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JOURNAL OF GERONTOLOGY AND GERIATRICS

Indexed in Embase, Excerpta Medica Database
and Scopus Elsevier Database

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ORIGINAL INVESTIGATION

Frailty status and the risk of fractures in older people: the Pro.V.A. Longitudinal study

C. Trevisan¹, B.M. Zanforlini¹, A. Bertocco¹, M. Mazzochin¹, S. Maggi², M. Noale², M. De Rui¹, S. Zambon^{2,3}, E. Perissinotto⁴, G. Crepaldi², E. Manzato^{1,2}, G. Sergi¹

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Background and aims. Frailty has been associated with an increased risk of fractures in older people, but the mechanisms behind this relationship have yet to be fully elucidated. We aimed to investigate which frailty criteria were more closely associated with the risk of fractures in community-dwelling older people.

Methods. This study analyzed data from 2,113 older men and women enrolled in the Progetto Veneto Anziani (ProVA) study and with no fractures at baseline. Frailty was assessed at baseline and defined as the presence of at least three out of five Fried criteria, pre-frailty was the presence of one or two criteria, while non-frailty was the presence of none of the criteria. Fractures after a mean 4-year follow-up were assessed on the basis of medical records, self-reports, and radiographic examinations.

Results. At follow-up, we identified 233 (11%) new cases of fracture, with an age- and gender-specific incidence rate of 22/1000 person-years (95% CI: 11-36). Compared with the non-frail, frail and pre-frail individuals carried a significant 59% (OR = 1.59, 95% CI: 1.31-1.93) and 21% (OR = 1.21, 95% CI: 1.09-1.34) higher risk of fractures, respectively. Among the frailty determinants, slow gait raised the likelihood of fractures by 56%, physical inactivity by 46%, exhaustion by 32%, and weakness by 31%. No significant associations with unintentional weight loss emerged after adjusting for potential confounders.

Conclusions. Frailty may predict the occurrence of fractures in older people, probably through mechanisms mediated by impaired physical performance and exhaustion. Slow gait seems to be the most relevant factor in increasing the risk of fractures in advanced age.

Key words: Frailty, Bone fractures, Older age, Prospective study

INTRODUCTION

Bone fractures represent one of the main causes of morbidity and disability in the elderly population, with consequent high costs for the healthcare system¹. The incidence of fractures increases exponentially with age, particularly for hip fractures, for which it reportedly rises by 1% a year for women over 80 with some geographical variations¹. The wrist, vertebra

and distal forearm are other common sites of fracture in older people, though their incidence may be underestimated because patients are less likely to need hospitalization.

The recognized major factors predisposing older adults to fractures are bone strength and recurrent falls^{2,3}. Both these conditions are strongly influenced by features typical of aging, such as sarcopenia, cognitive and functional impairments, depression and inflammatory

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states – which also describe the phenotype of frailty syndrome^{4,5}.

A two-way relationship between fractures and frailty has emerged from the current literature. In fact, frailty status may predispose individuals to falls^{2,6}, and a history of fractures has been associated with the onset of frailty^{7,8}. Moreover, a recent systematic review and meta-analysis including five prospective studies showed that the pooled risk of fractures was increased by 67% in frail and by 30% in pre-frail individuals, compared with non-frail people⁹.

While the link between frailty and bone fractures has been demonstrated in a large body of literature, little attention has been paid to which aspects of frailty could be more influential than others. Rothman et al. assessed the impact of frailty determinants on the occurrence of injurious falls in a cohort of community-living older individuals, finding slow gait speed at baseline the most significant predictor¹⁰. To the best of our knowledge, however, no studies have investigated which determinants of frailty are the most associated with the risk of fractures. Identifying the frailty determinants more strongly associated with the onset of fractures may enable targeted preventive action to reduce the risk of falls and bone fractures.

Based on these considerations, the aim of our study was to investigate the impact of frailty syndrome and its determinants on the incidence of bone fractures in a cohort of older persons over a 4.4-year follow-up.

SUBJECTS AND METHODS

DATA SOURCE AND SUBJECTS

The study population consisted of individuals included in the Progetto Veneto Anziani (Pro.V.A.), an observational cohort study that involved 3099 age- and sex-stratified community-dwelling adults aged 65 years and over (1245 men and 1854 women) living in northern Italy. Participants were randomly selected between 1995 and 1997 using a multi-stage stratified sampling method¹¹. The study data were collected by trained physicians and nurses at two out-patients' clinics or at participants' homes if they were housebound.

For the purposes of the present study, we analyzed participants' baseline data to identify cases of frailty syndrome, and then examined the cases of fracture after a mean follow-up of 4.4 ± 1.2 years.

Of the 3,099 participants initially enrolled in the study, 326 were excluded because they reported a history of fractures at baseline, 651 died before the follow-up, and 9 lacked sufficient follow-up data, so the final sample consisted of 2,113 older men and women.

The ethical committees of the University of Padua and

the Veneto Region's Local Health Units (USSL) no. 15 and 18 approved the study protocol, and participants gave their written informed consent.

