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ORIGINAL PAPER

The Syncope-Falls Index: a tool for predicting risk of syncope and complex falls in the older adult based on cumulative health deficits

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Summary

Background: Syncope is aetiologically diverse and associated with adverse outcomes; in older people, there is clinical overlap with complex falls presentations (i.e. recurrent, unexplained and/or injurious).
Aim: To formulate an index to predict future risk of syncope and falls in the Irish longitudinal study on ageing (TILDA).
Design/Methods: Using the frailty index methodology, we selected, from TILDA Wave 1 (2010), 40 deficits that might increase risk of syncope and falls. This syncope-falls index (SYFI) was applied to TILDA Wave 1 participants aged 65 and over, who were divided into three risk groups (low, intermediate and high) based on SYFI tertiles. Multivariate logistic regression models were used to investigate, controlling for age and sex, how SYFI groups predicted incident syncope, complex falls and simple falls occurring up to Wave 4 of the study (2016).
Results: At Wave 1, there were 3499 participants (mean age 73, 53% women). By Wave 4, of the remaining 2907 participants, 185 (6.4%) had reported new syncope, 1077 (37.0%) complex falls and 218 (7.5%) simple falls. The risk of both syncope and complex falls increased along the SYFI groups (high risk group: odds ratio 1.88 [1.26–2.80], $P = 0.002$ for syncope; 2.22 [1.82–2.72], $P < 0.001$ for complex falls). No significant relationship was identified between SYFI and simple falls.
Conclusion: The 6-year incidences of falls and syncope were high in this cohort. SYFI could help identify older adults at risk of syncope and complex falls, and thus facilitate early referral to specialist clinics to improve outcomes.

Introduction

Syncope refers to a transient loss of consciousness due to transient global cerebral hypoperfusion characterized by rapid onset, short duration and spontaneous complete recovery.[1] In younger cohorts, reflex vasovagal syncope is the most common form and does not reflect underlying pathology across physiological systems. However, in older adults, the aetiology of syncope can be more complex,[2] with multiple causes frequently identified for syncope in one individual.[3,4] In older people, the proportions of cardiac and orthostatic syncope are higher, and these types have a multiplicity of associated risk factors including pathologies across many different organ systems.[1] Multicause syncope is associated with poorer outcomes, with 77% vs.

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89% survival at 4 years in those with 2 or more causes identified for their syncope.[4] Additionally, syncope and falls have been linked to geriatric syndromes such as cognitive impairment, polypharmacy and frailty.[3,5,6] Given that frailty is defined as dysregulation in multiple physiological systems with increased risk of decompensation in the face of stressors,[7] the associations between frailty and syncope and frailty and falls, are biologically plausible in older adults.

In older people, there is a recognized clinical overlap between syncope and complex falls presentations (i.e. recurrent, unexplained and/or injurious).[3] The possible syncopal origin of complex falls in older people remains under appreciated in non-specialist settings. Alongside increased mortality, syncope and complex falls in the older adult can lead to premature disability, as well as reductions in confidence, functionality and quality of life and increased risk of institutionalization.[8–10] Early detection and specialist intervention in those at risk of syncope and complex falls has been shown to effectively reduce adverse outcomes.[11,12] Hence, it is important to bring this to the attention of non-specialist clinicians by offering simple tools that may help identify such patients.

In 2001, Mitnitski *et al.* formulated a Frailty Index (FI) methodology by which the cumulative burden of health deficits acts as a surrogate measure of frailty.[13] A FI can be constructed on any suitable health database provided that some requirements are met.[14] Most FIs have concentrated on the prediction of mortality[15] but it is possible to consider more specific health outcomes when selecting deficits for an FI.[16] Building on the clinical utility of FIs in predicting outcomes in the older population, we formulated an FI designed specifically to predict risk of syncope and falls and assess its predictive value on a population-based cohort.

