Mortality prediction of hospitalised type 2 diabetic foot ulcers using Wagner classification in Kaifeng, China: a retrospective cohort study

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Research Article

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Abstract

Background

To summarize the clinical characteristics of inpatients with type 2 diabetic foot ulcers (T2DFU) in a grade 3A hospital in China and observe the prediction effects of Wagner grades for the premature death.

Methods

309 Han Chinese inpatients who were diagnosed as T2DFU between September 2009 and November 2019 in a grade 3A hospital in Kaifeng, China. The patients were divided into six subgroups according to Wagner classification. The sociodemographic variables, clinical variables and mortality rate among the six subgroups were compared. Adjusted Cox proportional hazard regression models were conducted to estimate hazard ratios (HR) and 95% confidence interval (95% CI) for the six Wagner grade subgroups.

Results

Of the 309 patients, in comparison with Wagner grade 0, grade 4 and grade 5 showed a significantly higher cumulative mortality, respectively. In the unadjusted regression model of Wagner grades, the HR [95% CI] for Grade 1 ~ 5 subgroups were 0.86 [0.46–1.61], 0.97 [0.54–1.74], 1.42 [0.78–2.58], 2.20 [1.29–3.75], and 5.39 [2.77–10.51] with grade 0 subgroup as reference (P < 0.001); In a multiple regression model adjusted with age, cardiovascular diseases, peripheral neuropathy, and diabetic nephropathy, the HR [95% CI] for Grade 1 ~ 5 subgroups were 0.95 [0.51–1.77], 1.04 [0.57–1.89], 1.56 [0.86–2.86], 2.27 [1.33–3.89], and 6.39 [3.24–12.61] with grade 0 subgroup as reference (P < 0.001).

Conclusions

Mortality rate of T2DFU patients increased with Wagner grades, mainly from grade 4 through grade 5 in comparison with grade zero in the present study.

1. Background

The prevalence rate of diabetics in China has a marked increase in the past decades, from 0.67% in 1980 to 2.5% in 1994, 9.7% in 2008 and further to 11.6% in 2010[1–5]. Now, China has the largest population of diabetes mellitus (140.9 million persons with diabetes aged between 20–79 years in 2021) in the world and with extrapolation suggesting that this situation will continue until at least 2030[6, 7]. The increasing prevalence of diabetes has led to an unparalleled epidemic of diabetic foot ulcers (DFU), which will take approximately 25% of people with diabetes in their lifetime [8, 9]. Pengzi Zhang et al.[10] performed a systematic review and meta-analysis and found that diabetic foot ulcer prevalence rate was 4.1% in China. Yufeng Jiang et al. [11] shown that the estimated annual incidence of ulceration for persons with
The incidence of diabetic foot is increasing due to the prevalence of diabetes mellitus and the prolonged life expectancy of people with diabetes. DFU is a source of major suffering and financial costs for the patient, and also places a considerable burden on the patient’s family, health-care professionals and facilities, society, and in malnutrition in general [12, 13]. Diabetic foot ulcer severity is a more significant factor for subsequent mortality than coronary artery disease, peripheral arterial disease or stroke [14–16]. 70% of DFU remain unhealed after 20 weeks of treatment [17], and of these, 20% end in different levels of amputation [18]. A study in Spain by José Antonio Rubio showed that patients with a history of diabetic foot ulcers had very limited survival; estimated survival was reduced to 60% at 5 years [19]. Reducing early deaths is the primary goal of managing DFU [10, 20].

Data on studies of the association between mortality and severity of diabetic ulcers are limited. A study in Nigeria showed that the majority of deaths occurring among those with advanced ulcers [21]. Brennan et al. [16] used a simple classification, gangrene and osteomyelitis versus, and Amadou et al. [22], used the PEDIS classification (perfusion, extent, depth, infection, and sensation) studied the association of DFU and mortality. However, the study on the specific association between different Wagner grades and the rate of mortality after discharged from hospital is still insufficient, especially in China.

We aimed to summarize the clinical characteristics of inpatients with type 2 diabetic foot ulcers (T2DFU) and observe the prediction effects of Wagner grades for the premature death of the Han Chinese T2DFU patients when they were firstly admitted in a grade 3A hospital in China.

