Fall predictors in hospitalized patients living with cancer: a case–control study

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Abstract
Purpose To identify fall predictors and develop an assessment tool to be used for screening hospitalized cancer patients at risk for fall.
Methods A retrospective case–control study was conducted in 2018 at a cancer center in Northern Italy. The study participants were 448 adult cancer patients admitted to the oncology ward from 2009 to 2013. The case group consisted of 112 patients presenting at least one fall, while controls were randomly chosen by matching each case for age, sex, and admission period with three patients who did not fall. Data for the fall predictors were extracted from the electronic medical records. Conditional logistic regression was used to evaluate the association between patient’s characteristics and fall risk.
Results The overall prevalence of patients having at least one candidate fall predictor was high (98%). Seven of the studied variables showed an independent association with fall risk at multivariate analysis. These were tumor site, the presence of neurologic diseases, gait imbalance disorders, fatigue, and the assumption of certain medications such as diuretics, hypnotics, and opioids (odds ratios and 95% confidence intervals in brackets were 3.78 (1.78–8.13), 2.26 (1.08–4.77), 4.22 (1.87–9.52), 2.76 (1.45–5.26), 2.66 (1.52–4.66), 2.41 (1.20–4.85), and 3.03 (1.68–5.45), respectively).
Conclusions In this study, we identified falling risk factors in an Italian population of hospitalized cancer patients and developed a new risk assessment tool. An external validation is necessary before implementing our screening tool in clinical practice.

Keywords Hospitalized cancer patients · Fall predictors · Fall risk evaluation · Risk assessment tool

Introduction
Falls are a constant safety issue for healthcare providers, determining a heavy burden in terms of social, medical, and financial outcomes. Despite several studies have previously investigated fall predictors and evaluated fall prevention strategies, this event continues to be a frequently reported critical incident in acute care hospitals [1, 2]. Oncological diseases and their treatments may increase the risk of falls; indeed, patients with cancer present higher fall and injury rates compared to other patients. This population should be considered unique [3, 4] and in particular in older patients living with cancer the problem will continue to be of increasing importance [5].

Several studies on the topic have previously been conducted on hospitalized patients living with cancer [3–18]. However, studies evaluating fall risk tools in this clinical setting are few and the characteristics of study centers are not described in the published works. Given the great variability between the oncology wards in different countries, the lack of such information makes it difficult to apply the results of these studies in clinical practice [8]. Furthermore, a recent review concludes that currently there are no available recommendations about screening tools for the evaluation of fall risk in cancer populations because systematic reviews and meta-analyses are inconclusive [17].

The aim of the present study was to identify predictors of accidental falls and to develop an assessment/screening tool for evaluating the risk of falls in hospitalized patients living with cancer.
Methods

Study design

This was a retrospective case-control study conducted in 2018 at Istituto Scientiﬁco Romagnolo per lo Studio e la Cura dei Tumori (IRST) in Meldola, a research cancer center in the Northern Italy.

Inclusion criteria

The target population consisted of the adult cancer patients that had at least one admission to the Medical Oncology ward of IRST between January 1, 2009 and December 31, 2013. In our center, the role of the admission nurse in the oncology ward was introduced for the first time in October 2008. Therefore, we chose the period from 2009 to 2013 because that is when we started to systematically and electronically collect nursing assessment data.

Selection of cases

In the present study, an accidental fall event was defined as “an unexpected event in which patients come to rest on the ground, floor, or other lower level” [19]. All patients who had at least an accidental fall during the study period were included in the case group. For patients presenting more than one event during the study period, only the ﬁrst fall was considered. Falls were identiﬁed by the institutional fall incident report forms (FIRFs), routinely completed by the nurse and the physician at the time of each event. Date, time, location, circumstances of the fall, vital signs measurement, patient physical examination, and type of harm are recorded in the FIRFs. The Patient Safety Network deﬁnitions are used to categorize the severity of harms described in the FIRFs. According to these deﬁnitions, harms are classiﬁed as follows: no injury—fall resulted in no signs or symptoms of injury as determined by post fall evaluation; minor injury—fall resulted in application of a dressing, ice, cleaning of a wound, limb elevation, topical medication, bruise, or abrasion; moderate injury—fall resulted in suturing, application of steri-strips/skin glue, and splinting of muscle/joint strain; major injury—fall resulted in surgery, casting, traction, required consultation for neurological (basilic skull fracture, small subdural hematoma) or internal injury (rib fracture, liver laceration) or patients with coagulopathy who receive blood products as a result of the fall; and death—death as a result of injuries from the fall and not the physiological events causing the fall [19–21].

