RISK FACTORS FOR FOOT ULCERATION IN ADULTS WITH ESRD ON DIALYSIS

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Declaration of Financial Interests or Relationships

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I have no financial interest or relationship(s) to disclose.
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Prof Peter G Kerr
WHAT IS END-STAGE RENAL DISEASE (ESRD)?

- Chronic medical condition - significant loss of kidney function
- Dialysis or kidney transplant required for survival
- Dialysis removes metabolic waste products, water and toxic substances
- Leading causes of ESRD in Australia:
  - Diabetes mellitus (35%)
  - Nephritis (19%)
  - Hypertension (14%)
• High prevalence of foot ulceration (14.4%) and amputation (5.9%)
• Detrimental impact and financial burden
• Poor foot salvage and prognosis
• One and five year survival rates following a lower extremity amputation:
  • Haemodialysis (50.8%, 17.2%)
  • Moderate to severe CKD (76.6%, 40.9%)
  • Mild or no CKD (85.6%, 60.3%)
• There is limited high-quality evidence for the risk factors for foot ulceration

• Large multi-centre prospective cohort studies are needed
To investigate the risk factors for foot ulceration in adults with ESRD on dialysis
METHODS

- Multi-centre prospective observational cohort study
- 450 participants recruited

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESRD and clinically stable on dialysis (haemodialysis or peritoneal dialysis)</td>
<td>Insufficient English skills to provide informed consent or follow instructions during the project</td>
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<tr>
<td>≥18 years of age</td>
<td>Unwilling or unable to give informed consent to participate</td>
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<td>Cognitively aware (i.e. to provide informed consent)</td>
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**STUDY FLOW**

**RECRUITMENT**

- **Home-based participants**
  - Telephone screening

- **Satellite participants**
  - Face-to-face screening

**SCREENING FOR ELIGIBILITY**

- **BASELINE APPOINTMENT**
  - Interview
  - Review of medical record/blood tests
  - Health-status questionnaire
  - Foot assessment

**FOLLOW-UP APPOINTMENT**

- **(12 MONTHS)**
  - Evaluation of primary and secondary outcomes

**RELIABILITY STUDY**

- Additional foot assessment (1 week after baseline appointment)
DATA COLLECTION

- Participant characteristics
- Dialysis-related variables
- Comorbidities
- Blood results
- Foot complications
- Foot-health care behaviours
- Health status questionnaire
- Foot examination
NEUROLOGICAL ASSESSMENT

• Protective sensation (Semmes-Weinstein 5.07/10g monofilament)

• Vibration perception threshold (Neurothesiometer)
ARTERIAL ASSESSMENT

- Palpation of pedal pulses
- Ankle-brachial pressure index
- Toe-brachial pressure index (Systoe® automated system)
BIOMECHANICAL/FOOTWEAR ASSESSMENT

• 1st metatarsophalangeal joint (MTPJ) range of motion
• Peak plantar pressures (TekScan® MatScan system)
• Foot deformity
• Footwear (fit, type, condition)
Skin and nail pathology

• Corns/calluses
• Uraemic pruritus (itchy skin)
• Xerosis (dry skin)
• Calciphylaxis
• Onychomycosis (fungal nail)
• Onychocryptosis (ingrown nail)
• Onychauxis (thickened nail)
<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Secondary outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot ulceration</td>
<td>Number and time to onset of foot ulceration</td>
</tr>
<tr>
<td></td>
<td>Lower extremity amputations</td>
</tr>
<tr>
<td></td>
<td>Episodes of infection</td>
</tr>
<tr>
<td></td>
<td>Foot-related hospitalisations</td>
</tr>
<tr>
<td></td>
<td>Revascularisation procedures</td>
</tr>
<tr>
<td></td>
<td>Kidney transplantation</td>
</tr>
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<td>Mortality</td>
</tr>
</tbody>
</table>
• Cox proportional hazards analysis

• Multinomial logistic regression

• Risk estimates presented as HR, RR, OR (depending on model) and 95% CIs
## RESULTS: BASELINE

### Participant characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 450)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD, years</td>
<td>67.5 ± 13.2</td>
</tr>
<tr>
<td>Male, n(%)</td>
<td>64.7</td>
</tr>
<tr>
<td>Smoker, n(%)</td>
<td>12.0</td>
</tr>
<tr>
<td>Mean body mass index ± SD, kg/m²</td>
<td>28.2 ± 6.6</td>
</tr>
<tr>
<td>Living alone, n(%)</td>
<td>16.7</td>
</tr>
<tr>
<td>Haemodialysis, n(%)</td>
<td>94.0</td>
</tr>
<tr>
<td>Peritoneal dialysis, n(%)</td>
<td>6.0</td>
</tr>
<tr>
<td>Median dialysis duration (IQR), months</td>
<td>37 (17 to 70)</td>
</tr>
<tr>
<td>Diabetes mellitus, n(%)</td>
<td>50.2</td>
</tr>
<tr>
<td>Mean diabetes duration ± SD, months</td>
<td>256 ± 153</td>
</tr>
</tbody>
</table>

### Foot examination

<table>
<thead>
<tr>
<th>Examination</th>
<th>Total (n = 450)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy, n(%)</td>
<td>50.7</td>
</tr>
<tr>
<td>Peripheral arterial disease, n(%)</td>
<td>52.4</td>
</tr>
<tr>
<td>Arterial calcification, n(%)</td>
<td>40.9</td>
</tr>
<tr>
<td>Limited 1st MTPJ range of motion, n(%)</td>
<td>93.6</td>
</tr>
<tr>
<td>Foot deformity, n(%)</td>
<td>75.8</td>
</tr>
<tr>
<td>Skin pathology, n(%)</td>
<td>87.8</td>
</tr>
<tr>
<td>Nail pathology, n(%)</td>
<td>70.9</td>
</tr>
<tr>
<td>Inappropriate/ill-fitting footwear, n(%)</td>
<td>66.0</td>
</tr>
<tr>
<td>Poor foot-health care behaviours, n(%)</td>
<td>30.2</td>
</tr>
<tr>
<td>Podiatry attendance (last 12 months), n(%)</td>
<td>49.6</td>
</tr>
</tbody>
</table>
RESULTS: PRIMARY OUTCOME

