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Research Article

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The Effect of Glycemic Control on Rehabilitation Outcomes of Diabetic Patients Following Hip Fracture Repair

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Abstract

Background: This study examined the effect of glucose control during rehabilitation for surgical repair of hip fracture on rehabilitation outcomes.

Methods: Diabetic patients after hip fracture were recruited from a rehabilitation center. Glucose control was assessed by HbA1c and glucose measurements. Motor and cognitive functional status at admission and discharge from rehabilitation were estimated using the Functional Independence Measure (FIM). The patients were prospectively followed 3 months after discharge, and functional status assessed by telephone interview. Three-month mortality data were collected.

Results: A total of 64 patients were recruited (mean age 80.73±7.46 years, 78.12% women). Median HbA1c was 6.74±0.99% and mean glucose level was 143.72±26.41 mg/dl. No correlation was found between these variables and mortality, functional status at discharge or 3 months post-discharge. Higher pre-fracture functional status was associated with better functional status at discharge ($p=0.032$) and a non-significant trend towards reduced long-term mortality ($p=0.058$). Higher discharge FIM scores were associated with lower long-term mortality. Maximal glucose levels greater than 250 mg/dl during rehabilitation were associated with increased rate of readmission to the general hospital ($p=0.041$).

Conclusions: Glycemic control during rehabilitation following hip fracture did not influence short- or long-term functional outcomes or mortality.

Keywords: Rehabilitation; Diabetes; Glycemic Control; Hip Fracture

Introduction

The relationship between hyperglycemia and acute illness is complex and is often attributed to fluctuations in circulating stress hormones [1-3]. Regardless of cause, hyperglycemia during hospitalization for acute illness is an independent risk factor for poor outcome [4]. In-hospital mortality is even higher among patients with newly diagnosed hyperglycemia than it is for those with previously diagnosed diabetes [5]. For example, hyperglycemia among patients with diabetes admitted for acute myocardial infarction predicted both in-hospital and 1-year mortality [6].

Data regarding target glucose levels during hospitalization and the preferred method of glucose control are inconclusive. While some clinical studies have demonstrated benefit from tight glucose control [7], others, such as the NICE-SUGAR study, showed no effect or even increased risk of hypoglycemia and mortality [8].

Data regarding the effect of diabetes and glycemic control on rehabilitation outcomes is limited. Reistetter et al. demonstrated that diabetic patients tended to have longer rehabilitation admissions following hip fracture compared to their non-diabetic counterparts [9]. However, other population characteristics were not taken into account such as diabetes treatment or glycemic control. Lieberman et al. concluded that the odds for successful rehabilitation among diabetic patients were four-fold poorer compared to their non-diabetic peers [10], while a later publication by the same group of authors did not reaffirm the role of diabetes in rehabilitation following hip fracture [11]. Adunsky et al. found that diabetes had no effect on rehabilitation outcomes following hip fracture [12]. This study examined the effect of glycemic control during rehabilitation for surgical repair of hip fracture on short-term and 3-month outcomes.

Study Design

The study included patients aged 65 years and older who were admitted to the Geriatric Rehabilitation Unit affiliated with Meir Medical Center, a tertiary care facility. The Geriatric Rehabilitation Unit patient population includes neurologic (post-CVA) and orthopedic patients. The duration of hospitalization ranges from two weeks for post-surgical hip fracture repair to up to one month for neurologic patients. Patients included in our study were admitted to the unit following surgical repair of hip fracture (the index event) from January 2014 until June 2015. The study was approved by the hospital Ethics Committee. Informed consent was not required.

Data collected from hospital electronic medical records included demographics, diabetic treatment prior to hospitalization and during rehabilitation, comorbidities, type of surgical procedure, readmission, mortality during rehabilitation and mortality within 3 months of discharge. All patients had been diagnosed with type II diabetes mellitus prior to the hip fracture. Patients with a diagnosis of dementia at admission to rehabilitation were excluded, as were those on systemic glucocorticoid therapy.

The rehabilitation unit used a unified glucose control protocol. Diabetic patients were transferred to a basal-bolus insulin therapy regimen if they had at least 2 glucose values > 180 mg/dl. Patients on insulin therapy continued their regimen with adjustments according to glucose levels. Glucose control was achieved without intervention by the investigators.

Glycemic control was assessed using hemoglobin A1c (HbA1c) and glucose measurements. If HbA1c value within the 3 months preceding hospitalization was unavailable, it was measured at admission to rehabilitation using the D-10TM hemoglobin testing system (Bio-Rad, Hercules, CA, USA). Capillary glucose levels were measured at bedside using a glucometer and documented in the electronic medical record. Minimum, average and maximum glucose levels were abstracted from the patient's glucose chart. Hypoglycemia was defined as glucose level < 70 mg/dl. Severe hypoglycemia was defined as glucose < 50 mg/dl.