Materials and methods

Sample

The study utilized four waves of data from The Irish Longitudinal Study on Ageing (TILDA).[17–20] Authors accessed TILDA data via the Irish Social Science Data Archive (ISSDA)—www.ucd.ie/issda from July 2020 to December 2020. Full details of the recruitment and data collection process have previously been published.[21,22]

The first wave of data (Wave 1) was collected between October 2009 and February 2011 and included participants aged 50 or more, and some younger spouses of the latter. Subsequent data were collected ∼2-yearly and Wave 4 took place between January 2016 and December 2016. There was ∼6–10% reduction in sample size between waves due to attrition, with death of participants between waves contributing another 2–3% reduction. For the purpose of our analyses, we included only those who were aged 65 or older at time of first interview.

Measures

Outcomes

Syncope—participants were asked in each wave if they had a faint or blackout in the past 12 months (yes/no). A case of syncope was defined as having answered yes to this question at least once at Wave 2, 3 or 4.

Falls—participants were asked in each wave if they had experienced a fall in the past 12 months (yes/no). A case of fall was defined as having answered yes to this question at least once at Wave 2, 3 or 4. Participants were asked the following questions to further characterize their falls:

i. How many times had they fallen in the past 12 months? A *recurrent fall* was defined as any case with 2 or more falls in a 12-month period.
ii. Were any of these falls non-accidental, i.e. with no apparent or obvious reason? An *unexplained fall* was defined as any case who answered yes to this question.
iii. Were they injured seriously enough to require medical treatment? An *injurious fall* was defined as any case who answered yes to this question.

Based on the above responses, cases of fall were subdivided into *simple* and *complex*:

- *Simple falls*—defined as any case of fall that was not also documented as *recurrent*, *unexplained* and/or *injurious*.
- *Complex falls*—defined as any case of fall that was also documented to be *recurrent*, *unexplained* and/or *injurious*.

Each variable (syncope, simple fall and complex fall) was coded 1 if the case criteria were met, and 0 if they were not, producing a dichotomous variable for analysis.

Predictor variables

Syncope-Falls Index (SYFI). As per standard procedure (14), a FI can be constructed on any suitable database by considering a minimum of 30 deficits that need to satisfy the following criteria: (i) be associated with health status, and not simply attributes; (ii) cover a range of systems; (iii) not saturate too early and (iv) their prevalence must increase with age (excluding survivor effects). For SYFI, 40 deficits were identified a priori from the Wave 1 TILDA ISSDA database as potentially increasing the risk of syncope and falls (Table 1). Of the 40 SYFI items, 38 were collected via self-administered questionnaire; and handgrip strength and Mini Mental State Examination were collected by a trained interviewer.

As regards the grip strength measure in SYFI, cases were considered to have the deficit where grip strength was found to be in the range of the frailty phenotype[23] (see Table 1 for details). As regards medications, the list of anticholinergics, benzodiazepines and Z-drugs characterized in TILDA has been described elsewhere.[24] For the cognitive deficit, we selected an MMSE score of <24 points.[25]

Each deficit was coded 1 if it was present or 0 if it was not. In each case, the number of deficits recorded as present was divided by the total number of deficits considered (i.e. 40) to produce the SYFI. The continuous score was then divided into tertiles to define SYFI risk groups: low risk (first tertile), intermediate risk (second tertile) and high risk (third tertile). In addition, we operationalized the binary frailty cut-off recommended by Dent *et al.* (SYFY > 0.25).[26]

Age and sex

The age and sex of each participant were recorded at Wave 1. Age and sex have known influences on syncope.[2,27] The association between chronological age and the FI is typically small because the FI captures variation in health status within individuals of the same age.[28] Studies have shown that women consistently have higher frailty scores than men but lower overall mortality. Thus, we corrected for these demographics in our analysis.

