REVIEW ARTICLE

Link between cardiovascular disease and the risk of falling: a comprehensive review of the evidence

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KEY WORDS

ABSTRACT

cardiovascular conditions, falls, prevention Falls are associated with increased morbidity and mortality, rising hospital readmission rates, decreased patient independence, and strained healthcare resources. In aged populations and individuals with multimorbidity, cardiovascular conditions may contribute towards an increased propensity to fall. The prevalence of cardiovascular conditions generally increases with age, and understanding potential fall risk factors may help to minimize the risk of falls and develop preventive interventions. Acting on even one such risk factor or introducing an appropriate intervention may reduce the overall propensity for a patient to fall. Further prevention strategies primed towards cardiovascular ailments should be elucidated and trialed.

Introduction Falls are the world's second leading cause of accidental death, with an estimated 646 000 fatal falls occurring each year.¹ With approximately 37 million falls requiring medical attention annually,¹ interest in studying the factors contributing to an increased risk of falls has grown substantially. In effect, falls are associated with increased morbidity and mortality, increased hospital readmission rates, decreased patient independence, and strained healthcare resources.²

Multimorbidity is associated with an increased risk of falling,³ and adults over 65 years old experience the highest number of fatal falls.¹ Recent data showed that almost 17% of Poland's population is at or above the age of 65 years,⁴ with 69% having 2 or more chronic medical conditions.⁵ In terms of generalized fall data, an epidemiological study in Poland concluded that 23.1% of those aged 65 years and older experienced at least 1 fall in the last 12 months, with a slight predominance in women (26.8% vs 19.7%).⁶ Data from 2015 estimated that 1.2 million Polish adults at or above 65 years had fallen at least once in 2015, and current models estimate that 2.3 million people in this age group will be affected in 2050.^{6,7}

Falls are often multifactorial, and it may be challenging to elucidate specific causes or factors contributing to falls.⁸ In aged populations and individuals with multimorbidity, cardiovascular conditions may contribute to increasing the propensity to fall. Current projections estimate that one in every 4 people in Europe could exceed 65 years by 2050,⁹ and the rising prevalence of various comorbidities (eg, cardiovascular conditions) in proportion to age may be one of numerous sources of explanation for fall risk with increasing age.³ Most epidemiological data do not distinguish the etiology of a fall; this often renders it difficult to elucidate contributing factors for the resulting fall, and such data should only be used to understand the overarching picture of fall epidemiology. Knowledge of such fall risk factors may help to minimize the risk of falls and develop preventive interventions.⁸

Therefore, in this report, we aimed to: 1) characterize various cardiovascular conditions and their contribution towards the overall risk of falling; 2) analyze the link between quality of life and other patient outcome measures and falls; 3) review fall risk factors and fall-related epidemiological data as well as their association with current fall prevention strategies (TABLE 1).

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TABLE 1 Key points to remember

Falls are often multifactorial; in aged populations and individuals with multimorbidity, cardiovascular conditions may contribute to the increased propensity of falling.

Syncopal syndromes, arrhythmias such as atrial fibrillation, and heart failure have had consistent associations with an increased fall risk.

Unexplained falls and falls related to syncope may be difficult to discern; current guidelines cite a strong consensus of managing unexplained falls in the same way as unexplained syncope.

Treatment considerations, such as antihypertensive drug use, may be associated with fall risk or injury severity in some specific settings.

Responsible medication prescribing, proper patient education, and medication review may help to mitigate fall risk.

Future studies should continue to assess fall prevention strategies, especially in the context of cardiovascular comorbidities.

Methods Electronic searches of the major electronic databases (ie, PubMed, Scopus, Embase, Cochrane databases, and Google Scholar) using the key search terms fall, risk, prevention, and cardiovascular were performed. An additional manual search of references in the selected articles was performed to further localize relevant studies. The related links function in MEDLINE was used for additional possible references to maximize the search strategy. Only articles in English and Polish published up until April 2020 were included. Studies from a variety of settings, including hospitals, nursing homes, and institutions were included; articles concerning sports-related falls, occupational falls, and physical abuse-related falls were excluded. No formal limitations to the study types were established; 49 observational studies, 7 randomized controlled trials, 7 meta-analyses, and 7 systematic reviews were selected for inclusion in this review. Other publications, such as guideline summaries, editorials, and narrative reviews, were also included to review professional society recommendations and expand on visions for future research. Additional relevant epidemiological data from the World Health Organization were also searched and included.

Risk factors Falls may be accidental, typically due to slipping, tripping, or colliding with something, or unexplained, when there is no evident or apparent cause.¹⁰ It is essential to note the often multifactorial nature of risk factors contributing towards falls, and it is crucial to understand each factor's potential contributions towards the patient's propensity to fall.⁸ The prevalence of cardiovascular conditions generally increases with age, and the most frequently cited associations of fall risk in the elderly include carotid sinus syndrome (CSS), arrhythmias such as atrial fibrillation (AF), heart failure (HF), and vasovagal syndromes.¹¹⁻¹³

Advanced age and multimorbidity Advanced age is one of the most elementary factors increasing the risk of falling.¹ An age between 65 and 74 years was associated with a 31% risk of falling, which increased to 37% in the 80+ age group.¹⁴ While it is challenging to pinpoint age alone as an etiological factor behind the risk of falling,¹⁵ advanced age may be linked to multiple chronic comorbidities, driving up the fall prevalence mentioned previously.³ Some patients forget falls altogether, especially if the resulting fall does not result in injury.¹⁵ In settings with limited information, the simplest explanation possible may be sought, leaving some potential risk factors for falls unexplored.

