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ORIGINAL ARTICLE

Incidence and Recovery of Acute Kidney Injury in Diabetic and Nondiabetic Patients with Foot Infections

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Background: The aim of this study was to evaluate the incidence and recovery of acute kidney injury (AKI) in patients admitted to hospital with and without diabetes with foot infections.

Methods: We retrospectively reviewed 294 patients with diabetes and 88 without diabetes admitted to hospital with foot infections. KDIGO guidelines were used to define AKI. Recovery was divided into three categories: full, partial, and no recovery within 90 days of the index AKI.

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Results: AKI incidence was 3.0 times higher in patients with diabetes (DM 48.5% vs no DM 23.9%, CI 1.74-5.19, p<0.01). AKI incidence was similar at each stage in people with and without diabetes: Stage 1 DM 58.1% vs. no DM 47.6%, Stage 2 DM 23.3% vs. no DM 33.3%, and Stage 3 DM 18.6% vs. no DM 19.1%. Twenty-nine patients with diabetes had a second AKI event and four had a third event. In patients without diabetes one patient had a second AKI. Cumulative AKI incidence was 4.7 times higher in people with diabetes (DM 60.9% vs. no-DM 25.0%, CI 2.72-8.03, p<0.01). Patients with diabetes progressed to CKD or in CKD stage 39.4% of the time. Patients without diabetes progressed 16.7% of the time, but this trend was not significant (p=0.07). Complete recovery was 3.8 times more likely in patients without diabetes (CI 1.26-11.16, p=0.02). Conclusions: AKI incidence is higher in patients with diabetes and complete recovery after an AKI is less likely compared to patients without diabetes.

Keywords: Diabetic Foot, Infection, Osteomyelitis, Outcomes, AKI

Diabetic foot infections (DFI) are one of the most common underlying causes of hospitalization in people with diabetes [1, 2]. In addition to the stress of infection, these patients often have multiple co-morbidities, require multiple medications, undergo multiple surgeries and require prolonged exposure to antibiotics that predispose them to acute kidney injury (AKI). AKI is associated with increased mortality and progression of chronic kidney disease (CKD) that increases proportionally based on the severity of the event [3, 4]. Even in patients that recover, patients with AKI have worse long term clinical outcomes compared to patients with no history

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of AKI [5, 6]. We previously identified an incidence of AKI of 27% in a cohort of patients with diabetes and osteomyelitis [7]. The aim of this study was to evaluate the incidence and recovery of acute kidney injury in patients with and without diabetes admitted to the hospital with moderate and severe foot infections.

METHODS

Patient Selection

After approval by the institutional review board, medical records of patients treated between June 2009 and February 2017 for foot infection were reviewed. The records of ~~two hundred and ninety four~~ 294 patients with diabetes and 88 patients without diabetes were reviewed who were admitted to the hospital with an Infectious Diseases Society of America (IDSA) moderate or severe foot infection [8]. The diagnosis of diabetes was based on criteria from the American Diabetes Association [9]. Presence of a severe infection was identified by clinical recognition of two or more of the following systemic inflammatory response syndrome (SIRS) criteria [8]: heart rate >90 beats per minute, temperature >38ºC or <36ºC, respiratory rate >20 breaths per minute or PaCO2 <32 mmHg, white blood cell count (WBC) >12,000 cells/mm^3 or <4,000 cells/mm^3 or >10% immature bands. In addition, patient laboratory values including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum albumin, and hemoglobin were recorded.

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Identification of AKI

We used the Kidney Disease: Improving Global Outcomes (KDIGO) serum creatinine criteria for AKI diagnosis and staging [10]. AKI could be diagnosed if (1) there was an increase in serum creatinine by ≥0.3mg/dl (≥26.5 mol/l) within 48 hours in patients without CKD, or (2) an increase in creatinine to 1.5 times baseline in patients with and without CKD. The KDIGO AKI serum creatinine criteria states that stage 1 AKI is a creatine elevation 1.5–1.9 times baseline, stage 2 is 2.0–2.9 times baseline and stage 3 is 3.0 times baseline [10]. Urine output criteria was not considered as part of AKI criteria. Baseline creatinine was defined as the lowest creatinine measurement during hospitalization or, if available, the mean of all creatinine measurements 7-365 days before the index admission [11]. Patients with CKD Stage 5 were excluded.

