Falling and fall risk in adult patients with severe haemophilia

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Keywords
haemophilia, fall risk, adult

Summary
The objective of this study was to define fall rates and to identify possible fall risk factors in adult patients with severe haemophilia. Patients, material, methods: 147 patients with severe haemophilia A and B were evaluated using a standardized test battery consisting of demographic, medical and clinical variables and fall evaluation. Results: 41 (27.9 %) patients reported a fall in the past 12 months, 22 (53.7 %) of them more than once. Young age, subjective gait insecurity and a higher number of artificial joints seem to be risk factors for falling. Conclusion: Falls seem to be a common phenomenon in patients with severe haemophilia. Fall risk screening and fall prevention should be implemented into daily practice.

Advances in haemophilia care have resulted in increases in median life expectancy for patients with haemophilia (PWH) (1). Falls are a well-explored phenomenon in elderly non-haemophilic people. Ageing is known to be associated with a higher risk of falling, 28–35 % of the community-dwelling population aged ≥65 years fall at least once a year (2).

In addition to extrinsic risk factors (e.g. environmental hazards like slippery floors, poor lighting or inappropriate footwear), many intrinsic risk factors can increase the risk of falling, e.g.
• history of falls,
• impaired gait and mobility,
• visual impairments or
• fear of falling (3–5).

Many of the identified fall risk factors can be found in PWH. For PWH fall risk could be additionally increased by haemophilic arthropathy particularly affecting the lower limb (1, 6).

Data on falling and fall risk factors in PWH is very limited. To the best of our knowledge only 2 studies have been published so far that examined the occurrence of falls in PWH:
• Fearn et al. reported a fall incidence of 50 % in 20 patients with mild, moderate and severe haemophilia in the preceding 12 months (7).
• Sammels et al. reported a fall incidence of 32 % in 74 patients with moderate and severe haemophilia during the preceding 12 months (8).

The objective of the present study was to define fall rates and to identify possible fall risk factors in PWH. Additionally the relationship between scores on fall risk assessment tools and actual fall rates was evaluated.

Patients, material, methods
Design and sample
A descriptive, retrospective study was conducted. The data collection was performed between December 2014 and August 2015. The patients were recruited during their regular visit at the haemophilia care centre in Bonn. Written informed consent was obtained from all participants.
Community-dwelling adults aged 18 years or older with severe haemophilia A and B were included into the study.

Patients that were not independent in their mobility (e.g. patients that were fully bedridden or wheelchair-bound) and patients that suffered from other comorbidities that could influence the risk of falling (e.g. parkinsons’ disease, epilepsy) were excluded.

The study protocol was approved by the Medical Ethics Committee of the Rheinische Friedrich-Wilhelms-Universität Bonn.

Variables and measurement

Data was collected using a standardized test battery. General information like age and body mass index (BMI) were recorded. Medical variables were obtained from the patients’ records, such as type and severity of haemophilia, number of bleedings in the last 12 months, treatment modalities and factor concentrate consumption in the last 12 months.

Duration and reason of hospitalisation in the last 12 months and number of joint prosthesis were also recorded. The Haemophilia joint health score (HJHS) (9) is regularly assessed by the staff of the haemophilia care centre; results were obtained from the patients’ records as well.

A fall was defined as an “unexpected event in which the patient comes to rest on the ground, floor or lower level” (10). A fall questionnaire was designed, asking the patients about fall rates in the last 12 months. Concerning the last fall, data on cause, location and consequences (additional factor consumption, injuries, medical consultation, pain) were collected.

To gain insight into the patients’ subjective gait perception we included the statement “I often feel insecure when walking”. The patients were asked on how much they agreed with that sentence on a 5-step Likert scale from 1: “I strongly disagree” to 5: “I strongly agree”.

To explore possible fall risk factors the patients were asked to fill out questionnaires concerning fear of falling (Falls efficacy scale – international version; FES-I) (11), functional health status (Haemophilia activities list; HAL) (12) and quality of life (Short form 36; SF36) (13).

