with/without full weight-bearing for six weeks</td>
<td>26 (3.9)</td>
</tr>
<tr>
<td>Besse et al10</td>
<td>PS, SC</td>
<td>50</td>
<td>Not specified</td>
<td>Cast immobilisation for 45 days (up to 75), no weight-bearing for three weeks</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Haskell and Mann11</td>
<td>RS, MC</td>
<td>187</td>
<td>Not specified</td>
<td>Non-weight-bearing in a boot until the wound had completely healed</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Hobson et al4</td>
<td>RS, SC</td>
<td>123</td>
<td>Not specified</td>
<td>Touch weight-bear in plaster for six weeks</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Karantana et al12</td>
<td>RS, SC</td>
<td>52</td>
<td>Not specified</td>
<td>Short-leg walking cast with non-weight-bearing for six weeks</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Karantana et al13</td>
<td>RS, SC</td>
<td>10↑</td>
<td>LMWH, duration not specified</td>
<td>Below-knee walking cast or walker for six weeks</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Knecht et al14</td>
<td>RS, SC</td>
<td>132</td>
<td>Not specified</td>
<td>Not specified</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Kumar and Dhar15</td>
<td>RS, SC</td>
<td>50</td>
<td>LMWH, duration not specified</td>
<td>Full weight-bearing in a plaster splint for six weeks</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Lee et al16</td>
<td>RS, SC</td>
<td>50</td>
<td>Not specified</td>
<td>Non-weight-bearing in a short leg splint for three weeks</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Saltzman et al17</td>
<td>RS, SC</td>
<td>37</td>
<td>Not specified</td>
<td>Not specified</td>
<td>2 (5.4)</td>
</tr>
<tr>
<td>van der Heide et al18</td>
<td>RS, SC</td>
<td>58</td>
<td>0.3 ml nadroparin subcutaneously for six weeks</td>
<td>Walking cast for six weeks, weight-bearing after two weeks</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

* PS, prospective; SC, single-centre; RS, retrospective; MS, multicentre
† LMWH, low-molecular-weight heparin
‡ ten TARs were performed as a simultaneous bilateral procedure in five patients
cases where ultrasonography was performed because of clinical suspicion, no DVT was detected. No patient had a pulmonary embolus.

There were no bleeding complications, although in three patients (0.5%) the platelet count fell below 100 000/mm³, all on the seventh post-operative day. The administration of LMWH was halted and their thrombocytopenia improved.

The factors found to be significantly associated with an increased incidence of symptomatic DVT after TAR were obesity (a BMI $\geq 35$ kg/m²), ASA classification $\geq 2$, use of tobacco, previous VTE, prolonged operative time and post-operative mobilisation (Table IV). The regression model showed that a BMI $\geq 35$ kg/m², previous VTE and post-operative immobilisation without full weight-bearing were independently associated with an increased risk of symptomatic DVT in patients with TAR (Table V). The Hosmer-Lemeshow test indicated that the overall model fit was good ($p = 0.553$).

**Discussion**

To our knowledge, this is the first study to specifically address the incidence of and post-operative risk factors for symptomatic DVT after TAR. Our incidence of symptomatic DVT was 3.9%, which is comparable to that of symptomatic VTE in patients undergoing total hip replacement (THR) or total knee replacement (TKR) who receive thromboprophylaxis with LMWH.24 The reported incidence of symptomatic DVT in patients undergoing TAR is generally less than in our study (Table I). However, most studies of TAR reported functional outcomes and component stability, and do not specifically address the incidence of post-operative symptomatic DVT. Furthermore, most cases of clinical VTE in patients with joint replacement occur after discharge.25 Therefore, studies that analysed only in-patient results may provide biased rates of VTE.