Table 1. SYFI deficits and their definitions

	Deficit	Measure
1.	Polypharmacy	Taking five or more regular medications (excluding supplements)
2.	Anti-hypertensive treatment	Taking one or more anti-hypertensive medications
3.	Anti-cholinergic use	Taking one or more anti-cholinergic medications regularly (see Materials and Methods Section for details)
4.	Benzodiazepine use	Taking one or more benzodiazepines regularly (see Materials and Methods Section for details)
5.	Z-drug use	Taking one or more Z-drugs regularly (see Materials and Methods Section for details)
6.	Anti-depressant use	Taking one or more antidepressants regularly
7.	Weight loss	Self-reported weight loss of more than 4.5 kg or 10 lb in the past 12 months
8.	Poor eyesight	Self-rated eyesight as poor (with or without corrective lenses)
9.	Poor hearing	Self-rated hearing as poor (with or without a hearing aid)
10.	Poor smell	Self-rated sense of smell as poor
11.	Poor hearing	Self-rated sense of taste as poor
12.	Reduced grip strength	Two measures of handgrip strength were taken using a hydraulic hand dynamometer (Baseline, Fabrication Enterprises, Inc. White Plains, NY) from the dominant hand and the mean of these readings was calculated. Cut-offs: *Men:* 20.5 kg—body mass index (BMI) $<$ 24; 21.5 kg—BMI 24–26; 23 kg—BMI $>$26; *Women:* 11.5 kg—BMI $<$ 23; 13 kg—BMI $>$ 23
13.	Hypertension	Told by a doctor they had 'high blood pressure or hypertension'
14.	Angina	Told by a doctor they had 'angina'
15.	Myocardial infarction (MI)	Told by a doctor they had 'a heart attack (including MI)'
16.	Congestive cardiac failure	Told by a doctor they had 'congestive heart failure'
17.	Heart murmur	Told by a doctor they had 'a heart murmur'
18.	Arrhythmia	Told by a doctor they had an abnormal heart rhythm
19.	Stroke	Told by a doctor they had 'a stroke'
20.	Transient ischaemic attack (TIA)	Told by a doctor they had 'a mini-stroke or a TIA'
21.	Diabetes mellitus	Told by a doctor they had 'diabetes'
22.	Diabetic ulcers	Told by a doctor they had 'leg ulcers'
23.	Proteinuria	Told by a doctor they had 'protein in the urine'
24.	Peripheral neuropathy	Told by a doctor they had a 'lack of feeling or tingling pain in the legs and feet due to nerve damage'
25.	Diabetic retinopathy	Told by a doctor that they had 'damage to the back of the eye' related to diabetes
26.	Diabetic nephropathy	Told by a doctor they had 'damage to the kidneys' related to diabetes
27.	Chronic obstructive airway disease	Told by a doctor that they had 'chronic lung disease such as chronic bronchitis or emphysema'
28.	Asthma	Told by a doctor that they had 'asthma'
29.	Arthritis	Told by a doctor that they had 'arthritis (including osteoarthritis)
30.	Osteoporosis	Told by a doctor that they had 'osteoporosis or sometimes called thin or brittle bones'
31.	Malignancy	Told by a doctor that they had 'cancer or a malignant tumour (including leukaemia or lymphoma)'
32.	Mental health disorder	Told by a doctor that they had 'any emotional, nervous or psychiatric problem, such as depression or anxiety'
33.	Alcohol or substance abuse	Told by a doctor that they had 'alcohol or substance abuse'
34.	Gastric ulcers	Told by a doctor that they had 'stomach ulcers'
35.	Varicose ulcers	Told by a doctor that they had 'varicose ulcers or an ulcer due to varicose veins'
36.	Liver cirrhosis	Told by a doctor that they had 'cirrhosis or serious liver damage'
37.	Cognitive impairment	Score $<$24/30 in the Mini-Mental State Examination (MMSE) test
38.	Urinary incontinence	Self-reported 'loss of urine beyond their control' in past 12 months
39.	Unsteadiness on standing	Self-reported feeling unsteady on standing
40.	Unsteadiness on getting up from a chair	Self-reported feeling unsteady on getting up from a chair

Analysis

All statistical analyses were carried out with IBM SPSS Statistics version 25 (IBM Corp.: Armonk, NY). Descriptives were given as mean with standard deviation (SD), median with interquartile range (IQR) or proportion (%). The association between SYFI and age was measured with the two-sided Spearman's correlation coefficient (r_s). Associations between continuous and dichotomous variables were reported with the two-sided independent-samples Mann–Whitney U Test, and associations between dichotomous variables with the Chi-square test.

