Diabetic foot ulcer:
A diabetologist's perspective

Jong Chul Won, M.D., Ph.D.

Division of Endocrinology, Department of Internal Medicine, Sanggye Paik Hospital, College of Medicine, Inje University, Seoul
F/77yr. C/C Fever and discolored 5th toe, Rt.

DM for 20 yr with OAD (A1C: 10.4%)
F/77. C/C Fever and discolored 5th toe, Rt.
DM for 20 yr with OAD (A1C: 10.4%)

CPG: 296 mg/dL, WBC; 19,250/uL, ESR; 28.7mm/Hr, CRP; 5.9mg/dL
CT angiography: mild calcification in bilateral SFA
X-ray: lysis including 5th MTP joint
Emergent 5th toe amputation & Debridement
What do we know and what should we do to prevent or manage patients with diabetic foot disorder, especially diabetic foot ulcer (DFU)?

What’s the role of diabetologist?
What do we know and what should we do to prevent or manage patients with diabetic foot disorder, especially diabetic foot ulcer (DFU)?

What’s the role of diabetologist?

But, unfortunately, there are few things to do for diabetologist in patients with ulcerated foot.
1. Clinical implication of DFU
2. Diabetes and DFU
3. The role of diabetologist in the management of patients with DFU
4. Multidisciplinary management of patients with DFU
1. Clinical implication of DFU
2. Diabetes and DFU
3. The role of diabetologist in management of patients with DFU
4. Multidisciplinary management of patients with DFU
Complications of diabetes

Chronic complications of diabetes

- Blindness
- Kidney disease
- Nerve damage
- Amputation

Cardiovascular disease:
- Stroke
- Heart attack
- Loss of circulation in arms and legs
Nearly one third to half of patients with diabetes may have diabetic neuropathy.

Won JC, Diabetic Medicine, 2012
Won JC, DRCP, 2014
Won JC, DMJ, 2014
Diabetic neuropathy is the earliest complication and it’s prevalence is increased along the duration of diabetes

Temporal prevalence (%) of diabetic complications according to quartile of duration of diabetes (yr)

- Neuropathy
- Retinopathy
- Nephropathy
- Any macroangiopathy

All \( P \) for trend < 0.05

Won JC, Diabetic Medicine, 2012
Won JC, DRCP, 2014
Won JC, DMJ, 2014
In patients with diabetes, foot problems are...

The combination of nerve damage and insufficient blood supply in the legs and feet of people with diabetes often leads to painful ulcers, infection and gangrene. This can ultimately result in amputation and even death.
Diabetes in Korea, 2007

Foot amputation ($N=3,829$, 2003)  
- Diabetic: 55.2%  
- Non-diabetic: 44.8%

Foot ulcer ($N=8,495$, 2003)  
- Diabetic: 61.6%  
- Non-diabetic: 44.8%

KDA. Diabetes in Korea, 2007
DFU: a serious complication-incidence

- Among all patients with diabetes, UP TO 4% ANNUALLY will develop a DFU.
- Nearly a quarter of patients with diabetes will develop a diabetic foot ulcer (DFU).

DFU: a serious complication-complicated

- DFUs that persist more than 4 weeks have 5-fold higher risk of infection.
- Infected foot ulcer increases the risk for hospitalization 55.7 times and the risk for amputation 155 times.

M/72 yr. DM 20 YA with insulin. Bare foot in rice paddy. 4th toe OM. 4th ray amputation

Lavery et al. Diabetes Care. 2006
DFU: a serious complication - mortality

6 of 10 Patients Who Receive Their First Amputation Die within 5 Years

66% higher risk of death

Deaths Each Year per 1000

Diabetes - No Amputation  Diabetes - Amputation
DFU: a serious complication—mortality

- 5 yr mortality rate of DFU is comparable or worse than for most malignancies

The most serious problem:???

What do you think about the most serious problem in patients with DFU?
The most serious problem of DFU is “unawareness”

- Despite the high prevalence or available education program in each hospital, only 1 among the eight patients with DPN know about their foot problem.

