The Relationship Between Frailty and Treatment Compliance in Diabetic and Geriatric Patients Using Insulin

Diabetes Mellitus Tanılı Insulin Kullanan Geriatrik Hastalarda Tedaviye Uyum ve Kırılmanız Arasındaki İlişki

Aim: Understanding and detecting frailty makes convenience to healthcare providers for deciding on appropriate therapy and follow-up strategy. In this study, we tried to determine the relationship between compliance to therapy, hypoglycemia and frailty in the elderly diabetic patients under insulin therapy.

Materials and Methods: One hundred sixty-seven patients diagnosed with diabetes mellitus and under insulin therapy were recruited for the study. Criteria of frailty according to the Cardiovascular Health Study (CHS) were used to determine frailty. According to CHS, patients fulfilling three or more criteria out of five were regarded as frail elderly. Hypoglycemia rates and compliance to treatment were compared between the groups.

Results: 44.3% of our patients were regarded as frail elderly and the rate of hypoglycemia was higher in this group. A significant relationship between subgroups of frailty and insulin was detected. Frailty rate was 28.6% in the basal insulin therapy group, 37.1% in the basal-bolus therapy group and 40% in the premixed insulin group. In the frail elderly group, the rate of moderate hypoglycemia was significantly higher than in the non-frail group (40.2% vs 20%). Severe hypoglycemic episodes were observed more frequently in the frail elderly group than in the non-frail group (24.6% vs 12.7%).

Conclusion: Frailty increases the risk of moderate and severe hypoglycemia. Before planning and starting insulin therapy, frailty must be detected and taken into consideration.

Keywords: Diabetes mellitus, frailty, hypoglycemia, elderly

ABSTRACT

Amaç: Geriatrik hastalarda kırılganlığı anlamak ve tespit etmek, hastaları takip etmede ve uygulanacak tedavi seçiminde sağlıklık ekibine büyük kolaylık sağlayacaktır. Biz bu çalışmada diabetes mellitus tanılı insülin kullanan geriatrik hastalarda tedaviye uyum, hipoglisemi ve frailite arasındaki ilişkii belirlemeyi amaçladık.


INTRODUCTION

The population of our country has been reported as 83 million 154 thousand as of 2020. Looking at the population pyramid, it has a young population. However, as in the whole world, the elderly population is increasing rapidly in our country. According to the Turkish Statistical Institute 2020 data, the elderly population constitutes 9.1% of the country. The World Health Organization states that the number of geriatric people in the world will reach 1.2 billion by 2025. Due to the increase in the geriatric population and the changing lifestyle, chronic diseases are increasing in our country. The increasing elderly population brings with it problems specific to the elderly. One of these problems is the concept of frailty. The American Medical Association used the word “frailty” to describe “the patient group that presents the most complex and challenging problems for healthcare professionals.” While frailty is seen at a rate of 10-25% in people aged 65 and over, it increases to 30-45% in people aged 85 and over. Understanding and knowing the frailty in the geriatric population will provide great convenience to the healthcare team in following up the patients and choosing the treatment to be applied. With this study, we wanted to address frailty and frailty criteria in the geriatric population, while addressing frailty in the diabetic elderly patient group, which is an important problem. Insulin therapy should be carefully planned, especially in the diabetic elderly. Therefore, correct classification of cases is important. Indices used in patient selection exclude the concept of frailty. In this study, we aimed to investigate the relationship between compliance to treatment and frailty (weakness, weight loss, slowness, decreased physical activity, decreased stamina and energy) in patients aged 65 and over using insulin and diagnosed with diabetes mellitus.

MATERIALS AND METHODS

Our study is an analytical cross-sectional study and was conducted with a total of 167 patients aged 65 years and older, who were diagnosed with diabetes mellitus and were using insulin therapy, who applied to Ümraniye Training and Research Hospital Internal Medicine outpatient clinics or were hospitalized for various complications and chronic diseases. Ethics committee approval was obtained from the of Ümraniye Training and Research Hospital Ethics Committee for the study (decision number: 56, date: 24.09.2014). An informed consent form was signed by all patients participating in the study. Geriatric patients aged 65 years and older with diabetes mellitus using insulin were included in the study. Patients with congenital disability and malignancy and those who did not want to participate in the study were not included.

Frailty Assessment

For the assessment of frailty in the geriatric population, frailty criteria (fatigue, weight loss, slowness, decreased physical activity, decreased stamina and energy) according to the Cardiovascular Health Study (CHS) were used. According to the CHS criteria, patients with 3 or more of 5 characteristics were considered frail elderly. While scoring, frailty criteria and scoring recommended in the Canadian Health and Aging Study were used; classification was made as mild frailty (patients with 1 point), moderate frailty (patients with 2 points), and severe frailty (patients with 3 points).