Patient Follow-up and Outcomes

Patients were included in the study if they were followed for at least 12 months or until they expired. Patients with less than 12 months of follow up were excluded. The outcomes evaluated were the need for surgical intervention, lower-extremity amputation (LEA), hospital length of stay (LOS), wound healing, reinfection, readmission, and mortality.

AKI recovery was divided into 3 categories. Complete recovery was defined as patients who achieved a creatinine level that was within 115% of baseline levels [12], and partial recovery was defined as a creatinine level that remained 115% above baseline levels but less than 1.5 times

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baseline levels. No recovery was defined as a creatinine level that remained greater than 1.5 times the baseline value. CKD progression and estimated glomerular filtration rate values were determined by examining electronic medical records.

Statistical Analysis

Patient data were summarized using descriptive statistics. Median, mean and standard deviation were used for continuous variables while frequency and percentage were used for categorical variables. Characteristics and outcomes between patients with and without AKI were compared using parametric (Student *t* test, χ^2 test,) and non-parametric tests (Mann-Whitney *U* test, Fisher exact test) as appropriate.

RESULTS

AKI occurred in 150 patients (42.4%) with foot infections. There was a significant difference in the incidence of AKI between patients with and without diabetes. The incidence of AKI was 48.5% in patients with diabetes and 23.9% in patients without diabetes. There was no difference in timing (AKI present on admission, during hospitalization, or after discharge) in patients with and without diabetes. The incidence of the first AKI event during the index hospitalization was 3.0 times higher in patients with diabetes (48.5 vs. 23.9%, CI 1.74-5.19, $p<0.01$). The incidence of AKI was similar at each stage in people with and without diabetes: Stage 1 DM 58.1% vs. no DM 47.6%, ($p=0.37$), Stage 2 DM 23.3% vs. no DM 33.3% ($p=0.32$), and

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Stage 3 DM 18.6% vs. no DM 19.0% (p=0.96). Among patients with diabetes, 29 had a second AKI event and four had a third event. In patients without diabetes, only one had a second AKI event. Patients with diabetic foot infections were 10.6 times more likely to have multiple AKI events than patients without diabetes (DM 10.9% vs. no DM 1.1%, CI 1.43-79.33). The cumulative incidence of AKI was 4.7 times higher in people with diabetes (DM 60.9% vs. no DM 25%, CI 2.72-8.03, p<0.01) (Table 1).

After an AKI event, full recovery to baseline creatinine levels was more likely in patients without diabetes. Complete recovery was 3.8 times more likely in people without diabetes (72.2% vs 40.9%, CI 1.26-11.16, p=0.02). Patients with AKI and diabetes progressed to CKD or progressed in CKD stage 39.4% of the time. Patients without diabetes progressed at less than half the rate of patients with diabetes (16.7%, p=0.07) (Table 2).

DISCUSSION

To the best of our knowledge, this is the first study to compare the incidence AKI in patients treated for foot infections with and without diabetes. We report the incidence of the first AKI episode and the cumulative incidence of AKI, as well as the progression of renal disease after AKI in a cohort of 392 patients with foot infection. AKI is a frequent complication of hospitalization, and is associated with increased resource utilization [13], higher short-term and long-term mortality [13-15], progressive decline of renal function leading to the development of

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CKD and ESRD, as well as a decrease in quality of life [16]. Recent studies also suggest that AKI is a risk factor for cardiovascular disease, sepsis, malignancy, bone fracture and upper gastrointestinal hemorrhage [17-21]. Foot infection is a sentinel event that often necessitates multiple surgeries, repeated infections, multiple hospitalizations and prolonged exposure to parenteral and oral antibiotics [7]. Many of the risk factors for AKI are common in patients with foot infections including diabetes, sepsis, peripheral vascular disease, hypertension, congestive heart failure, and low serum albumin [6, 22]. In addition, upon presentation these patients often have pre-renal azotemia secondary to dehydration. This relative hypovolemia also increases the risk of renal injury from antibiotics. These shared risk factors for the development of AKI and foot infection, along with the high incidence of AKI we are reporting, have direct clinical relevance and implications on how to manage this patient population. Patient admitted to hospital with diabetes and foot infection often have multiple co-morbidities as demonstrated in Table 1.

