Arrythmia

Falls and Atrial Fibrillation in Elderly Patients

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Background: Atrial fibrillation is a common heart rhythm disorder in older adults, and its prevalence has increased rapidly in recent years. The health issues associated with atrial fibrillation are not limited to physiological problems, as it also contributes to an increased risk of falls, which may be related to cardiovascular co-morbidities and medication use. The aim of this study was to determine which cardiovascular co-morbidities and medication use are associated with falls in older adults with atrial fibrillation.

Methods: Four hundred and one patients 75 years of age or older (82.2 ± 0.2 years) were enrolled in a geriatric evaluation and management unit in Taiwan. Events associated with patient falls and medication use were recorded, and comprehensive geriatric assessment was conducted during admission.

Results: Among the study participants, 66 (16.5%) patients had atrial fibrillation and 234 (58.4%) patients had a history of fall. We found a significantly higher prevalence of falls in patients with atrial fibrillation [odds ration (OR) 1.98, 95% confidence interval (CI) 1.08-3.63, p = 0.026] compared with those without atrial fibrillation. Using multivariate logistic regression, we found that benzodiazepine use (OR 18.22, 95% CI 2.71-122.38, p = 0.003), a history of paroxysmal atrial fibrillation (OR 12.18, 95% CI 1.37-108.70, p = 0.025) and hypertension (OR 9.49, 95% CI 1.19-75.57, p = 0.034) were independent factors for falls in atrial fibrillation patients.

Conclusions: A diagnosis of atrial fibrillation in elderly patients is associated with falls. Benzodiazepine use, history of paroxysmal atrial fibrillation, and hypertension were associated with a high falling prevalence among patients with atrial fibrillation.

Key Words: Atrial fibrillation • Benzodiazepine • Falls • Hypertension

INTRODUCTION

Atrial fibrillation (AF) is a common rhythm disorder among older adults; aging is related to an increase in the incidence and prevalence of AF.[1,2] This arrhythmia has become more prevalent with the increase in the elderly population in recent years.[3] Additionally, AF is associated with many cardiovascular and other co-morbidities, such as hypertension, heart failure, diabetes mellitus, stroke, disability of daily living, and cognitive impairment.[3-5] Therefore, it could be expected that AF patients use more cardiovascular and other drugs than those who are not similarly afflicted.

Falling represents a major health threat for older adults. Previous studies have identified many factors associated with falls, including older age, gait and balance impairment, muscle weakness, depression, cognitive dysfunction, medications, limitations in daily activities, stroke, and orthostatic hypotension.[6-10] AF and other cardiovascular diseases, such as hypertension and dia-

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betes mellitus, are also considered as risk factors for falls in some studies.[8,9,11-13] Antihypertensives and other cardiovascular medications, such as calcium channel blocker, diuretics and alpha-blocker, have been known to be associated with an increased risk of falling.[8,9,11-13] Central nervous system active drugs, such as benzodiazepines, and muscle relaxants, which reduce muscle strength, are commonly used drugs associated with falls.[13,14] Furthermore, polypharmacy (the use of multiple medications) is also associated with an increase in fall risk.

Previous studies have suggested AF may result in unstable hemodynamic status.[15] As mentioned above, AF is associated with a variety of factors which are also related to falls. Until now, no research has focused on the effect of these factors as they relate to falling in elderly patients with AF. In this study, we examined if some of these cardiovascular co-morbidities and medications increase the prevalence of falling in AF patients.

