Incidence and Clinical Course of Limb Dysfunction Post Cardiac Catheterization
— A Systematic Review —

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Background: We systematically reviewed the available literature on limb dysfunction after transradial access (TRA) or transfemoral access (TFA) cardiac catheterization.

Methods and Results: MEDLINE and EMBASE were searched for studies evaluating any transradial or transfemoral procedures and limb function outcomes. Data were extracted and results were narratively synthesized with similar treatment arms. The TRA group included 15 studies with 3,616 participants and of these 3 reported nerve damage with a combined incidence of 0.16% and 4 reported sensory loss, tingling and numbness with a pooled incidence of 1.61%. Pain after TRA was the most common form of limb dysfunction (7.77%) reported in 3 studies. The incidence of hand dysfunction defined as disability, grip strength change, power loss or neuropathy was low at 0.49%. Although radial artery occlusion (RAO) was not a primary endpoint for this review, it was observed in 3.57% of the participants in a total of 8 studies included. The TFA group included 4 studies with 15,903,894 participants; the rates of peripheral neuropathy were 0.004%, sensory neuropathy caused by local groin injury and retroperitoneal hematomas were 0.04% and 0.17%, respectively, and motor deficit caused by femoral and obturator nerve damage was 0.13%.

Conclusions: Limb dysfunction post cardiac catheterization is rare, but patients may have nonspecific sensory and motor complaints that resolve over a period of time.

Key Words: Cardiac catheterization; Distal extremity function; Hand dysfunction; Leg dysfunction; Radial artery occlusion

Transradial access (TRA) is now considered the gold standard of care for percutaneous coronary intervention (PCI) across many countries, with the latest guidelines from the European Society of Cardiology placing a Class 1A level of evidence on the use of TRA.1 TRA is associated with reductions in access site complications, major bleeding and death in high-risk patients compared with transfemoral access (TFA).2–7 Although TRA is increasingly adopted as the first-choice access site, limitations of this approach include an increase in operator and patient radiation dose, particularly in the early phase of training,8 a longer learning curve,9 challenges with small arterial loops in the forearm,10 radial artery spasm (RAS)11 and radial artery occlusion (RAO).12–14 Interest around the potential for upper limb dysfunction following TRA has come to the fore in recent times, particularly with increasing adoption of TRA.15–17 At the vascular level, neurovascular injuries such as intimal thickening, endothelial dysfunction and nerve damage following TRA may lead to complaints of upper limb dysfunction. One of the first studies led by Campeau, describing an early experience of TRA in 100 consecutive patients, did not report any nerve damage
associated with TRA at 3 months.\textsuperscript{18} In more contemporary practice, a prospective randomized study of 338 participants reported that 10.5% developed extremity-related complaints after TRA.\textsuperscript{15}

In contrast, despite TFA being a widely used access site in many countries, there is limited data on lower extremity function following TFA. Access site-related bleeding and vascular complications are known to occur and the incidence is much higher in TFA groups compared with TRA in both randomized trials and observational studies.\textsuperscript{6,19–23} However, the relationship between TFA and lower limb dysfunction after cardiac catheterization is unclear. Finally, it is also important to note that the majority of studies reporting access site-related limb dysfunction are limited to TRA and have not included any TFA patients to provide a comparison between access sites. In the current review, we systematically appraised the literature around the incidence and long-term clinical effect of upper and lower limb dysfunction after TRA and TFA, respectively.

### Methods

We searched MEDLINE and EMBASE for TRA studies using broad search terms: (radial, transradial, or radial artery) and (catheterisation or catheterization or angiography or angiogram or angioplasty or percutaneous coronary intervention or PCI) and (hand function or grip strength or disability or dysfunction or sensation or paresthesia or

