Falling: should one blame the heart?
Jansen, Sofie

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CHAPTER THREE

ELECTROCARDIOGRAPHIC ABNORMALITIES IN PATIENTS ADMITTED FOR HIP FRACTURE
ABSTRACT

BACKGROUND
Several risk factors for falls and hip fractures have been recognized, but controversy still exists towards the importance of rhythm and conduction abnormalities as potentially modifiable risk factors for recurrent falls. The aim of this study was to determine the prevalence of clinically relevant ECG abnormalities in patients with a hip fracture versus controls.

METHODS
The study was designed as a case-control study within consecutive hip-surgery patients in an academic hospital. Cases: patients with traumatic hip fractures. Controls: patients undergoing planned hip surgery (non-traumatic). Cases and controls were 1:1 matched for age and gender. Inclusion criteria: age ≥50 years. Exclusion criteria: high energy trauma, pathological and/or previous hip fracture. ECGs were scored using predefined categories. Multivariate logistic regression was performed to calculate odds ratios (OR) and to correct for confounders.

RESULTS
We included 888 patients (444 cases). Mean age was 70.9 years (SD 9.3), 70% were female. After correction for potential confounders we found the following associations between clinically relevant ECG abnormalities and hip fractures: atrial fibrillation OR 2.7 (95%CI 1.2-6.1), abnormal QTc prolongation OR 3.9 (2.2-6.8), sinus tachycardia OR 5.0 (2.1-11.8) and sinus bradycardia OR 0.3 (0.1-0.5). Univariately, several markers for decreased cardiac function were associated with hip fractures also.

CONCLUSIONS
Hip fracture patients are at higher risk for ECG abnormalities than matched patients undergoing hip surgery for other indications. To potentially reduce the risk of future (injurious) falls, increased awareness of these ECG abnormalities is warranted to assess the need for further cardiovascular fall risk assessment.
CHAPTER 3

falling: should one blame the heart?

INTRODUCTION

Hip fractures in older persons form a substantial and growing health-care burden. Hip fractures lead to an excess one-year mortality rate of 25%, and 50% of survivors of hip fractures suffer from a significant decline in quality of life. Prevention of hip fractures is therefore of great importance. Since >90% of hip fractures are due to a fall, a multifactorial intervention is warranted when assessing treatable risk factors to prevent a (recurrent) injurious fall.

Several risk factors for falls and hip fractures have been recognised, including muscle weakness, history of falls and visual deficits. However, controversy still exists towards the importance of cardiac arrhythmias as a potentially modifiable risk factor for falls. Only a few studies have investigated the association between cardiac rhythm and conduction abnormalities and hip fractures. Although these studies suggest a potential association between cardiac arrhythmias and hip fractures, results were inconclusive due to small sample sizes and lack of adequate comparison groups.

If we could determine whether cardiac arrhythmias, conduction abnormalities and other electrocardiographic (ECG) abnormalities are indeed associated with hip fractures, this may provide us with new evidence on (potentially treatable) risk factors for injurious falls. In the current study we therefore investigated whether ECG abnormalities were more prevalent in hip fracture patients compared with planned hip surgery patients. We hypothesized that hip fracture patients have more clinically relevant ECG abnormalities, potentially explaining fall incidents, than study controls.

METHODS

Population

The study was conducted according to the principles expressed in the Declaration of Helsinki. The medical ethics committee of the Academic Medical Center (Amsterdam) approved the conduction of this study and waived the necessity for informed consent because of the observational design. The study was designed as a case-control study within consecutive patients undergoing hip-surgery. All patients admitted for either planned or emergency hip surgery from January 1996 to May 2011 in a tertiary university teaching hospital were screened for eligibility. Cases were defined as patients with traumatic hip fracture who underwent subsequent proximal femur fracture surgery. Controls were defined as patients who underwent elective hip surgery for non-traumatic reasons, mainly total hip replacement. Inclusion criteria were age ≥50 years and preoperative ECG present in hospital records. Exclusion criteria were previous hip fracture, high energy trauma and pathological fracture. Patients were individually matched 1:1 for age and gender. Age was categorized in groups of five years to increase likelihood of matching.

Baseline characteristics

For data collection, all electronic and paper medical records were retrieved. Admission duration was recorded in days. All functional limitations and comorbid diagnoses (noted in the medical records and/or referral letters) were recorded. Functional limitations included a previous fall (mention of a fall in the past medical history), use of a mobility aid (walker, cane or wheelchair), visual impairment or deafness. Further comorbid diagnoses included coronary artery disease (previous medical history of angina pectoris, myocardial infarction/percutaneous transluminal coronary angioplasty and/or coronary artery bypass graft-surgery), hypertension, heart failure, heart-valve disorder, cerebrovascular accident, atrial fibrillation, pacemaker or internal cardiac defibrillator, parkinsonism, cognitive impairment, alcohol abuse, diabetes mellitus, chronic obstructive pulmonary disease, hemiplegia/paraplegia and depression. As an overall measure of comorbidity, the Charlson Comorbidity-Index (CCI) was computed. Among other conditions, the CCI comprises myocardial infarction, congestive heart failure, cerebrovascular disease, peripheral vascular disease, diabetes, liver disease, renal disease and chronic pulmonary disease.