Syncope as a risk factor for falls One of the largest categories of risk factors includes syncope,¹³ usually defined as a temporary loss of consciousness following diminished blood flow to the brain.¹⁶ As the level of consciousness is altered, the propensity for falling increases,¹⁷ and if syncope occurs while a patient is upright, the patient may fall.¹⁰ The specific differentiation between an unexplained fall and a fall related to syncope may be difficult.^{10,16} They may be indistinguishable due to elements of retrograde amnesia, and thus falls can also be categorized into those that include transient loss of consciousness (TLOC) and those without.^{16,18} The current European Society of Cardiology (ESC) guidelines cite a strong consensus of managing unexplained falls in the same way as unexplained syncope (despite a lack of controlled trials).¹⁹ They further emphasize gathering history from patients and eyewitnesses to determine the presence or absence of TLOC, and if present, distinction of a potential origin of the TLOC. When syncope is suspected, the initial evaluation includes history taking and physical examination, supine and standing blood pressure measurements, and electrocardiography. Suspicion of particular cardiovascular causes may find diagnostic yield in further electrocardiographic monitoring, echocardiography, or other diagnostic testing specific to the suspected etiology.¹⁹ Further focus in this review will be maintained on syncope secondary to CCS, vasovagal syncope, orthostatic hypotension (OH), and causes of syncope occurring due to cardiac-specific conditions.

Carotid sinus syndrome Carotid sinus syndrome is characterized by syncope associated with an underlying carotid sinus hypersensitivity, leading to inappropriate carotid sinus function.²⁰ The diagnosis of CSS is often based on a clinical history and reproduction of symptoms during carotid sinus massage, leading to replication of hypersensitivity of the carotid sinus.¹⁹ One study analyzed patients over the age of 50 years presenting to the emergency department because of falls and reported that 1 in 3 patients attending due to nonaccidental falls had vasodepressor carotid sinus hypersensitivity, and simple testing for intact baroreceptor function may help to exclude other etiologies.²¹ There is potential to decrease the risk of falling in symptomatic patients by way of pacemaker insertion in appropriate patient groups.²¹⁻²⁵

Vasovagal syncope Vasovagal syncope, an autonomic neural reflex failure resulting in reduced cardiac output and cerebral hypoperfusion,²⁰ is among the most common causes of syncope, with one study estimating 24% of syncope workups to be classified as vasovagal.^{20,26} Although no studies have directly linked vasovagal syncope with falls, the premise of syncope increasing the propensity of falls maintains vasovagal syncope as a contributing factor to the risk of falls.^{11,18,27} Diagnostic mainstays include monitoring the cardiac electrical activity to exclude arrhythmias and the potential use of the tilt table test as a confirmatory assessment.^{21,28} They may also include the use of an internal loop recorder in the case of recurrent unexplained symptoms or high-risk patients.²⁸ Management generally begins with patient education and lifestyle modification, and may also include the use of counterpressure maneuvers, pharmacologic intervention, or modification of hypotensive medications.^{19,28} A severe or recurrent clinical course of a predominantly cardioinhibitory variant may lead to the consideration of cardiac pacing if asystole is the dominant feature. This is consistent with the recent ESC guidelines, which state that there is sufficient evidence that dual-chamber cardiac pacing should be considered when correlation between symptoms and electrocardiographic findings is established in patients over the age of 40 years with features of the ISSUE (International Study on Syncope of Uncertain Etiology) trial.^{19,28}

Orthostatic hypotension Orthostatic hypotension with syncope may also increase fall risk, characterized by functional or structural baroreflex impairment resulting in diminished compensatory responses to postural changes.²⁹ Drug-induced OH is the most common etiology, but it may also include volume depletion and autonomic failure.¹⁹ Decreased blood pressure without autoregulation may result in syncope and falls,³⁰ and reports have suggested that OH is a risk factor for falls over a long time.³¹ While previous studies have concluded it is a risk factor in falls in the institutionalized (but not ambulatory) adults, a prospective study with a median follow-up of 23 years suggested that the presence of OH in ambulatory middle-aged adults was associated with falls.³¹ Another longitudinal cohort study with a mean patient age of 61.5 years found that both OH with impaired blood pressure stabilization at 40 seconds after standing (relative risk [RR], 1.52; 95% CI, 1.03–2.26) and sustained OH (RR, 1.81; 95% CI, 1.06-3.09) were associated with an increased relative risk of unexplained falls.³² While orthostatic hypotension is classically associated with the elderly, studies have reported a prevalence of up to 15.9% in middle-aged adults, although this group is associated with a lower rate of falling.^{31,33}

Cardiac abnormalities Falls may also be attributed to syncope secondary to cardiac abnormalities;

they may include structural defects such as valvular disease or arrhythmias. Blood flow to the brain is impaired, and the resulting balance impairment increases the propensity of falling. While still multifactorial, the main causes may stem from patients' cardiovascular conditions.¹⁹ The presence of mitral, tricuspid, or pulmonary valve regurgitation on echocardiography was associated with a higher fall risk.³⁴ For example, AF has been reported to be an independent risk factor for nonaccidental falls in the older adult population.³⁵⁻³⁷ Proposed mechanisms include a directly diminished cardiac output as well as an association of the same disease process affecting other parts of the conduction system, which may be further compounded in those with autonomic dysfunction impairing protective reflexes.³⁵ Although requiring further studies to establish definitive causality, Jansen et al³⁷ reported that patients aged 65 to 74 years presenting with falls and adults aged 50+ years with self-reported syncope were twice as likely to have AF on examination.