Selection of controls

Patients with at least one admission to the oncology ward during the study period that did not fall were randomly selected as controls and matched (3:1 ratio) with cases by age (± 1 year), sex, and the admission date (± 1 month).

The electronic admissions database was used for this purpose.

Explored risk factors

The risk factors investigated in this study were selected through a literature review and consisted of tumor site, comorbidities, sensory-neurologic deﬁcits, mood and cognitive disorders (i.e., depression and delirium), previous fall history (it was assessed by the admission nurse by asking the patient and/or their caregiver if the patient had at least one fall in the last 6 months), treatment-induced fatigue, motor disorders requiring mobility assistance, medications (opioids, hypnotics, hypoglycemic agents, antihypertensives, diuretics), blood product use in the previous 24 h, medical devices limiting ambulation, and ambulatory aid use (i.e., crutches, cane, or walker) [3–18]. The short Confusion Assessment Method (short CAM) is used in our clinical practice to conﬁrm the delirium diagnosis [22].

Oncology ward characteristics

The oncology ward involved in this study is located inside the newly built cancer center in Meldola city. The facility was designed and furnished with the intent to maximize the humanization of care. The ward has 36 beds, of which 26 in double rooms and 10 in single rooms. Six of the single rooms are located in a low microbial load environment to allow care and protective isolation of the immunocompromised patients. All rooms are equipped with toilets and height-adjustable patient beds. In the inpatient setting, nursing activities are scheduled in three 8-h shifts to cover the 24 h. Depending on the distribution of clinical activities during each shift, the nursing staffing foresees the presence in the morning shift of 8 nurses. This includes the head nurse, one case manager, and one admission nurse. There are five nurses during the afternoon shift and three of them for the night shift. Three carers (health workers) for each shift during the day support nursing activities. The organizational model is based on the subdivision of responsibilities by sectors, in which there is a reference nurse in charge of nursing care of patients in each sector during working shifts. An institutional policy aimed at preventing accidental falls of patients is in place in our hospital. The average number of yearly admissions to the oncology ward is nearly 1700 patients with different types of advanced cancers. The most
Data on risk factors were extracted from the electronic medical records (EMRs) by two trained research nurses. The EMRs contain the documentation of all clinical activities and assessments made during the patient admission period. Such activities are timely registered in the dedicated sections of the EMRs: i.e., vital signs, nursing assessment scheme, nursing and doctor diaries and therapy cards. In our clinical practice, an accurate and holistic patient evaluation is made by the admission nurse, who daily interviews all new admitted patients and registers data related to the patient health status, vital signs, symptoms evaluation using the Edmonton Symptom Assessment System (ESAS), the presence and status of medical and walking aid devices, sensor or cognitive disorders, motor disorders, and the use of medications. Patient assessment data are updated daily by the staff nurses, and in case of changes in patient clinical conditions, additional focused assessments are made. Data related to symptoms as potential fall predictors in this study (e.g., fatigue, pain, depression, and anxiety) were collected as categorical depending on whether patients reported controlled/uncontrolled of the specific symptoms evaluated (i.e., the symptom fatigue was considered present in all patients reporting fatigue ≥ 4 when evaluated with ESAS scale). The medications in this study were collected as categorical, independently from the daily dose and frequency use, i.e., the “prescription and administration” (traceable from the therapy schema) in the 24 h preceding the event of the following medication categories: opioids, hypnotics, anxiolytics, neuroleptics, antidepressants, antidiabetics as well as antihypertensives and diuretics. Data related to patient comorbidities were reported as categorical for each secondary diagnosis that was reported by the oncologists in the anamnesis section of the EMRs.

