Renal Failure and the diabetic Foot

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Complications of Diabetes Affect Every Part of the Body

Microvascular Complications
- Diabetic Retinopathy
  NOT now Leading cause of blindness in working-age adults
- Diabetic Nephropathy
  Leading cause of end-stage renal disease
- Diabetic Neuropathy
  Leading cause of nontraumatic lower extremity amputations

Macrovascular Complications
- Stroke
  2- to 4-fold increase in cardiovascular mortality and stroke
- Heart Disease
- Peripheral Vascular Disease

“The art of medicine consists of amusing the patient while nature cures the disease”

Voltaire

Diabetes...

- an affliction that is not very frequent...being a melting down of the flesh and limbs into the urine...life is short, disgusting and painful...thirst unquenchable...the kidneys and bladder never stop making water...it may be something pernicious, derived from other diseases, which attack the bladder and kidneys

Areteus of Cappadocia (early 2nd century ad)

The Harsh Reality of Diabetes

- Most common cause of ESRD in Europe/USA
  - 140 per million in diabetes
  - 15-42 per million in non-diabetes

- Once on dialysis poor survival if diabetic
  - 5 year survival 30.2% if diabetic
  - 5 year survival 62.2% if non-diabetic

Incidence of End Stage Renal Disease

Proteinuria Is an Independent Risk Factor for Mortality in Type 2 Diabetes

Rossing P Diabetologia 2005;48:1439-1444

*P < 0.001 normoalbuminuria vs macroalbuminuria.
**Annual Transition Rates Through Stages of DN**

- **No nephropathy** → **2.0% (1.9% to 2.2%)** → **1.4% (1.3% to 1.5%)** → **DEATH**
- **Microalbuminuria** → **2.8% (2.5% to 3.2%)** → **3.0% (2.6% to 3.4%)**
- **Macroalbuminuria** → **2.3% (1.5% to 3.0%)** → **4.6% (3.6% to 5.7%)**
- **Elevated plasma creatinine or Renal replacement therapy** → **19.2% (14.0% to 24.4%)**

**Causal Pathways for Foot Ulceration**

- Neuropathy most important component cause (78%)
- Critical triad: neuropathy, deformity, and trauma present in 63%
- Ischemia component cause in 35%
- >80% of ulcers potentially preventable

**Risk Factors for foot ulceration in Diabetic Nephropathy**

- 84 patients studied
  - 4 groups: Microalbuminuria (MA), Albuminuria (A); Chronic Renal Failure (CRF) and non-nephropathic diabetes (N)
  - VPT, NCVs and dynamic foot pressures assessed

**Risk Factors for foot ulceration in Diabetic Nephropathy: Results**

- VPT, NCV and foot pressures significantly reduced in all 3 groups – eg., VPT: MA=21, A=28, CRF=39V.
- Past history of ulcers in 5% NN, 10% MA and A, and 40% CRF.
- Patients at all stages of nephropathy have increased DFU risk.
Other Associations with Foot Ulceration
End-stage Renal Disease

- Association between start of dialysis and incidence of foot ulceration
- Up to 40% of dialysis patients have past or current ulceration
- Related to lack of diabetes follow-up
- Ethnic protection lost

Game et al 2006, 2010; Ndip et al 2010

Incidence of Foot Ulcers & Amputation in ESRD

CKD associated risk independent of PAD

Margolis DJ, Hofstad O, Feldman HI. Diabetes Care 2008

Life on Dialysis

Nicholas Evans, BMJ 2012;345:e5262:
"Being on dialysis isn’t really a life: it’s not even half a life."

Renata Carey, BMJ 2012;345:e4492:
"Dialysis is brilliant, of course, but deeply horrendous."