### Table 1. Study Design and Participants’ Characteristics

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design/ country/year</th>
<th>No. of participants</th>
<th>Mean age (years)</th>
<th>% male</th>
<th>Participant inclusion criteria, sheaths and use of guide catheters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campeau (1989)\textsuperscript{18}</td>
<td>Cohort study; Canada; unclear</td>
<td>100</td>
<td>58 (median)</td>
<td>90</td>
<td>Participants had transradial coronary angiogram with 5Fr, 6Fr and 7Fr sheath</td>
</tr>
<tr>
<td>Kiemeneij (1995)\textsuperscript{24}</td>
<td>Cohort study; Netherlands; 1992–1993</td>
<td>100</td>
<td>62</td>
<td>77</td>
<td>Participants had transradial coronary angiography with 6Fr introducer and 6Fr-guide catheters</td>
</tr>
<tr>
<td>Lotan (1995)\textsuperscript{29}</td>
<td>Cohort study; Israel; 1994</td>
<td>100</td>
<td>61</td>
<td>79</td>
<td>Participants had transradial coronary angiography and angioplasty with 6Fr introducer and 6Fr guide catheters</td>
</tr>
<tr>
<td>de Beider (1997)\textsuperscript{34}</td>
<td>Cohort study; UK; unclear</td>
<td>75</td>
<td>Unclear</td>
<td>69</td>
<td>Participants had transradial coronary angiography and intervention and severe peripheral vascular disease with 5Fr or 6Fr sheath and 6Fr guide catheter</td>
</tr>
<tr>
<td>Chatelain (1997)\textsuperscript{37}</td>
<td>Cohort study; Switzerland; 1995–1997</td>
<td>159</td>
<td>60</td>
<td>82</td>
<td>Participants had transradial diagnostic and interventional cardiac procedures with 4Fr, 5Fr or 6Fr introducer sheath and guide catheters with RadialStop radial compression system</td>
</tr>
<tr>
<td>Benit (1997)\textsuperscript{38}</td>
<td>Randomized trial; Belgium; 1994–1995</td>
<td>56</td>
<td>577</td>
<td>100</td>
<td>Participants had transradial coronary angioplasty with 6Fr catheters and Palmaz-Schatz stent</td>
</tr>
<tr>
<td>Wu (2000)\textsuperscript{39}</td>
<td>Cohort study; USA; 1996–1998</td>
<td>40</td>
<td>65</td>
<td>88</td>
<td>Participants underwent 6Fr and 8Fr transradial procedure</td>
</tr>
<tr>
<td>Prull (2005)\textsuperscript{40}</td>
<td>Cohort study; Germany; unclear</td>
<td>93</td>
<td>625</td>
<td>806</td>
<td>Participants had transradial diagnostic cardiac catheterization with 5Fr or 6Fr sheath or transradial coronary intervention with 7Fr sheath</td>
</tr>
<tr>
<td>Tharmaratnam (2010)\textsuperscript{27}</td>
<td>Retrospective case control study; UK; 2005–2006</td>
<td>1,283</td>
<td>655</td>
<td>79</td>
<td>Participants had transradial coronary angiography and angioplasty</td>
</tr>
<tr>
<td>Zankl (2010)\textsuperscript{25}</td>
<td>Prospective cohort study; Germany; 2010</td>
<td>488</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Participants had transradial coronary angiography and angioplasty with 5Fr and 6Fr introducer, 4-, 5- and 6Fr catheters</td>
</tr>
<tr>
<td>Valgimigli (2014)\textsuperscript{31}</td>
<td>Prospective cohort study; Netherlands, Italy; 2014</td>
<td>203</td>
<td>60–77 (range)</td>
<td>73</td>
<td>Participants had transradial coronary angiography and angioplasty</td>
</tr>
<tr>
<td>van Leeuwen (2015)\textsuperscript{32}</td>
<td>Prospective cohort study; Netherlands; 2013–2014</td>
<td>286</td>
<td>64</td>
<td>72</td>
<td>Participants had transradial coronary angiography and angioplasty with 6Fr introducer sheath</td>
</tr>
<tr>
<td>Sciabasi (2016)\textsuperscript{33}</td>
<td>Prospective cohort study; Italy; unclear</td>
<td>99</td>
<td>66</td>
<td>73</td>
<td>Participants had transradial coronary angiography and angioplasty with 6Fr introducer sheath</td>
</tr>
<tr>
<td>van Leeuwen (2017a)\textsuperscript{34}</td>
<td>Prospective cohort study; Netherlands 2013–2015</td>
<td>300</td>
<td>64</td>
<td>72</td>
<td>Participants had transradial coronary angiography and angioplasty with 6Fr introducer sheath</td>
</tr>
<tr>
<td>van Leeuwen (2017b)\textsuperscript{34}</td>
<td>Prospective cohort study; Netherlands; 2014–2015</td>
<td>234</td>
<td>63</td>
<td>76</td>
<td>Participants had transradial coronary angiography and angioplasty with 6Fr introducer sheath</td>
</tr>
<tr>
<td>Femoral access studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benit (1997)\textsuperscript{38}</td>
<td>Randomized trial; Belgium; 1994–1995</td>
<td>56</td>
<td>584</td>
<td>100</td>
<td>Participants had transfemoral coronary angioplasty with 6Fr catheters and Palmaz-Schatz stent</td>
</tr>
<tr>
<td>Kent (1994)\textsuperscript{38}</td>
<td>Cohort study; USA; 1988–1993</td>
<td>9,585</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Participants had cardiac catheterization by femoral access with an average of 8.5Fr sheath</td>
</tr>
<tr>
<td>van Leeuwen (2015)\textsuperscript{32}</td>
<td>Prospective cohort study; Netherlands; 2013–2014</td>
<td>52</td>
<td>64</td>
<td>69</td>
<td>Participants had transfemoral coronary angiography and angioplasty with 6Fr introducer sheath A collagen plug (Angioseal) was applied at the end of procedure</td>
</tr>
<tr>
<td>El-Ghanem (2017)\textsuperscript{38}</td>
<td>Retrospective cohort study; USA; 2002–2010</td>
<td>15,894,201</td>
<td>64</td>
<td>61</td>
<td>Participants had transfemoral coronary angiography and angioplasty</td>
</tr>
</tbody>
</table>
Limb Dysfunction After Cardiac Catheterization