Statistical analysis

Continuous variables were reported as median, minimum, and maximum values and were compared between case patients and controls using the Student t-test or the Wilcoxon-Mann–Whitney test, as appropriate. Categorical variables were reported as natural frequencies and percentages and were compared using the chi-squared or Fisher’s exact test, as appropriate. Correlation among variables was mainly assessed by means of tetrachoric correlation. Conditional logistic regression was used to evaluate the association between patient’s characteristics and fall risk. Results were reported as odds ratios (ORs) and 95% confidence intervals (CIs). From an initial full model, containing all factors listed in Table 1, a final parsimonious model was obtained by means of backward selection procedure with significance level for variable removal of 0.05. From the final multivariable model, a score to easily screen oncologic patients at the moment of hospital admission was derived as follows: (i) a partial score was computed dividing the value of each regression coefficient by the smallest regression coefficient and the results were rounded to the nearest integer, or to the nearest integer + 0.5; (ii) a total score for each patient was obtained by adding their appropriate partial scores. To help the clinical applicability of the score, a cut-point was chosen by using the Youden index computed on the predicted probabilities obtained by fitting a logistic model for the risk of fall on the total score plus the matching variables [23] and taking the total score value corresponding to the found cut-point.

Thus, to use the above-mentioned screening tool on a new patient, it will be sufficient to sum the pertinent partial scores and to compare the obtained total score with the cut-off. If the patient’s total score will be greater than the cut-off, special attention will need to be paid during his/her hospital stay.

Multinomial logistic regression with fixed effects was used to investigate predictors of falls differentiating between falls without injuries and falls with a minor or moderate injury. The reference outcome category was represented by the control group.

All the statistical analyses were conducted using STATA statistical software version 15.1 (StataCorp, College Station, TX, USA).

Results

Four hundred and forty-eight adult cancer patients with at least one admission between 2009 and 2013 were included in the study. Of these, 112 were cases, i.e., patients that presented at least one event of accidental fall during the hospitalization period and 336 controls, i.e., patients without falls. Among the cases, 63 patients (56%) did not report injuries whereas 49 patients (44%) reported minor or moderate injuries. No events with major injuries or deaths were observed. The median hospital stay for cases was 12 days [range: 1–59] whereas for controls it was 3 days [range: 1–45]. The total number of admissions to the oncology ward during the 5-year period considered in this study was 9404, while the total number of patient hospital days was 53,876. The 5-year observed fall rate was 2.07 per 1000 patient hospital days and 1.19 per 100 patient hospital admissions. Data on patient characteristics and fall risk factors are shown in Table 1. About 60% of the patients were males with a median age of 66 years. The percentage of patients...
having at least one of the candidate fall predictors was 98.2. The number of previous falls was low for both groups (overall frequency less than 3%) even if case patients reported a higher frequency as compared to controls ($P = 0.077$). Cases also had a significantly longer median hospital length of stay than controls, 12 days vs. 3 days ($P < 0.001$). While solid tumors were the most frequent diagnoses in the study population (among them gastrointestinal and rare tumors were the most frequent), cases had a higher frequency of hematologic malignancies compared to controls, 22% vs. 10% ($P = 0.001$). With regard to other potential risk factors considered in this study, their overall prevalence was higher in cases than in controls. This was true in particular, for sensor-cognitive and mood disorders such as delirium, anxiety, and depression, neurological diseases (including CNS diseases such as brain tumors or brain metastases), motor disorders, the use of ambulation devices, and medications such as diuretics, hypnotics, and opioids (Table 1).

Results from univariable conditional logistic regression are shown in Fig. 1. Among studied risk factors, tumor type (hematological vs. solid malignancies); sensorial-cognitive and mood disorders such as impaired vision/hearing, delirium, anxiety, and depression; motor