Drugs were listed and grouped according to Anatomical Therapeutic Chemical (ATC) classification system. Medication categories adjusted for in our analysis were psychotropic medications: psycholeptics (N05*) and psychoanalptics (including anti-depressants) (N06*), and cardiovascular medications: cardiac therapy (cardiac glycosides, class I and III anti-arrhythmics, cardiac stimulants, vasodilators and other cardiac preparations) (C01*), antihypertensives (C02*), diuretics (C03*), peripheral vasodilators (C04*), beta blockers (C07*), calcium channel blockers (C08*), agents acting on the renin-angiotensin system (C09*), alpha-adrenoreceptor antagonists (G04CA) and beta blocker anti-glaucoma preparations (S01ED). QTc-prolonging drugs were defined according to the composite list with QT-drugs known to cause torsades de pointes.
RESULTS

The total cohort consisted of 3505 consecutive patients who underwent hip-surgery between January 1996 and May 2011. Of those, 1894 met the inclusion criteria. Within this eligible cohort, we were able to match 444 cases (311 females, mean age 70.9 years [SD 9.3]) to 444 controls (311 females, mean age 70.8 years [SD 9.2]). Further details on inclusion are shown in FIGURE 1. Of the cases, 305 patients underwent surgery for a femoral neck fracture, 129 for intertrochanteric fracture and 11 for subtrochanteric fracture. Among the controls, 431 underwent total hip replacement for osteoarthritis and 12 for avascular necrosis.

Electrocardiographic findings

Preoperative 12-lead ECGs were used for determination of ECG abnormalities (paper speed 25 mm/s and calibration 10 mm/mV), including ECGs that were performed before the date of admission. All ECGs were assessed and analyzed by a trained reviewer (SJ). If any doubts were present, a cardiologist (RWK/FJL) decided on final scoring. One in four ECGs was randomly checked by RWK. ECGs that showed a pacemaker rhythm were excluded from further analysis beyond assessment of potential pacemaker malfunction, as conduction intervals are usually distorted in these ECGs due to placement of the pacemaker lead.

Clinically relevant ECG findings were defined as: quantitative findings (ventricular rate, conduction intervals and electrical axis), rhythm and conduction abnormalities, electrical axis and voltage abnormalities, ectopic beats, QRS morphology and pathological Q wave and ST-T segment abnormalities. Information concerning ventricular rate, PR interval, QRS duration and electrical axis was taken from the automated ECG analysis. The QT interval was measured manually and corrected for rate through Bazett’s formula. Sinus tachycardia was defined as sinus rhythm with a rate of >100 beats/min. Sinus bradycardia was defined as sinus rhythm with a rate of <60 beats/min. Abnormally prolonged QTc interval was defined as a QTc interval of >450 ms in males and >470 ms in females 12.

Statistical analysis

To assess differences between cases and controls, paired t-tests were used for continuous variables and McNemar’s test for dichotomous variables. For non-normally distributed continuous data, Wilcoxon signed rank test was used. For associations, OR’s were calculated through conditional multivariate logistic regression analysis. A hierarchical modelling strategy was used, in which the first model contained the main determinant only (ECG abnormality) and the final model included potential confounders. The following covariates were considered as potential confounders: age, time between ECG and surgery, CCI, use of mobility aid, previous fall, hemiplegia, impaired cognition and use of psychotropic drugs. A p-value of <0.05 was used as threshold for statistical significance. For ECG abnormalities, the Bonferroni correction was used to adjust for multiple testing. Statistical analyses were performed using IBM SPSS Statistics (Version 19.0 for Windows. IBM Corp. Released 2010. Armonk, NY).
Baseline characteristics are shown in Table 1. Cases and controls showed significant differences in age, time of ECG to surgery and CCI. Use of mobility aid, hemiplegia and CVA were more prevalent in cases than controls. Other common fall-risk factors, such as previous fall, visual impairment, Parkinsonism, alcohol abuse and cognitive impairment were more prevalent among cases. Medical history of heart failure was significantly more prevalent in cases than controls, but medical history of other cardiovascular conditions such as hypertension, coronary artery disease and atrial fibrillation was equal in both groups. Use of psychotropic drugs was more common in cases, use of other drugs was equal in both groups.