Furthermore, joint pain was recorded using the visual analogue scale (VAS).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>non-fallers vs. fallers</th>
<th>one-time vs. multiple fallers</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>42.39±14.51 41.9±13.76 43.46±16.45</td>
<td>0.072 48.79±13.92 38.86±17.36 0.058</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.02±4.6 25.28±13.76 24.33±3.92</td>
<td>0.288 24.20±2.78 24.44±4.75 0.096</td>
</tr>
<tr>
<td>factor consumption past year (IU)</td>
<td>447893±463288 438551±470508 472567±448694</td>
<td>0.358 3661972±248729 567362±556319 0.151</td>
</tr>
<tr>
<td>number of bleedings past year</td>
<td>1.77±3.47 1.8±3.85 1.7±2.22</td>
<td>0.107 1.63±2.14 1.76±2.34 0.921</td>
</tr>
<tr>
<td>hospitalisation days past year</td>
<td>2.18±5.78 1.89±5.75 2.95±5.86</td>
<td>0.049* 3.16±7.31 2.77±4.43 0.435</td>
</tr>
<tr>
<td>number of joint prosthesis</td>
<td>0.35±0.77 0.27±0.70 0.56±0.91</td>
<td>0.024* 0.72±1.13 0.43±0.68 0.649</td>
</tr>
<tr>
<td>subjective gait insecurity</td>
<td>1.92±1.1 1.79±1.06 2.24±1.24</td>
<td>0.029* 2.11±0.99 2.36±1.43 0.765</td>
</tr>
<tr>
<td>TUG (s)</td>
<td>11.46±7.51 11.54±1.06 11.28±4.62</td>
<td>0.215 11.68±4.81 10.94±4.53 0.353</td>
</tr>
<tr>
<td>HAL</td>
<td>76.79±23.28 77.87±23.09 74.01±23.82</td>
<td>0.371 73.10±21.59 74.80±26.07 0.521</td>
</tr>
<tr>
<td>FES-I</td>
<td>21.63±8.08 20.9±7.31 23.54±9.47</td>
<td>0.089 23.05±8.44 23.95±10.46 0.635</td>
</tr>
<tr>
<td>SF36: PCS</td>
<td>43.72±11.90 43.84±12.13 43.39±11.45</td>
<td>0.757 43.97±9.70 42.88±12.99 1.000</td>
</tr>
<tr>
<td>SF36: MCS</td>
<td>52.51±11.23 53.29±10.32 50.53±13.21</td>
<td>0.423 52.79±13.61 48.57±12.84 0.100</td>
</tr>
<tr>
<td>number of painful joints</td>
<td>3.59±3.01 3.59±3.04 3.56±2.98</td>
<td>0.998 3.32±2.36 3.77±3.48 0.979</td>
</tr>
<tr>
<td>HJHS</td>
<td>23.57±23.41 22.16±22.47 27.18±25.62</td>
<td>0.448 30.79±26.47 23.90±25.02 0.316</td>
</tr>
</tbody>
</table>

Tab. 1 Comparison between non-fallers and fallers and between one-time fallers and multiple fallers (values given as mean ± standard deviation for normally distributed variables, respectively median (interquartile ranges) for non-normally distributed variables). Significant differences were evaluated with the Mann-Whitney-U-test for non-normally distributed data, normally distributed data were evaluated using the Student’s t-test. * statistically significant (p < 0.05).
Data collection was completed by a physical examination consisting of the Timed up and Go Test (TUGT) (14).

Statistics

Descriptive statistics of mean, standard deviation, percentages and frequencies were calculated for all variables.

Differences between the means of two groups (e.g. fallers vs. non-fallers) were assessed with independent t-test for normally distributed interval or ratio values.

Non-normally distributed interval or ratio values or ordinal variables were analysed using the Mann-Whitney-U-test.

Bivariate logistic regression was conducted to examine variables associated with falls. A value of p < 0.05 was considered statistically significant.

The data was analysed by using SPSS Version 22.0 (IBM Corp., Armonk, NY, USA) and Stata Statistical Software 14 (StataCorp LP, College Station, TX, USA).

Results

Description of the sample

147 male patients with severe haemophilia (factor level of < 1 %) participated in the study. The average age was 42.4 ± 14.5 years (range 18–74). 132 patients (89.8 %) had haemophilia A, 15 (10.2 %) haemophilia B.

4 patients (2.7 %) had inhibitors at the time of the examination. Almost all patients (142, 96.6 %) were under prophylactic treatment; the other 5 patients (3.47 %) applied clotting factor concentrates on demand. The average factor concentration in the last 12 months was 447 893 ± 463 288 IU. The average number of bleedings in the last 12 months was 1.77 ± 3.47 (range 0–26).

Fall rates, circumstances and consequences

41 patients (27.9 %) reported at least one fall within the last 12 months, 22 (53.7 %) of them more than one. Most of the falls occurred outside the patients’ home (70.7 %); 69 % of them outdoors, 31 % indoors. When asked for the cause of a fall, most patients answered “tripping” (44 %) or “slipping” (28 %); sports or physical activity were also frequently named (15 %).

More than half of the patients who fell (53.7 %) suffered from fall-related injuries afterwards:

- 9 patients (40.9 %) had mild injuries like superficial wounds or bruises,
- 11 (50 %) reported a bleeding after the fall and
- 2 (9.1 %) reported a fracture.