| Table 1 | Main characteristics of cases and controls (column percentages) |
|---------|-----------------------------------------------------------------|
|         | Total ($n=448$) | Cases ($n=112$) | Controls ($n=336$) | $P$ value |
| Female sex | 180 (40.2) | 44 (39.3) | 136 (40.5) | 0.824 |
| Median age, years [min–max] | 66.2 [20.6–83.2] | 66.17 [23.3–82.9] | 66.2 [20.6–83.2] | 0.998 |
| Tumor site | 0.001 |
| Solid tumors | 389 (86.8) | 87 (77.7) | 302 (89.9) | 0.979 |
| Hematologic malignancies | 59 (13.2) | 25 (22.3) | 34 (10.1) | 0.077 |
| Previous fall* | 13 (2.9) | 6 (5.4) | 7 (2.1) | 0.077 |
| Need help for walking* | 89 (20.0) | 39 (34.8) | 50 (15.0) | $<0.001$ |
| Comorbidities | 0.001 |
| Cardiovascular diseases* | 218 (49.0) | 59 (52.7) | 159 (47.8) | 0.367 |
| Endocrine diseases* | 113 (25.3) | 27 (24.1) | 86 (25.7) | 0.742 |
| Respiratory diseases* | 144 (32.3) | 41 (36.6) | 103 (30.8) | 0.259 |
| Sensor-cognitive disorders | 0.001 |
| CNS diseases* | 56 (12.6) | 26 (23.2) | 30 (9.0) | $<0.001$ |
| Peripheral neuropathy (neurotoxicity) | 22 (4.9) | 7 (6.3) | 15 (4.5) | 0.449 |
| Impaired vision/hearing | 19 (4.2) | 10 (8.9) | 9 (2.7) | 0.004 |
| Plegies | 6 (1.3) | 2 (1.8) | 4 (1.2) | 0.643 |
| Delirium | 31 (6.9) | 16 (14.3) | 15 (4.5) | $<0.001$ |
| Anxiety | 169 (37.7) | 52 (46.4) | 117 (34.8) | 0.028 |
| Motor disorders | 0.001 |
| Gait/balance disorders* | 55 (12.3) | 30 (26.8) | 25 (7.5) | $<0.001$ |
| Fatigue | 208 (46.4) | 72 (64.3) | 136 (40.5) | $<0.001$ |
| Hyposthenia of lower limbs | 46 (10.3) | 22 (19.6) | 24 (7.1) | $<0.001$ |
| Medications | 0.001 |
| Diuretics* | 183 (40.9) | 64 (57.1) | 119 (35.5) | $<0.001$ |
| Antihypertensives* | 120 (26.9) | 27 (24.1) | 93 (27.8) | 0.450 |
| Hypnotics* | 67 (15.0) | 31 (27.7) | 36 (10.8) | $<0.001$ |
| Hypoglycemic agents* | 61 (13.6) | 16 (14.3) | 45 (13.4) | 0.811 |
| Opioids | 221 (49.3) | 80 (71.4) | 141 (42.0) | $<0.001$ |
| Blood transfusion, previous 24 h* | 52 (11.7) | 11 (9.8) | 41 (12.3) | 0.478 |
| Enemas | 37 (8.3) | 11 (9.8) | 26 (7.8) | 0.493 |
| Medical devices | 0.001 |
| Has IV line or access* | 288 (64.4) | 61 (54.5) | 227 (67.8) | 0.011 |
| Ambulatory devices use* | 40 (9.0) | 19 (17.0) | 21 (6.3) | 0.001 |

*Frequency of missing values for each variable was <0.9%
disorders; the use of ambulation devices; and the use of some medications (diuretics, hypnotics, and opioids) resulted as predictors of accidental falls. The only factor showing a protective effect was having an intravenous (IV) access with infusion pump.

At multivariate analysis, seven variables showed an independent association with fall risk (Table 2). These were tumor site, the presence of CNS diseases, gait imbalance disorders, fatigue, and the assumption of certain medications such as diuretics, hypnotics, and opioids. Table 2 also shows the regression coefficients as well as the partial scores for each factor included in the multivariable model. The total score for a given patient was obtained by summing their appropriate partial scores. For example, for a patient with a solid tumor, a gait imbalance disorder, and taking opioids, the total score was $0 + 0 + 2 + 0 + 0 + 0 + 1.5 = 3.5$. The median total score computed on all patients was 2.5 [range: 0–7]. The total score cut-point was equal to 2. This was associated with a sensitivity of 92% and a specificity of 54%.