Our observations were novel as we evaluated a cohort of patients with and without diabetes admitted to the hospital with moderate and severe foot infections. We reviewed electronic medical records to evaluate serial creatinine levels to evaluate progression of disease. We identified a higher incidence of AKI in people with diabetes and a higher rate of multiple AKI events compared to patients without diabetes. Intuitively it makes sense that patients with diabetes have higher rates of AKI than non-diabetic patients. Patients with diabetic foot

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infections frequently have peripheral neuropathy, a comorbidity that is associated with microvascular changes common in diabetic patients with CKD.

The incidence of hospital induced AKI varies considerably, ranging from 6.4% [23] to 21% [24, 25] for all admissions. In high risk sub-populations, such as cardiac thoracic surgery (24.3%), sepsis, critical care (31.7%) or trauma patients (19.9%) the incidence is dramatically higher [25] among patients with diabetes the risk of AKI increases in high risk sub-populations. The incidence of AKI in patients with diabetes is much higher than patients without diabetes, and ranges from 20% after coronary artery bypass surgery [26] to 72.5% in patients admitted to intensive care for sepsis [27]. The three-fold increased risk of AKI in patients with diabetes and foot infections is the highest we have identified in the medical literature.

The consequences of an AKI event are important because AKI is associated with an increased risk of progression to CKD and death. Even among patients that have a full recovery, there is an increased risk of CKD, ESRD, and death [28]. For instance, in a retrospective study of a Veterans Health Administration database, Heung and colleagues evaluated 17,049 patients with AKI and 87,715 patients without AKI. Most of the AKI events were stage 1 (91%) with 71% of these patients achieving a full recovery within 2 days. Over the next year, 32% of AKI Stage 1 patients developed CKD 3 or higher [29]. In our current study, only 41% of patients with diabetes had a

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full recovery and returned to within 115% of their baseline creatinine levels within 90 days of the index AKI event. In contrast, 72% of patients without diabetes had a full recovery.

There are a number of ways baseline creatinine and return to baseline creatinine have been operationalized in the literature. The criteria we used to determine baseline was defined as the lowest creatinine measurement during hospitalization (KDIGO), or if available the arithmetic mean of all creatinine measurements 7-365 days before the index admission [30]. A common limitation of studying AKI is the unavailability of baseline creatinine in hospital datasets, prompting the use of surrogate estimates. The Acute Dialysis Quality Initiative advocates assigning a single estimated GFR of 75ml/min per 1.73 m^2 and "back calculation" of creatinine using the Modification of Diet in Renal Disease Equation for all patients with missing baseline creatinine data [31]. However, the advantages of this approach come at the risk for increasing misclassification, particularly among patients with CKD, who are at highest risk for AKI [30]. Because our study had a substantial proportion of these patients this method would have potentially overestimated disease incidence and severity while diluting or inflating associations between AKI and subsequent recovery. Another method used in many published reports is to base the definition of AKI on International Classification of Diseases (ICD) codes. In our review of electronic medical records and in studies that evaluate automated systems to identify AKI [32], many AKI events during hospitalization are not identified or recorded. The reports of AKI that rely on ICD codes probably underestimate the incidence of disease in the general population. In

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contrast, high risk patients, such as patients in intensive care for sepsis of after cardiac surgery, probably have more intensive monitoring for AKI events and better documentation. Since there are several criteria to define AKI, reporting will depend on the criteria used by treating physicians.