Comparison of non-fallers vs. fallers and one-time vs. multiple fallers

After dividing the patients into groups (non-fallers, fallers, one-time fallers and multiple fallers), differences between the medical and clinical variables of these groups were evaluated using the Mann-Whitney-U-test. Tab. 1 shows part of that comparison. Between fallers and non-fallers 3 significant differences were noted: 1. Fallers spent significantly more days in a hospital during the last year than non-fallers (2.95 ± 5.86 vs. 1.89 ± 5.75, p = 0.049). The days spent in inpatient care were all non-fall related and mostly due to elective orthopaedic procedures like joint replacement or radiosynoviorthesis. 2. Fallers had on average a higher number of joint prostheses than non-fallers (0.56 ± 0.91 vs. 0.27 ± 0.70, p = 0.024). 3. When asked for their subjective perception, fallers indicated a higher level of gait insecurity than non-fallers (2.24 ± 1.24 vs. 1.79 ± 1.06 on a 5-point Likert scale, p = 0.029).

In comparison of one-time fallers and multiple fallers, age was only the parameter that differed significantly: Multiple fallers were significantly younger than one-time fallers (38.86 ± 17.36 years vs. 48.79 ± 13.92 years, p = 0.043). Neither concerning the fall risk assessment tools (e.g. FES-I, TUGT), nor the joint status (HJHS) or pain levels (VAS) significant differences were found between the groups.

Taking these results into account a binary logistic regression was conducted. The following predictors were included into the regression model:

- age,
- subjective gait insecurity,
- duration of hospitalisation in the past year and
- number of joint prostheses.

Factors influencing fall risk in adult haemophilia patients. Logistic regression (n = 136), Pseudo R2 = 0.1475, *statistically significant (p < 0.05). Odds Ratios for „age“ and „subjective gait insecurity“ to be interpreted in relation to the reference category. Odds Ratios for „hospitalisation past year“ and „number of joint prostheses“ indicate the odds ratio for a one-unit change in the respective variable.

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31–40 years</td>
<td>0.12</td>
<td>0.02–0.66</td>
<td>0.019*</td>
</tr>
<tr>
<td>41–50 years</td>
<td>0.25</td>
<td>0.07–0.90</td>
<td></td>
</tr>
<tr>
<td>51–60 years</td>
<td>0.05</td>
<td>0.01–0.43</td>
<td></td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>0.03</td>
<td>0.00–0.34</td>
<td></td>
</tr>
<tr>
<td>subjective gait insecure</td>
<td>1.18</td>
<td>0.48–6.79</td>
<td>0.027*</td>
</tr>
<tr>
<td>2</td>
<td>3.69</td>
<td>1.35–23.96</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>10.68</td>
<td>1.93–58.97</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>31.04</td>
<td>1.88–512.33</td>
<td></td>
</tr>
<tr>
<td>5 (strongly agree)</td>
<td>0.97</td>
<td>0.88–1.08</td>
<td>0.629</td>
</tr>
<tr>
<td>hospitalisation past year (days)</td>
<td>2.81</td>
<td>1.87–6.66</td>
<td>0.019*</td>
</tr>
<tr>
<td>number of joint prostheses</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

1 reference category: 18–30 years
2 reference category: 1 (strongly disagree)
The outcome was defined as whether a patient did or did not fall in the past year. After excluding patients with missing values and identifying influential values (Cooks D > 4/47), 136 patients were included into the model. 3 of the 4 parameters showed significant influence on the outcome fall/no fall in the past year (Tab. 2). The probability of a fall is shown in Fig. 1, separately for the 3 significant variables age, gait insecurity and joint replacement.

Fall probability increased almost linear with gait insecurity and joint replacement: The more insecure the patients felt while walking or the more joints he had replaced, the higher was the probability to fall.

Concerning age as an independent predictor of a fall a decreasing fall risk with higher age was found. Based on the mathematical regression model patients between 18 and 30 years had the highest probability to fall (50 %). The probability of a fall decreased until it reached its minimum for patients older than 60 years (probability of fall: less than 10 %).

Discussion

Falls are usually multifactorial in their origin; especially in the elderly population many factors can contribute to an overall increased risk of falling. In addition to fall risk factors present in the general population, PWH show disease-specific characteristics that could lead to an increased risk of falling at a younger age (e.g. balance deficits, haemophilic arthropathy) (15).

So far there is a lack of literature on falls in PWH. Our study is the first study to examine exclusively adult patients with severe haemophilia aged 18 years and older. Patients with mild and moderate haemophilia rarely present with haemophilic arthropathy and associated musculoskeletal co-morbidities that could contribute to a higher risk of falling.