ANTHROPOMETRIC, DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Trained physicians and nurses conducted face-to-face interviews with study participants, and recorded information on their educational level, physical activity, and smoking and drinking habits. Participants' educational level was classified as ≤ 5 or > 5 years (primary school in Italy lasts 5 years), and monthly income as ≤ 500 or > 500 € (equivalent to one million lire), considering as a cut-off the mean pension of Italian retired people during the study period. Smoking status was classified as "never", "former" (for at least a year in the past) and "current" smokers. Drinking habits, defined as any use of any alcoholic beverage in the previous month, was categorized as yes/no. Body weight and height were measured, and the body mass index was calculated (BMI, kg/m²). Waist circumference was measured midway between the lowest rib and the iliac crest (with participants standing) and expressed in centimeters.

Functional status was evaluated with the Activities of Daily Living (ADL, score from 0 for complete dependence to 6 for total self-sufficiency) and the Instrumental Activities of Daily Living (IADL, score from 0 for total dependence to 8 for complete independence)¹² scales. Depressed mood was assessed using the 30-item Geriatric Depression Scale (GDS), a method validated for the elderly population, which indicates depressive symptoms for scores higher than 10¹³. Cognitive status was assessed by means of the Mini-Mental State Examination (MMSE)¹⁴. Lower extremity physical performance was tested by means of the Short Physical Performance Battery (SPPB), which evaluates gait speed, static balance, and time to rise from a chair. The total score on these three tests ranged from 0 (poor) to 12 (good) physical performance¹⁵. Handgrip strength was assessed using a JAMAR hand-held dynamometer (BK-7498, Fred Sammons, Inc.), and the highest score obtained with three technically-acceptable tests on the dominant side was considered in our analyses.

The participants' medical and hospital records, comorbidities, self-reported symptoms, and records of physical examinations and blood tests were collected by trained physicians and nurses. For the purpose of our analyses, we considered the presence of hypertension, diabetes, cardiovascular diseases (CVD), chronic obstructive pulmonary diseases (COPD), osteoporosis, cancer, lower limb osteoarthritis (OA), and cognitive impairment. Any use of calcium and vitamin D supplements, and bisphosphonates (assessed as yes/no) was also recorded. Diabetes was defined as fasting plasma

glucose levels ≥ 7.0 nmol/L, glycosylated hemoglobin (HbA1c) $\geq 6.5\%$, the use of glucose-lowering drugs, or a history of a 2 h post-load glucose ≥ 11.1 nmol/L¹⁶. CVD was defined as any of the following: congestive heart failure, angina requiring a stent, angioplasty or hospitalization, myocardial infarction and stroke. Osteoporosis was identified on participants' medical history or dual X-ray absorptiometry (DXA) scans, defining the disease as the presence of a T-score of -2.5 or lower at the hip, femoral neck, or spine¹⁷. Lower limb OA was assessed during the interviews with physicians and nurses by means of a clinical examination and participants' medical records, previous X-ray reports, and use of analgesics. A diagnosis of OA was subsequently confirmed by a rheumatologist using a standardized algorithm that also considered records of hospital admissions for OA and prostheses intended to relieve OA-related complications. Renal function was assessed from the estimated glomerular filtration rate (eGFR), calculated with the MDRD (Modification of Diet in Renal Diseases) formula¹⁸.

Biochemical parameters were also considered as potential confounders in our analyses. Serum concentrations of 25-hydroxyvitamin D (25[OH]D) and parathormone (PTH) were assessed. Serum 25OHD levels were measured by radioimmunoassay (RIA kit; DiaSorin) with intra- and inter-assay coefficients of variation (CV) of 8.1 and 10.2%, respectively. Serum intact PTH levels were measured using a two-site immunoradiometric assay kit (N-tact PTHSP; DiaSorin): the intra- and inter-assay CV were 3.0 and 5.5%, respectively.

FRAILTY ASSESSMENT AND DEFINITION

At baseline we assessed the presence of frailty and frailty determinants on the basis of Fried frailty criteria⁴. In particular, we defined frailty as the presence of at least three criteria of Fried frailty phenotype, and pre-frailty as the presence of one or two criteria⁴, among:

- self-reported unintentional weight loss of 5 kg or more over the previous year;
- exhaustion, defined as a GDS score higher than 10, and the answer "no" to the item "Do you feel full of energy?" (since data based on the Center for Epidemiological Studies scale for depression [CES-D] were unavailable). The GDS has been used to estimate and predict fatigue and exhaustion in other similar studies¹⁹;
- physical activity level, measured by estimating the energy expenditure on daily activities with a cutoff of 383 kcals/week, and 270 kcals/week for men and women⁴, respectively, to define low physical activity;
- gait speed, measured during a 4-meter walk, and adjusting for gender and height to define appropriate cut-offs for frailty⁴;

- grip strength, adopting specific cut-offs by gender and BMI to define the presence of weakness⁴.

ASSESSMENT OF FRACTURES

Information on fractures was obtained at the end of the study period from medical and hospital records, self-reports, and X-rays taken during the 4.4-year follow-up of any incident fractures involving the wrist, radius, or femoral or vertebral regions.