Post AKI renal function was assessed using creatinine values drawn closest to 90 days after the AKI episode. A 90-day time frame was used based on the KDIGO guidelines, which define CKD as a persistent decline in renal function lasting >90 days. We chose to stratify recovery into 3 categories. Complete recovery was defined as patients who achieved a creatinine level that was within 115% of baseline levels, and partial recovery was defined as a creatinine level that remained 115% above baseline levels but less than 1.5 times baseline levels. No recovery was defined as a creatinine level that remained greater than 1.5 times the baseline creatinine value. It was important to include the “partial recovery” category as population studies have shown that patients who achieve a recovery of creatinine level that remains above 115% of baseline levels still carry an increased mortality risk [12]. We believe the assessment of kidney function using creatinine drawn approximately 90 days after an AKI event may allow risk stratification for long term outcomes and assist in decision making with regard to ongoing follow up in this vulnerable patient population.

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There are several limitations to this study. This retrospective cohort study was conducted at a single center that serves a predominately low income, minority population. The sample size was relatively small, especially when AKI events were stratified into groups of patients with and without diabetes and then by the three stages of AKI. Another potential limitation is ascertainment bias. Patients that had soft tissue infection rather than osteomyelitis and patients that did not require surgery or amputation were more likely not to complete the one-year follow-up. They were therefore not included in the analysis. Sicker patients were probably more likely to stay in the system because they required treatment for other co-morbidities. These patients were more likely to have multiple creatinine values as well as longer exposure to nephrotoxic antibiotics that both required creatinine monitoring and increased the risk of AKI and CKD.

The incidence of AKI in foot infections is among the highest reported in the medical literature. Patients with diabetes are three times more likely to have an AKI episode and 10.6 times more likely to have two or more AKI episodes compared to patients without diabetes and a foot infection. Within 90 days after the index AKI event, most patients with diabetes did not return to their baseline creatinine (59%). New strategies should be put in place that focus on prevention, early detection and treatment of AKI in patients with diabetic foot infections to prevent the progression to CKD and end stage renal disease.

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CRediT Author Statement

Easton Ryan: Data curation, Investigation, Writing- Original draft preparation, Reviewing and Editing Peter **Andrew Crisologo:** Data Curation, Formal Analysis, Writing- Original draft preparation, Reviewing and Editing **Orhan K. Oz:** Reviewing and Editing **Javier La Fontaine:** Reviewing and Editing **Dane K Wukich:** Writing- Original draft preparation, Reviewing and Editing **Matthew Malone:** Reviewing and Editing **Lawrence A. Lavery:** Writing- Original draft preparation, Reviewing and Editing, Supervision

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References

1. Hicks CW, Selvarajah S, Mathioudakis N, et al. Burden of Infected Diabetic Foot Ulcers on Hospital Admissions and Costs. *Ann Vasc Surg*. May 2016;33:149-58. doi:10.1016/j.avsg.2015.11.025
2. Lavery LA, Lavery DC, Hunt NA, La Fontaine J, Ndip A, Boulton AJ. Amputations and foot-related hospitalisations disproportionately affect dialysis patients. *Int Wound J*. Oct 2015;12(5):523-6. doi:10.1111/iwj.12146
3. Fortrie G, de Geus HRH, Betjes MGH. The aftermath of acute kidney injury: a narrative review of long-term mortality and renal function. *Crit Care*. Jan 24 2019;23(1):24. doi:10.1186/s13054-019-2314-z
4. Horne KL, Packington R, Monaghan J, Reilly T, Selby NM. Three-year outcomes after acute kidney injury: results of a prospective parallel group cohort study. *BMJ Open*. Mar 29 2017;7(3):e015316. doi:10.1136/bmjopen-2016-015316
5. Lafrance JP, Miller DR. Acute kidney injury associates with increased long-term mortality. *J Am Soc Nephrol*. Feb 2010;21(2):345-52. doi:10.1681/ASN.2009060636