2. Methods

2.1 Study design, setting and participants

We carried out a retrospective cohort study at Huaihe Hospital of Henan University, a Grade 3A hospital located in Kaifeng, China. All case records of Han Chinese patients with T2DFU admitted to Huaihe Hospital of Henan University from 2009 to 2019 were enrolled. During their stay in hospital, all inpatients underwent comprehensive clinical examination and treatment. Patients’ files are securely stored in the hospital's electronic archives and contained phone contacts for the patients and at least one of their relatives.

2.2 Admission criteria

1. Patients admitted to Huaihe Hospital of Henan University from September, 2009 to November, 2019.
2. Patients diagnosed with type 2 diabetic mellitus.
3. Patients with at least one foot ulcer located at or below the ankle (Wagner classification: Grade 1–5), or who had foot problems but without any diabetic foot ulcer (Wagner grade: 0) [24].
4. Patients' hospital files with all the required information and containing a valid phone number.
5. Patients who were contactable directly or through their relative by phone calls, from May 1, 2020 to December 22, 2020.
6. Patients who are Han Chinese.
2.3 Exclusion criteria

1. Patients who were not reachable on the phone after a maximum of four calls over a period of 30 days.
2. Patients who did not consent to participate in the study.
3. Patients without Han nationality.
4. Patients without a confirmed diagnosis of type 2 diabetes.
5. Patients who had no required medical information for data analysis.

2.4 Data collection

All collected data were entered into structured dataset. Sociodemographic and clinical data were retrieved from hospital electronic records. The sociodemographic variables included age (20–96 years), sex (man vs. women), occupation (employee vs. non-employee), marital status (married vs. single/widow) and residence (urban vs. rural). The clinical variables included Wagner grade (0–5), amputation (no vs. yes), hypertension (no vs. yes), cardiovascular diseases (no vs. yes), cerebrovascular disease (no vs. yes), peripheral neuropathy (no vs. yes), diabetic retinopathy (no vs. yes), and diabetic nephropathy (no vs. yes).

First, we called the phone number provided on the patient’s hospital record to ascertain whether or not the patient was alive. In case a patient was dead, we expressed our condolences and sought for when and where the patient died. For patients who died at Huaihe Hospital of Henan University, time of death and the departments in which they died were further confirmed from hospital records.

2.5 Operational definitions for key variables were as follows:

1. Type 2 diabetic mellitus (T2DM): medical records (past medical and medication history), any patient diagnosed as such and confirmed by at least one attending doctor in accordance with The American Diabetes Association (ADA) guidelines [23] at admission.
2. Type 2 diabetic foot ulcers (T2DFU): Type 2 diabetic patient with diagnosed diabetic foot ulcers in the medical records at admission.
3. Wagner’s classification [24]: describe the most severe ulcer occurring during the observation period in all cases. Grade 0, skin lesions absent, but at risk of DFU; grade 1, superficial ulcer, skin and immediate subcutaneous tissue are ulcerated; grade 2, deep ulcer, lesions may penetrate to tendon, bone or joint capsule; grade 3 osteomyelitis and/or deep abscess, deep tissues are always involved; grade 4, partial foot gangrene, gangrene of some portion of the toes or forefoot; grade 5, the entire foot is gangrenous. The judgment of woundgrading was made by the first visited surgeon or physician. If there were multiple lesions, the grade of the most severe lesion was registered.
4. Hypertension: patients with a history of hypertension, using of antihypertensive medication, or systolic blood pressure $\geq 140$ mm Hg and/or diastolic $\geq 90$ mm Hg, confirmed by the attending doctor at admission.
5. Peripheral neuropathy (PN): patients with a history of peripheral neuropathy, or having met one or more of the following criteria at admission: (1) light sensory abnormalities, diagnosed with the 10g Semmes-Weinstein monofilament test [25]; (2) deep paraesthesia, diagnosed based on the final measured value of 128-Hz tuning fork tests [26].

6. Diabetic nephropathy (DN): patients with a history of diabetic nephropathy at admission, or urinary albumin excretion rate (UAER) > 30 mg/24 h (at least two measurements) [27], tested by using the 24-hour urine radioimmunoassay method.

7. Diabetic retinopathy (DR): patient with a history of diabetic retinopathy or identified on the basis of fundus photography reviewed by an ophthalmologist at admission.

In the end, after excluding 122 ineligible subjects from a total of 431 records that were reviewed, 309 patients (255 patients with Wagner grade 1–5 ulcers and 54 patients with Wagner grade 0 ulcers) of the Han Chinese patients who were diagnosed as T2DFU were included in the study (Fig. 1).