STATISTICAL ANALYSIS

The Pro.V.A. sample was generalized to the population in the two geographical areas where the participants lived, using a set of weights based on the gender and age distribution of the reference population (Italy, Census 1991) and the sample fraction.

Normal distributions of continuous variables were tested using the Shapiro-Wilk test. The data are shown as means \pm standard deviations for quantitative measures and as frequency percentages for all discrete variables. Differences in baseline characteristics between individuals classified by frailty status were compared through the ANOVA test, for continuous variables, and the Chi-square test, for the categorical ones. Levene's test was used to test the homoscedasticity of the variances, and Welch's ANOVA was used whenever its assumption was violated.

Multivariate logistic regression analyses were run, considering baseline frailty status as the independent variable and the onset of fractures during the follow-up as the dependent variable. Participants who were not frail were taken for reference in all analyses. Variables that significantly differed between baseline frailty groups and that could be potential confounders in the association between frailty and fractures were considered for inclusion in the fully-adjusted model. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated to estimate the strength of the associations between baseline frailty status and frailty criteria with the onset of frailty at follow-up.

All analyses were performed using the SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois). All statistical tests were two-tailed, and a p-value < 0.05 was assumed to be statistically significant.

RESULTS

The data on 2,113 participants (798 M, 1315 F, un-weighted data) were included for the purposes of our study. Across the sample as a whole, the mean age was 74.4 ± 7.0 years and the mean BMI was 27.9 ± 4.5 kg/m². At the baseline assessment, 216 (10.2%) participants, the majority of them women (79.6%), met at least three of the frailty criteria and were defined as

frail. Compared with the participants who reached the follow-up assessment, those who died during the study period were more likely to be older (mean age 81.5 ± 7.6 years) and to report higher prevalence of diabetes (21.5%), CVD (41.2%), COPD (17.1%), cancer (11.7%), cognitive impairment (26.7%), and frailty (41.9%). They were more likely to have lower BMI values (26.6 ± 4.5 kg/m²), to be dependent in activities of daily living and physically impaired. No significant differences were found instead on educational level, socioeconomic status, and drinking habits (data not shown). The characteristics of the sample as a whole, and divided by baseline frailty status are reported in Table I. Compared with non-frail and pre-frail subjects, those who were frail were significantly older, less physically active and more dependent in ADL. They reported lower educational levels and monthly incomes, and

were less likely to be drinkers and smokers. As regards comorbidities, the frail group had a higher prevalence of CVD, osteoporosis, cancer, lower limb OA, cognitive impairment and depressed mood.

After 4.4 years of follow-up, we found 233 (11%) new cases of fracture, with an age- and gender-specific incidence rate of 22/1000 person-years (95% CI: 11-36) in the sample as a whole. Figure 1 shows the cumulative rate of fractures reported at follow-up among participants divided by baseline frailty status. Significant differences emerged in the rate of new fractures between the groups, with 78 cases among the non-frail (8.7%), 118 among the pre-frail (11.8%), and 37 among the frail individuals (17.1%; $p < 0.0001$). Similarly, the presence at baseline of all determinants of frailty was associated with a higher incidence of fractures at follow-up ($p < 0.0001$ for all, Fig. 1).

Table I. Baseline characteristics of the sample as a whole, and by frailty status. Numbers are mean values (and standard deviations) or percentages (%), as appropriate (unweighted data).

Variables	Frailty status				P-values
	All (n = 2113)	Non-frailty (n = 894)	Pre-frailty (n = 1003)	Frailty (n = 216)	
Age (years)	74.4 ± 7.0	71.8 ± 5.5	75.4 ± 7.1	80.8 ± 7.0	< 0.001
Sex (women, %)	62.2	51.1	68.4	79.6	< 0.001
BMI (kg/m ²)	27.9 ± 4.5	27.7 ± 4.0	28.1 ± 4.8	27.4 ± 5.4	0.04
Waist (cm)	96.8 ± 11.6	96.5 ± 10.4	97.3 ± 12.2	95.6 ± 13.1	0.09
Diabetes (%)	15.1	14.3	15.2	18.5	0.30
CVD (%)	18.2	13.6	19.4	31.5	< 0.001
Osteoporosis (%)	39.6	32.7	43.3	51.4	< 0.001
Cancer (%)	6.8	4.9	8.0	8.8	0.01
COPD (%)	7.4	5.8	8.7	7.9	0.06
Lower limb OA (%)	24.4	15.3	28.4	43.5	< 0.001
Cognitive impairment (%)	4.2	0.2	2.9	26.9	< 0.001
Educational level > 5 years (%)	14.2	19.0	12.1	8.0	< 0.001
Current smokers (%)	9.4	12.5	7.5	5.2	< 0.001
Former smokers (%)	28.5	35.1	25.0	17.4	< 0.001
Monthly income > 500 € (%)	39.9	43.1	35.7	33.0	0.01
Drinking habits (%)	69.1	75.1	66.9	55.1	< 0.001
ADL (score)	5.3 ± 1.2	5.8 ± 0.5	5.2 ± 1.1	3.5 ± 2.0	< 0.001
IADL (score)	6.3 ± 1.8	7.2 ± 1.0	6.2 ± 1.6	3.5 ± 2.0	< 0.001
GDS (score)	9.4 ± 5.3	7.8 ± 3.6	10.4 ± 5.3	11.5 ± 8.3	< 0.001
MMSE (score)	24.3 ± 5.0	26.0 ± 3.3	24.0 ± 4.4	18.3 ± 8.4	< 0.001
SPPB (score)	8.5 ± 3.3	10.4 ± 1.5	8.0 ± 3.0	3.2 ± 3.0	< 0.001
25(OH)D (nmol/l)	83.2 ± 54.1	96.5 ± 55.9	77.3 ± 51.9	51.8 ± 36.1	< 0.001
PTH (ng/l)	40.3 ± 23.8	36.7 ± 18.9	42.2 ± 26.2	46.9 ± 28.2	< 0.001
GFR (ml/min)	69.9 ± 18.3	71.9 ± 16.9	69.1 ± 18.2	65.7 ± 23.2	< 0.001
Use of calcium supplements (%)	1.8	1.9	1.6	1.9	0.87
Use of vitamin D supplements (%)	1.0	0.7	1.2	1.4	0.43
Use of bisphosphonates (%)	1.4	1.5	1.4	0.9	0.83