Online Early
DOI: 10.7547/20-167

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6. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol*. Jan 2009;20(1):223-8. doi:10.1681/ASN.2007080837
7. van Asten SAV, Mithani M, Peters EJG, La Fontaine J, Kim PJ, Lavery LA. Complications during the treatment of diabetic foot osteomyelitis. *Diabetes Res Clin Pract*. Jan 2018;135:58-64. doi:10.1016/j.diabres.2017.06.002
8. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. Jun 2012;54(12):e132-73. doi:10.1093/cid/cis346
9. American Diabetes A. 2. Classification and Diagnosis of Diabetes. *Diabetes care*. Jan 2017;40(Suppl 1):S11-S24. doi:10.2337/dc17-S005
10. KDIGO: Clinical Practice Guideline for Acute Kidney Injury. *Kidney International*. 2012;(2):1-138.
11. Siew ED, Ikizler TA, Matheny ME, et al. Estimating baseline kidney function in hospitalized patients with impaired kidney function. *Clin J Am Soc Nephrol*. May 2012;7(5):712-9. doi:10.2215/CJN.10821011
12. Pannu N, James M, Hemmelgarn B, Klarenbach S, Alberta Kidney Disease N. Association between AKI, recovery of renal function, and long-term outcomes after hospital discharge. *Clin J Am Soc Nephrol*. Feb 2013;8(2):194-202. doi:10.2215/CJN.06480612
13. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol*. Nov 2005;16(11):3365-70. doi:10.1681/ASN.2004090740
14. Wang HE, Muntner P, Chertow GM, Warnock DG. Acute kidney injury and mortality in hospitalized patients. *Am J Nephrol*. 2012;35(4):349-55. doi:10.1159/000337487
15. Coca SG, Yusuf B, Shlipak MG, Garg AX, Parikh CR. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis*. Jun 2009;53(6):961-73. doi:10.1053/j.ajkd.2008.11.034
16. Ahlstrom A, Tallgren M, Peltonen S, Rasanen P, Pettila V. Survival and quality of life of patients requiring acute renal replacement therapy. *Intensive Care Med*. Sep 2005;31(9):1222-8. doi:10.1007/s00134-005-2681-6
17. Hansen MK, Gammelager H, Mikkelsen MM, et al. Post-operative acute kidney injury and five-year risk of death, myocardial infarction, and stroke among elective cardiac surgical patients: a cohort study. *Crit Care*. Dec 12 2013;17(6):R292. doi:10.1186/cc13158
18. Lai TS, Wang CY, Pan SC, et al. Risk of developing severe sepsis after acute kidney injury: a population-based cohort study. *Crit Care*. Oct 11 2013;17(5):R231. doi:10.1186/cc13054
19. Chao CT, Wang CY, Lai CF, et al. Dialysis-requiring acute kidney injury increases risk of long-term malignancy: a population-based study. *J Cancer Res Clin Oncol*. Apr 2014;140(4):613-21. doi:10.1007/s00432-014-1600-z
20. Wang WJ, Chao CT, Huang YC, et al. The impact of acute kidney injury with temporary dialysis on the risk of fracture. *J Bone Miner Res*. Mar 2014;29(3):676-84. doi:10.1002/jbmr.2061