METHODS

This study adopted a cross-sectional design in conjunction with our geriatric evaluation and management unit in Taichung Veterans General Hospital, a tertiary medical center in Taiwan. A total of 520 inpatients admitted for geriatric syndrome and falls evaluation and management were approached during the period from September 2008 to August 2010. Comprehensive geriatric assessments (CGA), including functional scales and evaluations of falling events, were implemented. The CGA database includes data of basic activities of daily living (BADL, measured by the Barthel Index), mini-mental state examination score (MMSE score, a scale for cognitive function evaluation), geriatric depression scale (GDS, with a maximum score of 15 points), timed up and go (TUG) test impairment (defined as impaired if the subject takes more than 10 seconds to finish the test),[16] functional reach (FR) test impairment (defined as a reach of less than or equal to 15 cm),[17] presence of polypharmacy (defined as using more than 4 kinds of drugs), co-morbidities and medication use. All enrolled patients' medical records were reviewed to collect data on co-morbidities and medication use from September 2007 to August 2010. Average systolic blood pressure was calculated from the systolic blood pressure (measured 2 to 4 times per day) of a patient before hospital discharge (for a total of 3 days). All subjects were interviewed by trained researchers, and subjects who did not complete the CGA (7 patients) or were less than 75 years of age (112 patients) were excluded. Eventually, 401 patients were available for statistical analysis. The average patient age was 82.2 $\pm$ 0.2 years, and 76% were male gender and 66 (16.5%) of them had a history of AF.

Among the valid study subjects, 66 (16.5%) patients were identified as having a history of AF by reviewing medical records, electrocardiogram (ECG) or ambulatory ECG reports. ECG data of AF patients were re-examined for assurance and to classify the type of AF. Paroxysmal AF was defined as AF which terminates spontaneously in less than 7 days (confirmed by a sinus rhythm ECG or by ECG monitoring for 24 hours), as described in the guidelines of the American College of Cardiology/American Heart Association/European Society of Cardiology.[18] Other co-morbidities were defined as recorded in charts. The history of falls was defined as any falling events from September 2007 to August 2010. We collected the fall data from the CGA databases and medical records. By definition, 234 (58.4%) patients had one or more falls in the study period. Recurrent fallers (defined as those who fell 3 times or more) within the group of AF patients were also identified by the same methods.

Statistic analysis

Continuous variables were expressed as mean $\pm$ standard error of the mean (SEM). Statistical comparisons of continuous variables were performed using the t test. Categorical variables were compared by the Chi-square test, Fisher's exact test or Yates' correction for continuity when appropriate. Factors probably associated with falls (with a p value < 0.1 between groups in univariate analysis) were entered into multivariate analysis. Multivariate logistic regression model was used to determine the independent factors for falls. Statistical significance was defined as a p value < 0.05 for all tests. SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA) was used to perform the statistical analysis.

RESULTS

Table 1 summarized the statistics on age, gender,

BADL, MMSE score, GDS, impaired TUG test, impaired FR test, polypharmacy, co-morbidities, medication use, and average systolic blood pressure. There were no differences in age (p = 0.53), gender (p = 0.825), BADL (p = 0.83), MMSE score (p = 0.25), GDS (p = 0.61), impaired TUG test (p = 0.53) and impaired FR test (p = 0.97) between patients with and without AF. Older adults with AF were significantly associated with a higher prevalence of polypharmacy (p = 0.042), stroke (p = 0.041) and heart failure (p < 0.001). No differences were found in diabetes mellitus, hypertension and myocardial infarction. The AF group was also associated with using more angiotensin-converting enzyme inhibitors/ angiotensin II receptor blocker (ACEI/ARB) (p = 0.005), diuretics (p < 0.001), aspirin (p = 0.046), warfarin (p < 0.001) and fewer muscle relaxants (p = 0.044). No differences were found in the use of beta-blocker, calcium channel blocker, alpha-blocker and benzodiazepine, or the systolic blood pressure distribution between patients with and without AF.