Patient pre- and post-fracture functional status was defined as independent (able to conduct all Activities of Daily Living [ADL]), dependent (need assistance with at least 3 ADL) or frail (neither independent nor dependent). Functional outcomes were measured using the Functional Independence Measure (FIM) scale, which includes18 items composed of 13 motor tasks (FIM_{motor}) and 5 cognitive tasks ($FIM_{cognitive}$). Tasks are rated on a 7-point ordinal scale that ranges from18 (indicating total assistance or complete dependence) to 126 (indicating complete independence). Patients are usually evaluated at admission and discharge.

To evaluate changes in functional status, a surrogate marker, termed ΔFIM_{motor}, was defined and calculated as the difference between the FIM_{motor} score at the beginning of rehabilitation and at discharge. Patients who were admitted to rehabilitation from December 2014 through June 2015 were contacted by telephone 3 months post-discharge. Functional status at this point was defined as independent, frail or dependent according to self-reported ADL function.

Statistical Analysis

Data were presented as numbers and percentages for nominal variables, and mean and standard deviation for continuous parameters. Chi-Square or Fishers' Exact test were conducted for non-metric parameters (each when appropriate) and t-test or Mann-Whitney non-parametric test for quantitative variables, according to variable distribution. $P<0.05$ was considered statistically significant. All statistical analyses were performed with SPSS-23 software.

Results

Patient Characteristics and Outcomes

A total of 64 patients with diabetes were recruited to the study. Two patients were lost to follow-up and 33 were available for long-term functional analysis. The demographics of the study population are presented in (Table 1). Functional status prior to hip fracture was the main determinant of rehabilitation outcome. Higher pre-fracture functional status correlated with lower mortality during hospitalization ($p = 0.032$). There was a trend toward an inverse correlation between pre-fracture functional status and mortality at 3 months ($p = 0.058$).

Higher FIM scores at discharge, as well as greater ΔFIM_{motor} were also significantly correlated with lower 3-month mortality ($p < 0.001$, $p < 0.001$ and $p < 0.001$ respectively). FIM_{motor} at the beginning of rehabilitation was inversely correlated with mortality at 3 months ($p = 0.009$).

Higher pre-fracture functional status correlated with greater ΔFIM_{motor} ($p = 0.009$). Patients with subcapital fracture had higher FIM_{motor} scores at discharge and ΔFIM_{motor} compared with patients with pertrochanteric fracture (65.24±11.16 vs. 53.08±19.07, $p < 0.006$; 25.04±11.12 vs. 13.47±17.36, $p < 0.004$). Jewish patients had greater ΔFIM_{motor} compared with Arab patients (19.98±13.67 vs. 2.71±25.85, $p < 0.007$).

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Variable	Total	Hemoglobin A1c		P-value
		≤6.5%	>6.5%	
Total, N	64	25 (40.0)	33 (51.6)	
Age, years (mean±SD)	80.73±7.47	80.95±8.47	80.31±6.73	0.748
Gender, N (%)				0.223
Male	14 (21.88%)	8 (13.8)	6 (10.3)	
Female	50 (78.12)	17 (26.56)	27 (42.19)	
Ethnicity, N (%)				1
Jewish	56 (87.50%)	22 (37.9	29 (50.0)	
Arab	8 (12.50%)	3 (5.2)	4 (6.9)	
Functional status before index event, N (%)				0.878
Independent	37 (57.81%)	15 (25.9)	18 (31.0)	
Frail	25 (39.06%)	9 (15.5)	14 (24.1)	
Dependent	2 (3.13%)	1 (1.7)	1 (1.7)	
Comorbidities at hospitalization, N (%)				
Osteoporosis	13	6 (10.3)	6 (10.3)	0.588
Cardiovascular diseases	35	14 (24.1)	19 (32.8)	0.904
Hypertension	53	19 (32.8)	29 (50.0)	0.302
Chronic renal insufficiency	17	9 (15.5)	8 (13.8)	0.33
Active malignancy	7	5 (8.6)	1 (1.7)	0.075
Past malignancy	13	7 (12.1)	6 (10.3)	0.375
Chronic lung disease	10	5 (8.6)	5 (8.6)	0.628
Duration of rehabilitation, days (mean±SD)	29.94±14.63	33.44±18.62	28.03±11.17	0.174
Motor FIM at the start of rehabilitation (mean±SD)	39.80±12.32	42.60±11.43	39.18±12.94	0.3
Cognitive FIM at the start of rehabilitation (mean±SD)	26.78±4.69	25.60±5.55	27.88±3.66	0.065
Motor FIM at the end of rehabilitation (mean±SD)	57.90±17.35	58.04±15.61	59.09±18.96	0.823
Cognitive FIM at the end of rehabilitation (mean±SD)	25.55±6.64	24.05±7.69	26.75±6.01	0.141
ΔFIM_{motor} (mean±SD)	20.78±10.64	15.91±16.45	19.25±16.82	0.376
Minimum glucose, mg/ml (mean±SD)	78.69±14.38	77.92±14.66	78.48±14.33	0.884
Average glucose, mg/ml (mean±SD)	143.72±26.41	133.56±19.05	150.09±28.98	0.016
Maximum glucose, mg/ml (mean±SD)	266.91±85.06	256.24±64.97	272.91±96.93	0.461
Hypoglycemia during hospitalization, N (%)	9 (14.06%)	4 (16.0)	5 (15.1)	1
Severe hypoglycemia during hospitalization, N (%)	2 (3.13%)	1 (1.7)	1 (1.7)	1
Readmission, N (%)	21 (32.81%)	8 (32.0)	11 (33.3)	0.915
Mortality during rehabilitation, N (%)	5 (7.82%)	1 (4.0)	4 (12.1)	0.378
Long-term mortality, N (%)	11 (17.19%)	4 (16.0)	6 (18.2)	1