Table 1. Baseline characteristics of hip fracture patients and controls

<table>
<thead>
<tr>
<th>Baseline characteristic</th>
<th>Cases n = 444</th>
<th>Controls n = 444</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.9 (± 9.1)</td>
<td>70.8 (±9.1)</td>
<td>0.012</td>
</tr>
<tr>
<td>Gender, female</td>
<td>235 (53.0%)</td>
<td>232 (51.9%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Time of ECG to surgery (days)</td>
<td>0.8 (0.4; 1.6)</td>
<td>1.9 (1.7; 2.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>52 (11.7%)</td>
<td>54 (12.1%)</td>
<td>0.629</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>26 (5.9%)</td>
<td>22 (5.0%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>123 (27.8%)</td>
<td>115 (26.1%)</td>
<td>0.184</td>
</tr>
<tr>
<td>Heart failure</td>
<td>129 (29.2%)</td>
<td>122 (27.5%)</td>
<td>0.246</td>
</tr>
<tr>
<td>Hypertension</td>
<td>311 (70.0%)</td>
<td>311 (70.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Heart valve disorder</td>
<td>21 (4.8%)</td>
<td>19 (4.3%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Atrial fibrillation/fibrillation flutter</td>
<td>27 (6.2%)</td>
<td>26 (5.9%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Right bundle branch block</td>
<td>23 (5.3%)</td>
<td>24 (5.5%)</td>
<td>0.036</td>
</tr>
<tr>
<td>Ectopic beats</td>
<td>56 (12.6%)</td>
<td>56 (12.6%)</td>
<td>0.987</td>
</tr>
<tr>
<td>Other comorbidities</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>52 (11.7%)</td>
<td>54 (12.1%)</td>
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</tr>
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Table 2 shows the proportion of ECG findings and abnormalities in cases and controls. Four cases and five controls showed pacemaker rhythm and were therefore excluded from further ECG analyses. None of the paced ECGs showed signs of pacemaker malfunction. Because of the paired character of the analysis, 18 patients were therefore excluded from further analysis, yielding a population of 435 cases and 435 controls for ECG analysis.
Cases and controls showed significant differences in the occurrence of several rhythm and conduction abnormalities: abnormal QTc prolongation (22.1% of cases vs. 4.8% of controls), sinus bradycardia (4.1% of cases vs. 18.4% of controls), sinus tachycardia (10.8% of cases vs. 2.1% of controls) and atrial fibrillation or flutter (6.2% of cases vs. 2.9% of controls). Electrical axis and voltage abnormalities that were significantly different between cases and controls were: right-axis deviation (2.8% of cases vs. 0.5% of controls), low QRS voltage (4.8% of cases vs. 0.9% of controls) and left ventricular hypertrophy (5.3% of cases vs. 2.3% of controls). Pathological Q waves was more frequently observed in cases (8.7% of cases vs. 4.6% of controls), as were non-specific ST-T changes (21.6% of cases vs. 13.1% of controls).

Prevalence of first-degree atrioventricular (AV) block and supraventricular tachycardia was equal in both groups, as were all bundle branch abnormalities, bifascicular and trifascicular blocks. One case had a third degree AV-block (vs. none in the control group) and left posterior fascicular block was observed in one case (vs. none in the control group).

All quantitative ECG abnormalities that were univariately associated with hip fractures were tested multivariately (FIGURE 2). The following cofactors were included in the final model: age, time of ECG to surgery, CCI, use of mobility aid, previous fall, hemiplegia, impaired cognition and use of psychotropic drugs. ECG abnormalities that remained significantly associated with hip fractures after adjustment in the final model were abnormal QTc prolongation (OR 3.9 [95% CI 2.2-6.8]), sinus bradycardia (0.3 [0.1-0.5]), sinus tachycardia (5.0 [2.1-11.8]) and atrial fibrillation (2.7 [1.2-6.1]). Adjustment for use of QTc-prolonging drugs did not alter odds ratios between abnormal QTc prolongation and hip fractures.
Our study showed that clinically relevant rhythm and conduction abnormalities, such as atrial fibrillation, QTc prolongation, sinus bradycardia and tachycardia, were associated with hip fractures in patients undergoing hip-surgery.

An association between atrial fibrillation and hip fractures has not been shown before. Two recent studies, however, found atrial fibrillation to be an independent risk factor for falls in older patients. Our results support this finding, as >90% hip fractures are due to a fall. Atrial fibrillation can lead to decreased cardiac output because of an increased ventricular rate, irregular ventricular response and loss of the atrial kick. Furthermore, atrial fibrillation is associated with decreased baroreflex sensitivity, which can result in a decrease in orthostatic tolerance. Since orthostatic hypotension is a cause for syncope and falls in older persons, this may provide an extra pathophysiological explanation for the association between atrial fibrillation and falls.