The numbers of patients with an event and the total patients were collected and the total percentages were determined. Where meta-analysis and pooled analysis were not possible, descriptive synthesis was used to report study results.

**Results**

**Upper Extremity Dysfunction after TRA**

A total of 15 studies reporting hand dysfunction post-TRA were included in the pooled analysis (Table 1). The process of study selection is shown in Figure. There were 12 cohort studies, 2 randomized control trials and 1 case-control study. There were 3,616 participants in total, with the largest study of 1,283 and the smallest study of 40 participants. The mean age reported in 10 studies was 62.7 years and over two-thirds of participants were male (78%). The results of the pooled analysis of hand function and vascular complications are presented in Tables 2, 3, S1. These results are narratively described below.

**Nerve Damage After TRA**

A total of 3 studies reported a combined incidence of nerve damage post-TRA of 0.16%. The only observation of radial nerve damage was made by Zankl et al in a study of 488 participants where only 1 patient (0.25%) experienced nerve damage post-TRA. In contrast, the other studies by Campeau and Benit et al did not observe any cases of nerve damage in their cohorts.

**Sensory Loss, Tingling and Numbness After TRA**

The pooled incidence of sensory loss, tingling and numbness was also low, at 1.61% in 4 studies.

Tharmaratnam et
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Measure of hand function and vascular complications</th>
<th>Follow-up postprocedure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campeau (1989)</td>
<td>Patients were re-examined or questioned over telephone about local complications</td>
<td>1–3 months</td>
<td>No nerve injury: 0/100 RAO: 1/100 Radial artery dissection: 1/100</td>
</tr>
<tr>
<td>Kiemeneij (1995)</td>
<td>Examination and ultrasound study performed if radial artery pulsations or flow were absent</td>
<td>1–3 months</td>
<td>Functional disability of the hand: 0/100 Pseudoaneurysm: 2/100 Absent radial pulse at discharge 10/100, 5 had follow-up recanalization</td>
</tr>
<tr>
<td>Lotan (1995)</td>
<td>Assessment methods unclear</td>
<td>1 month follow-up</td>
<td>Small hematoma in wrist: 3/100 Small pseudoaneurysm: 2/100 Numbness of the thumb and index finger: 1/100 No flow on Doppler: 2/100 Long-term no flow (RAO): 0/100</td>
</tr>
<tr>
<td>de Belder (1997)</td>
<td>Clinical evaluation</td>
<td>4–6 weeks</td>
<td>Hematoma and paresthesia postprocedure: 1/75 Hand sensation and function at 4–6 weeks: 0/75</td>
</tr>
<tr>
<td>Chatelain (1997)</td>
<td>Physicians assessed for any clinical events</td>
<td>Assessment prior to discharge</td>
<td>Paresthesia of right thumb during exercise: 1/159 RAO 1/159 Small hematoma: 15/159</td>
</tr>
<tr>
<td>Benit (1997)</td>
<td>Local complications assessed in clinic</td>
<td>1 month</td>
<td>Nerve damage documented by EMG: 0/50 Local pain: 0/50 Radial thrombosis (RAO): 2/50</td>
</tr>
<tr>
<td>Wu (2000)</td>
<td>Ultrasound assessment for RAO, aneurysm or dissection. Grip strength based on dynamometer results. Palmar pinch, key pinch and tip pinch strength tests were assessed by dynamic endurance test</td>