Abbreviations. BMI: body mass index; CVD: cardiovascular diseases; COPD: chronic obstructive pulmonary disease; ADL: activities of daily living; IADL: instrumental activities of daily living; GDS: geriatric depression scale; MMSE: mini mental state examination; SPPB: short physical performance battery; 25(OH)D: 25-hydroxyvitamin D; PTH: parathormone; GFR: glomerular filtration rate.

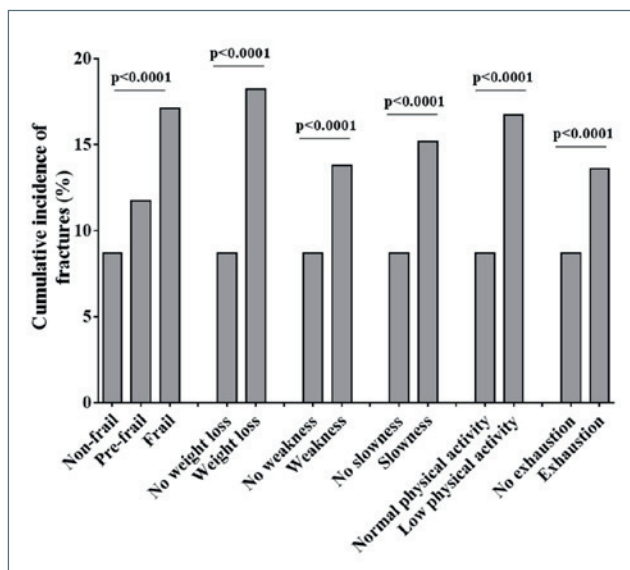


Figure 1. Cumulative incidence of fractures occurring during the 4.4-year follow-up in participants divided by frailty status and presence/absence of frailty criteria at baseline.

Logistic regression analyses confirmed the association between baseline frailty status and fractures at follow-up also after adjusting for potential confounders, with the fracture risk 20% higher for the pre-frail, and 56% higher for the frail individuals (OR = 1.56, 95% CI: 1.31-1.87, $p < 0.001$), compared with those who were not frail (Tab. II). When the frailty criteria were considered separately, the risk of fractures was significantly associated with low baseline walking speed (OR = 1.51, 95% CI: 1.34-1.70, $p < 0.001$), low physical activity (OR = 1.62, 95% CI: 1.31-2.00, $p < 0.001$), weakness (OR = 1.35, 95% CI: 1.22-1.51, $p < 0.001$), and exhaustion (OR = 1.23, 95% CI: 1.09-1.39, $p = 0.001$). No significant results emerged for the association between unintentional weight loss and fractures at follow-up.

DISCUSSION

Our longitudinal study confirmed that frailty and pre-frailty significantly increased risk of fractures occurring over a period of 4.4 years in a cohort of community-dwelling older adults. The determinants of frailty most strongly associated with fractures were slow gait, physical inactivity, exhaustion and weakness.

The sample considered in our study revealed a higher prevalence of frailty than in similar samples of older people (10.2 vs 6.9%⁴ and 8.8%²⁰), while large cohorts of women showed an even higher prevalence of frailty than ours, ranging from 16% in two American

works²¹⁻²² to 22% in the GLOW international study²³. These differences in frailty prevalence may be attributable to a variability of the participants' characteristics depending on the inclusion criteria adopted and/or on the different tools used to assess frailty, particularly weight loss, physical activity and exhaustion.