- High rate of education, but low level of awareness their having DPN

---

**Awareness**
- Yes: 12.6%
- No: 87.4%

**Education**
- 27.2%
- 72.8%

Won JC, Diabetic Medicine, 2012
Won JC, DRCP, 2014
Won JC, DMJ, 2014
1. Clinical implication of diabetic DFU
2. Diabetes and DFU
3. The role of diabetologist in management of patients with DFU
4. Multidisciplinary management of patients with DFU
Diabetes: biochemical diseases

- Cellular senescence
- Growth factor/Cytokine deficiency
- Diminished angiogenesis
- MMP/TIMP imbalance
- Matrix degradation and turnover

Diabetes: biochemical and biomechanical disease

- “Diabetes mellitus is a biochemical disease, but a large number of lower extremity complications of the disorder are due to biomechanical dysfunction.”

- Diabetics may have altered biomechanics; or present with a complication of any pre-existing neurovascular or biomechanical dysfunction
Three main risk factors for DFU

- Neuropathy
  - Sensory
  - Autonomic
  - Motor
  - Risk factors for neuropathy include: High levels of glycaemia, elevated triglycerides, high BMI, smoking & hypertension.
- Excessive plantar pressure
- Trauma
Risk factors for DFU

- Sensory Neuropathy
  - Largest single risk factor for diabetic foot ulcers
    - Burning, tingling, "pins & needles", numbness or "dead" feeling
    - Repeated unrecognized stress, pressure, friction & shearing.
  - Lack of sensation to feel foreign objects, heat changes, discomfort or pain.

M/57 yr (DM 20YA)
A1C, 7.4%
Insensate feet
S/P 5th ray amputation
Risk factors for DFU

- Autonomic Neuropathy
  - Impairs skin integrity, sweat regulation & blood flow.
  - Leads to thick, dry cracked skin, fissures and callus build-up at pressure points
Risk factors for DFU

- Motor Neuropathy results in
  - Loss of muscle tone in the foot
  - Foot deformities:
    - Hammer toes
    - Claw toes
    - Metatarsal heads become prominent
    - Changes in pressure distribution & gait pattern
Risk factors for DFU

- In real practice setting (busy clinic)
  - Under-diagnosis of neuropathy could be fundamental problem in primary care.
  - Impedes early identification, management & prevention of complicated DFU.

M/53 yr
A1C, 11.7%

Self-diagnosis
“Dr, please see my foot”

CT angio: Severe stenosis of both CIA and Rt dorsalis pedis
S/P Lisfranc amputation
We need time and
.
.
.
chair to look at patients’ feet!
Contributory factors for DFU

- Chronic hyperglycemia results in triad;
  - Neuropathy
  - Ischemia
  - Infection

- Incidentally, a Korean study reported higher prevalence of peripheral artery disease in patients with diabetic peripheral neuropathy (OR 5.29, 95% CI 3.06-9.16, \( P < 0.01 \)).
  - These share common risk factors such as co-morbidities, duration of diabetes, atherosclerosis

High risk of infection in patients with diabetes

- Why are diabetics prone to infection?
  - Immune system defects
    - Abnormalities in cell-mediated immunity
    - PMN dysfunction: Impaired migration, phagocytosis, intracellular killing, chemotaxis
  - Other considerations: Decreased vascularization, compromised local circulation, colonization by microorganisms

- Infections cause imbalance in glucose control: counter-regulatory hormone, cytokines
1. Clinical implication of diabetic DFU

2. Diabetes and DFU

3. The role of diabetologist in management of patients with DFU

4. Multidisciplinary management of patients with DFU
Inside perspective: the role of the diabetologist in DFU

- Prevention of development of DFU
  - Screening to Identify Patients at Risk
  - Educational Interventions
  - Clinical Interventions

- Treatment of diabetic patients with acutely diseased foot to prevent further problems
  - Management of hyperglycemia and other risk factors
  - Perioperative management
Prevention of development of DFU
Preventing DFU begins with identifying “at-risk” foot