According to our stated definition, 234 subjects (58.4%) had a history of falls (Table 2). Compared with

Table 1. Clinical characteristics of the 401 study subjects by presence of atrial fibrillation

Variable	Total (n = 401)	Atrial fibrillation		p value*
		No (n = 335)	Yes (n = 66)	
Age (years)	82.2 ± 0.2	82.1 ± 0.2	82.6 ± 0.6	0.435
Male	76%	76%	74 %	0.825
BADL	65.7 ± 1.6	65.8 ± 1.7	65.1 ± 3.9	0.856
MMSE score	22.4 ± 0.3	22.6 ± 0.3	21.8 ± 0.7	0.316
GDS	4.9 ± 0.2	4.8 ± 0.2	5.0 ± 0.4	0.612
Impaired TUG test	87%	87%	83%	0.525
Impaired FR test	76%	76%	77%	0.966
Polypharmacy	74%	72%	85%	0.042
Co-morbidities				
Diabetes mellitus	34%	34%	35%	0.999
Hypertension	78%	77%	79%	0.920
Stroke	27%	25%	38%	0.041
Heart failure	17%	12%	41%	< 0.001
Myocardial infarction	6%	6%	8%	0.569
Medication use				
ACEI/ARB	53%	50%	70%	0.005
Beta-blocker	30%	29%	38%	0.179
Calcium channel blocker	56%	55%	58%	0.829
Diuretics	46%	42%	68%	< 0.001
Alpha-blocker	58%	57%	62%	0.528
Benzodiazepine	52%	52%	52%	0.999
Muscle relaxant	31%	33%	20%	0.044
Aspirin	51%	49%	62%	0.046
Warfarin	8%	2%	36%	< 0.001
Average systolic blood pressure				0.308
< 101 mmHg	2%	2%	3%	
101-120 mmHg	24%	24%	21%	
121-140 mmHg	50%	50%	50%	
141-180 mmHg	22%	22%	20%	
> 180 mmHg	2%	2%	6%	

* Comparison of prevalence from chi-square test and means from t test by presence of atrial fibrillation.

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; BADL, basic activities of daily living, measured by the Barthel Index; FR, functional reach; GDS, geriatric depression scale; MMSE, mini-mental state examination; TUG, timed up and go.

non-fallers, fallers had a significantly lower BADL score (p = 0.017), higher GDS (p = 0.002), higher prevalence of impaired FR test (p = 0.002), polypharmacy (p = 0.034) and AF (p = 0.029), and had increased benzodiazepine (p < 0.001) and muscle relaxant use (p = 0.015) in univariate analysis. No significant difference was noted in systolic blood pressure distribution between patients with and without falls. By using multivariate logistic regression, we found that a history of AF [odds ratio (OR) 1.98, 95% confidence interval (CI) 1.08-3.63, p = 0.025], benzodiazepine use (OR 1.93, 95% CI 1.24-3.02, p = 0.004) and higher GDS (OR 1.07, 95% CI 1.00-1.14, p = 0.048) were independent factors for falls in older adults (Table 3).

Among the AF patients, 47 patients (71.2%) had a history of falling (Table 4). Compared with non-fallers, fallers were significantly older (p = 0.016), with a higher prevalence of polypharmacy (p = 0.027), paroxysmal AF (p = 0.018) and benzodiazepine use (p < 0.001) in univariate analysis. None of the cardiovascular drugs (including aspirin and warfarin) were associated with a higher prevalence of falls in our study. Systolic blood pressure distribution showed no difference between AF patients with and without falls. Using multivariate logistic regression, we found that benzodiazepine use (OR 18.22, 95% CI 2.71-122.38, p = 0.003), history of paroxysmal AF (OR 12.18, 95% CI 1.37-108.70, p = 0.025) and hypertension (OR 9.49, 95% CI 1.19-75.57, p = 0.034) were independent factors for falls in older adults with AF (Table 5). Prevalence of falls in AF subjects had a linear relationship (p per trend < 0.001) to the total number of these independent factors for falls (benzodiazepine use, paroxysmal AF and hypertension) (Figure 1). Prevalence of recurrent falls also had a similar linear

Table 2. Comparison between the study subjects with or without a history of falls