When we investigated the association between the occurrence of fractures and the presence of frailty phenotype, we found a 56 and 20% higher risk of fractures in frail and pre-frail individuals, respectively, compared with their non-frail counterparts. Our results confirm the findings of previous studies^{6-8,9,22,24,25}. In particular, similar prospective studies on older women showed an increase in the risk of fractures ranging from 11-31% for the pre-frail, and from 25-57% for frail subjects²¹⁻²³, with a marked variability due mainly to the site of fracture considered. Consistently, the risk of falls – a factor that, combined with declining bone strength, may significantly influence the risk of fractures – seems to rise in frail individuals too^{4,7,8,26,22-24}. However, the results of a recent study that compared the simplified Women's Health Initiative and the standard Cardiovascular Health Study frailty phenotypes in predicting adverse health-related outcomes in older women found that both phenotypes were associated with increased rates of falls and mortality, but neither could predict incident hip fractures²⁷.

In addition to bone strength²⁸, other well-recognized factors promoting falls and fractures in older people are also common features of the frailty syndrome, such as poor physical performance, impaired balance and mobility, low body mass index and reduced lean mass, loss of vision, cognitive decline and polypharmacy²⁹. The overall impact of these factors on the likelihood of fractures was demonstrated in our study too when frailty determinants were analyzed separately, with slow gait, physical inactivity, weakness and exhaustion all associated with a higher risk of fractures.

Many authors have identified low walking speed as the strongest predictor of such adverse outcomes as cardiovascular diseases, chronic disability and mortality^{10,30}. Rothman et al. also found that this factor was the only frailty criterion capable of predicting injurious falls¹⁰, since it is an indicator of impaired mobility and physical inactivity, both conditions potentially predisposing older people to fractures³¹. Weakness is another marker of scarce physical performance that could raise the risk and consequences of falls in older people³². Loss of muscle strength, together with a reduction in muscle mass, are the hallmarks of sarcopenia, a condition closely associated with osteoporosis and higher risk of falls^{28,33}. Our study confirmed that weakness increases the chances of fractures, even after adjusting for any presence of osteoporosis, suggesting that this

Table II. Association between the baseline frailty status and frailty determinants with the presence of fractures at follow-up.

Odds ratios and 95% Confidence Intervals of Incident Fractures				
	Age- and sex-adjusted model	P-value	Fully-adjusted model*	P-value
Baseline frailty status				
Non-frailty	1 [ref]		1[ref]	
Pre-frailty	1.19 (1.08-1.31)	< 0.001	1.20 (1.09-1.33)	< 0.001
Frailty	1.67 (1.44-1.94)	< 0.001	1.56 (1.31-1.87)	< 0.001
Unintentional weight loss	1.69 (1.16-2.46)	0.01	1.34 (0.91-1.98)	0.14
Weakness	1.37 (1.23-1.51)	< 0.001	1.35 (1.22-1.51)	< 0.001
Slowness	1.50 (1.35-1.67)	< 0.001	1.51 (1.34-1.70)	< 0.001
Low physical activity	1.79 (1.50-2.13)	< 0.001	1.62 (1.31-2.00)	< 0.001
Exhaustion	1.29 (1.15-1.44)	< 0.001	1.23 (1.09-1.39)	0.001

*Adjusted for: sex (male/female), age, body mass index (20-24.9 vs < 20/25-29.9/≥ 30 kg/m²), cardiovascular diseases, osteoporosis, lower limb osteoarthritis, cancer, cognitive impairment (all as yes vs no), educational level (≤ 5 vs > 5 years), smoking habits (never vs current vs former), monthly income (< vs > 500 euros), drinking habits (yes vs no), serum levels of parathormone (≤ 55 vs > 55 ng/l), serum levels of 25-hydroxivitamin D (< 75 vs ≥ 75 nmol/l), activities of daily living (as continuous variable).

frailty criterion has an independent role in raising the risk of fractures, probably through endocrine-immune mechanisms involved in the musculoskeletal frailty typical of advanced age^{33,34}. The incidence of fractures in our sample also rose for people reporting exhaustion at baseline. The feeling of tiredness and depression have been associated with a higher likelihood of falls due to a worse physical performance, slow reaction time and gait, and an impaired balance, mediated by both cognitive and physical mechanisms^{35,36}. Falls and the fear of falling can negatively affect motor and psychological well-being, adding to the risk of fractures³⁷. Finally, when we considered unintentional weight loss, we found no significant independent association with the onset of fractures, although there are reports of reductions in lean mass and BMI being associated with higher risks of falls and fractures^{38,39}.

The present study has some limitations. First of all, our not having assessed vertebral fractures by means of morphometric measurements means that we may have underestimated the incidence of such fractures in our sample because most mild and early vertebral body deformations are asymptomatic in older people. Second, we did not consider a history of falls as a potential confounder in the association between frailty and the occurrence of new fractures, though having excluded individuals reporting fractures at baseline minimizes this potential bias. Third, our assessment of frailty syndrome may be biased because self-reported information was considered regarding weight loss and daily physical activities, and the GDS scale was used to define exhaustion.