Metabolic Parameters

Plasma glucose of all patients was measured by enzymatic test; HPLC method was used to measure glycosylated hemoglobin; total cholesterol, high-density lipoprotein cholesterol, calcium, phosphate and triglyceride concentration were measured by enzymatic colorimetric test; and creatinine was measured by the Jaffe’ method [Hitachi 747 autoanalyzer (Mito, Ibaragi, Japan)]. Blood samples were taken from the patients between 08:00 and 10:00 on an empty stomach. Blood samples were collected into tubes with SST II, LH PST II and EDTA and analyzed simultaneously.

Statistical Analysis

IBM Statistical Package for the Social Sciences Statistics 22.0 IBM Software program was used for statistical analysis. While evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation), the One-Way ANOVA test was used to compare the parameters with normal distribution between groups in the comparison of quantitative data, and the Tukey HSD test was used to determine the group that caused the difference. Chi-square test was used to compare qualitative data. Spearman correlation analysis was used to examine the relationships between parameters that did not conform to the normal distribution. Significance was evaluated at the p<0.05 level.

RESULTS

A total of 167 patients were evaluated. In the sample distribution, 92 (55.1%) of the cases were female and 75
patients over 65 years of age using insulin, and the rate of frailty was 44.3% in patients using basal-bolus insulin and 14.3% in the group using mixed insulin. In the correlation analysis between frailty and age groups, hypoglycemia groups and hypoglycemia rate above 10 was 18.6% in the group using basal insulin, it was 24.6% in the frail group and severe hypoglycemia was 2 times higher in the frail group. While the rate of severe hypoglycemia was 12.7% in patients without frailty, this rate was 42.1% in frailty patients and while the rate of moderate hypoglycemia was 8.2% in patients without frailty, it was 9.2% in the frail group.

In the evaluation we made between the frailty groups and the insulin groups, there was 28.6% frailty in the basal insulin group, 37.1% in the basal-bolus group and 40% in the mixed insulin group. The frailty rate was found to be higher in patients using basal-bolus and mixed regimen insulin (Table 4). A significant correlation was found between the HbA1c levels above 10 was 18.6% in the group using basal insulin, it was 35.5% in the group using basal-bolus insulin and 14.3% in the group using mixed insulin. In the correlation analysis between frailty and age groups, hypoglycemia groups and HbA1c groups; a positive significant correlation was found between frailty and age groups and hypoglycemia.

**DISCUSSION**

In this study, we found that the rate of frailty was 44.3% in patients over 65 years of age using insulin, and the rate of hypoglycemia was higher in patients with frailty compared to those without. We found a positive correlation between frailty and hypoglycemia. We showed that frailty increased as the degree of hypoglycemia increased. Life expectancy has been prolonged due to many important developments such as the success achieved in the treatment of diseases, the control of...
approach should be taken towards the general care of elderly
were "bad" and it was concluded that a multidisciplinary
(41.2%), 75-80 years (43.8%) and 85-90 years (40%) were
patients between the ages of 65-70 years (52.5%), 70-75 years
studies on the life activities of the elderly are not sufficient in
emphasize the inadequacies in this regard. Considering that
studies are carried out to find the most appropriate method
for detecting frailty or to draw attention to frailty and to
cooperation with their families, the morbidity and mortality
loss
increases. In our study, the frail group was found to be older
than the non-fragile group. While this rate was 24% for the
60-70 age group, it was 49% for the 70-80 age group. We have
shown that frailty increases with age and decreased physical
activity is also related to increased frailty, and care and
treatment approaches for the elderly population change. In a
study it is stated that in elderly patients with diabetes for
several years and complications, tight glycemic control reduces
the risk of microvascular events, but does not reduce
macrovascular events or mortality, better glycemic control is
associated with less disability and better organ function, but
observation of severe hypoglycemia in advanced age is a risk
factor for intensive treatment13. Again, in the same study, OAD
basal-bolus therapy was compared and it was noted that frailty
that increases with age is associated with decreased functions
and increased mortality, and that elderly diabetic patients tend
to be more frail7. In people with multiple comorbidities, the
high functional variability and limited life expectancy suggest
that the benefit of intensive therapy is minimal. The decision
to recommend tighter or milder glycemic control is made
according to the degree of weakness, and it is noted that the
patients with moderate or more severe weakness should not
have strict glycemic control because they have a reduced life
expectancy, and that when glycemic control is tried to be
better in these patients, maybe less pronounced hyperglycemia
episodes are seen, but serious episodes of hypoglycemia are
more frequent10. It is recommended that insulin treatment
regimens in the elderly be individualized and determined by
considering the safety of the patient. It has been concluded
that pre-mixed insulin analogues can be used after meals and
are associated with better control compared to basal insulins,
but they cause more frequent hypoglycemia and more weight
loss11,12. Our study showed a positive relationship between
frailty and age and hypoglycemia. While severe hypoglycemia
was 39.3% in the 60-70 age group, this rate was 50% in the
70-80 age group. No significant relationship was found
between age groups and hypoglycemia, but a significant
relationship was found in the relationship analysis between
frailty groups and insulin groups. The frailty rate was 24.6%
in the basal insulin group, 39.3% in the basal bolus group, and it
was higher with 40% in the mixed insulin group. We believe
that frailty should be taken into account when administering
insulin therapy in the elderly patient group and treatment
regimens should be adjusted accordingly. The least
hypoglycemia was seen in the basal treatment group, and
hypoglycemia rates increased significantly in both the mixed
and basal bolus groups. In a study by Kim et al.13, it was stated
that geriatric frailty is a syndrome and it affects treatment
options. It was pointed out that the development and
application of the statement-based frailty index in older adults
should be determined and adjusted in pharmacoepidemiological
studies, and that more research is needed. In a study by Sourial