Atrial fibrillation therapy A recent study found that the use of antiarrhythmic therapy increased the risk of fall-related injury and syncope compared with rate-lowering monotherapy, with the highest risk during the first 14 days.³⁸ Applicable AF patient populations may use anticoagulants to diminish stroke risk, and while serving a protective effect, it may be considered a potential modifier of the severity of injury following falls due to increased bleeding risk.^{35,39-42} Among patients with AF and appropriate criteria for anticoagulation, a previous fall history was associated with delayed oral anticoagulation that was, on average, a 53-day delay.⁴³ A 2012 prospective study concluded that patients at high risk of falls who took oral anticoagulants were not at a significantly increased risk of major bleeding as compared with low-fall risk patients, suggesting that a heightened fall risk alone should not discourage the use of oral anticoagulants in patients with AF.⁴⁴ Others have similarly concluded that anticoagulation does not increase the risk of a significant bleeding injury,^{45,46} but may increase mortality due to a bleeding injury.⁴⁵ Another study concluded that older direct anticoagulant users with traumatic head injury following low-level falls did not have increased morbidity or mortality as compared with warfarin or nonanticoagulant users.⁴⁷ Several studies have suggested that following trauma, direct oral anticoagulation is associated with fewer major bleeding events as compared with warfarin^{40,48-50} and better outcomes,⁵¹ although others have suggested no difference between warfarin and direct oral anticoagulants.^{52,53} Many authors have concluded that while the benefits of anticoagulation most often outweigh the risks,⁵⁴ a case-by-case basis should be undertaken to properly balance all possible outcomes.^{41,42,55} The most recent ESC guidelines state that anticoagulation among patients with AF and a fall history should only be withheld from

patients with severe uncontrolled falls (eg, epilepsy or multisystem atrophy), or in situations in which compliance and adherence cannot be guaranteed.⁵⁶

Use of antihypertensive drugs Several studies have concluded that the chronic use of antihypertensives is not associated with an increased risk of falls,^{57,58} and 2 meta-analyses found that it did not increase the risk of falls or fall injuries.^{59,60} Data analysis from the REGARDS (Reasons for Geographic and Racial Difference in Stroke) study demonstrated that the number of antihypertensive medication classes used was not associated with an increased fall risk.⁶¹ Intensive treatment of blood pressure (with a systolic blood pressure target under 120 mm Hg) was associated with an increased risk of hypotension, but not falls.⁶² Some studies have found an association between antihypertensives and severe fall injuries (especially those with previous fall injuries),63 associations between loop diuretics and falls,^{58,64} and associations within the setting of first-time or acute use of antihypertensive agents.^{57,59,65,66} Even with careful administration and use of the lowest effective doses, hypotensive medications may precipitate a fall or syncope in the early stages of use.^{57,59,66} This stresses the importance of thorough communication between the clinician, pharmacist, and patient, ensuring that an appropriate dosage has been established and potential side effects have been explained.

Blood pressure and falls A study looking at fall rates among patients over the age of 70 years who had undergone 24-hour ambulatory blood pressure monitoring (ABPM) found that after 1 year, those who had fallen had a significantly lower 24-hour diastolic blood pressure as well as a higher 24-hour pulse pressure as compared with those who did not experience fall injuries.⁶⁷ The study was limited by the reasoning for referral to 24-hour ABPM, as the indications were generally unknown and may have included a suspicion of orthostatic hypotension. As low diastolic blood pressure is common among elderly patients with hypertension, strategies to potentially identify at-risk patients may be useful.

Heart failure A long-term prospective cohort study undertaken in patients aged 60 to 93 years concluded that symptomatic HF is a risk factor for falls, with an age- and sex-adjusted odds ratio of 1.88 (95% CI, 1.17–3.04).⁶⁸ The effects of HF are multifactorial and the increased risk may be attributed to the disease process itself, the cardio-vascular system's attempt to compensate, or even be secondary to treatment. Pinpointing the exact etiology of a fall in this group can be difficult, although some predispositions may be identified, such as dehydration or electrolyte imbalance.^{68,69} As patients in later stages of HF face disturbances across multiple organ systems, a balance between symptomatic relief and treatment

of the underlying issues must be reached. Among hospitalized patients with recent incidence of cardiovascular disease—including HF, myocardial infarction, and AF—the fall risk score was high in 22% of patients and was associated with an increased risk of death and 30-day readmission.¹²

In-hospital versus out-of-hospital falls Fall risk protocols, staff training, and continuous observation and monitoring of patients are often scrutinized in healthcare settings. The quantification of falls is sometimes used as a healthcare quality indicator, which has led to the development of fall prevention strategies in the clinical setting.⁷⁰ Although such strategies are used, falls continue to occur, and even patients assessed to be at lowest risk may still fall.⁷¹ One prospective study aiming to elucidate the epidemiology of in--hospital falls found an occurrence rate of 2.97 per 1000 patient-days in the cardiology ward. This rate was higher than for surgery (with 2.18 falls per 1000 patient-days) and orthopedics (0.8 per 1000 patient-days), but was lower than for neurology (6.12 per 1000 patient-days) and oncology (3.75 per 1000 patient-days).⁷² As suggested by the authors, it is possible that falls not resulting in injury may have been underreported. This may also occur in the setting of self-reporting at general wellness check-ups.⁷³ Decreased self-reporting may be associated with the stigma of attributing an injury to a fall, and addressing such issues could improve prevalence data and help to develop strategies to diminish mortality and morbidity and allow appropriate fall risk reduction measures to be initiated for a patient.⁷³

Falls that occur outside the healthcare setting may prove to be more challenging to explain, especially when a patient-reported history of a fall may be unreliable or even nonexistent. Without a credible history or even a witness, it may be difficult to determine factors increasing the risk of falling, which may lead to worse patient outcomes.⁷⁴ Patients who experienced a fall and are further admitted into hospitals after presentation have been quoted to have in-hospital mortality as high as 6% in those above the age of 75 years; in these patients, AF and myocardial infarction were among cardiovascular factors for independent predictors of short-term mortality.²