On the other hand, a strength of our work lies in the prospective design of the study and the inclusion of a large sample of older subjects living in the community. Having adjusted our analyses for multiple covariates

also strengthens our results, ruling out any influence of confounders on the association between frailty and the occurrence of fractures. A novel aspect of our study lies in that we investigated how frailty status was associated with the risk of fractures by focusing on single frailty determinants.

In conclusion, frail and pre-frail older adults carry a higher risk of fractures than their non-frail peers. Physical inactivity and slow gait, in particular, but also weakness and exhaustion seem to exacerbate the fracture risk in older people. Assessing older people for any presence of these factors may help to identify those at higher risk of fractures and enable targeted preventive action.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Differences in one year outcome after primary total hip and knee arthroplasty in elderly patients with osteoarthritis: a cohort study

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Background. Patients submitted to primary total hip (THA) and knee (TKA) arthroplasty show better clinical outcomes, improved quality of life and increased participation in leisure activities. However, the discrepancy between primary THA and TKA in elderly patients are unknown.

Aim. To compare the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) scores and WOMAC change scores, the Medical Outcomes Study 12-item short-form version 2 (SF-12) mental and physical health scales, satisfaction, and frequency of participation in leisure activities in elderly osteoarthritis patients (≥ 65 years) who underwent primary THA and TKA, respectively.

Methods. Data from 170 THA and 169 TKA patients were collected one week preoperatively through self-reporting of WOMAC scores, and SF-12. One year postoperatively, the latter parameters and satisfaction frequency for participation in leisure activities were collected by self-reporting questionnaires.

Results. THA group patients showed better WOMAC scores ($p < 0.05$), WOMAC change scores ($p < 0.05$), physical component summary (PCS) of SF-12 ($p < 0.01$), and PCS change scores ($p < 0.01$) compared with the TKA group. In addition, THA patients showed higher overall satisfaction (91.90 vs 83.60%), pain relief satisfaction (87.20 vs 77.40%), and functional improvement satisfaction (90.10 vs 83.08%) in comparison with TKA patients. Furthermore, higher frequency of participation in leisure activity was obtained in THA patients, except the intellectual leisure activity.

Conclusions. Our findings suggest that primary THA offers superior clinical outcomes, quality of life, satisfaction, and participation in leisure activity compared with primary TKA in elderly patients.

Key words: THA, TKA, Leisure activity, Quality of life, Elderly patients

INTRODUCTION

Total hip and knee arthroplasty (THA and TKA) are considered to be cost-effective and reliable, enhancing the quality of life and maintaining independence in patients with osteoarthritis (OA) ¹. Hip and knee OA is the major cause of lower extremity disability among elderly adults ^{2,3}. Previous studies have predicted that approximately 60% of the U.S. population aged ≥ 65 years will have arthritis by 2030 ⁴. The conservative treatments for hip and knee OA are effective in the early

stages. However, their efficacy gradually declines with disease progression. THA and TKA are considered to be the optimum selections for end-stage hip or knee OA. Both procedures can relieve pain, restore function, and improve the quality of life ^{5,6}. Consequently, the primary THA and TKA rates have increased, respectively, by 16 and 42% per 100,000 persons between 1991 and 2004 in the UK ⁷. Investigators have predicted an increase of as much as 174 and 673%, respectively, for THA and TKA by 2030 ⁸.

THA and TKA have been used successfully, with higher

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patient satisfaction in the treatment of advanced OA⁹; nevertheless, multiple scholars believe that THA is better than TKA in pain relief and function improvements¹⁰. Indeed, Ethgen et al.¹¹ carried out a meta-analysis and demonstrated that although both surgeries are valid in enhancing health-related outcomes, patients treated with THA have a better function than those who received TKA. In addition, Bachmeier et al.¹² reported a better improvement in SF-36 scores (except emotional) and Western Ontario and McMaster's University Osteoarthritis Index WOMAC scores for patients who underwent THA than those treated with TKA. Similar results were observed in other studies^{13,14}. Liang et al.¹⁵ found no significant differences regard to the improvement Quality of Well-Being Scale between patients undergoing THA and TKA. Ritter et al.¹⁶ found substantial improvement in the quality-of-life after THA and TKA, and no significant difference was found between patients treated with THA and TKA, respectively. These findings indicated that patients treated with THA obtain greater pain relief and functional recovery compared with those receiving TKA, although it was not clear which of these surgeries provides the best quality of life. The previous studies aimed at evaluation the total population, and no work was specifically focused on elderly individuals. Leisure activities are defined as activities different from work or daily life duties, which could bring individuals enjoyment or wellbeing¹⁷. Leisure activities belong to the top 5 concerns of patients undergoing joint replacement¹⁸. Patients with end stage OA participate in far less leisure activities¹⁹. After joint replacement, patients greatly improve their ability to participate in leisure activities, but approximately a quarter of them find these activities difficult to undertake^{20,21}. A study revealed that the patient's leisure activity expectations were likely not to be fulfilled one year after TKA²². However, leisure activities are rarely included in the assessment of patient outcomes after joint replacement²³. Little is known about the difference in leisure activity participation between elderly patients treated with THA and TKA, respectively.