- We should pay attention to patients with high risk foot.
  - H/O foot ulcer [RR, 1.6; 95% CI 1.2-2.3, P = 0.004]
  - S/P L/E amputation [2.8; 1.8-4.3, P < 0.001]
  - Duration of diabetes (>10yr) [OR, 3.0, P<0.03]
  - A1C >9% [OR, 3.2, P<0.03]
  - Visual acuity < 20/40 [RR, 1.9;1.4-2.6, P<0.001]
  - Structural abnormalities (calluses, hammer or claw toes, flat feet, bunions), reduced joint mobility, dry or fissured skin, tinea, or onychomycosis
Screening to identify patients at risk for DFU

- Screening for Loss of Protective Sensation
- Screening for Peripheral Vascular Disease
Screening to identify patients at risk for DFU

● Screening for Loss of Protective Sensation
  - Monofilament
  - Biothesiometer
  - Tuning Fork

F/73 yr
A1C, 14.76%
Insensate foot
S/P 1st ray amputation
Monofilament is the most simple, inexpensive and accurate method

- Screening methods of increased risk of DFU

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Monofilament</th>
<th>Biothesiometer</th>
<th>Turning Fork</th>
<th>Pressure Mat</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/S(%)</td>
<td>≥1 insensate site</td>
<td>VPT&gt;25V</td>
<td>Loss of vibration</td>
<td>≥59 - 87.5N/cm²</td>
</tr>
<tr>
<td>S/P(%)</td>
<td>66-91</td>
<td>83-86</td>
<td>55-61</td>
<td>57-70</td>
</tr>
<tr>
<td>Comment</td>
<td>Inexpensive, quick, widely available</td>
<td>Similar to monofilament, less available</td>
<td>Inexpensive, less predictive</td>
<td>Device-specific</td>
</tr>
</tbody>
</table>
Monofilament to detect loss of protective sensation

- Monofilament (10 sites vs. 4 sites): While authorities recommend testing 8-10 anatomic sites, testing just 4 plantar sites on the forefoot identifies 90% of patients with an insensate site.

Litzelman DK et al, Ann Intern Med, 1993
Screening peripheral arterial diseases by ABI

- ABI (ankle brachial index)
  - <0.9, PAOD; >1.1, falsely elevated pressure (medical arterial calcinosis)

- Transcutaneous oximetry

M/69 yr (DM, 30YA)
A1C, 9.0%
Rt calf multifocal stenosis
S/P Bypass and amputation

M/50 yr
A1C, 13.6%
CRF and Severe occlusion of bilateral popliteal arteries
S/P Fasciotomy (failed revascularization)
Educational interventions to prevent DFU

- **Patients education**
  - Modestly reduce risk of DFU.
  - Which format? How long? Long term effectiveness?

- **Physician education**
  - To improve clinicians’ performance with patient education (i.e., computerized register reminder’)
  - Implementing foot care clinical practice guideline
    - Annual foot examination
    - Risk stratification category
Clinical interventions to prevent DFU

- Optimizing Glycemic Control: DCCT, UKPDS
- Quit Smoking: strong predictor of amputation
- Foot examination by physician vs timely appropriate specialist referrals
- Custom footwear and orthotics, debridement of calluses
- Foot specialist and multidisciplinary team care
- Prophylactic foot surgeries
- Revascularization surgery
Treatment of diabetic patients with acutely diseased foot
Patients with diabetic foot disorders

- Patients with diabetic foot disorders have typically have significant comorbidities and concurrent hyperglycemia, CV disease, renal disease, and anemia.
  - So we need a multidisciplinary approach: Diabetologist, cardiologists, nephrologists, infectious disease specialist.

- The goal of management of patients with DFU is correcting hyperglycemia and avoiding hypoglycemia
A case control study of 108,593 patients who underwent non-cardiac surgery.

*Odds ratio for perioperative mortality is 1.19 (95% CI 1.1–1.3) per mmol/l increase of glucose level.
## In-hospital glycemic targets

### American Diabetes Association

**“Standards of Medical Care”**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Fasting</th>
<th>Non-Fasting</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical surgical</td>
<td>110 mg/dL</td>
<td>110 mg/dL</td>
<td>A</td>
</tr>
<tr>
<td>Critical non-surgical</td>
<td>&lt;140</td>
<td>&lt;140</td>
<td>C</td>
</tr>
<tr>
<td>Noncritical</td>
<td>&lt;126 mg/dL</td>
<td>&lt;180-200 mg/dL</td>
<td>E (Expert Consensus)</td>
</tr>
</tbody>
</table>