Our patients who developed symptomatic DVT presented at a median of 15 days post-operatively (Fig. 2), which is comparable with studies on THR or TKR. In our cohort, most thrombi were localised distally in the peroneal and tibial veins, similar to symptomatic DVT reported elsewhere.26

Asymptomatic patients were not screened for DVT, and it could be that those with classic risk factors for DVT, such as obesity, would be more likely to be scanned, thereby introducing possible bias. However, our decision to perform duplex sonography was based strictly on clinical criteria and not on demographic data or hypothesised risk factors for DVT. Whereas 20 of 26 patients with symptomatic DVT had at least one risk factor, only four of those 26 patients with negative ultrasonography had one risk factor, and none had more than one.

Colour duplex sonography is used increasingly as an alternative non-invasive method for the diagnosis of DVT. Although the high sensitivity and specificity of duplex compression ultrasonography and colour-flow Doppler imaging is recognised, its efficacy as a screening tool...
in asymptomatic patients with proximal thrombi remains controversial.\textsuperscript{29} Our results are considered reliable because they were performed by experienced vascular radiologists.\textsuperscript{30}

A number of classic risk factors for DVT have been identified.\textsuperscript{8,29,31} A previous VTE provided the highest OR in our study, and this is supported by other studies which have addressed DVT after TKR.\textsuperscript{32,33} Another powerful risk factor

\begin{table}[h]
\centering
\caption{Patient data, laboratory findings and surgical characteristics of 665 patients (701 ankles) who underwent total ankle replacement (TAR)}
\begin{tabular}{lcccc}
\hline
Parameter\textsuperscript{*} & All patients & DVT\textsuperscript{†} & No DVT & p-value\textsuperscript{‡} \\
\hline
Number of patients (ankles) & 665 (701) & 26 (26) & 639 (675) & - \\
Mean age (range) (yrs) & 60.6 (19.8 to 90) & 61.4 (28.4 to 83.9) & 60.5 (19.8 to 90) & 0.736\textsuperscript{§} \\
Gender male:female\textsuperscript{**} & 350:328 & 11:15 & 339:313 & 0.332 \\
Right:left (ankles) & 378:323 & 9:17 & 369:306 & 0.044 \\
Mean BMI (range) (kg/m\textsuperscript{2}) & 26.8 (15.2 to 40) & 31.6 (22.8 to 40) & 26.7 (15.2 to 39.5) & < 0.001\textsuperscript{§} \\
Aetiology of ankle osteoarthritis (%) & & & & \\
Post-traumatic & 570 (81.3) & 21 (80.8) & 549 (81.3) & 0.942 \\
Secondary\textsuperscript{¶} & 77 (11.0) & 3 (11.5) & 74 (11.0) & 0.927 \\
Primary & 54 (7.7) & 2 (7.7) & 52 (7.7) & 0.998 \\
ASA classification\textsuperscript{22} (%) & & & & \\
1 & 521 (76.8) & 16 (61.5) & 505 (72.4) & 0.062 \\
2 & 144 (21.2) & 7 (27.0) & 137 (21.1) & 0.483 \\
3 & 13 (2.0) & 3 (11.5) & 10 (1.5) & < 0.001 \\
4 & - & - & - & - \\
Tobacco use yes:no & 113:565 & 12:14 & 101:551 & < 0.001 \\
Previous VTE yes:no\textsuperscript{**} & 73:605 & 13:13 & 60:592 & < 0.001 \\
Mean APTT (range) (seconds) & 29 (22 to 36) & 29 (26 to 32) & 29 (22 to 36) & 0.812\textsuperscript{§} \\
Mean duration of surgery (range) (mins) & 78 (54 to 131) & 85 (54 to 128) & 78 (54 to 131) & 0.089\textsuperscript{§} \\
Anesthesia spinal:general\textsuperscript{**} & 446:232 & 17:9 & 429:223 & 0.965 \\
Additional surgical procedures yes:no & 201:500 & 10:16 & 191:484 & 0.261 \\
Bilateral simultaneous TAR yes:no & 46:665 & 0:26 & 46:629 & 0.168 \\
Post-operative mobilisation cast:brace & 340:361 & 17:9 & 323:352 & 0.079 \\
Post-operative mobilisation with full weight-bearing yes:no & 610:91 & 15:11 & 595:80 & < 0.001 \\
\hline
\end{tabular}
\textsuperscript{*} BMI, body mass index; ASA, American Society of Anesthesiologists; VTE, venous thromboembolism; APTT, activated partial thromboplastin time (normal range 26 s to 32 s) \\
\textsuperscript{†} DVT, deep-vein thrombosis \\
\textsuperscript{‡} chi-squared test, unless otherwise stated \\
\textsuperscript{§} unpaired samples t-test \\
\textsuperscript{¶} including rheumatoid arthritis, haemochromatosis, haemophilia, clubfoot, avascular talus necrosis, osteochondrosis dissecans and post-infection arthritis \\
\textsuperscript{**} out of a total of 678 procedures. A total of 23 patients had simultaneous bilateral procedures, counted here as a single operation
\end{table}