To investigate the ability of SYFI to predict risk of future *syncope*, *complex falls* and *simple falls* after adjusting for age and sex, binary logistic regression was performed on each of the dependent variables. For regression analysis purposes, SYFI was entered as an ordinal predictor where Group 1 acted as control for calculation of the odds ratios (OR) of Group 2 and Group 3.

Confidence intervals (CI) of 95% for ORs were calculated. The level of significance was set at $P < 0.05$.

In the main analysis, participants for whom the SYFI was calculated at wave 1 but did not have outcomes measured in subsequent waves were omitted from analysis. A sensitivity analysis was performed by re-running the logistic regression models after performing multiple imputation of missing outcome data.

Results

Of 8504 Wave 1 participants, 3499 were aged 65 or more years. Among the latter, the mean (SD) age was 72.6 (5.2) years, 52.5% were women and all had SYFI information. In $N = 3499$, the r_s between age and SYFI was 0.214 ($P < 0.001$). Figure 1 shows the typical gamma distribution of SYFI across Wave 1 participants ($N = 3499$). At baseline, SYFI tertiles were: Group 1 or low-risk (SYFI < 0.05), Group 2 or intermediate-risk (SYFI 0.05–0.13) and Group 3 or high-risk (SYFI > 0.13). 126 (3.6%) Wave 1 participants had an SYFI of more than 0.25.

By Wave 4, 592 participants (16.9% of Wave 1 sample), did not have information on outcomes. Table 2 shows a comparison of Wave 1 characteristics between participants with and without data for outcomes at Wave 4. The median age of participants without Wave 4 outcomes was three years older, but there were no significant differences in sex or median SYFI.

Of the 2907 with outcome data, 185 (6.4%) reported new syncope, 1077 (37.0%) complex falls and 218 (7.5%) simple falls. By frailty status (SYFI > 0.25), 9.2% ($N = 9$) of the frail vs. 6.3% ($N = 176$) of the non-frail had new syncope (Chi-squared test; $P = 0.245$); the proportions for complex falls were 62.2% ($N = 61$) and 36.2% ($N = 1016$) ($P < 0.001$) and for simple falls, 6.1% ($N = 6$) and 7.5% ($N = 212$) ($P = 0.599$), respectively.

The results of the multivariate binary logistic regression models (Table 3) showed that baseline SYFI had a statistically significant independent association with events of syncope and complex falls between Wave 1 and Wave 4, with incremental effects by tertiles. In contrast, SYFI did not show any statistically significant association with future simple falls. Age and sex were not shown to be significant predictors of simple falls or syncope. A small-magnitude association was observed with age and complex falls. Female sex appeared to be a significant independent predictor of complex falls (Table 3).

Appendix Table A1 shows a sensitivity analysis of the regression models utilizing SYFI dichotomized as per frailty cut-off (> 0.25). Results showed that SYFI > 0.25 was an independent predictor of complex falls, but the syncope prediction lost significance. Appendix Table A2 shows another sensitivity analysis with imputation of missing data. Using age as a predictor for the imputation, we imputed values of missing outcomes data by using the SPSS automatic multiple imputation procedure. Results were unchanged compared to the main analysis.

Discussion

Using data from a large, community-based, nationwide study, we were able to compile an index (SYFI) that predicts, independently of age and sex, risk of future syncope and complex falls in community-dwelling older adults.