Variable	History of falls		p value*
	No (n = 167)	Yes (n = 234)	
Age (years)	81.7 ± 0.3	82.6 ± 0.3	0.066
Male	77%	76%	0.909
BADL	69.9 ± 2.3	62.7 ± 2.1	0.021
MMSE score	22.9 ± 0.5	22.1 ± 0.4	0.158
GDS	4.2 ± 0.2	5.3 ± 0.2	0.002
Impaired TUG test	83%	89%	0.074
Impaired FR test	68%	82%	0.002
Polypharmacy	68%	78%	0.034
Comorbidities			
Atrial fibrillation	11%	20%	0.029
Diabetes mellitus	36%	33%	0.665
Hypertension	79%	76%	0.630
Stroke	22%	31%	0.053
Heart failure	18%	16%	0.750
Myocardial infarction	8%	4%	0.134
Medication use			
ACEI/ARB	53%	53%	0.999
Beta-blocker	28%	32%	0.390
Calcium channel blocker	50%	59%	0.088
Diuretics	44%	47%	0.605
Alpha-blocker	56%	59%	0.664
Benzodiazepine	41%	59%	< 0.001
Muscle relaxant	24%	36%	0.015
Aspirin	51%	50%	0.833
Warfarin	7%	9%	0.469
Average systolic blood pressure			0.258
< 101 mmHg	1%	3%	
101-120 mmHg	22%	25%	
121-140 mmHg	50%	50%	
141-180 mmHg	26%	19%	
> 180 mmHg	1%	3%	

* Comparison of prevalence from chi-square test and means from t test by presence of a history of falls.
ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; BADL, basic activities of daily living, measured by the Barthel Index; FR, functional reach; GDS, geriatric depression scale; MMSE, mini-mental state examination; TUG, timed up and go.

Table 3. Independent factors for falls in the study subjects from multivariate logistic regression

Variable	Odds ratio (95% CI)	p value*
Atrial fibrillation	1.98 (1.08-3.63)	0.025
Benzodiazepine use	1.93 (1.24-3.02)	0.004
Higher GDS	1.07 (1.00-1.14)	0.048
Muscle relaxant use		0.06
Impaired FR test		0.07
Age		0.16
Stroke		0.33
Calcium channel blocker use		0.48
Polypharmacy		0.57
Impaired TUG test		0.76
BADL		0.81

* Covariates entered simultaneously into multivariate logistic regression model.
BADL, basic activities of daily living, measured by the Barthel Index; CI, confident interval; FR, functional reach; GDS, geriatric depression scale; TUG, timed up and go.

Table 4. Comparison between the atrial fibrillation study subjects with or without a history of falls

Variable	History of falls		p value*
	No (n = 19)	Yes (n = 47)	
Age (years)	80.8 ± 0.7	83.3 ± 0.8	0.016
Male	74%	74%	0.999
BADL	67.9 ± 6.7	63.9 ± 4.7	0.647
MMSE score	22.7 ± 1.2	21.4 ± 0.9	0.402
GDS	4.9 ± 0.6	5.1 ± 0.5	0.822
Impaired TUG test	84%	83%	0.999
Impaired FR test	74%	79%	0.748
Polypharmacy	68%	91%	0.027
Co-morbidities			
Paroxysmal atrial fibrillation	16%	51%	0.018
Diabetes mellitus	21%	40%	0.226
Hypertension	63%	85%	0.092
Stroke	21%	45%	0.131
Heart failure	47%	38%	0.688
Myocardial infarction	11%	6%	0.621
Medication use			
ACEI/ARB	63%	72%	0.661
Beta-blocker	26%	43%	0.342
Calcium channel blocker	42%	64%	0.180
Diuretics	74%	66%	0.750
Alpha-blocker	58%	64%	0.865
Benzodiazepine	16%	66%	< 0.001
Muscle relaxant	11%	23%	0.318
Aspirin	58%	73%	0.653
Warfarin	37%	36%	0.959
Average systolic blood pressure			0.848
< 101 mmHg	5%	2%	
101-120 mmHg	16%	23%	
121-140 mmHg	58%	47%	
141-180 mmHg	16%	21%	
> 180 mmHg	5%	6%	