To determine the WOMAC scores, SF-12, and satisfaction, we contrasted the therapeutic effect of primary THA with primary TKA in elderly patients after one year. In addition, we compared the patients that received these treatments with regard to participation in leisure activities.

PATIENTS AND METHODS

To explore this research, a large population-based cohort study was conducted at the First Affiliated Hospital of Guangzhou Medical University. OA patients ≥ 65

years, who had undergone primary TKA or THK in the period from January 2013 to March 2015, were eligible to participate in this study. Six orthopedic doctors from the same department implemented the operations. During follow-up (1 year post-operation), patients who had other lower-limb surgery, died, were diagnosed with malignant diseases, had cognitive limitations, or were unable to answer the questionnaires were excluded. The inclusion criteria were met by 374 consecutive patients, while 35 were eliminated, 6 had other lower-limb surgery, 9 had died between the time of surgery and follow-up end (2 from lung cancer, 1 pneumonia patient, 3 myocardial infarction victims, 1 traffic accident victim, 2 unidentified deaths), 4 were diagnosed with malignant diseases, 5 had cognitive limitations and were unable to answer the questionnaires; 11 were lost to follow-up. The study collected 319 effective questionnaires, including 170 and 149 individuals treated with THA and TKA, respectively. This research had approved by the Ethics Committee at the First Affiliated Hospital of Guangzhou Medical University.

Baseline data and preoperative questionnaires were collected from patients 1 week before surgery. The baseline data included age, gender, weight and height (used to figure out body mass index), comorbidity, living status (live alone: yes/no). The preoperative questionnaire included WOMAC, SF-12 and the Self-Administered Comorbidity Questionnaire (SCQ)²⁴. One-year postoperative questionnaire surveys were collected by mail, and included WOMAC, SF-12, patient satisfaction, and leisure activity. Data were collected by the same group of surgeons and postgraduates. In order to obtain maximum response rates, we reminded the patients to perform survey after they received the questionnaires.

PAIN, STIFFNESS, AND FUNCTIONAL LEVEL ASSESSMENT

WOMAC score is a 3 domains (pain, stiffness, physical function) index including 24 items²⁵, and the index were ranged on a numerical scale from none (0), mild (1), moderate (2), severe (3) to extreme (4), which lower score reflected a better state. In orthopedics, raw WOMAC scores are commonly transformed and normalized into a 0 to 100 scale, with 0 to 100 reflecting worst to best state change²⁶. The alteration of WOMAC score takes a great part in pre-operational and post-operational evaluation which measured by subtracting the pre-operational WOMAC score from the one obtained 1-year post-operation.

QUALITY OF LIFE ASSESSMENT

The health-related quality of life was evaluated using the SF-12 questionnaire²⁷, which consists of 12 questions from eight domains (physical functioning, role

limitation because of physical health problems, bodily pain, general health, vitality, social functioning, role limitation due to emotional problems and mental health) about health-related quality of life. Physical and mental component summary (PCS and MCS) scores of the SF-12 were gathered according to the scores, and higher scores represent a better quality of life. It has been validated for the Chinese population²⁸.

SATISFACTION

The assessment of patient satisfaction used a survey which included three questions: (1) global satisfaction of patients with surgery; (2) patients satisfaction on pain remission; and (3) patients satisfaction about functional improvement. Each answer was graded and categorized as satisfaction (satisfied, very satisfied) and dissatisfaction (neutral, dissatisfied, very dissatisfied)²⁹.

LEISURE ACTIVITY ASSESSMENT

To our knowledge, there is no consistent assessment scale to measure leisure activities. Moreover, there are significant differences in leisure activities among various populations due to distinct cultural backgrounds. To select leisure activity items, we used the experience of Hong Kong for elderly people because of the two regions having similar habits and Cultural backgrounds³⁰. The leisure activity questionnaire included 4 categories: (1) the intellectual portion comprised reading, web surfing or computer operation, gambling or cardplaying, finance and stock investment, taking part in open forum events or debates, drawing, painting, playing a musical instrument, writing, and doing artwork and crafts; (2) the social category included participating the interest group, involving in voluntary activities, visiting the museum, joining exhibitions, catching various shows, and meeting people; (3) the recreational category was composed of enjoying music, movies, shopping, having pets, cooking, fishing, facial and massage; (4) the physical part comprised running, hiking, practicing Chinese martial arts and Chinese traditional sports, playing ballgames and exercise machines, swimming, and cycling. All leisure activity which participants involved in were summarized. The frequency of participation was recorded as “daily (which got 7 points)” “several days

per week (which got 4 points)” “once weekly (which got 1 points)” “occasionally (which got 0 points)” or “never (which got 0 points)”.

COMORBIDITY ASSESSMENT

SCQ is a short, easily understood survey which is efficient to assess comorbidity in clinical and health services research^{28,36}, and can be completed by individuals with no medical background. It includes 13 defined medical problems that might impact functioning and 3 optional non-specified medical problems. For each condition, it was asked whether (1) it was present (yes/no); (2) treatment was received (yes/no); and (3) it imposed functional limitations (yes/no). Every ‘yes’ is given one point. So, the maximum total score was 45 points (the open-ended items used).