The fall incidence we found was considerably lower than the one Fearn et al. reported in 2010 (27.9 vs. 50 % in the last 12 months) (7). Fearn et al. included 20 patients with mild, moderate and severe haemophilia (average age 39.4 years, range: 22–58) and compared them to a non-haemophilic control group. The higher fall in-
Swinkels et al. suppose a reduction in
Levinger et al. on the other side found
Tinetti ME, Speechley M, Ginter SF. Risk factors
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102Rehm H et al. Fall risk in adults with haemophilia
incidence might be due to the very small
sample size.
Sammels et al. reported a fall incidence
of 32% in 74 patients with moderate and
severe haemophilia, which is comparable
to the incidence we found (8).
So far there has only been one study that
systematically evaluated different fall risk
factors in PWH (8). Up to this point our
study is the largest study examining falling
and fall risk factors in PWH: Age, number
of joint prostheses and subjective gait inse-
curity have a significant influence on falls
in PWH. In the general population high
age is often associated with a higher risk of
falling (2).

Unexpectedly, in our study younger PWH
showed a higher probability to fall com-
pared to elderly patients. This can most likely
be explained with higher activity levels
combined with a higher willingness to take
risks in young PWH.

Due to the treatment opportunities avail-
able nowadays even patients with severe
haemophilia can lead almost normal lives.
In our study the probability to fall in-
creased almost linearly with the number
of joint prostheses. This is in accordance
with the study of Sammels et al., who found a
higher incidence of joint replacement in
multiple fallers compared to non-fallers
(8). In the general population the literature
is inconsistent regarding joint replacement
as a fall risk factor:
• Swinkels et al. suppose a reduction in
  fall prevalence for patients after knee
  replacement surgery (16).
• Levinger et al. on the other side found
  an increased fall risk in patients after
  knee replacement surgery (17).

In PWH both knee and hip replacement
have been shown to improve function and
reduce pain (18–20). However, according
to our results, the probability to fall in-
creases with the number of joint prostheses.
On the one hand joint arthroplasty results in
an improvement of function and reduction
of pain, but on the other hand propriocep-
tive deficits and reduced muscle strength
are reported regularly (21, 22). Both pro-
prioceptive deficits and reduced muscle
strength can lead to gait impairments and
thereby gait insecurity. Impaired lower ex-
tremity proprioception – especially in pa-
tients with multiple joint prostheses –
could lead to the strong increase in fall risk.
Interestingly none of the fall risk assess-
ment tools showed significant differences
between fallers and non-fallers. No signifi-
cant difference between fallers and non-fal-
lers in the results of the TUG was found. It
is often suggested, that the TUG is a good
measure for basic mobility and therefore
also a good indicator of fall risk (23, 24).
Even though not statistically significant, we
found that both fallers and multiple-fallers
were on average faster in completing the
TUG than non-fallers.

The TUG seems to be a good fall risk as-
essment tool for elderly patients; when
assessing young patients its results seem
to be less conclusive.

In contrast to the comparatively complica-
ted and time-consuming assessments like
the TUG or the FES-I the simple question
“Do you feel insecure when walking” seems
to be a good indicator of fall risk: The more
insecure patients felt when walking (i.e. the
more strongly they agreed to the state-
ment) the higher was the probability to fall.
Multiple factors can influence a patients’
subjective perception of gait (in)security,
e.g. gait, fear of falling and history of fal-
ling. To ask the patient directly about
his/her perception of gait (in)security
might be a fast and easy way to identify pa-
tients with a higher risk of falling.

Limitations
The main limitation of our study is the re-
trospective study design. Studies have
shown that retrospective studies underesti-
mate the fall incidence by up to 13–32%.
Recalling a fall in the past 12 months can
be difficult for patients, especially if the fall
did not have serious consequences (“recall
bias”) (25). The close contact between pa-
tients and health care professionals in haem-
ophilia care centres helped us to minimi-
ze these recall bias by double checking the
information with the patients’ records.
Another limitation is the lack of a non-
haemophilic control group. To identify fall
risk factors specific for PWH a prospective
multicentric study with a large sample of
adult PWH and a non-haemophilic control
group should be conducted.

Conclusion
Falls seem to be a common phenomenon
in patients with haemophilia. Screening for
fall risk factors like age, joint replacement
and gait insecurity should be implemented
into the daily practice of haemophilia care
to prevent falling. Both patients and
healthcare professionals need to be aware
of the ailing risk and the possible conse-
quences a fall might have – especially for
elderly patients.
Fall prevention strategies such as phy-
siotherapy should be stimulated.

Authorship contribution
Hanna Rehm, Jan Schmolders and Peter
Pennekamp performed chart review, data
collection and wrote the paper. Rahel Bor-
nemann, Georg Goldmann and Sebastian
Koob performed chart review and collecti-
on of clinical data; Andreas Strauss and
Johannes Oldenburg analysed results and
edited the manuscript.

Conflict of interest
Peter H. Pennekamp and Andreas C.
Strauss have received funding for research
carried out in this work. The other authors
declare that they have no interests which
might be perceived as posing a conflict or
bias.

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