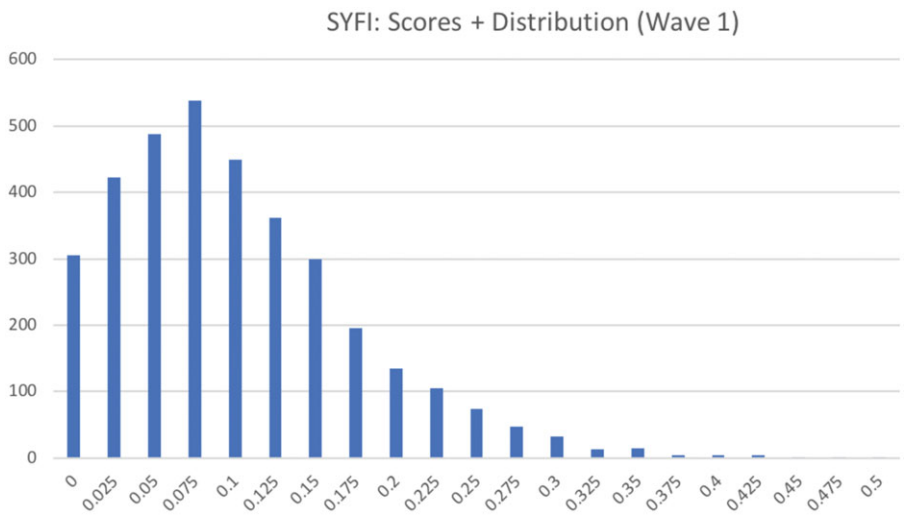

Figure 1. Distribution of SYFI across Wave 1 participants ($N = 3499$).

Table 2. Comparison of Wave 1 characteristics between participants with ($N = 2907$) and without ($N = 592$) data for outcomes at Wave 4

	Outcome data available ($N = 2907$)	Outcome data missing ($N = 592$)	*P*-value
Median age, years (IQR)	72 (9)	75 (10)	<0.001[a]
Female sex (%)	52.6	50.0	0.870[b]
Mean SYFI (SD)	0.08 (0.10)	0.10 (0.10)	0.440[a]

IQR, interquartile range.

[a]Independent-samples Mann–Whitney *U* test.

[b]Chi-square test.

Table 3. Baseline SYFI groups (tertiles) as predictor of outcomes: results of the binary logistic regression models controlling for age and sex

Predictor	OR [95% CI]	*P*-value
Future syncope		
SYFI Group 1	*Control*	*Control*
SYFI Group 2	1.51 [1.03–2.21]	0.034
SYFI Group 3	1.88 [1.26–2.80]	0.002
Age	1.02 [0.99–1.05]	0.218
Female sex	1.06 [0.78–1.43]	0.724
Future complex fall		
SYFI Group 1	*Control*	*Control*
SYFI Group 2	1.34 [1.12–1.61]	0.002
SYFI Group 3	2.22 [1.82–2.72]	<0.001
Age	1.01 [1.00–1.03]	0.033
Female sex	1.51 [1.29–1.76]	<0.001
Future simple fall		
SYFI Group 1	*Control*	*Control*
SYFI Group 2	1.09 [0.79–1.51]	0.596
SYFI Group 3	0.96 [0.66–1.39]	0.831
Age	1.00 [0.97–1.03]	0.961
Female sex	1.14 [0.86–1.50]	0.370

Syncope in older people is known to be complex and multifactorial. Advancing age, polypharmacy and multiple comorbidities are associated with physiological impairments in cardiovascular autoregulatory mechanisms, cerebral blood flow and neurohumoral stability.[29,30] Frailty, cognitive decline and reductions in functional status associated with ageing also contribute to the risk of syncope.[3] SYFI was designed to reflect this complex interplay between contributing factors, made up of a heterogenous group of 40 potential deficits that allows calculation of cumulative risk.

One of the clinical challenges in addressing syncope and complex falls is the underreporting and mislabelling of syncopal events. Atypical syncope presentations are common in older adults, the most prevalent being unexplained falls.[12,31] We found that the risk of complex falls similarly rose for patients as they moved up SYFI risk groups. This suggests, as often clinically suspected, that complex falls in older people may have an underlying syncopal aetiology.[32] Female sex was in significant association with complex falls and this is also in keeping with known sex differences in syncope and falls epidemiology.[27]

Contrastingly, we found that SYFI was not predictive of future simple falls. The overlap in cardiovascular risk factors for both syncope and non-accidental falls has previously been described in this cohort.[32] In clinical practice, verifying whether non-accidental falls in older people have underlying syncopal aetiology has remained a challenge.[12,33] General consensus supports the treatment of unwitnessed or unexplained falls as possible syncope[1,5] but this is still underappreciated in non-specialist settings. Significant overlap in risk profiles was identified in our study which further supports the mandate that unexplained, recurrent and/or injurious falls in older people be considered as potential syncope. Therefore, in patients with a high SYFI risk, it would be prudent to refer falls presentations for further investigation. This could be particularly helpful in busy Emergency Departments or primary care settings, where access to currently validated investigations for syncope, such as tilt-table testing, is limited.