Renata Carey, BMJ 2012;345:e4492:
"On the dialysis unit, patients suddenly appear with amputations: and often before that with heavily bandaged feet, rapidly followed by crutches and then wheelchairs."
Dialysis and Foot Ulceration

- Dialysis is an independent risk factor for foot ulceration
- When compared to ESRD patients not on dialysis, 4.2x increased risk of foot ulceration
- Mortality after amputation - 290% increase in hazard for those on dialysis
- Need for foot care on dialysis units

Ndip A et al, Diabetes Care 2010;33: 878-880 and 33:1811-1816

<table>
<thead>
<tr>
<th>Factor</th>
<th>No-dialysis (n=187)</th>
<th>Dialysis (n=139)</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalent foot ulcer (%)</td>
<td>4.8</td>
<td>21</td>
<td>5.1 (2.9 to 11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior amputation (%)</td>
<td>6.4</td>
<td>15</td>
<td>2.6 (1.2 to 5.6)</td>
<td>0.008</td>
</tr>
<tr>
<td>PAD (%)</td>
<td>43</td>
<td>64</td>
<td>2.4 (1.5 to 3.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neuropathy (%)</td>
<td>65</td>
<td>79</td>
<td>2.0 (1.2 to 3.3)</td>
<td>0.006</td>
</tr>
<tr>
<td>Prior foot ulcer (%)</td>
<td>20</td>
<td>32</td>
<td>1.9 (1.1 to 3.1)</td>
<td>0.011</td>
</tr>
<tr>
<td>Deformity (%)</td>
<td>33</td>
<td>22</td>
<td>0.6 (0.4 to 1.0)</td>
<td>0.019</td>
</tr>
<tr>
<td>IWGDF risk categories (%)</td>
<td>16 vs 85</td>
<td>7 vs 34</td>
<td>2.7 (1.2 to 5.8)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Patient care

- Use of bespoke footwear (%)  8       16  2.6 (1.2 to 4.3)  0.026
- Walking barefoot at home (%) 28     43  2.0 (1.2 to 3.1)  0.004
- Routine podiatry attendance (%) 70  44  0.3 (0.2 to 0.5)  <0.0001
- Daily inspection of foot (%)  70    29  0.2 (0.1 to 0.3)  <0.0001

ADA TASK FORCE REPORT

Risk factors for foot ulcers
- Previous amputation
- Past foot ulcer history
- Peripheral neuropathy
- Foot deformity
- Peripheral vascular disease
- Visual impairment
- Diabetic nephropathy (especially those on dialysis)
- Poor glycemic control
- Cigarette smoking

Boulton AJM et al, Diabetes Care 2008;31:1679.

Mortality after amputation in CKD & Haemodialysis

- CKD and dialysis treatment are independent risk factors for mortality after lower extremity amputation.
- 10-year mortality among patients on dialysis who have an amputation X 3 greater than patients that require amputation without CKD.
- Mortality in this population is higher than many other disease processes such as coronary artery disease and cancer

Mortality, Dialysis and Foot Ulceration

- 192 diabetic dialysis patients followed for 2 years
- Overall 2 yr mortality 53%: 59% if foot ulcer at baseline; 74% if amputation: p<0.001.
- Mortality after amputation - 290% increase in hazard for those on dialysis
- Need for foot care on dialysis units

Recommendations

3. Vascular Assessment

- Foot pulse assessment – dichotomous
  IF ANY PULSE ABSENT or Hx of PVD, then
- Ankle Brachial Index if possible.

Recommendations

What about the ABI?

- ADA/ACC recommend that all those patients >50 years old should have an annual ABI
- Is this practical
- Could this give rise to a false sense of security?
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Charcot neuroarthropathy (CNA):
The osteolysis/vascular calcification paradox
Contrasting fortunes: Chalk or Cheese

RANKL/OPG and Vascular Calcification

- RANKL/OPG signaling pathway plays a role in vascular calcification
- Human VSMCs cultured in serum from CN patients show accelerated osteoblastic differentiation
- This pathway is a potential target for intervention

Ndip A et al, Diabetes 2011;60:2187

Multidisciplinary team

- Diabetologists
- Interventional Radiologists
- Nurses
- Orthotist
- Patient
- Podiatrist
- Surgeons

No conflicting advice

For one mistake made for not knowing, ten mistakes are made for not looking.

J A Lindsay