Online Early
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21. Wu PC, Wu CJ, Lin CJ, Wu VC, National Taiwan University Study Group on Acute Renal Failure G. Long-term risk of upper gastrointestinal hemorrhage after advanced AKI. *Clin J Am Soc Nephrol*. Mar 6 2015;10(3):353-62. doi:10.2215/CJN.01240214
22. Bucaloiu ID, Kirchner HL, Norfolk ER, Hartle JE, 2nd, Perkins RM. Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. *Kidney Int*. Mar 2012;81(5):477-85. doi:10.1038/ki.2011.405
23. Wonnacott A, Meran S, Amphlett B, Talabani B, Phillips A. Epidemiology and outcomes in community-acquired versus hospital-acquired AKI. *Clin J Am Soc Nephrol*. Jun 6 2014;9(6):1007-14. doi:10.2215/CJN.07920713
24. Sawhney S, Fraser SD. Epidemiology of AKI: Utilizing Large Databases to Determine the Burden of AKI. *Adv Chronic Kidney Dis*. Jul 2017;24(4):194-204. doi:10.1053/j.ackd.2017.05.001
25. Susantitaphong P, Cruz DN, Cerda J, et al. World incidence of AKI: a meta-analysis. *Clin J Am Soc Nephrol*. Sep 2013;8(9):1482-93. doi:10.2215/CJN.00710113
26. Hertzberg D, Sartipy U, Holzmann MJ. Type 1 and type 2 diabetes mellitus and risk of acute kidney injury after coronary artery bypass grafting. *Am Heart J*. Nov 2015;170(5):895-902. doi:10.1016/j.ahj.2015.08.013
27. Venot M, Weis L, Clec'h C, et al. Acute Kidney Injury in Severe Sepsis and Septic Shock in Patients with and without Diabetes Mellitus: A Multicenter Study. *PLoS One*. 2015;10(5):e0127411. doi:10.1371/journal.pone.0127411
28. Patel SS, Palant CE, Mahajan V, Chawla LS. Sequelae of AKI. *Best Pract Res Clin Anaesthesiol*. Sep 2017;31(3):415-425. doi:10.1016/j.bpa.2017.08.004
29. Heung M, Steffick DE, Zivin K, et al. Acute Kidney Injury Recovery Pattern and Subsequent Risk of CKD: An Analysis of Veterans Health Administration Data. *Am J Kidney Dis*. May 2016;67(5):742-52. doi:10.1053/j.ajkd.2015.10.019
30. Siew ED, Peterson JF, Eden SK, Moons KG, Ikizler TA, Matheny ME. Use of multiple imputation method to improve estimation of missing baseline serum creatinine in acute kidney injury research. *Clin J Am Soc Nephrol*. Jan 2013;8(1):10-8. doi:10.2215/CJN.00200112
31. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure–definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Critical care*. 2004;8(4):R204.
32. Kothari T, Jensen K, Mallon D, Brogan G, Crawford J. Impact of Daily Electronic Laboratory Alerting on Early Detection and Clinical Documentation of Acute Kidney Injury in Hospital Settings. *Acad Pathol*. Jan-Dec 2018;5:2374289518816502. doi:10.1177/2374289518816502

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TABLE 1. Demographics, Comorbidities, and Laboratory Values

	Diabetes N=266	**No Diabetes N=88**	**P-value**	**OR (95% CI)**
Demographics				
Age, years	53.0, 52.6 (10.7)	52.0, 50.2 (15.1)	0.10	
Male gender	204 (76.7)	65 (73.9)	0.59	1.16 (0.67-2.03)
Race			0.05	
White	74 (27.8)	34 (38.6)	0.06	0.61 (0.37-1.02)
African American	65 (24.4)	28 (31.8)	0.17	0.69 (0.41-1.18)
Asian	4 (1.5)	1 (1.1)	0.80	1.33 (0.15-12.04)
Hispanic/Latino	120 (45.1)	25 (28.4)	**0.01**	2.07 (1.23-3.49)
Body Mass Index, kg/m^2	30.6, 32.3 (9.9)	26.5, 28.0 (6.4)	**<0.01**	
Comorbidities				
Retinopathy	79 (29.7)	0	**<0.01**	75.05 (4.60-1224.34)
Neuropathy	240 (90.2)	47 (53.4)	**<0.01**	8.05 (4.50-14.42)
Previous ulcer	170 (63.9)	32 (36.4)	**<0.01**	3.10 (1.88-5.12)
Previous Amputation	93 (35.0)	9 (10.2)	**<0.01**	4.72 (2.26-9.83)
Chronic Kidney Disease	101 (38.0)	17 (19.3)	**<0.01**	2.56 (1.43-4.59)
Peripheral Arterial Disease	180 (67.7)	33 (37.5)	**<0.01**	3.49 (2.11-5.76)
Laboratory values				
Glycated Hemoglobin, %	9.2, 9.4 (2.4)	5.5, 5.4 (0.5)	**<0.01**	
Glycated Hemoglobin, mmol/mol	77, 79	37, 36		
WBC, cells/mm^3	9.6, 10.7 (4.4)	8.8, 9.6 (4.0)	**0.04**	
Serum Albumin, mg/dL	3.4, 3.4 (0.6)	3.7, 4.1 (3.5)	**<0.01**	
CRP, mg/dL	4.1, 7.3 (8.5)	2.1, 4.7 (7.0)	**<0.01**	

