ORIGINAL ARTICLE

Hypoglycemia and hyperglycemia are risk factors for falls in the hospital population

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Abstract

Objective To determine the role of hypoglycemia, hyperglycemia or the combination of both as independent risk factors for falls in a hospital population. Secondary objectives included evaluation of other risk factors for falling and their relationships with glucose levels.

Research design and methods Retrospective cohort study over 2 years on hospitalized subjects ($N = 57411$) analyzing in-hospital-falls and capillary glucose values. Bivariate analysis (χ^2 test) and multivariate analysis (logistic regression) were performed to test for correlation of glucose values, age, sex, Charlson index, service of care, diagnosis at discharge and diabetes treatment with risk of in-hospital-falls.

Results The comparison of patients who experienced a fall (fall population) with the non-fall population suggested that: glucose determinations were significantly more frequent in the fall population (OR 3.45; CI 2.98–3.99; $p < 0.0001$); values of glucose below 70 mg/dl and over 200 mg/dl were significantly associated to falls during hospitalization (OR 1.76; CI 1.42–2.19; $p < 0.001$) as compared to glycemic values between 70 and 200 mg/dl; diabetes treatment was significantly correlated to risk of fall (OR 2.97; CI 2.54–3.49; $p < 0.001$); the frequency of glycemia measurements below 70 mg/dl and over 200 mg/dl in the same subject was significantly associated to falls during hospitalization (OR 1.01; CI 1.01–1.02; $p < 0.001$).

Conclusion Hypoglycemia and hyperglycemia during hospital stays are correlated with an increased risk for falls in the hospitalized population. Presence of diabetes, use of insulin or glucose variability could potentially constitute risk factors for falls inside the hospital as well.

Keywords Falls · Hyperglycemia · Hypoglycemia · Glucose variability · Diabetes · In-hospital · Insulin · Hypoglycemic agents

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Background

Patient falls are frequent adverse events in hospitals and are associated to potentially severe consequences in terms of morbidity and mortality, such as further deterioration of physical and mental wellbeing and increased inpatient time, which conversely worsens prognosis and increases economic and social costs. The frequency of falls in the hospitalized population is between 4 and 12 falls every 1000 days of hospitalization [1], which may result in femoral fractures [2] and more rarely in the formation of subdural hematomas [3] among the other potentially harmful consequences. Many of the features relevant to inpatient falls, such as patient characteristics, circumstances (e.g., location, time, patient's activity) and other risk factors, as well as interventions to prevent patient falls during hospitalization, have been investigated before. Multiple-fall risk factors have been identified in the past, such as specific medical conditions [4–7], history of falls, age, visual impairment, pain, cognitive decline, and medications like antiarrhythmics, beta-blockers, benzodiazepines, antidepressants, and calcium channel antagonists [8–11].

Hyperglycemia has been associated with increased morbidity and mortality in hospitalized patients with or without a prior diagnosis of diabetes [12], whereas hypoglycemia has been linked to increased mortality in the intensive care unit [13]. Moreover, increased glycemic variability during hospitalization was found to be independently associated with longer permanence and increased mortality in long-term follow-up of non-critically ill patients [14–16].

Previous studies suggested that hypoglycemia is associated with increased risk of falls in elderly type 2 diabetic patients. In these studies the prevalence of falls increased with the frequency of hypoglycemic events in the outpatients setting [17] and similar results were also found in younger subjects affected by type 1 diabetes [18]. Risk for hip fractures in patients with type 2 diabetes was found to be linked to severe hypoglycemia and falling was likely the main cause [19, 20]. Yau et al reported that hyperglycemia, as well as poor physical balance, were risk factors for injuries requiring hospitalization in elderly diabetic patients, in particular in those using insulin [21].

Nowadays, our knowledge regarding the association of glycemia to falls with their causes is still somehow quite limited. Likewise, the effect of other risk factors in the general hospitalized population, irrespective of the presence of diabetes is largely unknown and a matter of active investigation.

Aim of the study

The purpose of this study was to investigate the role of hypoglycemia, hyperglycemia, or the combination of both (glucose variability), as independent risk factors for falls in a hospitalized population.

Secondary aims were to identify other variables associated with in-hospital falls, to explore their relationship with hypoglycemia or hyperglycemia and to investigate a potential connection between falls and the diagnosis of diabetes among hospitalized subjects.

Materials and methods

We performed a retrospective cohort study that included all subjects admitted to Humanitas Research Hospital, Milan, Italy between January 2015 and December 2016 (108 weeks). Patients admitted to the Intensive Care Units (ICU) were excluded, due to their high level of dependency and immobilization, being completely bedridden and unable to walk around.