### Table 3. Comparison of hypoglycemia and HbA1c levels and frailty status

<table>
<thead>
<tr>
<th>Hypoglycemia</th>
<th>Frail</th>
<th>None-frail</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>14</td>
<td>14</td>
<td>.01</td>
</tr>
<tr>
<td>Moderate</td>
<td>22</td>
<td>24</td>
<td>.01</td>
</tr>
<tr>
<td>Mild</td>
<td>9</td>
<td>5</td>
<td>.88</td>
</tr>
<tr>
<td>Normal</td>
<td>65</td>
<td>75</td>
<td>.99</td>
</tr>
<tr>
<td>&lt;6.5</td>
<td>17</td>
<td>12</td>
<td>.11</td>
</tr>
<tr>
<td>6.5-8.5</td>
<td>46</td>
<td>26</td>
<td>.01</td>
</tr>
<tr>
<td>8.5-10</td>
<td>24</td>
<td>8</td>
<td>.14</td>
</tr>
<tr>
<td>&gt;10</td>
<td>29</td>
<td>11</td>
<td>.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>Frail</th>
<th>None-frail</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6.5</td>
<td>17</td>
<td>12</td>
<td>.11</td>
</tr>
<tr>
<td>6.5-8.5</td>
<td>46</td>
<td>26</td>
<td>.01</td>
</tr>
<tr>
<td>8.5-10</td>
<td>24</td>
<td>8</td>
<td>.14</td>
</tr>
<tr>
<td>&gt;10</td>
<td>29</td>
<td>11</td>
<td>.01</td>
</tr>
</tbody>
</table>

### Table 4. Comparison of insulin regimes and frailty status

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>Basal-bolus</th>
<th>Mix</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frail</td>
<td>50</td>
<td>39</td>
<td>21</td>
<td>.01</td>
</tr>
<tr>
<td>None-frail</td>
<td>20</td>
<td>23</td>
<td>14</td>
<td>.01</td>
</tr>
</tbody>
</table>