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ESR, mm/h	65.0, 71.5 (36.7)	32.0, 38.1 (24.9)	**<0.01**	
ABI	1.1, 1.2 (0.5)	1.2, 1.1 (0.3)	0.68	
Incidence and Timing of AKI				
Total	129 (48.5)	21 (23.9)	**<0.01**	3.00 (1.74-5.19)
At Admission	24 (18.6)	2 (9.5)	0.32	2.17 (0.47-9.96)
During Hospitalization	86 (66.7)	15 (71.4)	0.67	0.80 (0.29-2.21)
After Discharge	19 (14.7)	4 (19.1)	0.61	0.73 (0.22-2.42)
Multiple AKIs	29 (10.9)	1 (1.1)	**0.02**	10.6 (1.43-79.34)
Cumulative AKI	162 (60.9)	22 (25.0)	**<0.01**	4.67 (2.72-8.03)
AKI Incidence and Stage				
Total	129 (48.5)	21 (23.9)	**<0.01**	3.00 (1.74-5.19)
Stage 1	75 (58.1)	10 (47.6)	0.37	1.53 (0.61-3.85)
Stage 2	30 (23.3)	7 (33.3)	0.32	0.61 (0.22-1.64)
Stage 3	24 (18.6)	4 (19.1)	0.96	0.97 (0.30-3.15)

Descriptive variables are described as N (%).
Continuous variables are described as mean (SD).
OR=Odds Ratio; 95% CI=95% Confidence Interval; WBC=White Blood Cell Count; CRP=C-Reactive Protein; ESR=Erythrocyte Sedimentation Rate; ABI=Ankle Brachial Index

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Table 2. AKI Stages and Recovery

	Diabetes N=127	No Diabetes N=18	P-value	OR (95% CI)
Full Recovery	52 (40.9)	13 (72.2)	**0.02**	0.27 (0.09-0.79)
Partial Recovery	55 (43.3)	5 (27.8)	0.22	1.99 (0.67-5.90)
No Recovery	20 (15.7)	0	0.18	7.06 (0.41-121.80)
Stage 1	74	8	0.27	1.75 (0.65-4.72)
Full Recovery	36 (48.7)	7 (87.5)	0.07	0.13 (0.02-1.16)
Partial Recovery	32 (43.2)	1 (12.2)	0.13	5.33 (0.62-45.57)
No Recovery	6 (8.1)	0	0.75	1.61 (0.08-31.24)
Stage 2	29	6	0.33	0.59 (0.20-1.72)
Full Recovery	12 (41.4)	4 (66.7)	0.27	0.35 (0.05-2.25)
Partial Recovery	11 (37.9)	2 (33.3)	0.69	1.50 (0.23-9.59)
No Recovery	6 (20.7)	0	0.13	3.60 (0.18-72.57)
Stage 3	24	4	0.74	0.82 (0.25-2.70)
Full Recovery	4 (16.7)	2 (50.0)	0.16	0.20 (0.02-1.87)
Partial Recovery	12 (50.0)	2 (50.0)	1.00	1.00 (0.12-8.31)
No Recovery	8 (33.3)	0	0.32	4.64 (0.22-96.61)
CKD Progression				
Total	50 (39.4)	3 (16.7)	0.07	3.25 (0.89-11.79)
AKI Stage 1	24 (32.4)	1 (12.5)	0.42	3.36 (0.39-28.88)
AKI Stage 2	10 (34.5)	1 (16.7)	0.64	2.63 (0.27-25.72)
AKI Stage 3	16 (66.7)	1 (25.5)	0.27	6.00 (0.54-67.28)

Variables are presented as N (%).

OR=Odds Ratio; 95% CI=95% Confidence Interval

*Number of patients reflect the number of patients with an AKI, absent patients who did not have follow up serum creatinine values.