Abnormal QTc prolongation was also associated with hip fractures. QTc prolongation can cause torsades-de-pointes, which in turn can lead to syncope. Ventricular tachy-arrhythmias may contribute to syncope as the cause of a fall. Nevertheless it is unlikely that all traumatic hip fracture patients suffered from torsades. Although speculative, it is possible that the effects of acute-phase response due to hip fracture or poor general condition contributed to QTc prolongation through as yet unknown mechanisms. A previous study has found an association between QTc prolongation and increased C-reactive protein levels which supports this theory.

To our surprise, we found that study controls had a higher prevalence of sinus bradycardia on the ECG, whereas hip fracture significantly more often showed sinus tachycardia. This difference may be explained by the fact that hip fracture patients will more often have an increased heart rate due to pain, anemia and stress, leading to sinus tachycardia, or to the finding of sinus rhythm in patients that normally would have sinus bradycardia. Use of beta-blockers, which potentially could have explained this finding as well, did not change the results in a multivariate model.

Univariately, we found that other markers for decreased cardiac function were associated with hip fractures, namely low QRS voltages, inverted T waves, non-specific ST-T changes, pathological Q waves and left ventricular hypertrophy. As these abnormalities are usually the result of either previous myocardial damage (e.g. due to ischaemia) and/or heart failure, patients with these abnormalities could be prone to (near) syncope when physical demands outweigh the capability of the heart to generate the required cardiac output. Three large population cohort studies found that risk of (hip) fracture was significantly increased in patients after a diagnosis of heart failure. Although markers for decreased cardiac function were only univariately associated with hip fractures in our cohort, this trend is in line with the findings of these population cohort studies.

Many of the potential explanatory findings in rhythm or conduction abnormalities such as complete heart block, severe bradycardias or tachycardias that may cause syncope can be transient and therefore be missed on the admission ECG. Abnormalities in ECG findings that were significantly more prevalent in hip fracture patients are by themselves not an explanation for a fall, but may be considered as ‘proxies’ for an abnormality that can cause a fall or syncope. However, this was not the case for conduction abnormalities. A complete third-degree heart block can be suspected when less advanced block is observed such as a bifascicular or trifascicular block, first or second degree AV block, but this was only present in a small number of subjects. It can therefore only potentially explain the fall in a small minority of patients.

Some limitations must be mentioned. One limitation of this study is the design. Although registration of all patients was performed prospectively, detailed data on comorbidity and drug use were collected from medical records, and we can therefore not rule out incomplete data collection during admission. It is known that retrospective collection of falls-data is less reliable than prospective collection. However, there is little reason to assume that missing data are differential for the groups, and therefore potential confounding by indication is unlikely. Another limitation is the fact that we compared patients in an acute setting with study controls in a more stable situation. This reflects in differences in median time from ECG to surgery between the two groups. ECGs for hip fracture patients were more often made directly preoperatively or on the day of admission, whereas ECGs for patients undergoing planned hip surgery were more often made during preoperative assessment by anaesthesiologists in the outpatient department. For most of the hip fracture patients, the ECG recording was performed after the actual outcome event (hip fracture). As some of the ECG abnormalities that we found (e.g. atrial fibrillation and tachycardia, were associated with hip fractures in patients under-
and sinus tachycardia) are known to be elicited by stress\textsuperscript{23}, the increased prevalence these abnormalities in hip fracture patients could be partly due to stress of the hip fracture. To account for the differences in timing of the ECG we adjusted for time of ECG to surgery in our analyses. As it is questionable whether hospital populations are fit to serve as controls because controls should preferably resemble the general population, we hypothesized that patients undergoing planned hip-surgery would resemble the general population most\textsuperscript{24}. Also, as the prevalence of ECG abnormalities in our control group was similar to ECG abnormalities found in the general population, we believe that our control group was adequate to make meaningful comparisons\textsuperscript{25,26}. Finally, we used Bazett’s formula for correction of the QT interval for heart rate, as it is the most frequently used formula in clinical practice. However, it is known that this correction method can overestimate QT interval at higher heart rates\textsuperscript{27}, and we should take this into consideration when interpreting the results of this study.

Hip fractures, with their associated morbidity and mortality, are among the most feared consequences of falls, and recognition of potentially modifiable risk factors in this group is therefore of great importance. The results of our study show that hip fracture patients are at much higher risk for heart rhythm and conduction abnormalities than a matched cohort of patients undergoing hip surgery for other indications. Thus, a higher degree of caution and observation during perioperative management is warranted, as well as increased awareness of the need to undertake cardiovascular fall risk assessment when an older adult presents with one of these ECG findings to potentially reduce the risk of future falls. Further research, however, is warranted to confirm our findings in a prospective study. Additionally, it is necessary to study the effects of treatment of these abnormalities on fall incidence rates and fall-related morbidity and injury.

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REFERENCES