<td>Late follow-up 315 days</td>
<td>Hand complication in-hospital: 0/40 RAO: 1/40 Late radial occlusion: 5/34 Radial artery aneurysm: 0/40 Radial artery dissection 0/40 Grip strength: baseline 68±34, post-catheterization 69±35 Palmar pinch: baseline 18±10, post-catheterization 17±6 Key pinch: baseline 19±7, post-catheterization 19±6 Tip pinch: baseline 14±6, post-catheterization 14±4 Endurance: median for 6Fr and 8Fr is 78 [IQR 53–108] and 58 [IQR 32–68] respectively, post-catheterization 58 [IQR 47–84] and 56 [IQR 38–80], respectively</td>
</tr>
<tr>
<td>Tharmaratnam (2010)</td>
<td>Questionnaire posted to address and clinical notes for significant clinical events</td>
<td>Unclear</td>
<td>Problem with radial access site: 166/1,283 (12.9%) Pain at puncture site: 95/1,283 (7.4%) Swelling: 46/1,283 (3.6%) Bruising: 30/1,283 (2.5%) Nonspecific sensory abnormalities either pain or paresthesia in hand: 22/1,283 (1.71%)</td>
</tr>
<tr>
<td>Zankl (2010)</td>
<td>Assessment with ultrasound</td>
<td>4 weeks follow-up</td>
<td>RAO at 1 day: 51/488 (10.45%) Persistent RAO at 4 weeks: 21/488 (4.3%) Radial nerve paralysis: 1/488 (0.2%) Persistent hematoma: 0/488 (0%)</td>
</tr>
<tr>
<td>Valgimigli (2014)</td>
<td>RAO by duplex echocardiographic examination. Hand grip strength test with dynamometer</td>
<td>Just after procedure, 1 day, 30 days and 1 year</td>
<td>RAO at day 1: 5/203 RAO at 1 year: 3/203 Change in handgrip strength test: 0/203 Ischemic vascular or bleeding complications: 0/203</td>
</tr>
<tr>
<td>van Leeuwen (2015)</td>
<td>Quick DASH and CISS questionnaires. Patients asked to describe any procedure-related extremity complaints or loss of function at 1 month</td>
<td>Preprocedure and at 1 month</td>
<td>Procedure-related extremity problems in TRA group 56/286 (19.6%) Procedure-related extremity problems in TRA group at 30 days 6/286 (10.5%) Temporary upper limb complaint (&lt;30 days): 26/286 (9%) Persistent upper limb complaint (&gt;30 days): 31/286 (11%) Pain: 13/286 Numbness: 2/286 Tingling: 3/286 Stiffness: 2/286 Less power: 2/286 Upper limb function by QuickDASH at 30 days: no change over time, baseline 455 [IQR 0–13.64], follow-up 227 [IQR 0–9.32]</td>
</tr>
<tr>
<td>Sciahbasi (2016)</td>
<td>RAO by ultrasound test. Hand grip strength by Jamar Plus dynamometer. Thumb and forefinger pinch test by Jamar Plus electronic pinch gauge</td>
<td>Day of procedure and at least 30 days follow-up</td>
<td>RAO: 9/99 (9.1%) Hand grip strength change at follow-up: 0/99 Thumb and forefinger pinch test change at follow-up: 0/99</td>
</tr>
</tbody>
</table>

(Table 2 continued the next page.)
Limb Dysfunction After Cardiac Catheterization

The largest study reporting pain post-TRA procedure was conducted by Tharmaratnam et al, where the pain was reported in 7.4% of participants.

Hand Function, Disability, Grip Strength Change, Stiffness, Power Loss and Neuropathy After TRA

Hand function complications such as disability, grip strength, stiffness, power loss and neuropathy were also described in their retrospective case-control questionnaire-based study, found the highest incidence of sensory abnormality in the form of pain and paresthesia in hand at 1.71% (22/1,283) post-TRA.  