Burden on healthcare and patient quality of life Patients with a previous history of falls and/or increased fall risk may be affected at both physical and mental levels.⁷⁵ Although it is not specific to individuals with cardiovascular disease, both admitted and nonadmitted patients who experienced a fall have reported reduced quality-of-life scores up to even 9 months after the incident, and those who had been hospitalized following a fall had more frequently cited problems with mobility, selfcare, and performance of usual activities.⁷⁵ A prospective study of adults aged 60 to 93 years, of whom 42.5% had at least 1 comorbid condition, concluded that fallers scored significantly lower in health-related quality of life metrics and life satisfaction at baseline and after 6 years compared with nonfallers.⁷⁶ Even a single traumatic event may diminish the sustainability of independence in a patient, and a previous history of falls has also been implicated in associations of recurrent falls and subsequent hospitalizations.74,77 A new fall history in a patient suffering from a chronic disease, such as that of cardiovascular disease, can suggest disease progression into a state in which the balance between the pathologic process and cardiovascular compensation (even under pharmacotherapy) may begin to become disharmonious. One study quoted that more than half of hospitalized patients with a recent diagnosis of cardiovascular disease (including HF, myocardial infarction, and AF) was at moderate or high risk of falls, and a greater fall risk score was tied to a significant increase in the risk of readmissions as well as death.¹²

This leads to further implications in the necessary care for patients following falls; one such alternative is institutionalization. In a study of 1352 patients older than 65 years who were admitted because of ground-level falls, 12% died, 51% were discharged to a skilled nursing facility, 33% went home without assistance, 6% went home with assistance, and 5% were referred to inpatient rehabilitation care.⁷⁸ Of these patients, 44.6% were readmitted, and for patients discharged alive, the 1-year mortality rate was 24%; patients discharged to a skilled nursing facility had a 3-fold higher risk of 1-year mortality than those discharged home without assistance.⁷⁸

The effects do not remain exclusive to the patient; the burden on healthcare resources worldwide is immense. The financial impact of both fatal and nonfatal falls in the United States population aged 65 years and older was estimated to have reached almost 50 billion USD during 2015.⁷⁹ While it is extremely difficult to stratify the direct impact specific cardiovascular diseases may have on this quantification of falls, there is no doubt of the contribution, even in the form of associated risk factors.

Prevention strategies Many strategies are currently employed worldwide to diminish the risk of falling. The most basic within the healthcare settings involve the use of fall risk assessment screening, aiming to expose hidden or potentially modifiable factors, and patient education.^{80,81}

Cardiovascular condition–specific interventions In patients with identified risk factors, especially those pertaining to cardiovascular conditions, strategies undertaken are often specific to etiologies.⁸⁰ For example, one study proposed implantable loop recording to monitor the presence of arrhythmias in patients who had experienced subsequent unexplained falls. With this measure, at the following fall, 20% could be attributed to arrhythmia, additionally guiding further management of the patients.⁸² Patients in

whom symptomatic arrhythmia may be suspected, or those presenting with suspected syncope, may benefit from such diagnostic workup, which could lead to the introduction of prevention strategies, lowering fall risk.^{19,27,82,83} One such pillar of management, especially in the syncope setting related to sinus node dysfunction, can be the implantation of a permanent pacemaker.¹⁹ A study of patients with this condition showed a significant reduction in the number of falls following such an intervention.²³ Although the study did not establish direct causality due to the lack of randomization and a control group (attributed to patient circumstances and ethical reasons), pacemaker implantation was associated with a reduction in the incidence of falls in the 12 months following implantation as compared with the preceding 12 months.²³ Irrespectively, the most recent ESC guidelines recommend pacemaker therapy when intermittent sinus arrest or sinoatrial block is tied to electrocardiographic evidence during documented syncope.¹⁹ In patients with symptomatic carotid sinus hypersensitivity, pacemaker implantation was also used as an intervention to attempt to lower the possible risk of falls. The mean number of falls was considerably lower in patients who were paced versus those who were not, with a decrease even by over two-thirds.^{21,22} A Cochrane review found that pacing in cardioinhibitory carotid sinus hypersensitivity was associated with a reduction in the rate of falls, but not the risk of falling,⁸⁴ and pacing continues to be considered for symptomatic patients based on clinical practice.85

Within the realm of monitoring techniques, 24-hour ABPM has been suggested as a useful examination in detecting hypotensive episodes in patients at risk, especially in the elderly who have low diastolic blood pressure and increased pulse pressure.⁶⁷ Further confirmation of such parameters should point to the need to stabilize blood pressure in such at-risk patients. These patients (as well as those with confirmed orthostatic hypotension) should at the very least receive additional consideration when prescribing new medications, which may compound the effects of orthostatic hypotension, such as those that may decrease alertness.³¹

Medication review The use of a medication review as a tactic to diminish fall risk has been subject to controversy and conflicting opinions, and while this form of intervention has demonstrated some success in small-scale studies, other studies have not found the same benefits or cost-effectiveness.^{86,87} A study by van der Velde et al⁸⁶ concluded that the withdrawal of unnecessary fall risk–increasing drugs (FRIDs) was safe and effective, with an absolute risk reduction reaching even 19%. Risk reduction was especially prominent in the class of cardiovascular medications; however, the control group was composed of patients who were ineligible for FRID withdrawal. A more recent study using FRID withdrawal found

that compliance was difficult and did not affect the time to the first or second fall, or time to first fall-related general practitioner consultation.87 Subgroup analysis of cardiovascular FRIDs did find an increased time to the first general practitioner consultation and could be a continued direction of future research.⁸⁷ Identifying patients and their medications that can increase fall risk may be relatively clear-cut, but difficulty can come from the necessity to switch to other medications while maintaining the same clinical effect; communication between pharmacists and physicians may help to increase successful outcomes.^{87,88} This sentiment is particularly true among classes of cardiovascular drugs, where FRIDs are often not suitable for modification compared with other drug classes.⁸⁸ Few studies have shown a substantial and consistent reduction of risk following medication reviews, but this should not exclude their use: a reasonable balance must be undertaken to facilitate the appropriate treatment without an increased risk of falling.⁸⁹ The clinical benefits of medications (for example, treating a patient for significant hypertension) should not be compromised owing to the belief that such continued use may increase the risk of falling.^{57,61,62} On the other hand, some FRIDs taken concomitantly for other conditions may be modified in appropriate cases. Insomnia, for example, may be caused or exacerbated by HF. If this underlying cause is confirmed and treatment is optimized, the discontinuation of a FRID such as a benzodiazepine receptor agonist may be considered.⁹⁰ It is the clinician's duty, by consulting a pharmacist when needed, to ensure that each medication is adequately prescribed, establish reasonable dosages, and provide proper patient education on possible side effects.⁸⁹ It should be the intent of every physician to review the medications currently being taken by the patient before initiating new ones.