FOOT ULCERATION

• 81 participants (18%)

• 211 foot ulcers (200 new, 11 reoccurring)

• Majority located on the toes (61%)

• Time to onset 164 ± 127 days

• Annual incidence 122 per 1,000 person-years
RESULTS: SECONDARY OUTCOMES

LOWER EXTREMITY AMPUTATION

• 12 participants (2.7%)

• 20 amputations (18 minor, 2 major)

• Reason for amputation: PAD/gangrene (45%), infected foot ulcer (40%), osteomyelitis (15%)
RESULTS: SECONDARY OUTCOMES cont...

EPISODES OF INFECTION

- 96 participants (21.3%), 182 episodes
- Common infections: cellulitis (10.9%), local wound infection (8.2%), osteomyelitis (5.3%)

REVASCULARISATION PROCEDURES

- 24 participants (5.3%), 42 procedures
- 81% angioplasties
RESULTS: SECONDARY OUTCOMES cont...

FOOT-RELATED HOSPITAL ADMISSIONS
- 42 participants (9.3%)
- 74 admissions
- Length of stay 25 ± 23 days
- Admitted due to infected foot ulcer (28.4%)

KIDNEY TRANSPLANT
- 30 participants (6.7%)
RESULTS: SECONDARY OUTCOMES cont...

ALL-CAUSE MORTALITY

- 52 participants (11.6%)
- Common causes: myocardial infarction (23.1%), withdrawal from dialysis (15.4%), pneumonia (15.4%)

FOOT-RELATED MORTALITY (n = 6)

- Sepsis secondary to infected foot ulcer (n = 5)
- Due to complications of PAD (n = 1)
## RESULTS: RISK FACTORS

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy</td>
<td>3.02 (1.48 to 6.15)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Previous foot ulceration</td>
<td>2.86 (1.53 to 5.34)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.82 (0.98 to 3.36)</td>
<td>0.057</td>
</tr>
</tbody>
</table>
## Results: Risk Factors

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>Risk factor</th>
<th>Relative Risk (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Never ulcerated</strong></td>
<td></td>
<td>Reference Category</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>New foot ulceration</strong></td>
<td>27</td>
<td>Diabetes mellitus</td>
<td>0.68 (0.28, 1.63)</td>
<td>0.388</td>
</tr>
<tr>
<td>(no past/baseline ulcer)</td>
<td></td>
<td><strong>Peripheral neuropathy</strong></td>
<td>2.66 (1.04, 6.82)</td>
<td>0.040*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peripheral arterial disease</td>
<td>0.58 (0.24, 1.41)</td>
<td>0.229</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cerebrovascular disease</td>
<td>1.37 (0.54, 3.50)</td>
<td>0.511</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Nail pathology</strong></td>
<td>3.85 (1.08, 13.75)</td>
<td>0.038*</td>
</tr>
<tr>
<td><strong>New foot ulceration</strong></td>
<td>54</td>
<td>Diabetes mellitus</td>
<td>1.84 (0.75, 4.48)</td>
<td>0.180</td>
</tr>
<tr>
<td>(past/baseline ulcer)</td>
<td></td>
<td><strong>Peripheral neuropathy</strong></td>
<td>11.23 (3.16, 39.87)</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Peripheral arterial disease</strong></td>
<td>7.15 (2.24, 22.82)</td>
<td>0.001**</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Cerebrovascular disease</strong></td>
<td>2.08 (1.04, 4.16)</td>
<td>0.037*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nail pathology</td>
<td>1.02 (0.43, 2.45)</td>
<td>0.953</td>
</tr>
</tbody>
</table>
• Peripheral neuropathy and previous foot ulceration are major risk factors for foot ulceration.

• Nail pathology and neuropathy are risk factors in those without history of ulceration.

• Neuropathy, peripheral arterial disease and cerebrovascular disease are risk factors in those with history of ulceration.

• Diabetes is not a primary or significant risk factor, as other comorbidities (such as neuropathy and peripheral arterial disease) have stronger associations with ulceration.
CLINICAL IMPLICATIONS

• First study to identify longitudinal risk estimates for foot ulceration in a large dialysis cohort
• Clearer understanding of risk factors and identification of those at the highest risk
• Highlights a clear need for foot care provision to dialysis patients
• Risk factors identified may help to reduce the incidence of foot ulceration and its associated complications
FUTURE RESEARCH

• Direct health care prioritisation - develop prevention and early treatment programs

• Inform the design of randomised clinical trials that target the risk factors for ulceration in the dialysis population
CONCLUSION

• There is a high prevalence and incidence of foot ulceration
• Peripheral neuropathy and previous foot ulceration are major risk factors
• Risk factors differ between those with and without a history of ulceration
• Diabetes is not a significant risk factor on its own
• These findings should help reduce the incidence of foot ulceration and its associated complications
THANK YOU

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RELIABILITY STUDY

• 20 participants recruited
• Foot assessment on 2 separate occasions (one week apart)
• Intra-examiner reliability for the monofilament, neurothesiometer, palpation of pedal pulses, ABPI, TBPI, 1\textsuperscript{st} MTPJ ROM tests

RESULTS

• ICCs ranged between 0.87 and 0.99
• All weighted kappa values equalled 1.00 (absolute % agreement ranged from 95 to 100%)