**Pain After TRA**

Pain was the most common complaint and reported at 7.77% in 3 studies. It was described as perioperative procedural pain. The largest study reporting pain post-TRA procedure was conducted by Tharmaratnam et al, where the pain was reported in 7.4% of participants.

**Table 3. Summary of Pooled Results for Hand Dysfunction or Vascular Complications Post-Transradial Procedure**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Measure of hand function and vascular complications</th>
<th>Follow-up postprocedure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Leeuwen (2017a)</td>
<td>Quick DASH and CISS questionnaires. Patients asked to describe any procedure-related extremity complaints or loss of function at 1 year</td>
<td>Preprocedure and at 1 year</td>
<td>QuickDASH scores at baseline and 1 year were same. Overall upper extremity complaints: 3% Pain 43.2%, Other 26.7%, Tingling 10%, Numbness 6.7%, Stiffness 6.7%, Less power 6.7%. Upper limb function by QuickDASH at 1 year: no change over time, baseline 239 [IQR 0–13.64], follow-up 0 [0–11.02]. Cold intolerance not associated with access route at 1 year</td>
</tr>
<tr>
<td>van Leeuwen (2017b)</td>
<td>Quick DASH and CISS questionnaires</td>
<td>Preprocedure and at 2-year follow-up</td>
<td>Incompleteness of SPA: 99/234 (46%) Incompleteness of DPA: 0% Incompleteness of SPA and DPA: 0% Increase in QuickDASH scores at 2-year follow-up With SPA incompleteness: 31% Without SPA incompleteness: 25% Increase in CISS score With incompleteness of SPA: 16% Without incompleteness of SPA: 14% RAO: 4.9%</td>
</tr>
<tr>
<td>Benit (1997)</td>
<td>Local complications assessed in clinic</td>
<td>1 month</td>
<td>Nerve damage documented by EMG: 0/50 Local pain: 0/50</td>
</tr>
<tr>
<td>Kent (1994)</td>
<td>Extensive review of patient’s symptoms and disability</td>
<td>Telephone interview with review of patient’s symptoms and disability</td>
<td>Peripheral neuropathy 20/9,585 (0.21%) Localized groin injury causing sensory neuropathy of the medial and intermediate cutaneous branches of the femoral nerve 4/9,585 (0.04%) Large retroperitoneal hematomas with sensory neuropathy of the femoral nerve 16/9,585 (0.17%) Motor deficits of the femoral and obturator nerves 13/9,585 (0.13%) Sensory neuropathy at mean follow-up of 41 months: 5/9,585 Follow-up tingling in inner thigh and upper calf: 5/9,585 Follow-up with motor symptoms: 1/9,585</td>
</tr>
<tr>
<td>van Leeuwen (2015)</td>
<td>Patients asked to describe any procedure-related extremity complaints or loss of function</td>
<td>1 month</td>
<td>Procedure-related extremity problems in TFA group= 9/52 (17.3%) Procedure-related extremity problems in TFA group at 30 days=6/52 (11.5%)</td>
</tr>
<tr>
<td>El-Ghanem (2017)</td>
<td>Hospital diagnostic codes</td>
<td>In-hospital</td>
<td>Femoral neuralgia, peripheral neuropathy (sensory, motor neuropathies) 597/15,894,201 (0.00004%)</td>
</tr>
</tbody>
</table>

CISS, Cold Intolerance Symptom Severity; DPA, deep palmar arch; EMG, electromyography; IQR, interquartile range; RAO, radial artery occlusion; SPA, superficial palmar arch.
low at a pooled rate was 0.49% across 6 studies.\textsuperscript{31, 36} The largest study investigating hand function was conducted by van Leeuwen et al, reporting an incidence of 9% and 11% for temporary (<30 days) and persistent (>30 days) upper limb complaints respectively.\textsuperscript{15} The same investigators in the ACRA trial reported loss of hand function in approximately 4% of participants at 2-year follow-up.\textsuperscript{31} However, the majority of studies evaluating hand function, disability, grip strength change, stiffness, power loss and hand complications did not report any hand dysfunction at all.\textsuperscript{31, 35}