* Comparison of prevalence from chi-square test and means from t test by presence of a history of falls.
ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; BADL, basic activities of daily living, measured by the Barthel Index; FR, functional reach; GDS, geriatric depression scale; MMSE, mini-mental state examination; TUG, timed up and go.

relationship (p per trend = 0.020) to the total number of these independent factors for falls.

DISCUSSION

The major findings of this study were that benzodiazepine use, history of paroxysmal AF and hypertension were independent factors for falls in older adults with AF. Prevalence of falls or recurrent falls in our AF subjects showed a linear relationship to the total number of the independent factors for falls. From our review of the literature, these findings have not yet been described elsewhere.

Table 5. Independent factors for falls in the atrial fibrillation study subjects from multivariate logistic regression

Variable	Odds ratio (95% CI)	p value*
Benzodiazepine use	18.22 (2.71-122.38)	0.003
Paroxysmal atrial fibrillation	12.18 (1.37-108.70)	0.025
Hypertension	9.49 (1.19-75.57)	0.034
Polypharmacy		0.074
Age		0.086

* Covariates entered simultaneously into multivariate logistic regression model.
CI, confident interval.

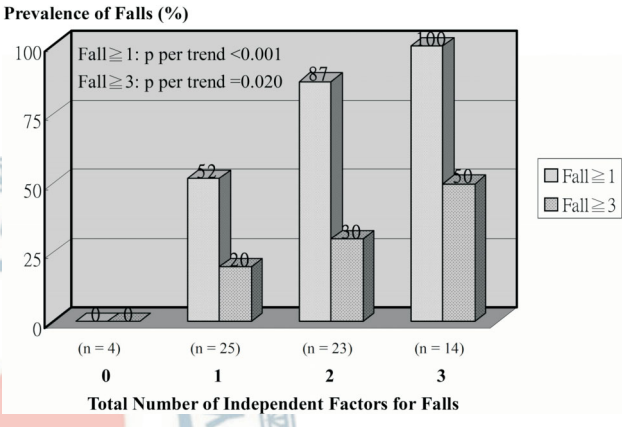

Figure 1. *Prevalence of falls in the atrial fibrillation study subjects (bars) by total number of independent factors for falls (benzodiazepine using, paroxysmal atrial fibrillation, hypertension).*

The higher prevalence of paroxysmal AF in fallers might be due to the 24-hour ECG monitoring and thus more likely to capture AF events, while non-fallers were not similarly monitored. Another possible reason for the higher falling risk in patients with paroxysmal AF may be related to bradycardia after AF with rapid ventricular rate. Syncope or falls may also occur due to the long pause after termination of a paroxysmal AF.[15] The preliminary research suggests that both speculations warrant further study. Our investigation showed that a history of hypertension contributed to falls in older adults with AF. Hypertension has been shown to be a

risk factor for falls.[7,19] A small study performed by Hausdorff et al. showed that increased blood pressure disturbed the balance and gait in elderly patients, and thus increased their falling risk.[20] There are two explanations why hypertension is involved in increasing the risk of falls in the elderly. First, hypertension exacerbates age-related abnormalities in blood pressure homeostasis, which may cause transient hypoperfusion in the brain.[21] Second, high blood pressure damages some of the brain structures related to gait control.[22,23]

AF is a common heart rhythm disorder in older adults and its prevalence increases with age, affecting 0.5% of the population at 40 years and 10% at 80 years.[3] Our studied subjects had a high prevalence of AF (16.5%) and were older than those subjects in earlier studies. Among patients with AF, 41% of our patients were diagnosed with paroxysmal AF, a slightly higher ratio than previous reports (26-32%).[24,25] AF is known to be associated with cardiovascular events, such as stroke and heart failure,[1-3,5] and our study showed similar results. We also found that patients with AF had a higher prevalence of polypharmacy as well as antihypertensives use (ACEI/ARB and diuretics) than those without AF.