Exercise and fall risk There is also evidence pointing towards the use of exercise interventions to decrease fall risk.⁹¹ Apart from increasing muscle strength and balance, exercise may help patients to perform daily activities without falling or the fear of falling.⁹¹ One such potential intervention is the use of supervised tai-chi exercises,⁹¹ which may also help to improve hemodynamic parameters.⁹² Exercise protocols, including tai chi, may thus be considered a potential option for decreasing fall risk, especially when combined with other interventions.

Tailored prevention plans The hypothesized pinnacle of decreasing fall risk is to introduce an individualized plan tailored to the patient, ^{93,94} and several studies have attempted to compare the effectiveness of such strategies. One study recently undertaken in Malaysia showed no significant differences in the number of falls in patients who had their medications reviewed, had been educated on falls, and had undergone interventions as needed, compared with patients receiving just generalized health advice.⁹⁵ Possible cultural differences and family influences limited the study; a similar investigation was conducted in Italy, although it inquired about the use of continuous care while regularly providing educational input. The study demonstrated the effectiveness of a telerehabilitation program, including nursing and medical monitoring concerning falls number reduction, with relative risk dropping to 0.6 (95% CI, 0.44–0.83).⁹⁶ Another study showed that a tailored intervention program for fall reduction for community-dwelling patients was associated with an 11% reduction in fall risk at 1 year and a 33% lower incidence of claims for long-term care services compared with a control group.⁹⁷ In an inpatient setting, the formation of a fall reduction working group (using methods such as patient education and informing staff of patient fall risk using wristbands) was associated with a decrease of falls from 2.1% to 1.3% over 5 years.⁹⁸ A 2018 Cochrane review concluded that although multifactorial interventions may reduce the rate of falls, there may be little or no difference in other fall-related outcomes,⁷⁰ and a recent meta-analysis has called the use of multifactorial interventions to decrease falls into question; the study found insufficient evidence and calls for further research in such patients over the age of 60 years.99 Although none of the multifactorial prevention strategies were primed exclusively to cardiovascular disorders, implementation and future research among patients suffering from such conditions would surely be feasible, especially in patients suffering from multiple comorbidities.¹⁰⁰

Summary This review was limited by the number of studies directly assessing associations of cardio-vascular conditions and the risk of falling, as well as specific interventions towards such risk factors and their tie to the propensity of falling. More studies should continue to assess the outcomes of tailored intervention programs, which could be used among patients with specific subsets of cardiovascular conditions and comorbidities.

In cardiology alone, relatively firm associations of increased fall risk among conditions such as carotid sinus hypersensitivity, AF, and HF have been established. Further studies are needed to fully understand the multifactorial inputs towards fall risk, such as orthostatic hypotension and syncope, which may be attributed to cardiovascular ailments. As unexplained falls and falls related to syncope may be difficult to differentiate, the current guidelines encourage managing the initial workup for unexplained falls in the same way as unexplained syncope. Some potential risk factors for falls may be treated directly through therapeutic interventions; others require a step-by--step approach to reduce risk.

With current knowledge, a cardiologist should focus on clear-cut actions: assessing conditions that may be causing increased risk with specific interventions, medication review and tailoring, and furthering patient education and rehabilitation. The assessment of a patient's potential risk factors for falling, especially in the context of cardiovascular comorbidities, can help to lead to appropriate diagnostic workups and interventions to mitigate the risk of falling. As the cause of a fall may often be stratified into multiple contributing factors, reducing even one such risk factor or introducing an appropriate intervention may reduce the overall propensity for a patient to fall.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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REFERENCES

1 Falls. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/falls. Accessed May 8, 2020.

2 Siracuse JJ, Odell DD, Gondek SP, et al. Health care and socioeconomic impact of falls in the elderly. Am J Surg. 2012; 203: 335-338.

3 Sibley KM, Voth J, Munce SE, et al. Chronic disease and falls in community-dwelling Canadians over 65 years old: a population-based study exploring associations with number and pattern of chronic conditions. BMC Geriatr. 2014; 14: 1-11. C²

4 Sowada C, Sagan A, Kowalska-Bobko I, et al. Poland: health system review. Health Syst Transit. 2019; 21: 1-234.

5 Garin N, Koyanagi A, Chatterji S, et al. Global multimorbidity patterns: a cross-sectional, population-based, multi-country study. J Gerontol A Biol Sci Med Sci. 2016; 71: 205-214. ☑

6 Mossakowska M, Więcek A, Blędowski P, eds. Medical, psychological, sociological, and economic aspects of aging in Poland [in Polish]. International Institute of Molecular and Cell Biology in Warsaw. Poznań: Termedia; 2012.

7 Kłak A, Raciborski F, Targowski T, et al. A growing problem of falls in the aging population: a case study on Poland – 2015–2050 forecast. Eur Geriatr Med. 2017; 8: 105-110.

8 WH0. WH0 Global Report on Falls Prevention in Older Age. 2007. https://extranet.who.int/agefriendlyworld/wp-content/uploads/2014/06/ WHo-Global-report-on-falls-prevention-in-older-age.pdf. Accessed May 8, 2020.

9 Nations U. World population prospects 2019. https://population.un.org/ wpp/Publications/Files/WPP2019_Highlights.pdf. Accessed May 22, 2020.

10 Alboni P, Coppola P, Stucci N, et al. Differential diagnosis between 'unexplained' fall and syncopal fall: a difficult or impossible task. J Cardiovasc Med. 2015; 16: 82-89.