**Vascular Complications After TRA**

The pooled incidence of vascular complications, including bruising, hematoma, pseudoaneurysm and dissection, was reported as 2.42% among 9 studies.\textsuperscript{8, 25, 27, 29, 31, 33, 35, 36} All these complications were based on clinical judgment and occurred around the periprocedural time. For instance, Lotan et al reported a 5% rate of vascular complications in their postprocedure assessment.\textsuperscript{29} Only 3 studies reported nearly 3% of access site-related hematoma.\textsuperscript{27, 28} None of the studies described clinically significant functional outcomes at follow-up. Minor bruising related to access site was reported by Tharmaratnam et al in a cohort of 1,283 participants with an incidence of 2.3%.\textsuperscript{37}

**RAO After TRA**

Overall incidence of RAO was 3.57% of vascular complications across 8 studies.\textsuperscript{18, 25, 29, 31, 33, 36, 37} Zankl et al noted 10.4% of participants with RAO, in whom spontaneous recanalization was observed in the majority at a 4-week follow-up, where the incidence of RAO was 4.3%.\textsuperscript{21} In contrast, only Wu et al reported late RAO (14.7% of participants) at nearly 1 year follow-up.\textsuperscript{33}

**Ascertainment of Outcomes After TRA**

In our pooled analysis of 15 TRA studies, we observed a significant heterogeneity in ascertainment of outcomes of hand dysfunction, both in methodology and timing of ascertainment. For instance, the timing of measurement of outcomes and follow-up varied from just after the procedure\textsuperscript{35, 37} and at 2 years.\textsuperscript{36} Similarly, studies used various subjective questionnaires and tests to measure different forms of hand dysfunction. Campeau\textsuperscript{38} and Zankl et al\textsuperscript{28} evaluated nerve damage at 1–3 months postprocedure either by physical examination or via a telephone questionnaire. Only Benit et al used electromyography (EMG) at 1-month follow-up and no nerve damage was observed.\textsuperscript{26} The majority of studies reported sensory loss by clinical examination based on patient symptoms. Only van Leeuwen et al used a well-recognized and widely accepted objective method in the form of the cold intolerance symptom severity (CISS) questionnaire to assess the sensory component of hand function at 1 month, 12 months’ and 2 years’ follow-up (Table S2).\textsuperscript{15, 30, 36}

In addition, methods of measuring power strength ranged from the Quick DASH questionnaire (Table S3)\textsuperscript{45} to detailed measures of hand function by Wu et al,\textsuperscript{33} which included grip strength, palmar pinch, key pinch, tip pinch and endurance, and Wu reported no significant difference before or after TRA procedure. Finally, the majority of studies used ultrasound to assess the incidence of RAO post-TRA.\textsuperscript{25, 29, 32, 33}

**Lower Extremity Dysfunction After TFA**

In contrast to the 15 studies found for the TRA cohort, there were only 4 studies that met the inclusion criteria for limb dysfunction post-TFA, with 15,903,894 participants.\textsuperscript{26, 30, 36, 39} El-Ghanem et al studied the National inpatient sample (NIS) database to investigate the incidence of femoral neuralgia (sensory and motor neuropathy of lower extremity) post-TFA, reporting only 597 events in a weighted sample of 15,894,201 participants (0.0004%).\textsuperscript{39} In another retrospective cohort study of 9,585 patients, only 20 patients developed femoral neuropathy.\textsuperscript{38} Assessment was based on clinical judgment and extensive review of each patient’s symptoms and disability following telephone interviews. There was an average delay of 37 h from catheterization to the recognition of symptoms. Almost 50% of patients complained of severe pain even before the onset of neuropathic symptoms. Motor neuropathy was observed in 13 of 20 patients, but all patients reported sensory neuropathy. This translated into an overall rate of leg dysfunction of 0.21% in the study (Table 4).

**Retropertitoneal Hematoma**

Large retropertitoneal hematomas were the most common cause of sensory neuropathy across 1 study, from involvement of the femoral nerve and lateral femoral cutaneous branches, and were observed in 0.17% of participants (16/9,585).\textsuperscript{38} Motor deficits of the femoral (weakness of quadriceps and psosas muscles) and obturator nerves (inability to adduct the thigh) were observed in 0.13% of participants (13/9,585). Only 1 patient in this group required surgical intervention because of an expanding retropertitoneal hematoma. As a result, 6 patients reported severe initial deficit (2 were unable to walk and 4 required assistance in the form of a walker, crutches or leg brace). The size of the retropertitoneal hematoma did not correlate with the severity of sensory or motor deficit.\textsuperscript{38}

**Other Neurovascular Complications**

Localized access site complications such as groin hematoma and femoral false aneurysm resulted in sensory neuropathy in 0.04% (4/9,585) of the patients caused by involvement of
the medial and intermediate cutaneous branches of the femoral nerve. Two patients were found to have aneurysms on clinical examination and confirmed with ultrasonography. The remaining 2 had groin hematoma and 1 required surgical drainage.