*ADA/AACE statement March 09 promised new guidelines and recommended targets similar to the "conventional" arm of NICE-SUGAR*

### American Heart Association: Hyperglycemia and Acute Coronary Syndrome

<table>
<thead>
<tr>
<th></th>
<th>Fasting</th>
<th></th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical</td>
<td>90-140 mg/dL</td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>Noncritical</td>
<td>&lt;180 mg/dL</td>
<td></td>
<td>C</td>
</tr>
</tbody>
</table>

### International Guidelines for Management of Severe Sepsis and Septic Shock

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical</td>
<td>&lt;150 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

### The Endocrine Society - Position Statement

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical</td>
<td>&lt;144-180 mg/dL</td>
</tr>
</tbody>
</table>
Basal-bolus regimen achieves better control than sliding scale alone

Protocols for glycemic control

Modified Alberti's Method

1. 측정대상
   FBS < 180mg/dL (일주일) 혹은 HbA1C < 8% (3개월) 이면서, 항목 중 하나라도 해당되는 경우
   ① 대수달
   ② 수달 후 급식이 24시간 이상
2. 측정일: 수술 전 날 오후6시 이후 (또는 저녁식사 후부터 시작)
1. Check BST q2hr
2. Electrolyte (2 회, q (12) hr)
*검사차원: comment: 시작 시점부터 1회는 4시간 간격, 그 이후 12시간 간격으로 측정
3. D10W 1L + 2 M KCl (15) cc mix IV with (100) cc/hr
4. N/S 500cc + RI 50unit mix IV with (10) cc/hr 혹은 1u/hr
5. 다음과 같이 BST에 따라 fluid의 주입 속도를 조절함.
   - BST가 120 mg/dL 미만이면 4번 fluid을 이전 속도보다 20 cc/hr (인슐린량은 2u/hr) 감소
   - BST가 120 - 200 mg/dL 이면 4번 fluid을 이전 속도 그대로
   - BST가 201 - 300 mg/dL 이면 4번 fluid을 이전 속도보다 5 cc/hr (인슐린량은 0.5u/hr) 증가
   - BST가 301 이상이면 4번 fluid을 이전 속도보다 10 cc/hr (인슐린량은 1u/hr) 증가
6. 다음과 같은 electrolyte (potassium 수치) 값에 따라 2 M KCL의 주입량 조절함.
   - K가 4 미만이면 2M KCl 30 cc 섞은 것으로 교체
   - K가 4-5면 그대로 유지
   - K가 5를 넘으면 KCL을 별 것으로 교체
7. 탁의 주입속도는 환자의 상태에 따라 초기 주입 속도를 다음을 참조하여 변경할 수 있다.
   ① 배합 (BMI >30), 만성 간질환, 스테로이드 사용, 감염(폐혈증)): 3u/hr 혹은 그 이상
   ② 심장수술 (cardiopulmonary bypass) 사용하거나 CAGB시행 등: 3u/hr 혹은 그 이상
   ③ 기존 인슐린 치료 중인 환자로서 일일 인슐린 투여량이 20 단위 이상이었던 경우: 2u/hr 이상
8. 주의 사항
   - 상기 방법으로 (Modified Alberti method) 혈당 조절 시에는 시작 후 최소시간 동안 측정한 혈당이 200mg/dL이상으로 높더라도 바로 인슐린 주입속도를 올리지 않고 관찰한다.
   - 현재 측정된 혈당이 늘어나도 떨어지는 추세가 있으면 인슐린 주입속도를 올리지 않고 그대로 유지하고, 같은 주입속도에서도 혈당이 계속 떨어지는 경우에는 혈당이 200mg/dL이하로 떨어지는 시간에서 주입속도를 시간당 1단위 줄이고 나서 다음 혈당을 관찰
   - 환자가 급식이 아닌 식사를 하는 경우에는 식전 30분 이내에 소초효성 인슐린 (novorapid, Apidra, 또는 humalog)을 4-6 단위 병위 내에서 피하주사를.