2.6 Statistical analysis

Categorical variables were presented as number of cases (percentage). The mortality rate was expressed as deaths per 100 person-years and the cumulative mortality rate as deaths per 100 T2DFU patients. Chi square test was used to compare sociodemographic variables, clinical variables and mortality between six grade subgroups. Then, survival curves were generated using the Kaplan-Meier method. Cox proportional hazards regression analysis was used to calculate the hazards ratio (HR) and 95% Confidence Interval (95% CI). The relationship between different Wagner classification and mortality were first analysed using univariate Cox proportional hazards model. Then, in order to further determine the relationship, four resulting main Cox multiple regression models were fitted. In model 2, we adjusted the sociodemographic variables. In model 3, we adjusted the clinical variables. In model 4, we adjusted the sociodemographic and clinical variables. In model 5, we adjusted with age, CVD, peripheral neuropathy, diabetic nephropathy that were independently associated with the risk of death in our previous study (unpublished manuscript). These adjusted variables were then analysed in a multivariate Cox proportional hazards regression model, respectively. All participants included in the data analysis had no missing data for any specific analysis. P value less than 0.05 was considered statistically significant. Data were analysed using the Stata software version 14 (Stata Corporation, College Station, TX, USA).

3. RESULTS

3.1 General characteristics of patients in Wagner grade subgroups

The baseline demographic details for the subjects are summarized in Table 1. Of the 309 patients with T2DFU, 168 were men (54.4%), and 122 were above 70 years of age (39.5%). The percentages of T2DFU patients who had amputation, hypertension, CVD, CBD, PN, DR and DN at admission were 6.2%, 74.8%,
52.4%, 48.9%, 57.3%, 46.9% and 48.5%, respectively. Statistical analysis showed that there was a different distribution of age (P < 0.001), residence (P = 0.041), amputation (P < 0.001) and diabetic retinopathy (P < 0.001) among six grade subgroups. With the increase in Wagner grade from 0 to 5, ratio of patients who were older than 70 years and amputation tended to increase and the patients who were rural residents and diabetic retinopathy tended to decrease.
Table 1
Demographic data, risk factors, and comorbidities of the study population by Wagner classification

<table>
<thead>
<tr>
<th>Wagner classification</th>
<th>Total</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>309</td>
<td>54</td>
<td>61</td>
<td>69</td>
<td>43</td>
<td>64</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Man</td>
<td>168</td>
<td>27</td>
<td>32</td>
<td>40</td>
<td>21</td>
<td>36</td>
<td>12</td>
<td>0.764</td>
</tr>
<tr>
<td>Age, &gt;70 years</td>
<td>122</td>
<td>27</td>
<td>20</td>
<td>18</td>
<td>10</td>
<td>39</td>
<td>8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-employee</td>
<td>285</td>
<td>46</td>
<td>56</td>
<td>65</td>
<td>39</td>
<td>61</td>
<td>18</td>
<td>0.249</td>
</tr>
<tr>
<td>Married</td>
<td>277</td>
<td>47</td>
<td>56</td>
<td>62</td>
<td>38</td>
<td>56</td>
<td>18</td>
<td>0.673</td>
</tr>
<tr>
<td>Rural</td>
<td>136</td>
<td>14</td>
<td>32</td>
<td>31</td>
<td>24</td>
<td>28</td>
<td>7</td>
<td>0.041</td>
</tr>
<tr>
<td>Amputee</td>
<td>19</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>231</td>
<td>41</td>
<td>46</td>
<td>49</td>
<td>32</td>
<td>49</td>
<td>14</td>
<td>0.979</td>
</tr>
<tr>
<td>CVD</td>
<td>162</td>
<td>30</td>
<td>35</td>
<td>35</td>
<td>18</td>
<td>35</td>
<td>9</td>
<td>0.702</td>
</tr>
<tr>
<td>CBD</td>
<td>151</td>
<td>27</td>
<td>33</td>
<td>30</td>
<td>19</td>
<td>33</td>
<td>9</td>
<td>0.839</td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>177</td>
<td>31</td>
<td>35</td>
<td>38</td>
<td>29</td>
<td>37</td>
<td>7</td>
<td>0.487</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>145</td>
<td>27</td>
<td>36</td>
<td>33</td>
<td>28</td>
<td>17</td>
<td>4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>150</td>
<td>29</td>
<td>36</td>
<td>36</td>
<td>20</td>
<td>22</td>
<td>7</td>
<td>0.091</td>
</tr>
</tbody>
</table>

Data are presented as number of cases (percentage) for categorical variables. *P-value for comparison between men and women (Chi square test for categorical data; Wilcoxon rank-sum (Mann-Whitney) test for person-years. CVD, cardiovascular diseases; CBD, cerebrovascular disease. P-values less than 0.05 are indicated in bold.