11 Drootin M. Summary of the updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. J Am Geriatr Soc. 2011; 59: 148-157.

12 Manemann SM, Chamberlain AM, Boyd CM, et al. Fall risk and outcomes among patients hospitalized with cardiovascular disease in the community. Circ Cardiovasc Qual Outcomes. 2018; 11: e004199. C

13 Jansen S, Bhangu J, de Rooij S, et al. The association of cardiovascular disorders and falls: a systematic review. J Am Med Dir Assoc. 2016; 17: 193-199.

14 Kwan E, Straus SE. Assessment and management of falls in older people. Can Med Assoc J. 2014; 186: E610-E621.

15 Ganz DA, Higashi T, Rubenstein LZ. Monitoring falls in cohort studies of community-dwelling older people: effect of the recall interval. J Am Geriatr Soc. 2005; 53: 2190-2194.

16 Alpert JS. Syncope in the elderly. Am J Med. 2019; 132: 1115-1116.

18 McCarthy F, Fan CW, Kearney PM, et al. What is the evidence for cardiovascular disorders as a risk factor for non-syncopal falls? Scope for future research. Eur Geriatr Med. 2010; 1: 244-251.

19 Brignole M, Moya A, De Lange FJ, et al. 2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J. 2018; 39: 1883-1948. ☑

20 Goyal P, Maurer MS. Syncope in older adults. J Geriatr Cardiol. 2016; 13: 380-386.

21 Kenny RAM, Richardson DA, Steen N, et al. Carotid sinus syndrome: a modifiable risk factor for nonaccidental falls in older adults (SAFE PACE). J Am Coll Cardiol. 2001; 38: 1491-1496.
^C
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22 Crilley JG, Herd B, Khurana CS, et al. Permanent cardiac pacing in elderly patients with recurrent falls, dizziness and syncope, and a hypersensitive cardioinhibitory reflex. Postgrad Med J. 1997; 73: 415-418. C²

23 Brenner R, Ammann P, Yoon S II, et al. Reduction of falls and fractures after permanent pacemaker implantation in elderly patients with sinus node dysfunction. Europace. 2017; 19: 1220-1226.

24 Chen BW, Wang ZG, Lv NQ, et al. The role of cardiac pacing in carotid sinus syndrome: a meta-analysis. Clin Auton Res. 2014; 24: 127-134.

25 Rivasi G, Solari D, Rafanelli M, et al. Incidence and predictors of syncope recurrence after cardiac pacing in patients with carotid sinus syndrome. Int J Cardiol. 2018; 266: 119-123.

C

26 Bădilă E, Negrea C, Rîpă A, et al. The etiology of syncope in an emergency hospital. Rom J Intern Med. 2016; 54: 173-178.

27 Anpalahan M. Neurally mediated syncope and unexplained or nonaccidental falls in the elderly. Intern Med J. 2006; 36: 202-207.

28 Kenny RA, McNicholas T. The management of vasovagal syncope. QJM. 2016; 109: 767-773. 🖸

29 Mol A, Bui Hoang PTS, Sharmin S, et al. Orthostatic hypotension and falls in older adults: a systematic review and meta-analysis. J Am Med Dir Assoc. 2019; 20: 589-597.e5.

30 Lipsitz LA. Orthostatic hypotension and falls. J Am Geriatr Soc. 2017; 65: 470-471.

31 Juraschek SP, Daya N, Appel LJ, et al. Orthostatic hypotension in middle-age and risk of falls. Am J Hypertens. 2017; 30: 188-195.

32 Finucane C, O'Connell MDL, Donoghue O, et al. Impaired orthostatic blood pressure recovery is associated with unexplained and injurious falls. J Am Geriatr Soc. 2017; 65: 474-482.

33 Wu JS, Yang YC, Lu FH, et al. Population-based study on the prevalence and correlates of orthostatic hypotension/hypertension and orthostatic dizziness. Hypertens Res. 2008; 31: 897-904.

34 van der Velde N, Stricker BHC, Roelandt JRTC, et al. Can echocardiographic findings predict falls in older persons? PLoS One. 2007; 2: e654.

35 Sanders NA, Ganguly JA, Jetter TL, et al. Atrial fibrillation: an independent risk factor for nonaccidental falls in older patients. Pacing Clin Electrophysiol. 2012; 35: 973-979.

36 Malik V, Gallagher C, Linz D, et al. Atrial fibrillation is associated with syncope and falls in older adults. Mayo Clin Proc. 2020; 95: 676-687. ☑

37 Jansen S, Frewen J, Finucane C, et al. AF is associated with selfreported syncope and falls in a general population cohort. Age Ageing. 2015; 44: 598-603.

38 Dalgaard F, Pallisgaard JL, Numé AK, et al. Rate or rhythm control in older atrial fibrillation patients: risk of fall-related injuries and syncope. J Am Geriatr Soc. 2019; 67: 2023-2030.

39 Banerjee A, Clementy N, Haguenoer K, et al. Prior history of falls and risk of outcomes in atrial fibrillation: the Loire valley atrial fibrillation project. Am J Med. 2014; 127: 972-978. ☑

40 Rao MP, Vinereanu D, Wojdyla DM, et al. Clinical outcomes and history of fall in patients with atrial fibrillation treated with oral anticoagulation: insights from the ARISTOTLE trial. Am J Med. 2018; 131: 269-275.e2. ∠

41 Brook R, Aswapanyawongse O, Tacey M, et al. Real-world direct oral anticoagulant experience in atrial fibrillation: falls risk and low dose anticoagulation are predictive of both bleeding and stroke risk. Intern Med J. 2020; 50: 1359-1366. C⁴

42 Büchele G, Rapp K, Bauer JM, et al. Risk of traumatic intracranial haemorrhage is increased in older people exposed to oral anticoagulation with phenprocoumon. Aging Clin Exp Res. 2020; 32: 441-447. ☑

43 Khurshid S, Weng LC, Hulme OL, et al. Factors associated with anticoagulation delay following new-onset atrial fibrillation. Am J Cardiol. 2017; 120: 1316-1321.