infectious diseases, and the improvement of living conditions,
and accordingly, the elderly population is increasing rapidly in
our country as in the world. Malnutrition, incontinence,
inaactivity, delirium, depression, falls, dementia, pain, gait
disorders, osteoporosis, frailty and pressure sores are the most
common problems in the elderly. Frail elderly syndrome has
many different definitions. The definition with the greatest
consensus is increased susceptibility to external stresses due to
age-related physiological reserves, neuromuscular, metabolic,
and immune system dysfunction. The frailty rate increases with
age and reaches 30% over the age of 90. Frail elderly people
are the group that will benefit most from a comprehensive
geriatric assessment. By identifying these elderly people and
taking the necessary preventive and therapeutic measures in
cooperation with their families, the morbidity and mortality
rate can be reduced. In the literature, there are not enough
studies on frailty in the diabetic elderly patient group. However,
when the studies on frailty are examined, we see that these
studies are carried out to find the most appropriate method
for detecting frailty or to draw attention to frailty and to
emphasize the inadequacies in this regard. Considering that
studies on the life activities of the elderly are not sufficient in
our country, in a study in which 400 patients aged 65 and over
were included in a private hospital and their daily living activity
indices were examined, the life activity performances of the
patients between the ages of 65-70 years (52.5%), 70-75 years
(41.2%), 75-80 years (43.8%) and 85-90 years (40%) were
found to be "very good", only 50% of patients aged 90-95 were
"bad" and it was concluded that a multidisciplinary
approach should be taken towards the general care of elderly
patients. According to the results of this study, it has been
shown that care and treatment approaches change as age
et al.14, it was aimed to evaluate 129 combinations of seven indicators of weakness (cognition, energy, mobility, mood, nutrition, physical activity, and strength) and to determine their predictive accuracy regarding age, gender, and number of chronic diseases. When 129 combinations of weakness indicators from the best model to the worst fit model are compared, it was found that the inclusion of multiple indicators generally improved performance and single markers gave the worst performance result. The results also suggest that frailty as a diagnostic tool, may play a more important role in the 80 and older age group. Although the "CHS model" and the "count model" are among the best models, it was concluded that both were not optimal. Compared to these two studies, our study used frailty criteria (fatigue, weight loss, slowness, decreased physical activity, decreased stamina and energy) according to the CHS to evaluate frailty and adherence to treatment in the geriatric population. In addition, hypoglycemia and other comorbid diseases were also questioned in the diabetic patient population over 65 years of age. While there was no significant relationship between frailty and hypertension and chronic kidney disease, a significant relationship was found between the presence of heart failure, cerebrovascular accident, dementia, hypoglycemia and frailty groups. The frailty rates were 35.1% in those with heart failure, 31.6% in those with cerebrovascular accident, and 31.6% in those with dementia. Both moderate and severe hypoglycemia were observed 2 times more in the frail group. Based on this, we can say that the presence of frailty significantly increases the risk of moderate and severe hypoglycemia, and if insulin therapy is planned, frailty should be detected and this should be taken into account when arranging the treatment. In another study, it was stated that elderly diabetic patients are constantly at high risk of geriatric syndrome, and are at risk for functional impairment, depression, falls, urinary incontinence, malnutrition, and cognitive impairment. It was concluded that the treatment of diabetic patients with geriatric syndrome should focus on a strategy to prevent exacerbation of frailty15. In a published guideline, it is recommended that the treatment targets of blood glucose in elderly people with diabetes be individually determined according to age, life expectancy, patient preference, presence of geriatric syndrome, depression, pain, falling, incontinence, polypharmacy, and cognitive impairment16. In a study by Gregg et al.17, which included 6,588 residents aged 60 and over, it was reported that 32% of diabetic women and 15% of men with diabetes did not have the capacity to walk a quarter of a mile, do housework or climb stairs, this rate for those without diabetes was detected as 14% for women and 8% in men. In a study by Amer et al.18 in which 104 elderly patients were included, similar to our study, it was seen that in physically frail cases the rate of associated chronic diseases, diabetes, ischemic heart diseases, hypertension, stroke, vision and hearing loss was significantly higher than others.

**Study Limitations**

Our study had some limitations. First, our study was a single-center cross-sectional analysis. Second, frailty was assessed at a single time point. Third, the presence of hypoglycemia was based on one-time measurement.

**CONCLUSION**

In conclusion, with this study, we wanted to draw attention to frailty in diabetic patients and to examine the effect of hypoglycemia on frailty. In all studies in the literature, it is not considered beneficial to try to keep blood glucose normoglycemic with intensive antidiabetic therapy in elderly diabetic patients19. Elderly diabetic patients have many risk factors such as a history of cardiovascular disease and other comorbid diseases. All these risk factors outweigh the benefits of intensive antiglycemic therapy in the elderly diabetic population. In the Action to Control Cardiovascular Risk in Diabetes study; it has been shown that giving intensive antiglycemic therapy and trying to reduce the HbA1c target below 6% increase the risk of death from other causes or cardiovascular causes4. Similarly, it was found in the Veterans Affair Diabetes Trial study that excessive glycemic control failed to have benefit in cardiovascular endpoints20. In our study, we found that frailty increases the risk of hypoglycemia in the geriatric patient population using insulin. We also showed that other comorbid conditions, such as dementia and Alzheimer, are also associated with increased frailty. This revealed the necessity of considering comorbid conditions apart from activities of daily life when assessing frailty. We observed that frailty increases with increasing age. Considering that the majority of the diabetic patient population will be over the age of 65 in the near future, frailty syndrome will have even more importance. This shows that for elderly diabetic patients, these geriatric syndromes should be evaluated and the treatment should be arranged with this perspective. In addition to the agent to be chosen in the treatment of diabetic patients, attention should be paid to the issue of hypoglycemia. Ultimately, frailty will be beneficial for health improvement only if it is reversible or if adverse outcomes can be changed or at least improved. If the use of insulin is absolutely necessary in elderly individuals, choosing the regimen after considering the frailty will ensure compliance with the treatment and protect the individuals from complications.

**Acknowledgement**

We thank Ümraniye Training and Research Hospital for its support.
Ethics

**Ethics Committee Approval:** The study were approved by the Ümraniye Training and Research Hospital Ethics Committee (decision number: 56, date: 24.09.2014).

**Informed Consent:** An informed consent form was signed by all patients participating in the study.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**


**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

**References**