The incidence of falls was assessed among patients who met the inclusion criteria. Analyses were performed on all glucose readings available from each individual hospitalization. Patient characteristics included in the analysis were: sex, age, hospital access (emergency vs elective admission), hospital discharge diagnosis (surgical vs medical), clinical severity [assessed through Diagnosis Related Group (DRG) weight and Charlson Index] [22, 23].

Approval for our retrospective study was obtained from the Institutional Review Board.

Data collection

Data were extracted from the Electronic Medical Record system used in our hospital (EMRS Lutech wHospital® 26.3.12.6098 version). Blood glucose concentrations were measured from capillary blood obtained by finger stick with a standard system (ACCU-CHECK Aviva® Roche). The results of these capillary blood glucose tests, along with patient details, time and date of testing are routinely uploaded to a central network system for storage and were subsequently available to us for analysis. As follows, information concerning clinical details, a summary of all drugs administered, service of care (medicine or surgery), ICD-9 codification (discharge diagnosis) were also documented and available on EMRS.

Hypoglycemia was defined as any episode of capillary blood glucose below 70 mg/dl during the hospital stay, while hyperglycemia was defined as any episode of

capillary blood glucose above 200 mg/dl during the hospital stay.

A fall was defined as any unexpected and unintentional event in which the patient came to rest on the ground, floor or a lower level. In any of these cases the event was registered in the central network system of the hospital and was available for analysis (EMRS).

The Charlson index is a tool for predicting health outcomes by classifying or weighing comorbid conditions (comorbidities) based on the International Classification of Diseases (ICD) diagnosis codes found in the administrative data of hospitalized patients [24].

Statistical analysis

Bivariate analysis was employed to test for association between the occurrence of falls and every categorical variable (capillary glucose determinations, glucose values, diabetes medications, and glycated hemoglobin) by applying Chi squared test.

For the multivariate analysis a logistic regression was employed to identify the variables that were significantly associated with a fall. Hence, the fall was considered the dependent variable while the other variables were independent variables, that could explain the occurrence of a fall.

Results

Subjects

Based on the exclusion criterion (patients admitted to the intensive care unit), the final sample consisted of the medical records of 57,411 patients.

The clinical characteristics of the study subjects are summarized in Table 1.

In brief, the mean age was 60.7 (50–74), of which 52.7% were males ($N = 30,271$) and 47.3% females ($N = 27,140$). 62.4% had a medical diagnosis at discharge ($N = 35,804$), while 37.6% had a surgical diagnosis at discharge ($N = 21,607$). 13,065 patients were admitted to the hospital from the emergency department (23.7%), while 43,806 were elective patients (76.3%). When employing the Charlson index to determine the degree of diagnosis complexity at discharge, 11.7% ($N = 6717$) had a score of 2, while 6.6% ($N = 3789$) scored 1, and 81.7% ($N = 46,905$) scored 0.

Falls and capillary glucose determinations

759 subjects experienced a fall during their hospital stay among the total of 57,411. We thus considered two different cohorts: a fall population ($N = 759$) and a non-fall population ($N = 56,652$).

Table 1 Characteristics of subjects admitted to the hospital and included in the study between January 2015 and December 2016

Patients characteristics		(%)
Mean age (years)	60.7 (50–74)	
Gender		
Male	30,271	52.7
Female	27,140	47.3
Total number of patients	57,411	
Hospital discharge diagnosis		
Medical	35,804	62.4
Surgical	21,607	37.6
Admissions		
Elective	43,806	76.3
From ER	13,605	23.7
Charlson index		
0	46,886	81.7
1	3799	6.6
2	6726	11.7

The number of patients with at least one capillary glucose determination in the non-fall population was 13,025 (23%), while in the fall population it was 385 (50.7%), (odds ratio 3.45, confidence interval 2.98–3.99; $p < 0.001$).

In the group in which there was no any capillary glucose measurement ($N = 43,627$), there were 374 falls (0.8%). In the group, which had at least one capillary glucose measurement ($N = 13,410$), 385 falls were documented (2.9%) ($p < 0.001$) (Table 2).