\begin{table}[h]
\centering
\caption{Additional procedures performed along with primary total ankle replacement}
\begin{tabular}{lc}
\hline
Additional procedure & Ankles \\
\hline
Osteotomies & \\
Supramalleolar osteotomy & 21 \\
Medial displacement calcaneal osteotomy & 22 \\
Dwyer calcaneal osteotomy & 2 \\
Z-shaped calcaneal osteotomy & 1 \\
Medial cuneiform osteotomy & 4 \\
Dorsiflexion first metatarsal osteotomy & 5 \\
Arthrodeses & \\
Double-hindfoot arthrodesis (subtalar and talonavicular arthrodesis) & 32 \\
Subtalar arthrodesis & 32 \\
Talonavicular arthrodesis & 16 \\
Ligament/tendon procedures & \\
Lateral ligament augmentation & 42 \\
Medial ligament augmentation & 8 \\
Peroneus longus transfer & 10 \\
Tendo Achillis lengthening & 75 \\
\hline
\end{tabular}
\end{table}
for DVT after TAR was a BMI $\geq 35$ kg/m$^2$, which is also the case in patients undergoing THR or TKR.

Patients who were not fully weight-bearing post-operatively have a higher risk for symptomatic DVT, as do patients with a cast and prolonged immobilisation after tendo Achillis injury. Conversely, early mobilisation after TKR resulted in a 30-fold reduction in the risk of DVT.

We believe that without full weight-bearing, muscular activity and venous blood flow are probably reduced, as shown with Doppler ultrasound.

Neither advanced age nor female gender was identified as a risk factor in our study. This is consistent with findings in studies of THR and TKR, although some reports have linked advanced age with an increased incidence of DVT after THR and TKR. Although smoking has been identified as a possible risk factor for DVT in univariate analysis, it has not been reported as an independent risk factor.

Anaesthetic technique is an important variable in the aetiology of post-operative DVT in elective orthopaedic surgery.

### Table IV. Univariate analysis of potential risk factors giving the odds ratio (OR) with 95% confidence intervals (CI) for the development of deep-vein thrombosis (DVT) after total ankle replacement (TAR)