44 Donzé J, Clair C, Hug B, et al. Risk of falls and major bleeds in patients on oral anticoagulation therapy. Am J Med. 2012; 125: 773-778.

45 Chiu AS, Jean RA, Fleming M, et al. Recurrent falls among elderly patients and the impact of anticoagulation therapy. World J Surg. 2018; 42: 3932-3938. ☑

47 Batey M, Hecht J, Callahan C, et al. Direct oral anticoagulants do not worsen traumatic brain injury after low-level falls in the elderly. Surgery. 2018: 164: 814-819. 48 Miao B, Alberts MJ, Bunz TJ, et al. Safety and effectiveness of oral factor Xa inhibitors versus warfarin in nonvalvular atrial fibrillation patients at high-risk for falls. J Thromb Thrombolysis. 2019; 48: 366-372. C^{*}

49 Chopard R, Piazza G, Hurwitz S, et al. Fatal warfarin-associated intracranial hemorrhage in atrial fibrillation inpatients. J Thromb Thrombolysis. 2019; 47: 331-335. ☑

50 Feeney JM, Santone E, Difiori M, et al. Compared to warfarin, direct oral anticoagulants are associated with lower mortality in patients with blunt traumatic intracranial hemorrhage: a TQIP study. J Trauma Acute Care Surg. 2016; 81: 843-848.

51 Shin SS, Marsh EB, Ali H, et al. Comparison of traumatic intracranial hemorrhage expansion and outcomes among patients on direct oral anticoagulants versus vitamin K antagonists. Neurocrit Care. 2020; 32: 407-418.

52 Martinez BK, Sood NA, Bunz TJ, et al. Effectiveness and safety of apixaban, dabigatran, and rivaroxaban versus warfarin in frail patients with nonvalvular atrial fibrillation. J Am Heart Assoc. 2018; 7: 1-11.

53 Pozzessere A, Grotts J, Kaminski S. Dabigatran use does not increase intracranial hemorrhage in traumatic geriatric falls when compared with warfarin. Am Surg. 2015; 81: 1039-1042.

54 Hilkens NA, Algra A, Greving JP. Predicting major bleeding in ischemic stroke patients with atrial fibrillation. Stroke. 2017; 48: 3142-3144.

55 Hagerty T, Rich MW. Fall risk and anticoagulation for atrial fibrillation in the elderly: a delicate balance. Cleve Clin J Med. 2017; 84: 35-40. ♂

56 Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016; 37: 2893-2962. C^{*}

57 Lipsitz LA, Habtemariam D, Gagnon M, et al. Reexamining the effect of antihypertensive medications on falls in old age. Hypertension. 2015; 66: 183-189. ☑

58 Marcum ZA, Perera S, Newman AB, et al. Antihypertensive use and recurrent falls in community-dwelling older adults: findings from the health ABC study. J Gerontol A Biol Sci Med Sci. 2015; 70: 1562-1568.

59 Kahlaee HR, Latt MD, Schneider CR. Association between chronic or acute use of antihypertensive class of medications and falls in older adults. A Systematic review and meta-analysis. Am J Hypertens. 2018; 31: 467-479. ℃

60 Zang G. Antihypertensive drugs and the risk of fall injuries: a systematic review and meta-analysis. J Int Med Res. 2013; 41: 1408-1417. ♂

61 Bromfield SG, Ngameni C, Colantonio LD, et al. Blood pressure, antihypertensive polypharmacy, frailty, and risk for serious fall injuries among older treated adults with hypertension. Hypertension. 2017; 70: 259-266.

62 Sink KM, Evans GW, Shorr RI, et al. Syncope, hypotension, and falls in the treatment of hypertension: results from the randomized clinical systolic blood pressure intervention trial. J Am Geriatr Soc. 2018; 66: 679-686.

63 Tinetti ME, Han L, Lee DSH, et al. Antihypertensive medications and serious fall injuries in a nationally representative sample of older adults. JAMA Intern Med. 2014: 174: 588-595. C

64 de Vries M, Seppala LJ, Daams JG, et al. Fall-risk-increasing drugs: a systematic review and meta-analysis: I. cardiovascular drugs. J Am Med Dir Assoc. 2018; 19: 371.e1-371.e9.

65 Butt DA, Mamdani M, Austin PC, et al. The risk of falls on initiation of antihypertensive drugs in the elderly. Osteoporos Int. 2013; 24: 2649-2657. ☑

66 Musich S, Wang SS, Ruiz J, et al. Falls-related drug use and risk of falls among older adults: a study in a US medicare population. Drugs Aging. 2017; 34: 555-565. C⁴

67 Jonas M, Kazarski R, Chernin G. Ambulatory blood-pressure monitoring. antihypertensive therapy and the risk of fall injuries in elderly hypertensive patients. J Geriatr Cardiol. 2018; 15: 284-289.

68 Stenhagen M, Nordell E, Elmståhl S. Falls in elderly people: a multifactorial analysis of risk markers using data from the Swedish general population study 'Good Ageing in Skåne'. Aging Clin Exp Res. 2013; 25: 59-67. ♂

69 Michalik C, Matusik P, Nowak J, et al. Heart failure, comorbidities, and polypharmacy among elderly nursing home residents. Pol Arch Med Wewn. 2013; 123: 170-175. ♂

70 Hopewell S, Adedire O, Copsey BJ, et al. Multifactorial and multiple component interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev. 2018; 7: CD012221.

71 Kobayashi K, Imagama S, Ando K, et al. Analysis of falls that caused serious events in hospitalized patients. Geriatr Gerontol Int. 2017; 17: 2403-2406.

72 Hitcho EB, Krauss MJ, Birge S, et al. Characteristics and circumstances of falls in a hospital setting: a prospective analysis. J Gen Intern Med. 2004; 19: 732-739.