Falls and glucose values

In the subgroup which had at least one capillary glucose measurement ($N = 13,410$), subjects with at least one glycemic value out of the range (> 200 mg/dl or < 70 mg/dl) had an odds ratio for falling of 1.76 as compared with patients with glucose values within the 70–200 mg/dl range (confidence interval between 1.42 and 2.19; $p < 0.001$) (Table 2). Values below 70 mg/dl (hypoglycemia) conferred a higher risk of falling (odds ratio 2.18; confidence interval 1.69–2.8, $p < 0.001$) as compared with values over 200 mg/dl (hyperglycemia) (odds ratio 1.7; confidence interval 1.38–2.11 $p < 0.001$) (Table 2).

Falls and diabetes medications

When considering the subjects treated with diabetes medications ($N = 7579$), (hypoglycemic agents including insulin), prescription of hypoglycemic treatment was significantly associated with values of glucose > 200 mg/dl and < 70 mg/dl. 233 out of 7579 (3.07%) fell, while in subjects not receiving hypoglycemic agents, the percentage of falls was 1.05% (526

Table 2 Associations between glucose values and falls

	Non-fall population $N = 56,652$	Fall population $N = 759$	
No glucose determination	43,627 (77%)	374 (49.3%)	OR 3.45, CI 2.98–3.99 $p < 0.0001$
Glucose determination	13,025 (23%)	385 (50.7%)	
Glucose value < 70 mg/dl	1557 (12%)	88 (22.9%)	OR 2.18, CI 1.69–2.80; $p < 0.001$
Glucose value > 70 mg/dl	11,468 (88%)	297 (77.1%)	
Glucose value < 200 mg/dl	7064 (54.3%)	158 (41%)	OR 1.70, CI 1.38–2.11; $p < 0.001$
Glucose value > 200 mg/dl	5961 (45.7%)	227 (59%)	
Glucose value < 70 mg/dl or > 200 mg/dl	6412 (49.2%)	243 (63.1%)	OR 1.76, CI 1.42–2.19; $p < 0.001$
Glucose value between 70 and 200 mg/dl	6613 (50.8%)	142 (36.9%)	

Table 3 Associations between the use of hypoglycemic agents or Insulin and falls

	Non-fall population $N = 56,652$	Fall population $N = 759$	
Subjects not treated with hypoglycemic agents	49,306 (87%)	526 (69.3%)	OR 2.97, CI 2.54–3.49; $p < 0.001$
Subjects treated with hypoglycemic agents	7346 (13%)	233 (30.7%)	
Subjects not treated with insulin	52,128 (92%)	601 (79.2%)	OR 3.03 CI, 2.53–3.63; $p < 0.001$
Subjects treated with insulin	4524 (8%)	158 (20.8%)	

out of 49,832) (odds ratio 2.97, confidence interval of 2.54 and 3.49; $p < 0.001$). (Table 3). Insulin treatment (4682 subjects) was more significantly associated with the risk of falls, 158 out of 4682 subjects treated with insulin (3.3%) fell, while in subjects not receiving insulin, 601 out of 52,729, (1.1%) fell, (odds ratio 3.03, confidence interval 2.53–3.63, $p < 0.0001$) (Table 3).

Multivariate analysis

In a multivariate analysis, sex, age, admission to the hospital (from ER/elective), drugs for diabetes, service of care (medicine or surgery) and Charlson index for discharge diagnosis were significantly associated with falling and the presence of at least one out of range glycemic value (over 200 or below 70 mg/dl) also conferred an odds ratio for fall of 1.57 (confidence interval of 1.20 and 1.86; $p < 0.001$) (Fig. 1a).

Age (in a linear regression), diagnosis at discharge and disease complexity were independent risk factors for falls in the hospital setting, as well as the number of glycemic values out of range (over 200 or below 70) which conferred an odds ratio for fall of 1.01 (confidence interval of 1.01 and 1.02; $p < 0.001$) (Fig. 1b).

Discussion

Inpatient hyperglycemia or hypoglycemia are frequent and important phenomena, which have been explored within the hospital setting and have been associated with

increased mortality and morbidity, increased duration of hospitalization and poorer outcomes [12–16].

Falls in the hospital population are common complications of hospital care, which result in significant morbidity and mortality, including serious injuries, prolonged hospitalization, decreased quality of life and increasing hospital financial liability [25–30].

In the non hospitalized population, diagnosis of diabetes and presence of hypoglycemia are known to increase the risk of falls requiring hospitalization, as a result of several established factors such as the presence of peripheral neuropathy, decreased cognitive performance, impaired vision, and decreased physical performance [17–21].

We have therefore decided to study the impact of hypoglycemia, hyperglycemia, and their combination (glucose variability) in our hospitalized population.