**Ascertainment of Outcomes After TFA**

We observed that the length of follow-up ranged from 1 month to 26±17 months across the 4 studies. In the first group, partial resolution of sensory neuropathy was observed at the time of discharge; 50% of patients had complete resolution of symptoms by the end of 2 months. On the other hand, 5 patients had persistent sensory neuropathy at 41 months' follow-up. Motor symptoms resolved in all patients except 1 who occasionally required a stick to walk because of quadriiceps weakness. All of the patients in the second group had complete resolution of symptoms immediately after repair of false aneurysm and 5 months after drainage of groin hematoma. In one of the recent studies from contemporary practice, van Leeuwen et al reported a higher incidence of lower extremity-related symptoms in their TFA cohort at 17.3% immediately postprocedure, which decreased to 11.5% at 1-month follow-up.

**Discussion**

In this systematic review, we narratively describe the incidence of limb dysfunction after TRA and TFA cardiac catheterization. We found that the incidence of limb dysfunction following TRA or TFA is very low, at 0.26% and 0.21%, respectively. We observed significant heterogeneity among the studies with regard to definitions, methods and timing of assessment of limb dysfunction. The most striking finding was that despite being the oldest and widely practised access site for cardiac catheterization, limb dysfunction is rarely evaluated or reported after TFA. Finally, our study supported the fact that most operators, whether radial or femoral, very rarely refer patients for specialist input or for further rehabilitation as the majority of the symptoms resolve without any significant long-term disability.

The exact mechanism of limb dysfunction (motor or sensory) following TRA or TFA cardiac catheterization is unclear, though there are many possible explanations. Firstly, the flexor carpi radialis, flexor pollicis longus tendons and median nerve lie next to the radial artery at the wrist from lateral to medial, respectively, and the femoral nerve just lateral to the femoral artery. These structures can be directly damaged during cannulation of the radial or femoral arteries. Direct injury and hematoma lead to edema (inflammatory reaction) with secondary compression of underlying structures (e.g., carpal tunnel syndrome, compartment syndrome) leading to motor and sensory deficits. Additionally, extrinsic pressure to achieve hemostasis may lead to transient or permanent ischemia of the main nerves or branches, resulting in motor or sensory deficits. Hematoma formation is a common manifestation of access site-related bleeding. More frequently encountered in patients undergoing TFA cardiac catheterization procedures. Large, rapidly expanding hematomas can also cause intrinsic compression of adjacent neurological structures, resulting in damage. Although this mechanism of neurological damage was not well reported in these studies, there are isolated case reports. Another mechanism for the development of limb dysfunction is direct ischemic injury. For instance, RAO is a recognized complication of TRA that can lead to transient or permanent mild ischemia of the hand. Such ischemic insults following RAO may contribute to hand dysfunction. Interestingly, in a recent study by Zwaan and colleagues, a higher incidence of RAO (9.8%) was observed in patients experiencing hand dysfunction compared with those with normal hand function (0% RAO). Although in most patients there is collateral blood flow from the ulnar artery and palmar arches, the authors postulate that RAO might still lead to a reduction in blood supply to hand muscles and thus ischemia. In contrast, van Leeuwen et al's ACRA trial reported no loss of hand function related to incompleteness of the palmar arches. In the RADAR study, Valgimigli et al used a more objective method of detecting hand ischemia in patients undergoing TRA by measuring lactate with normal, intermediate and abnormal Allen's test. Lactate did not differ among the 3 study groups after the procedure and, more importantly, there were no differences in handgrip strength test results and discomfort ratings across the 3 groups. It is important to note that anatomic variations may also play an important role in neurovascular injuries. For instance, radial artery anomalies such as high-bifurcating radial origins, full radial loops and extreme radial tortuosity are well known to increase the risk of procedural failure of TRA. Increased instrumentation and catheter exchanges can also cause vascular damage, at both the endothelial and vascular level. Furthermore, once trauma has occurred to the vasculature and nerves, its effect may depend on how early it is identified and managed. For example, a small hematoma may not be recognized until it has caused significant swelling and possible extension proximally or distally.