73 Hoffman GJ, Ha J, Alexander NB, et al. Underreporting of fall injuries of older adults: implications for wellness visit fall risk screening. J Am Geriatr Soc. 2018; 66: 1195-1200. ☑

74 Matusik P, Tomaszewski K, Chmielowska K, et al. Severe frailty and cognitive impairment are related to higher mortality in 12-month follow-up of nursing home residents. Arch Gerontol Geriatr. 2012; 55: 22-24.

75 Hartholt KA, Van Beeck EF, Polinder S, et al. Societal consequences of falls in the older population: injuries, healthcare costs, and long-term reduced quality of life. J Trauma. 2011; 71: 748-753.

76 Stenhagen M, Ekström H, Nordell E, et al. Accidental falls, healthrelated quality of life and life satisfaction: a prospective study of the general elderly population. Arch Gerontol Geriatr. 2014; 58: 95-100. ♂

77 Sri-on J, Tirrell GP, Bean JF, et al. Revisit, subsequent hospitalization, recurrent fall, and death within 6 months after a fall among elderly emergency department patients. Ann Emerg Med. 2017; 70: 516-521.e2.

78 Ayoung-Chee P, McIntyre L, Ebel BE, et al. Long-term outcomes of ground-level falls in the elderly. J Trauma Acute Care Surg. 2014; 76: 498-503.

79 Florence CS, Bergen G, Atherly A, et al. Medical costs of fatal and nonfatal falls in older adults. J Am Geriatr Soc. 2018; 66: 693-698.

80 Perell KL, Manzano MLP, Weaver R, et al. Outcomes of a consult fall prevention screening clinic. Am J Phys Med Rehabil. 2006; 85: 882-888. ☑

81 Cimilli Ozturk T, Ak R, Unal Akoglu E, et al. Factors associated with multiple falls among elderly patients admitted to emergency department. Int J Gerontol. 2017; 11: 85-89. ☑

82 Bhangu J, McMahon CG, Hall P, et al. Long-term cardiac monitoring in older adults with unexplained falls and syncope. Heart. 2016; 102: 681-686.

83 De Ruiter SC, Wold JFH, Germans T, et al. Multiple causes of syncope in the elderly: diagnostic outcomes of a Dutch multidisciplinary syncope pathway. Europace. 2018; 20: 867-872. ♂

84 Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev. 2012; CD007146.
☐

85 Parry SW, Matthews IG. Update on the role of pacemaker therapy in vasovagal syncope and carotid sinus syndrome. Prog Cardiovasc Dis. 2013; 55: 434-442.

86 van der Velde N, Stricker BHC, Pols HAP, et al. Risk of falls after withdrawal of fall-risk-increasing drugs: a prospective cohort study. Br J Clin Pharmacol. 2007; 63: 232-237.

87 Boyé NDA, van der Velde N, de Vries OJ, et al. Effectiveness of medication withdrawal in older fallers: results from the improving medication prescribing to reduce risk of falls (IMPROveFALL) trial. Age Ageing. 2017; 46: 142-146. C²

88 Browne C, Kingston C, Keane C. Falls prevention focused medication review by a pharmacist in an acute hospital: implications for future practice. Int J Clin Pharm. 2014; 36: 969-975.

89 Marvin V, Ward E, Poots AJ, et al. Deprescribing medicines in the acute setting to reduce the risk of falls. Eur J Hosp Pharm. 2017; 24: 10-15.

90 Lee JY, Farrell B, Holbrook AM. Deprescribing benzodiazepine receptor agonists taken for insomnia: a review and key messages from practice guidelines. Pol Arch Intern Med. 2019; 129: 43-49. Z^{*}

91 Sherrington C, Fairhall NJ, Wallbank GK, et al. Exercise for preventing falls in older people living in the community. Cochrane Database Syst Rev. 2019; CD012424.

92 Sam-Kit Tin T, Daniel Weng CH, dos Santos Vigário P, et al. Effects of a short-term cardio tai chi program on cardiorespiratory fitness and hemodynamic parameters in sedentary adults: a pilot study. JAMS J Acupunct Meridian Stud. 2020; 13: 12-18. ☑

93 Barker A, Cameron P, Flicker L, et al. Evaluation of RESPOND, a patient--centred program to prevent falls in older people presenting to the emergency department with a fall: a randomised controlled trial. PLoS Med. 2019; 16: 1-18.

94 Khow KSF, Visvanathan R. Falls in the aging population. Clin Geriatr Med. 2017; 33: 357-368. ☑

95 Tan PJ, Khoo EM, Chinna K, et al. Individually-tailored multifactorial intervention to reduce falls in the Malaysian Falls Assessment and Intervention Trial (MyFAIT): a randomized controlled trial. PLoS One. 2018; 13: 1-16. C⁴

96 Bernocchi P, Giordano A, Pintavalle G, et al. Feasibility and clinical efficacy of a multidisciplinary home-telehealth program to prevent falls in older adults: a randomized controlled trial. J Am Med Dir Assoc. 2019; 20: 340-346.

97 Cohen MA, Miller J, Shi X, et al. Prevention program lowered the risk of falls and decreased claims for long-term services among elder participants. Health Aff. 2015; 34: 971-977. ♂

98 Kobayashi K, Ando K, Inagaki Y, et al. Measures and effects on prevention of fall: the role of a fall working group at a university hospital. Nagoya J Med Sci. 2017; 79: 497-504.

99 Morello RT, Soh SE, Behm K, et al. Multifactorial falls prevention programmes for older adults presenting to the emergency department with a fall: systematic review and meta-analysis. Inj Prev. 2019; 25: 557-564. ☑

100 Luiting S, Jansen S, Seppälä LJ, et al. Effectiveness of cardiovascular evaluations and interventions on fall risk: a scoping review. J Nutr Heal Aging. 2019; 23: 330-337. ^[2]