Our data suggest that subjects undergoing capillary blood glucose monitoring experience more falls than patients in whom this degree of monitoring is deemed not necessary, regardless of the diagnosis of diabetes or treatment for this disease. Patients undergoing glucose monitoring in the clinical setting, independently from the presence of diabetes or a medical history of diabetes, might represent a subgroup of a "fragile" population, such as subjects being treated with high-dosage steroids (respiratory failure, cancer patients and others) and therefore be at higher risk of falling. Moreover, we have found a strong correlation between hypoglycemia/hyperglycemia and the risk of falling, confirmed by multivariate analysis with other risk factors like age, disease complexity, discharge diagnosis, and others. We also observed a
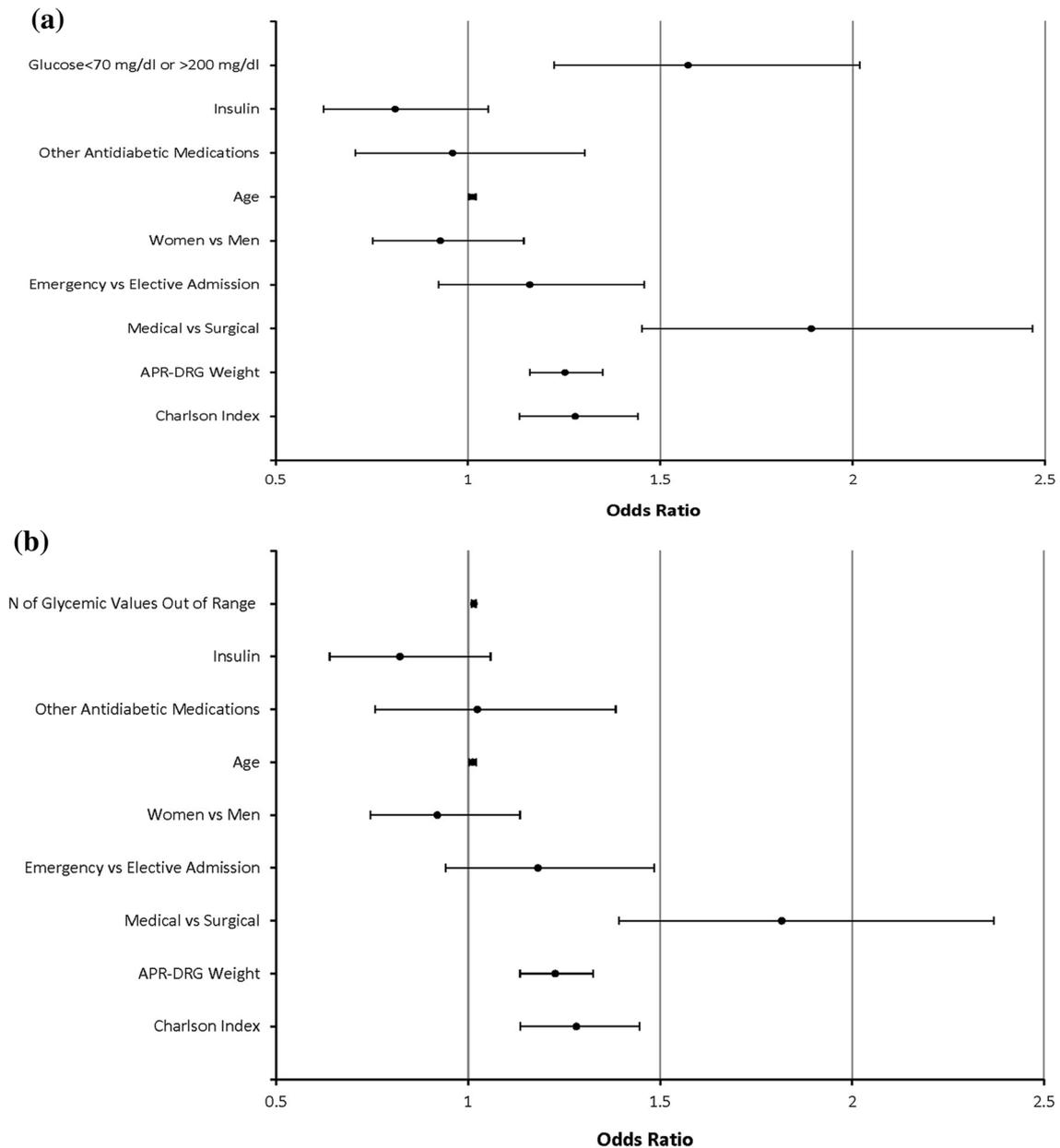
Fig. 1 **a** Multivariate analysis for sex, age (in linear regression), hospital admission (from ER/elective) surgical or medical discharge diagnosis, Charlson index, drugs for diabetes, presence of at least one glycemic value more than 200 or lower than 70. The presence of at least one glycemic value more than 200 or lower than 70 confers an odd-ratio for fall of 1.57 (confidence interval between 1.20 and 1.86; $p < 0.001$). **b** Multivariate analysis according with the number of glycemic values out of range (more than 200 or lower than 70) confers an odd-ratio for fall of 1.01 (CI between 1.01 and 1.02; $p < 0.001$)