N - Number of patients; SD - Standard deviation; FIM - functional independence measure; ΔFIMmotor = (motor FIM score at discharge - motor FIM score at beginning of rehabilitation). All continuous variables are stated as mean±SD

Table 1: Demographic data according to hemoglobin A1c values.

Long-term functional status reported at telephone interview correlated with pre-fracture functional status (p = 0.029). FIM scores at the end of rehabilitation and ΔFIM_{motor} also correlated with functional status 3 months after rehabilitation.

Total mortality rate in our study was 17.2% (5 patients died during rehabilitation and 6 died during the 3-month follow-up). No association was found between epidemiologic characteristics of the patients and the outcomes measured, including mortality during rehabilitation, mortality at 3 months, rate of readmission to the general hospital and duration of rehabilitation.

Glycemic Control and Outcomes

Anti-diabetic drugs most frequently used during rehabilitation were metformin (57.81%), short-acting insulin analogues (25.00%) and long-acting insulin analogues (39.10%). Four patients (6.25%) did not require anti-diabetic agents before hospitalization. One of these patients had hyperglycemia during rehabilitation and was started on metformin. Sulfonylureas and metformin were discontinued in two patients (3.13%) due to adequate glycemic control.

HbA1c levels were available for 58 patients (90.63%). Patients were stratified into 2 groups: HbA1c ≤ 6.5% and HbA1c > 6.5%. HbA1c data are presented in Table 1. There was no correlation between the HbA1c and the rate of hypoglycemia (p = 1.000), the rate of readmission to the general hospital (p = 0.915), mortality during rehabilitation (p = 0.378), 3-month mortality (p = 1.00) or duration of rehabilitation (p = 0.174).

Data regarding correlation of glucose levels with rehabilitation outcomes and hypoglycemic events are summarized in (Table 2). There was no correlation between the minimum, average or maximum glucose levels and mortality during rehabilitation, 3-month mortality or duration of rehabilitation. Minimum glucose levels were not correlated with rate of readmission to the general hospital. Patients with lower maximum glucose levels were less likely to be readmitted to the general hospital (p = 0.041). There was a trend towards correlation between lower average glucose level and lower rate of readmission to the general hospital (p = 0.054).

Variable	Average glucose level			Maximum glucose level		
	≤140	>140	P-value	≤250	>250	P-value
Total, N (%)	38 (59.38)	26 (40.62)		33 (51.56)	31 (48.43)	
Hypoglycemia, N (%)	3 (7.9)	6 (23.1)	0.142	3 (9.1)	6 (19.4)	0.296
Readmission, N (%)	9 (23.7)	12 (46.2)	0.054	7 (21.2)	14 (45.2)	0.041
Mortality during rehabilitation, N (%)	3 (7.9)	2 (7.7)	0.677	2 (6.1)	3 (9.7)	0.667
Long-term mortality, N (%)	9 (23.7)	2 (7.7)	0.089	5 (15.2)	6 (19.4)	0.656
Duration of rehabilitation (days, mean±SD)	31.11±13.91	28.23±15.74	0.445	30.45±14.75	29.39±14.72	0.773
Motor FIM at hospitalization	40.45± 12.597	38.85±12.09	0.614	40.39±13.81	39.16±10.71	0.693
Motor FIM at discharge	56.79±20.64	59.60±10.77	0.534	57.58±18.68	58.27±16.08	0.876
ΔFIM_{motor}	16.34±17.42	20.68±13.89	0.3	17.18±17.35	19.03±14.91	0.653
Cognitive FIM at hospitalization	26.68±5.15	26.92±4.04	0.839	26.81±4.98	26.74±4.46	0.953
Cognitive FIM at discharge	24.76±7.95	26.72±3.85	0.257	25.66±6.98	25.43±6.37	0.896
Status 3 months' post-discharge, N (patients recruited starting December 2014)			0.098			0.454
Independent	5	2		5	2	

Frail	6	7		7	6	
Dependent	3	4		2	5	
N - Number of patients; SD - Standard deviation; FIM - functional independence measure; ΔFIMmotor = (motor FIM score at discharge - motor FIM score at beginning of rehabilitation). All FIM scores are stated as mean±SD						

Table 2: The relationship between the average and maximum glucose levels and rehabilitation outcomes.