### 3.2 Mortality rate of patients in Wagner grade subgroups

During a total of 948.7 person-years of follow-up for the 309 patients, 147 died, resulting in a mortality rate of 15.5 per 100 person-years and a cumulative mortality rate of 47.6%. Statistical analysis showed
that there was a marginal significant trend of increase in mortality rate (P = 0.062) and a significant trend of increase in cumulative mortality (P = 0.014) with the increase in Wagner grades (Table 2).

Table 2. Mortality rate of the study population by Wagner classification

<table>
<thead>
<tr>
<th>Wagner classification</th>
<th>Total</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>309</td>
<td>51</td>
<td>58</td>
<td>71</td>
<td>44</td>
<td>66</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>948.7</td>
<td>172.6</td>
<td>202.3</td>
<td>231.7</td>
<td>142.7</td>
<td>175.4</td>
<td>23.9</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>147</td>
<td>20</td>
<td>20</td>
<td>25</td>
<td>23</td>
<td>43</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Mortality rate (%)</td>
<td>15.5</td>
<td>11.6</td>
<td>9.9</td>
<td>10.8</td>
<td>16.1</td>
<td>24.5</td>
<td>66.9</td>
<td>0.062</td>
</tr>
<tr>
<td>Cumulative mortality (%)</td>
<td>47.6</td>
<td>39.2</td>
<td>34.5</td>
<td>35.2</td>
<td>52.3</td>
<td>65.2</td>
<td>84.2</td>
<td>0.014</td>
</tr>
</tbody>
</table>

1 deaths per 100 person-years, 2 deaths per 100 subjects

3.3 Hazard ratio (HR) and 95% CI of patients in Wagner grade subgroups

There were a significant association of mortality rate of T2DFU with Wagner grades among patients in both unadjusted and four adjusted models (P < 0.001). In model 1 (unadjusted model), patients with Wagner grade 1–3 showed an non significant differences in risk of death (grade 1: HR = 0.86, 95% CI = 0.46–1.61; grade 2: HR = 0.97, 95% CI = 0.54–1.74; (grade 3: HR = 1.42, 95% CI = 0.78–2.58) in comparison with grade 0. Patients with Wagner grade 4–5 showed a significant increase in risk of death than grade 0 (grade 4: HR = 2.20, 95% CI = 1.29–3.75, grade 5: HR = 5.39, 95% CI = 2.77–10.51). In model 2, we adjusted the sociodemographic variables that included sex, age, occupation, marriage, living area. In model 3, we adjusted the clinical variables that included amputation, hypertension, CVD, CBD, PN, DN, and DR. In model 4, we adjusted the sociodemographic and clinical variables as listed in model 2 and model 3. In model 5, we adjusted with age, CVD, PN, and DN that were independently significantly associated with the risk of death in our previous study (unpublished manuscript). The four adjusted models showed a robust association of Wagner grade with risk of death of the T2DFU in our present population (Table 3).

Table 3. Hazard ratio and 95% CI of the T2DFU as graded by Wagner classification
Wagner classification, HR (95%CI)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.86 (0.46-1.61)</td>
<td>0.97 (0.54-1.74)</td>
<td>1.42 (0.78-2.58)</td>
<td>2.20 (1.29-3.75)</td>
<td>5.39 (2.77-10.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1</td>
<td>0.99 (0.53-1.87)</td>
<td>1.04 (0.57-1.89)</td>
<td>1.49 (0.80-2.75)</td>
<td>1.83 (1.06-3.15)</td>
<td>6.41 (3.23-12.69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>0.87 (0.46-1.63)</td>
<td>0.97 (0.53-1.76)</td>
<td>1.74 (0.94-3.23)</td>
<td>2.77 (1.61-4.76)</td>
<td>6.30 (3.08-12.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>0.86 (0.46-1.63)</td>
<td>0.96 (0.53-1.76)</td>
<td>1.55 (0.82-2.92)</td>
<td>2.23 (1.28-3.89)</td>
<td>7.34 (3.53-15.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>0.95 (0.51-1.77)</td>
<td>1.04 (0.57-1.89)</td>
<td>1.56 (0.86-2.86)</td>
<td>2.27 (1.33-3.89)</td>
<td>6.39 (3.24-12.61)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Model 1: no adjustment.