Insulin-glucose infusion protocol (DIGAMI protocol)

1. 적응 대상
   - 염증적인 혈당 조절이 필요한 경우 (감염증, 신근경색증, 수술 전후, 또는 지속적인 고혈당)
2. 저항력
   1. Check BST q2hr
   2. 혼합량:
      5% Dextrose Water (5%DW) 500 ml + Insulin aspart (NovoRapid®) 80 IU with (60) cc/hr
* 상기 혼합액의 경우, 인슐린 농도는 1 IU/6 cc
3. 1시간 후 혈당측정 후 다음 프로토콜에 따라 혼합 용액 주입 속도를 조절하며, 주입 속도를 변경한 경우에는 반드시 변경 1시간 후에 혈당을 측정함. 만약, 주입 속도를 변경하지 않은 경우에 는 2시간마다 혈당을 측정.
* 혈당 조절의 목표는 126-180 mg/dl입니다.
* 혼합용액의 주입속도

<table>
<thead>
<tr>
<th>혈당 값 (mg/dL)</th>
<th>조치</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 270</td>
<td>Novorapid 8 IU IV (bolus injection) 후에 주입속도를 6 cc/hr 증가</td>
</tr>
<tr>
<td>200 - 270</td>
<td>주입속도를 3 cc/hr 증가</td>
</tr>
<tr>
<td>126 - 200</td>
<td>변화 없음</td>
</tr>
<tr>
<td>70 - 126</td>
<td>6 cc/hr 감소</td>
</tr>
<tr>
<td>&lt; 70</td>
<td>15분 동안 주입 중단 후 혈당이 126 mg/dL가 될 때까지 15분 간격으로 혈당 측정. 저혈당 증상이 발현될 경우 (의사 판단) 50% 포도당 용액 50 cc 정맥주사 후 15분 간격으로 혈당 측정. 혈당이 126 mg/dL이 상이 되었을 경우 주입속도를 6 cc/hr로 다시 조정</td>
</tr>
</tbody>
</table>

4. 주의사항
   - 환자가 급식이 아닌 식사를 하는 경우에는 식전 30분 이내에 Novorapid를 4 - 6 IU 병위 내에서 피하주사.
   - 현재 측정된 혈당이 높더라도 떨어지는 추세에 있으면 (최초 1시간 내 혈당 감소가 60 mg/dL 이상인 경우) 용액의 주입속도를 변경하지 말고 그대로 유지할 것.
1. Clinical implication of diabetic DFU
2. Diabetes and DFU
3. The role of diabetologist in management of patients with DFU
4. Multidisciplinary management of patients with DFU
Eight essential skills to manage patients with DFU: multidisciplinary

1. The ability to perform hemodynamic and anatomic vascular assessment with revascularization intervention.

2. The ability to perform neurological workup using rapid assessment of this at the bedside should be performed using various validated techniques.

3. The ability to perform site-appropriate deep culture technique to direct antibiotic therapy.

4. The ability to perform wound assessment and staging/grading of infection and ischemia using a suitably validated wound classification system.

Eight essential skills to manage patients with DFU: multidisciplinary

5. The ability to perform **site-specific bedside and intraoperative incision and debridement** to decompress limb-threatening abscesses.

6. The ability to **initiate and modify culture-specific and patient-appropriate antibiotic therapy** after an initial course of broad spectrum antibiotic therapy.

7. The ability to perform appropriate **postoperative monitoring** to reduce risk of reulceration and infection.

8. The ability to **provide basic foot care education and referral to a self-management education program**.

Among them the most important tip is the leader’s role in multidisciplinary team

“The leader of the team can be from any specialty, with the major asset being a passion for this type of work”

Wukich DK et al. Diabetes Care 2013
Conclusion

- Foot problems are a major cause of morbidity & mortality in patients with diabetes.

- Management of DFU requires an interdisciplinary approach (glycemic control, infection, vascular status, foot wear & wound care).

- Uncontrolled hyperglycemia may result in immunopathy and deleterious effects on glycemic control.

- Awareness & intervention can prevent many problems with the diabetic foot.
Thank you for your attention!

Special thanks to Prof. Hyung Jin Chung (Sanggye Foot and Ankle Center, Inje University) for sharing of clinical cases.