significant correlation between the incidence of out-of-range values (below 70 mg/dl or over 200 mg/dl) in the same subject and the patient's odds risk for falling, suggesting that glucose variability may also play an important role.

Hypoglycemia is a well recognized risk factor for falling in outpatient diabetic subjects [31–34]. Our study also confirms this finding in the non-diabetic population. However, as mentioned above, one must consider that the subgroup

of subjects not treated with hypoglycemic agents (including insulin) experiencing hypoglycemias, might exemplify subgroups of "fragile" subjects like cancer patients, liver failure patients, septic states or patients with malnutrition. It is important to notice that mild hyperglycemia (indicated as a value > 200 mg/dl, which is extremely common during hospitalization) was identified as an independent risk factor for in-hospital falls [35].

Patients treated with diabetes medications are certainly affected by diabetes. Thus, in addition to out-of-range glycemic values, diagnosis of diabetes is itself related to a higher risk of falling. Approximately one-third of the patients experiencing falls have diabetes (around 30%), compared to 14% in the no-falls population. If we exclusively analyze data of patients receiving insulin treatment vs all other therapies (including metformin, the first-line oral agent prescribed for diabetes) a very high odds ratio for risk of fall is observed. Insulin treatment is necessary in around 1/3 of type 2 diabetic patients at some point, because of the progressive decrease in beta cell mass in the natural history of type 2 diabetes mellitus to around 20/30% of the original beta cell mass, which can be attributed to apoptotic beta cell death [36–42].

We further noticed that almost half of the population undergoing glucose monitoring was not being treated with diabetes drugs at the time. Independently of the values found, this points out the importance of sensitizing health care providers to improving the management of metabolic control in hospitalized subjects as we pointed out in a previous work [43].

The main limitation of our retrospective analysis is the difficulty we experienced in assessing the presence of diagnosis of diabetes in our subjects. The only confirmed diabetic subjects were those with a prescription for diabetes treatments. We also attempted evaluating Hb1Ac dosages in our population but scarce availability of these data limited their usefulness. Diabetic subjects undergoing acute hospitalization often do not require dosage of glycated hemoglobin and not in all newly diagnosed diabetics these exams are routinely ordered. Regardless, also the subgroup with an available dosage of Hb1ac had a major risk for falls in our population compared to the other subjects, with a major increase for values above 7.5% (data not shown).

When we considered the possibility of a relationship between the variables studied and damage as a consequence of the falls, we found that almost one-third of falls resulted in a damage, but the distribution between different subgroups was superimposable with the population undergoing our study, so no significant difference was found in all the subgroups analyzed (data not shown).

In conclusion, the results of our study indicate that hypoglycemia and hyperglycemia are correlated with risk of falls in a hospitalized population, consisting of over 57 thousands subjects over a period of 2 years.

These data resulted from the analysis of all blood glucose concentrations revealed by finger sticks in hospitalized patients independent of the diagnosis of diabetes.

Both hypoglycemia and hyperglycemia are independent risk factors for falls, with odds ratio values mounting in concomitance with the number of glucose values out of range, suggesting that also glycemic variability, albeit with a far lower statistical significance, could play an interesting role in risk of falling in the inpatient population.

If we consider the subgroup of patients taking diabetes medications, the use of insulin was significantly correlated with glucose variability but also with the risk of falls, indicating that diabetes and use of insulin, although necessary at the present time in around 1/3 of patients with type 2 diabetes mellitus, are both important risk factor for falls inside the hospital.

Our study also confirms that age, discharge diagnosis and disease complexity are independent risk factors for falls in the hospital. Combined with a diagnosis of diabetes, altered glucose values could in future facilitate identification of high-risk subjects, who may require more attention in the prevention of falls.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the Ethical Committee of the Humanitas Research Hospital, Rozzano, Milano, Italy.

Informed consent All clinical and laboratory informations came from retrospective analysis from non identifiable data, informed consent was not deemed necessary by the Ethical Committee.

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