Model 2: adjusted with sex, age, occupation, marriage, living area.

Model 3: adjusted with amputation, hypertension, CVD, CBD, peripheral neuropathy, diabetic nephropathy, diabetic retinopathy

Model 4: adjusted with occupation, marriage, living, age, sex, amputation, hypertension, CVD, CBD, peripheral neuropathy, diabetic nephropathy, diabetic retinopathy

Model 5: adjusted with age, CVD, peripheral neuropathy, diabetic nephropathy

Kaplan-Meier survival curve analysis also showed that patients within Wagner grade 0–3 subgroups had an non significant difference in overall survivals (OS), while patients with grade 4–5 had a significant decrease of OS during follow-ups in comparison with Grade 0 subgroup (Fig. 2).

4. DISCUSSION

Our study shows a mortality rate of 15.5 per 100 person-years and a cumulative mortality rate of 47.6% over a median follow-up period of 2.7 years in Han Chinese T2DFU patients. There was a significant trend of increase in cumulative mortality (P = 0.014) along with the increase in Wagner grades from grade 1 through 5, with grade 4 and 5 showing a significantly decrease OS than the grade 0. To the best of our knowledge, this is the first report to address the specific association of different Wagner grades with OS of T2DFU in Han Chinese subpopulation.

Wagner classification is a system for classifying diabetic, neuropathic, and dysvascular foot lesions [24]. Because the Wagner grading criteria is currently the most commonly used grading scale, all patient’s foot ulcers were classified with Wagner’s classification in the present study. Few studies have focused on foot
ulcer classification systems as predictors of premature death of T2DFU. The current study offered an evidence for the specific relationships between OS of patients with T2DFU and Wagner grades 1–5, respectively in comparison with Grade 0.

A study by Jason H. Calhoun et al. [28] show that the proportion of patients in different Wagner grades was similar to what we did. Deep ulcer (grade 2) were seen most frequently, followed by partial foot gangrene (grade 4), superficial ulcer (grade 1), and osteomyelitis and/or deep abscess (grade 3). There were few patients with entire foot gangrene (grade 5), perhaps because most were treated earlier before they progressed to grade 5.

A study have shown that as the Wagner grade increased from 0 to 5, the percentages of DN, PN of patients increased[13]. However, this rule is not reflected in our study, so far as to, diabetic retinopathy decreased as the Wagner grade of diabetic foot increased. Several studies have shown that complications in patients—DN, PN, DR, CBD, CVD, may increase the mortality of diabetic foot[29–32]. However, there may be no difference between different Wagner grades of diabetic foot. The first explanation is that the occurrence of complications might have alerted the patients, strengthen the early treatment of diabetic foot patients, and potentially delayed the progress of T2DFU; the second is that both patients and attending doctors paid more attention to screening of complications of T2DFU at early stages, but medical priorities would be diverted to the foot itself at later stage; and the third is that patients with higher Wagner grade may not actively receive early treatment in regular hospitals due to economic reasons, and they often refuse to be screened for complications due to financial reasons, and their mobility was not convenient and screening for associated complications.

Our study showed that there was no significant difference when Wagner grade 1,2 or 3 compared with Wagner grade 0 in mortality. The rates of complications of patients with Wagner grade 0–3 is similar. Possibly, this suggests that patients’ physical conditions may be similar, and the ulcer does not cause gangrene in the foot,so the healing speed is faster in the Wagner grade 0–3. A study by Huifen Chen et al. [33]shown that compared to DFU patients with Wagner grader 1, DFU patients with Wagner grader 2 had more effectively maintaining self-management and more voluntarily cooperated with family members, nurses and physicians, eventually, DFU patients with Wagner grader 2 benefiting to a greater extent. In addition, one study showed that a wound with Wagner grade 2 might have better tissue reserve with less ulcer lesion. The wound healing could proceed with proper infection control[34]. In our study, patients with Wagner grader 3 who over 70 years old, with CVD, with CBD were the least compared with other Wagner graders. In addition, patients with Wagner grader 3 have some increase in mortality compared to Wagner grader 0–2, but not significant.