Additional exploratory analyses were performed distinguishing the cases between those who reported a minor or moderate injury and those who did not report an injury. Supplementary Table S1 shows the distribution of patient characteristics among the three groups. Hospitalization length was longer for cases reporting an injury compared to the other patients (median of 10 days [range: 1–59] vs. 3 [range: 1–45], respectively). In addition, such patients reported a slightly higher prevalence of hematologic tumors and need for a walking aid. The
frequency of sensor-cognitive and mood disorders was higher in patients not reporting a fall injury compared to other patients with the exception of anxiety or depression. A similar pattern was observed with regard to motor disorders with the exception of fatigue, more prevalent among patients reporting an injury. Hypnotics were more prevalent among cases without injuries whereas hypoglycemic medications among those reporting a minor or moderate injury.

To investigate predictors of fall without injury and fall with minor or moderate injury, a multinomial logistic regression was applied. Controls were chosen as reference category. Results from univariate analyses showed in Supplementary Table S2 were substantially consistent to those obtained by considering the binary outcome. However, few differences were observed. Previous falls, the use of infusion pumps in patients with IV lines and of medical devices as well as the presence of a neurologic disorder resulted as predictors only for the risk of fall without injury. Conversely, anxiety/depression resulted associated only to the risk of fall with injury (minor or moderate). At multivariate analysis, tumor site, the presence of gait/balance disorder, and the use of opioids were factors associated with the risk of fall with and without injury whereas fatigue was a predictor of risk of fall with injury and the use of hypnotics and diuretics of the risk of fall without harm (Table S3).

### Discussion

Our study was aimed at identifying fall predictors in hospitalized patients with cancer and developing an assessment tool for screening patients at risk for fall at admission to the hospital. Even though several studies conducted in different countries have investigated the issue before, ours is the first study conducted in an Italian population in the cancer setting [3–18]. Risk for fall varies according to type and specificity of oncology wards [8]. The need to implement an assessment tool based on our patients and organizational characteristics justified the study. Hospitalized patients with different types of advanced cancer diseases were included in this study. The median age of the study population was in line with Stone et al., while the prevalence of falls with minor or moderate injuries (44%) was in line with two previous studies [9, 24], but lower if compared with Tsai et al. (84.8%) [12]. Forty percent of study participants were women, 86.8% had solid tumors, and 13.2% were affected from hematologic malignancies.

Because the fall rates and injuries and the environment and organizational characteristics of included centers are not constantly described in the previous studies focusing on fall predictors, a full comparison of our findings with them is not possible. The fall rate per 1000 patient days in this study resulted lower than in Weed-Pfaff, Fischer and Pautex et al.: respectively 2.07 vs. 3.41, 3.83, and 6.89. This also applies to the fall rate per 100 patients compared to Lorca, Weed-Pfaff, and Capone’s studies (i.e., respectively 1.19% vs.1.98%, 2.4%, and 3%) [3, 8, 11, 15, 24]. Clinical characteristics of patients and organizational variables may partially explain such differences in fall rates between studies.

In line with previous studies, we found for the most of the candidate fall predictors higher prevalences in the case group as compared to controls. This applies to the need for walking aid, having a neurologic disease, impaired vision/hearing, delirium, anxiety/depression, gate imbalance disorders, fatigue, hyposthenia of lower limbs, use of ambulatory devices, diuretics, hypnotics, and opioids [3, 8–11, 13]. Conversely, in contrast with previous studies, we found no statistically significant differences in prevalences of having comorbidities such as cardiovascular, endocrine, and respiratory diseases, treatment-induced neuropathy, the presence of plegies, and the use of antihypertensive, hypoglycemic agents, and having received blood products transfusions in the last 24 h. History of previous fall prevalence in the study population resulted low (2.6%) with no statistically significant difference between fallers and not fallers.

Having a hematologic malignancy (tumor site), neurologic disease (including brain metastases or other
neurologic diseases), gait imbalance disorders, fatigue, and the use of diuretics, hypnotics, and opioids resulted as independent predictors for fall.

Patients with hematologic malignancies at our center are hospitalized mainly for receiving high-intensity treatments (e.g., high-dose chemotherapy, bone marrow transplantation) or for the management of serious toxicities that cannot be managed in outpatient settings. Treatment regimens of such patients could explain having hematologic malignancies as a fall predictor. This result is in line with the studies of Capone et al., Weed-Pfaff et al., and Jun et al., who reported that hematologic patients receiving bone marrow transplantation present higher risk for falls [3, 11, 13].