Our analysis demonstrated that pain and neurological symptoms were the most common forms of limb dysfunction reported. The pooled incidence of pain post-TRA/-TFA was 6.67% and 0.21%, respectively. Although patients frequently reported pain following the procedure, the majority of these settled over time without any significant residual symptoms. Neurological symptoms can be more worrying because they can impair the day-to-day function of the individual. In a landmark study evaluating limb function post-TRA/-TFA, van Leeuwen and colleagues reported that nearly 20% of the patients developed subjective neurological complications in the form of numbness, tingling, stiffness, and less power post-TRA. Reassuringly the majority of these symptoms resolved at 30-day follow-up. More recently, the investigators published the results of the same study at 1-year follow-up, illustrating that although limb-related complaints were reported equally in both TRA and TFA groups, they diminished significantly over time without any clinical sequelae. The transient nature of these complications is important because the resolution of symptoms raises doubt around long-term clinical relevance in clinical practice, which supports the theory of a temporary inflammatory reaction to local injury leading to sensory and motor deficits.

There is currently no consensus regarding the definition of limb dysfunction post-TRA/-TFA cardiac catheterization and no agreement on the optimal method of assessing limb function. Studies to date have used a wide range of tests such as visual analog scale (VAS: a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot
easily be directly measured, for example, pain). Boston carpal tunnel questionnaire (BCTQ: a measure of symptom severity and functional status) (Table S4), Disabilities of Arm, Shoulder and Hand (QuickDASH: a measure of physical function, symptoms, and its consequences on daily life) and CISS (a measure of intolerance to cold) questionnaire. It is important to note that these tests have been mainly developed and validated in noncardiac intervention settings. In the evaluation of limb dysfunction, it is important to consider procedural and patient characteristics such as repeated puncture, size of the sheath, number of catheters used, and presence of spasm or underlying peripheral vascular disease, diabetes and pharmacological agents used during the procedure to tackle the RAS. Postprocedural factors such as the method of achieving hemostasis, compression and any immediate complications may also play an important role. Although studies have been undertaken to systematically study hand dysfunction post-TRA, there have been no studies to date that focus on lower limb dysfunction following TFA despite the femoral artery being used for cardiac catheterization for over 50 years. With the growth of larger bore femoral access for structural heart interventions that are becoming increasingly common practice, future work should focus on leg/foot dysfunction, particularly in these clinical situations.

Our study is the first to compare and systematically present the incidence of limb dysfunction post-TRA/-TFA. We found that majority of the literature around limb dysfunction involved patients undergoing TRA and only 2 studies have assessed limb dysfunction post-TFA. While we were able to provide a comprehensive summary of the current literature, our review has few limitations. The evidence is poor and not of sufficient quality to permit a meta-analysis. We also identified significant heterogeneity in the studies’ designs and methodology, such as the various ways of assessing limb function. However, our findings showed there are limited data on location, severity, causality, treatment and long-term outcome of limb dysfunction after cardiac catheterization. Finally, baseline demographics and procedural characteristics such as age, body mass index, sex, wrist size, and sheath size are known to be associated with increased risk of vascular injury particularly in the TRA setting. However, studies included in the current review lacked consistency in reporting the association of such variables with the development of limb dysfunction.

Conclusions

Limb dysfunction post-TRA/-TFA cardiac catheterization is a rare entity. There is a lot of variability in the methodology and reporting of studies investigating limb dysfunction post-TRA/-TFA. Participants may have nonspecific sensory and motor complaints that resolve over a period of time. More robust and pragmatic approaches are required in future studies to measure the clinical relevance of such complications.

Disclosures

None relevant to this study.

References


40. Araki T, Itaya H, Yamamoto M. Acute compartment syndrome of the forearm that occurred after transradial intervention and was not caused by bleeding or hematoma formation. *Catheter Cardiovasc Diag* 2010; 75: 362 – 365.


### Supplementary Files

#### Supplementary File 1

**Table S1.** Baseline characteristics and predictors of limb dysfunction

**Table S2.** Cold Intolerance Symptoms Severity (CISS) questionnaire

**Table S3.** Disabilities of Arm, Shoulder and Hand (QuickDASH) questionnaire

**Table S4.** Boston Carpal Tunnel Syndrome Questionnaire (BCTQ)

Please find supplementary file(s): http://dx.doi.org/10.1253/circj.C3-18-0389