Patients with Wagner grade 4 and 5 showing a significantly decrease OS than the grade 0, which was consistent with the clinical observation. Jui-Hung Sun et al. [34]demonstrated that high grade of Wagner classification (≥ grades 3) markedly increased the risk of death, and that more extensive wounding was associated with an increased risk of death. This is easy to understand that a diabetic foot ulcer of Wagner grade 4 or 5 shows focal or total gangrene change, which implies extensive necrosis and poor
circulation in the tissue, and under such catastrophic circumstances, often causes irreversible damage to the affected limb.\[35\] In addition, as the severity of diabetic foot ulcers increases, the nutritional status of the patients deteriorated \[13, 36\], and the amputation rate increased\[37, 38\]. Therefore, patients have a worse quality of life and a higher mortality rate.

Few studies have shown that with the increase of the Wagner grade of diabetic foot, how does the patients' mortality change. However, with the increase of the Wagner grade of diabetic foot, the mortality of patient increased. These statements may not be quite right. Because compared to Wagner grade 0 patients there was no significant increase in mortality in Wagner grade 1,2,3 patients, the significant increase in mortality was only seen in Wagner grade 4–5 patients. Therefore, our study showed that only Wagner grade 4–5 was a predictor of increased mortality in patients with diabetic foot. Study by Olufunmilayo O Adeleye et al. \[21\] also showed that Wagner grade $\geq 3$ was a risk factor for death. However, few studies have analyzed the relationship between Wagner grade and mortality, and Winkley et al. \[18\], using the Texas classification, found no association with mortality, which may be interpreted that as patients with Wagner grade 1,2,3 who usually accounted for a large proportion in the diabetic foot patients, attenuating the effect of Wagner grade on mortality.

From this study, we feel that something needs to be done. First, every attempt must be made to prevent further development of diabetic foot. Second, if the severity of DFU is underestimated, the optimal treatment time is delayed or lost, it will increase the difficulty of treatment. So, foot care education for the patients, their families, and their primary care physicians, enhance recognition of the need for aggressive treatment of even minor foot trauma in the diabetic is very necessary. Finally, once DFU does develop, patients should be taken care of by a multidisciplinary team, including internists, general and vascular surgeons, endocrinologists, orthopedists, diagnostic and interventional radiologists (including nuclear medicine), and anesthesiologists, as well as podiatrists, dieticians, and psychologists.

We are cognizant of the limitations of the present study. First, the small sample size in Wagner grade 5 resulted in an unbalanced distribution of some clinical indicators in different groups, which may limit the power of data analysis. Second, the Wagner grade of diabetic foot was determined by attending doctors from different clinical departments, and some observational bias would be difficult to avoid. Third, all variable data were obtained at the beginning of the study, but we could not analyze how they changed during the follow-up period. Nevertheless, the present study is the first to demonstrate the specific association between different Wagner classification and the rate of mortality of T2DFU in Han Chinese patients from a grade 3A university hospital.

5. CONCLUSION

In conclusion, there were significant differences in mortality among T2DFU patients with different Wagner grades. Wagner grade 0–3 had very little difference in mortality, however, patients with gangrene (Wagner grade 4–5) are at particularly high risk of death. Every attempt must be made to prevent further
development of diabetic foot, and foot care education for the patients, their families, and their primary care physicians is very necessary.

**Declarations**

**Conflict of interest**: none

**Ethical considerations**: The present study was approved by the Ethics Committee of the Huaihe Hospital of Henan University. All participants or their relatives provided verbal consent to participate in the study.

**Author contributions**

YMZ: conceptualisation, data curation, writing-review and editing. YQL: conceptualisation, interpretation, writing-review and editing, formal analysis. HL: data collection, writing-original draft, interpretation, writing-review and editing. All authors reviewed and approved the final version of the manuscript.

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**Data availability statement**: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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**References**


**Figures**
Hospital files for subjects with type 2 diabetic foot and Han nationality
\(N = 431\)

Subjects that could be reached for followed-up
\(n = 334\)

Wrong phone number \(n = 43\)
Blank phone number \(n = 41\)
Phone number was out of use \(n = 13\)

No answer to the phone \(n = 11\)
No answer to questions \(n = 9\)
Refused to offer consent \(n = 5\)

Eligible diabetic foot ulcer subjects
\(n = 309\)
\(\text{Men } = 168, \text{ Women } = 141\)

Figure 1

Legend not included with this version
Figure 2

Legend not included with this version