Having a neurologic disease resulted as an independent fall predictor. Indirectly, this finding confirms the study conducted by Stone et al. in 2012, in which having primary brain cancer or brain metastases resulted as a hospital fall predictor [9].

Gait imbalance disorders, asthenia of lower limbs, and fatigue resulted as independent fall predictors as well. These factors are mutually influenced and are related with disease itself as well as cancer treatment side effects. Besides, patients experiencing fatigue likely have hyposthenia of lower limbs which may result in gait imbalance. These fall predictors were frequently found in most if not all of previous studies [3, 6, 7, 11–13, 26–29].

The use of diuretics resulted as an independent predictor of fall in the study population. It is known the need for elimination as result of the effect of this medication category and the hypotensive effect of diuretics, which can explain such predictor. In fact, having elimination issues has resulted as fall predictor in other studies before [7, 25]. Among studied medications, the use of hypnotics and opioids resulted as independent fall predictors in line with findings reported from previous authors [3, 8–10, 29–31]. Both these two medication categories have effects on patient's cognitive status by influencing their space and time orientation and motor capabilities, which may explain this finding [7–9, 11].

The presence of medical devices in the study population was analyzed singularly for each medical device limiting ambulation and by considering having at least one of them (i.e., nose-gastric tube, having infusion lines, drainage tubes, urinary catheter). In our study population, having an IV line resulted protective for fall since the prevalence of patients with IV lines was higher in the control group (OR 0.54; 95% CI 0.34–0.85; P value = 0.008). This finding may be explained by the characteristics of the drip stands used in our hospital for infusions and with the fact that patients with an IV line probably use them as an ambulatory aid while walking.

Among fall predictors, tumor site, gait imbalance disorders, fatigue, and sensor-cognitive disorders such as anxiety/depression resulted related with falls with injury, while previous falls, use of diuretics, hypnotics, and opioids were associated with falls without harms.

It is worth noting that despite the retrospective study design, the quality of the information contained in the EMRs helped minimize the known risk of recall bias. However, our study has certain limitations. Since it was conducted in a single center, its generalizability still needs to be ascertained. Given that the study refers to data from a few years ago, its findings may not be entirely up to date: recently introduced treatment options could have a different impact on the risk of falls (e.g., by causing potentially different adverse events when compared to previously available treatments).

Thus, further research is needed to externally and temporally validate our results and investigate the clinical utility of our screening tool.

In conclusion, the definition of a screening tool able to identify patients at higher risk for fall based on patients, organizational, and facility characteristics represents the first step for implementing tailored evidence-based strategies for fall prevention. We believe that having described the characteristics of the study center, including facility, staffing, and nursing organization, could help other researchers evaluate if the results of our study can apply to their own context. This could also promote further studies to validate our results and investigate the influence of hospital and organizational features on the risk of falls in cancer patients during their hospitalization.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00520-022-07208-x.

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Author contribution AZ, SM, GM, and MTM designed the study and provided the training of research nurses involved in the study. MG, GM, and IM were involved in data collection and registration. EP was responsible for data analysis. AZ, ON, and EP contributed to the drafting of the manuscript and all authors critically reviewed the draft and approved the final version for submission.

Data availability All data relevant to the study are included in the article or uploaded as supplemental information. The authors confirm that the data supporting the findings of this study are available within the article and/or its supplemental materials. The authors have full control of primary data and agree to allow the journal to review their data if requested.

Declarations

Ethics approval The study protocol was approved by the relevant medical, scientific, and ethics committees of Area Vasta of Romagna (Prot. N. 2741/2013/1.5/113) and has been conducted in accordance with good clinical practice and the principles of the Helsinki Declaration.

Consent to participate Given the retrospective nature of the study, it was not possible to obtain the informed consent from patients.
because most of them were not reachable (dead or in critical conditions). In research centers and universities in Italy, the use of patient data for research purposes can be authorized by the General patients Authorization 2018 [32].

**Consent for publication** Not applicable. Specific precautions were put in place to warrant the confidentiality of participants. In particular, the study data extracted from the EMRs were initially registered in a dedicated encrypted database with limited access to study nurses only. The completed database was permanently anonymized by deleting patients’ identity data and by assigning a unique numerical code to each study participant.

**Competing interests** The authors declare no competing interests.

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