One of the advantages of the SYFI is that, although it incorporates a wide range of deficits, the vast majority were measured using a self-administered questionnaire, which could easily be recreated in a clinical setting. In addition, the SYFI only requires the measurement of grip strength (handheld dynamometer), BMI (weight and height) and administration of the MMSE. This lends itself to implementation as a risk assessment tool in non-specialist clinical settings. Early detection and intervention for those at risk of syncope or complex falls, e.g. referral to a syncope unit, comprehensive geriatric assessment and/or cardiac monitoring devices, have been associated with favourable outcomes.[3,11,34] The SYFI could hence be used to identify those who might benefit from these interventions.

A limitation of the SYFI is its strong reliance on self-report. However, self-reported FIs have been validated elsewhere.[35] In our study, we found that 4.9% of the Wave 1 sample had cognitive impairment (MMSE < 24). This is likely to be of higher in real clinical settings. Even without cognitive impairment, we cannot exclude recall bias as a potential limitation of our study.

Another limitation is that only 126 Wave 1 participants had an SYFI of more than 0.25, which is reflective of a generally healthy community-based sample with low proportions of severe frailty. Results showed that SYFI >0.25 was an independent predictor of complex falls, but the syncope prediction lost significance probably due to the low numbers involved.

Conclusion

Using data from the TILDA cohort spanning 6 years, we were able to conceive an adapted FI that significantly predicts future risk of syncope and complex falls in those aged 65 years and over. Further assessment of the SYFI in clinical settings is recommended.

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Ethical approval

Ethical approval for each wave was obtained from the Faculty of Health Sciences Research Ethics Committee at Trinity College Dublin, Ireland. All participants provided written informed consent prior to inclusion in the study.

Conflict of interest. None declared.

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Appendix Table A1. Baseline SYFI groups (frail: SYFI > 0.25 vs. non-frail) as predictor of outcomes: results of the binary logistic regression models controlling for age and sex

Predictor	OR [95% CI]	*P*-value
Future syncope		
SYFI Frail	1.46 [0.72–2.95]	0.295
Age	1.03 [1.00–1.06]	0.066
Female sex	1.08 [0.80–1.45]	0.623
Future complex fall		
SYFI Frail	2.82 [1.86–4.29]	<0.001
Age	1.03 [1.01–1.04]	<0.001
Female sex	1.54 [1.32–1.79]	<0.001
Future simple fall		
SYFI Frail	0.80 [0.34–1.84]	0.593
Age	1.00 [0.97–1.03]	0.967
Female sex	1.14 [0.86–1.50]	0.370

Appendix Table A2. Baseline SYFI groups (tertiles) as predictor of outcomes: results of the binary logistic regression models controlling for age and sex, with multiple imputation of missing outcome data

Predictor	OR [95% CI]	*P*-value
Future syncope		
SYFI Group 1	*Control*	*Control*
SYFI Group 2	1.54 [1.05–2.25]	0.026
SYFI Group 3	1.89 [1.26–2.82]	0.002
Age	1.02 [0.99–1.05]	0.261
Female sex	1.04 [0.77–1.41]	0.781
Future complex fall		
SYFI Group 1	*Control*	*Control*
SYFI Group 2	1.35 [1.12–1.62]	0.001
SYFI Group 3	2.22 [1.82–2.71]	<0.001
Age	1.02 [1.00–1.03]	0.031
Female sex	1.51 [1.29–1.76]	<0.001
Future simple fall		
SYFI Group 1	*Control*	*Control*
SYFI Group 2	1.09 [0.79–1.51]	0.584
SYFI Group 3	0.96 [0.66–1.40]	0.843
Age	1.00 [0.97–1.03]	0.971
Female sex	1.14 [0.86–1.50]	0.369