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The effect of creatinine clearance on the short-term outcome of neuropathic diabetic foot ulcers

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ABSTRACT

Reduced creatinine clearance is related to an increased risk for diabetic foot ulcer development. Wound healing has been reported to be worse in diabetic patients with impaired kidney functions than general diabetic population. This study aimed to investigate the effect of creatinine clearance on the short-term outcome of neuropathic diabetic foot ulcers.

Data from 147 neuropathic diabetic foot ulcer episodes were included in this observational study. Patients were admitted to Dokuz Eylul University Hospital between January 2003 and June 2008. Patients were excluded if they had limb ischemia. Diabetic nephropathy was investigated by 24 h urinary albumin excretion and serum creatinine levels. Creatinine clearance was calculated according to Cockcroft–Gault formula. Foot ulcers were followed up for 6 months to determine the outcome.

Our short-term follow-up revealed that neuropathic diabetic ulcers healed worse in patients with decreased creatinine clearance than in those who had normal creatinine clearance. Amputation rates were also found to be higher.

Our results suggest that creatinine clearance is an important factor affecting wound healing in patients with neuropathic diabetic foot ulcers.

1. Introduction:

Diabetic foot ulcers precede 85% of non-traumatic lower-extremity amputations [1]. Diabetic neuropathy accounts for the majority of cases presenting with diabetic foot ulcers. The outcome is insensitive feet which are vulnerable to repeating traumas such as stepping on a sharp object or, simply, injury due to ill-fitting shoes [2]. Neuropathy is also associated with impaired innervation of foot muscles which leads to muscular atrophy and deformities, diminished sweating which results in dry skin and callus formation, and loss of proprioception, all of which are major risk factors for ulcer formation [3].

Diabetic nephropathy is a major chronic complication of diabetes, which is associated with morbidity and reduced survival. Diabetic nephropathy usually accompanies retinopathy and neuropathy [4]. Renal failure due to diabetic nephropathy is associated with an increased risk for developing a diabetic foot ulcer [5]. The amputation rate is significantly higher among diabetic patients with impaired kidney functions than

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general diabetic population [6,7]. This increased amputation risk has been mostly associated with arterial calcifications, namely with the severity of peripheral artery disease [5,8–10]. However, animal studies have shown that uraemia, per se, is associated with poor wound healing [11,12].

Creatinine clearance (CCre) is widely used to estimate glomerular filtration rate (GFR) in clinical practice [13]. The error margin of CCre is acceptable considering the ease of its assay in routine practice [14]. CCre can be simply calculated by Cockcroft–Gault formula [15]. The aim of this observational study was to determine the effect of the creatinine clearance on the ulcer outcome in patients with neuropathic diabetic foot ulcers in the short-term.

2. Materials and methods

This observational study includes the data of 147 neuropathic diabetic foot ulcer episodes in patients who admitted to Dokuz Eylul University Hospital between January 2003 and June 2008. Data were collected prospectively, and used retrospectively to compare the outcome of patients with various degrees of renal impairment. Neuropathic foot ulcers were followed up for 6 months to determine the outcome.

Diabetic neuropathy was evaluated by 10 g monofilament test. Loss of vibration perception was evaluated by a biothesiometer on the pulp of the hallux. Symptoms of neuropathy were questioned. Further neurological assessments were done when required. Limb ischemia was evaluated by palpation of the peripheral pulses and ankle brachial pressure index (ABI) using a handheld Doppler. Patients with absent or reduced pedal pulses or ABI < 0.9 were excluded from the study. Ulcer episodes were excluded if they could be followed for less than 6 months.

Characteristics of patients were recorded at presentation. Weight was measured. A photograph of the ulcer was taken. The site and the largest diameter of the ulcer were noted. Depth of the ulcer was determined by inspection, with additional use of a sterile probe if indicated. Ulcers were classified according to the Wagner classification. Wagner classification grades were as follows: 0 (risk for development of foot ulcer), 1 (ulcerated skin and subcutaneous tissue), 2 (deeper lesions may penetrate to tendon, bone, or joint capsule, there is yet no abscess or osteomyelitis), 3 (deep tissues are involved, abscess, osteitis or osteomyelitis are present), 4 (local gangrene), 5 (diffuse gangrene). Plain X-ray films of affected bones were taken. Magnetic resonance imaging (MRI) of the extremity was performed in selected patients. Infection was defined according to the Infectious Diseases Society of America guidelines, as the presence of purulent wound drainage or ≥3 (designated systemic or local inflammatory findings.

Baseline serum albumin, glycosylated haemoglobin (A1c), and haemoglobin levels were recorded. Diabetic nephropathy was investigated with 24 h urinary albumin excretion and serum creatinine levels. CCre was calculated according to Cockcroft–Gault formula. Because of our relatively small

Table 1 – Baseline characteristics of patients with various levels of CCre.

	Group A CCre ≥90 ml/min/1.73 m^2 (n = 33)	Group B CCre 30–89 ml/min/1.73 m^2 (n = 97)	Group C CCre <30 ml/min/1.73 m^2 (n = 17)
Age (years)[*] [†]	51.94 ± 1.24	63.2 ± 0.95	61.06 ± 3.27
Male	23 (69.7%)	54 (55.7%)	10 (58.8%)
Diabetes duration (years) [*],[†],[‡]	11.03 ± 1.07	16.39 ± 0.84	23.65 ± 2.54
Smoking	11 (33.3%)	24 (24.7%)	5 (29.4%)
BMI (kg/m^2)	28.55 ± 4.49	26.77 ± 3.88	26.83 ± 3.98
Site of ulcer			
Toe	17 (51.5%)	45 (47.9%)	9 (52.9%)
Fore-foot	9 (27.3%)	20 (20.6%)	3 (17.6%)
Mid-foot	4 (12.1%)	9 (9.3%)	1 (5.9%)
Hind-foot	0	17 (17.5%)	4 (23.5%)
Leg	3 (9.1%)	6 (6.2%)	0
Wagner score			
1	1 (3%)	9 (9.3%)	2 (11.8%)
2	21 (63.6%)	49 (50.5%)	10 (58.8%)
3	9 (27.3%)	34 (35.1%)	5 (29.4%)
4	2 (6.1%)	5 (5.2%)	0
5	0	0	0
Ulcer diameter (cm)	4.5 ± 0.59	4.57 ± 0.41	5 ± 1.25
Osteomyelitis	9 (27.3%)	33 (34%)	5 (29.4%)
Hemoglobin (g/dl)[†],[‡]	12.61 ± 0.29	12.38 ± 0.28	10.97 ± 0.52
Albumin (g/dl)	4.05 ± 0.55	3.92 ± 0.59	3.81 ± 0.36
A1c (%)[†],[‡]	9.59 ± 0.42	9.27 ± 0.23	8.1 ± 0.74

A1c: hemoglobin A1c, BMI: body mass index, CCre: creatinine clearance, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, WBC: white blood cell count.

[*] CCre ≥ 90 ml/min/1.73 m^2 vs. CCre 30–89 ml/min/1.73 m^2, $p < 0.05$.

[†] CCre ≥ 90 ml/min/1.73 m^2 vs. CCre < 30 ml/min/1.73 m^2, $p < 0.05$.

[‡] CCre 30–89 ml/min/1.73m2 vs. CCre < 30 ml/min/1.73 m^2, $p < 0.05$.