The incidence of hypoglycemia during hospitalization was 14.06%. Only 2 patients (3.12%) experienced severe hypoglycemia, with no clinical consequences. There was no correlation between hypoglycemia and mortality during rehabilitation (p = 0.141), 3-month mortality (p = 0.177) or patient functional status at the end of the follow-up period (p = 0.883).

With regard to functional outcomes, there was no correlation between HbA1c, minimum, average or maximum glucose values and FIM scores at discharge (Tables 1 and 2). For patients who participated in the follow-up telephone interview, there was no correlation between glycemic control variables and status 3 months post-discharge (p = 0.288).

Discussion

Diabetic patients are at increased risk for hip fractures [13]. Some clinical factors were associated with this increase including HbA1c above 9% [14], insulin treatment [15] and glucose variability [16]. Moreover, mortality after hip fracture is up to 30% higher in diabetic patients compared to non-diabetic patients [17-19].

Nevertheless, data pertaining to the effect of glycemic control on rehabilitation outcomes following hip fracture is limited. It has been shown that diabetic patients tend to remain in rehabilitation longer compared to non-diabetic patients. Studies addressing the influence of glycemic control on rehabilitation outcomes have presented conflicting results [9,12].

In the current study, several different parameters of glycemic control did not correlate with rehabilitation outcomes after hip fracture. We established a link between higher maximal glucose levels and increased hospital readmission rate. Although poor glycemic control is considered a risk factor for perioperative complications such as cardiovascular events and infections and readmissions [20,21], it is difficult to ascertain whether hyperglycemia underlies the higher rate of complications or reflects the severity of the patient's illness secondary to circulating stress hormones.

The total mortality rate in our study was 17.2% (5 patients died during rehabilitation and 6 died during the 3-month follow-up). An association between glucose control and mortality was not found, possibly due to the homogeneity of the patients; 68.42% had HbA1c levels ≤ 7%. These relatively low HbA1c levels are surprising considering the high prevalence of uncontrolled diabetes mellitus in the general population and the lower fracture risk among elderly patients with low HbA1c levels (6.5-6.9%) [14,21]. However, strict glycemic control may also come at a risk of hypoglycemia, which can lead to recurrent falls and fractures [22]. The relatively low HbA1c levels in our study may be partially explained by post-operative anemia and administration of blood transfusions, which could have diluted patients' hemoglobin. This hypothesis may be refuted by the good correlation of the HbA1c levels with the glucose levels (Table 1).

In accordance with previous studies [22-25], pre-fracture functional status in our study was a strong predictor of patient outcome following hip fracture. Independent patients with diabetes tended to survive longer, to achieve a greater change in FIM scores and to return to their pre-fracture status compared with frail or dependent patients with diabetes. This may be linked to better mental status at the time of fracture [26], a factor that represents a commitment to acquire new abilities, such as using assistive devices for walking, and to regain previous activity levels. The correlation between higher FIM_{motor} and $FIM_{cognitive}$ scores at discharge and survival and long-term functional status found in our study supports this concept.

The strengths of this study include the analysis of the glycemic control and its effect on rehabilitation using HbA1c and minimum, average and maximum glucose levels. In addition, glycemic control was also evaluated in relation to patients' functional status pre- and post-fracture. To the best of our knowledge, previous studies did not analyze glycemic control to this depth. Another strength of the study is the 3-month follow-up after rehabilitation.

The main limitation of this study is the small number of participants. In addition, patients with poor glucose control were under-represented in our cohort. Moreover, evaluation of 3-month functional status by telephone interview which was limited to 3 categories (independent, frail or dependent) rather than using formal FIM scoring may have led to imprecision. Self-reporting may also be a cause of bias.

Conclusion

In this study, we demonstrated that pre-fracture status rather than glucose control parameters was the main determinant of rehabilitation outcome among patients with diabetes following hip fracture. However, higher maximal glucose levels were correlated with an increased rate of readmissions to the general hospital. This may reflect the severity of the medical condition necessitating the readmission. Future studies with larger populations from multiple centers, with longer follow-up periods and more sophisticated evaluation of post-rehabilitation functional status is necessary to establish these results.

Declaration of Interest: The authors report no conflict of interests.

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