Warfarin is effective for stroke prevention and current published guidelines have recommended its use for high-risk AF patients.[26] Falls are the most common reason for not using anticoagulants.[27-30] Physicians often feel uncomfortable prescribing anticoagulants due to the fear of complications, such as intracranial bleeding after falls. Many studies have documented that warfarin has been underused around the world, especially in older patients.[26,27,31-33] Thus, assessment and management of fall risk are important for proper prescription of anticoagulants and management in older adults. Reducing the falling related injuries in patients, assessment and management of fall risk will also help physicians to withstand their "fear of falls". Physicians should evaluate and modify potentially reversible patient factors while prescribing anticoagulant in these high falling risk patients. (i.e. stop using benzodiazepine in patient with paroxysmal AF)

The presence of AF, benzodiazepine use and higher GDS were independent factors for falls, and previous fall studies have showed similar results.[8,13,14,34] Although AF has been considered as a risk factor for falls, few studies have addressed this issue. In a recent retrospective study for aged-care inpatients, AF was identified as an independent risk factor for recurrent falls with an odds ratio of 2.5 (95% CI 1.1-5.5).[9] Despite the fact that the definition of falls in our study was different from that of the above study, our data showed a similar finding with an odds ratio of 1.98 (95% CI 1.08-3.63) for AF being a factor for falls. Maurer et al. hypothesized some potential mechanisms by which AF may induce hemodynamic compromise in older adults.[15] One of these mechanisms is that diastolic dysfunction develops during aging as the heart becomes less compliant.[1] Thus, a slowed early diastolic filling develops and a greater atrial contraction for diastolic filling is needed. However, AF results in the dysfunction of atrial contraction and then hemodynamic compromise occurs. This condition may cause falls or syncope in some situations.

There were some limitations in this study. First, our study was a cross-sectional study design and we could not observe the causes of falls due to its retrospective nature. The data revealed associated factors for falls, rather than true risk factors or actual causes of falls. Second, our participants were older Asians with a predominance of male subjects. Thus, the results may be applicable only to that segment of the population deemed elderly. Third, drug-induced orthostatic hypotension is considered to be another mechanism for hypertension being a risk factor of falls.[35,36] However, our dataset included information on antihypertensive use but not orthostatic hypotension. As a result, the effects of antihypertensive drugs could not be evaluated. However, because our AF patients had a significantly higher prevalence of polypharmacy as well as an increased use of antihypertensives, it is likely that drug-induced orthostatic hypotension may play an important role in the risk of falls in this disease population. Fourth, the relatively small number of AF patients included in the current study limited our ability to find more associated factors for falls. Fifth, selection bias cannot be ruled out in our study. Theoretically, to make a valid inference on AF and falls, the underlying reasons that led to geriatric evaluations should not be associated with exposure. Those seeking treatment due to falls were more likely to be diagnosed with AF because a thorough and proper falling evaluation was conducted (i.e. a 24-hours ECG monitoring). This may cause the prevalence of AF in fallers to be overestimated. Finally,

measurement errors and information bias in recording AF and falls are possible. Further well-designed prospective studies may be needed for evaluating other risk factors and identifying the mechanisms of these associated factors for falls.

CONCLUSIONS

In conclusion, AF was associated with a significantly increased prevalence of falls in patients 75 years of age and older. Benzodiazepine use, history of paroxysmal AF and hypertension were independent factors for falls in older adults with AF. Ultimately, disease control and reduction in the use of benzodiazepine are important in an effort to prevent or minimize fall risk in elderly AF patients.

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