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>DVT (%)</th>
<th>No DVT (%)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\geq 60$ years (393 patients)</td>
<td>16 (4.1)</td>
<td>377 (95.9)</td>
<td>1.06 (0.78 to 1.45)</td>
<td>0.707</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>328 patients</td>
<td>15 (4.6)</td>
<td>313 (95.4)</td>
<td>1.20 (0.86 to 1.69)</td>
<td>0.332</td>
</tr>
<tr>
<td>Obesity: BMI $\geq 35$ kg/m$^2$ (29 patients)</td>
<td>6 (20.7)</td>
<td>23 (79.3)</td>
<td>6.54 (2.92 to 14.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ASA classification $\geq 2$ (157 patients)</td>
<td>10 (6.4)</td>
<td>147 (93.6)</td>
<td>1.69 (1.02 to 2.81)</td>
<td>0.059</td>
</tr>
<tr>
<td>Tobacco use (113 patients)</td>
<td>12 (10.6)</td>
<td>101 (89.4)</td>
<td>2.98 (1.90 to 4.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Previous VTE (73 patients)</td>
<td>13 (17.8)</td>
<td>60 (82.2)</td>
<td>5.43 (3.45 to 8.56)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Surgery duration $\geq 120$ min (47 ankles)</td>
<td>3 (6.4)</td>
<td>44 (93.6)</td>
<td>1.77 (0.59 to 5.33)</td>
<td>0.315</td>
</tr>
<tr>
<td>Spinal anaesthesia (446 ankles)</td>
<td>17 (3.8)</td>
<td>429 (96.2)</td>
<td>0.99 (0.75 to 1.32)</td>
<td>0.965</td>
</tr>
<tr>
<td>Additional surgical procedures (201 ankles)</td>
<td>10 (5.0)</td>
<td>191 (95.0)</td>
<td>1.36 (0.82 to 2.24)</td>
<td>0.261</td>
</tr>
<tr>
<td>Bilateral simultaneous TAR (46 ankles)</td>
<td>0 (0.0)</td>
<td>46 (100.0)</td>
<td>1.07 (1.05 to 1.11)</td>
<td>0.168</td>
</tr>
<tr>
<td>Post-operative mobilisation with cast (340 ankles)</td>
<td>17 (5.0)</td>
<td>323 (95.0)</td>
<td>1.37 (1.02 to 1.83)</td>
<td>0.079</td>
</tr>
<tr>
<td>No full weight-bearing post-operatively (91 ankles)</td>
<td>11 (12.1)</td>
<td>80 (87.9)</td>
<td>3.57 (2.18 to 5.86)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* BMI, body mass index; ASA, American Society of Anesthesiologists; VTE, venous thromboembolism

### Fig. 2

Bar chart showing the time of clinical presentation of symptomatic deep-vein thrombosis in 26 patients.
Our rate of DVT was comparable in patients having both spinal and general anaesthesia.

In patients undergoing bilateral simultaneous THR or TKR, the incidence of asymptomatic DVT is higher than in unilateral cases. In our study symptomatic DVT did not occur in any of the 23 patients undergoing bilateral simultaneous TAR, as was also reported by Karantana et al. However, such small patient groups do not exclude the bilateral simultaneous procedure as a possible risk factor owing to the doubling of the anaesthetic and tourniquet times and reduced post-operative mobility.

Our study has limitations. First, routine post-operative surveillance with colour duplex sonography was not undertaken. Therefore, the true incidence of post-operative asymptomatic DVT in the cohort is unknown. Secondly, the regression analysis must be interpreted with caution. It cannot adjust for all unidentified risk factors which could have different frequencies in the two groups, thus limiting extrapolation of the results. Logistic regression is sensitive to the number of explanatory variables and the number of patients. It is possible that several risk factors did not reach statistical significance owing to the small number of patients who had a DVT.

Thromboprophylaxis remains a controversial subject in elective orthopaedic surgery, particularly foot and ankle surgery, and there are no studies specifically addressing the efficacy of chemical thromboprophylaxis in patients undergoing TAR. Although we used LMWH routinely, our results do not provide the evidence to advocate the routine use of such agents in this patient group.

The authors wish to thank colleagues from the Radiology Department of Kantonsspital Liestal for their support and G. J. Stoddard from University of Utah for his contributions to the statistical analyses.

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### References


### Table V. Independent risk factors for the development of deep-vein thrombosis from multivariate logistic regression analysis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity, BMI ≥ 35 kg/m²</td>
<td>6.94</td>
<td>2.22 to 21.68</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous VTE</td>
<td>7.07</td>
<td>2.99 to 16.73</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No full weight-bearing post-operatively</td>
<td>4.53</td>
<td>1.86 to 11.00</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*BMI, body mass index; VTE, venous thromboembolism
†OR, odds ratio
‡CI, confidence interval