STATISTICAL ANALYSIS

The results were expressed as means \pm SD, and frequencies and percentages were used for better understand. Statistical were analyzed with SPSS software version 17 (SPSS Inc, Chicago, IL). The socio-demographic characteristics of the two groups, gender (men/women), living alone and patient satisfaction were compared using the chi-square test. Differences in age, BMI, SCQ, WOMAC scores, SF-12 scores, leisure activity scores, the difference between WOMAC scores were evaluated by the Student’s t-test. Differences in SF-12 change scores were evaluated by the Mann-Whitney U test. An outcome was considered statistically significant with $P < 0.05$.

RESULTS

Totally, 44 patients (21 THA, 23 TKA) did not answer the questionnaires. The response rates remain 85.90% (149 patients) in the THA and 84.25% (126 patients) in the TKA groups. The demographics and characteristics of patients received presented no significant differences in age, sex, SCQ, BMI, and live alone (Tab. I), and there were no significant different variables between non-responders and the responders.

Pre-operational WOMAC total scores (all three domains)

Table I. Demographic distributions of the primary total hip and knee arthroplasty.

Joint demographics	Hip	Knee	P-value
Age (mean + SD)	75.38 (6.85)	75.13 (7.57)	0.770
Body mass index (mean + SD)	25.32 (5.52)	25.54 (6.14)	0.745
Female (%)	63.80%	67.10%	0.543
Live alone (%)	20.10%	19.20%	0.836
SCQ (mean + SD)	2.66 (1.47)	2.97 (1.46)	0.081

did not suffer significant differences between the THA and TKA groups. However, significant differences were obtained in postoperative WOMAC total scores as well as in individual domain scores (Tab. II); in addition, patients treated with primary THA presented more effective than those underwent primary TKA in the light of pain relief, joint stiffness, function, and total scores which reflected in WOMAC change scores (Tab. III).

There were no significant differences in preoperative SF-12 scores (PCS, MCS) between both groups. Interestingly, significant differences were obtained in postoperative PCS but not MCS (Tab. II). The PCS change scores were better in the THA group than in TKA treated patients (Tab. III).

The patients who underwent THA obtained higher leisure activity scores ($p < 0.01$) in the social, recreational, and physical categories compared with those treated with TKA, indicating that THA patients had a reduced hindrance to participating in leisure activities, except for the intellectual leisure activity (Tab. IV).

One-year after surgery, the patients treated with THA reported greater global, pain relief, and functional improvement satisfaction than those who underwent TKA (Tab. V).

DISCUSSION

The present research confirmed the capture joint-specific and generic quality of life outcomes, patient satisfaction, and leisure activity scores through reported patient measures. These comprehensive questionnaires allow for assessment of actual differences between primary THA and TKA. We found that elderly patients treated with primary THA had a better outcome and greater improvement in joint-specific and generic quality of life outcomes, patient satisfaction, and leisure activity scores compared with those who underwent primary TKA. A relationship was found between pain or function and part of leisure activity 1-year after joint replacement.

Table II. Comparison of WOMAC and SF-12 between patients who underwent primary THA and TKA.

	THA	TKA	P-value
Preoperative WOMAC (SD)			
Pain	40.07 (17.77)	41.89 (15.34)	0.347
Stiff	39.56 (16.09)	41.05 (16.55)	0.433
Function	41.19 (16.48)	40.87 (15.51)	0.868
Total	40.27 (10.32)	41.27 (8.26)	0.359
Postoperative WOMAC (SD)			
Pain	88.79 (15.40)	84.91 (12.84)	0.020
Stiff	85.42 (13.37)	78.49 (14.73)	< 0.001
Function	85.23 (15.29)	79.90 (14.23)	0.002
Total	86.48 (8.67)	81.10 (7.50)	< 0.001
Preoperative SF-12 (SD)			
PCS	26.09 (6.52)	27.38 (6.08)	0.080
MCS	47.13 (10.61)	47.24 (11.28)	0.934
Postoperative SF-12 (SD)			
PCS	43.01 (6.72)	39.99 (7.63)	< 0.001
MCS	51.86 (10.36)	51.47 (8.93)	0.732

Table III. Improvement in WOMAC and SF-12 of patients who underwent primary THA and TKA.

	THA	TKA	P-value
WOMAC change scores			
Pain	48.72 (16.99)	43.03 (16.34)	0.004
Stiff	45.87 (17.45)	37.44 (15.46)	< 0.001
Function	44.04 (14.77)	39.03 (14.60)	0.004
Total	46.21 (9.74)	39.83 (8.58)	< 0.001
SF-12 change scores			
PCS	17 (12,21.5)	12 (6,18)	< 0.001
MCS	4 (0,9)	4 (-1,8)	0.991

Table IV. Comparison of leisure activities between patients who underwent primary THA and TKA.

Leisure activity	THA	TKA	P-value
Preoperative			
Intellectual	7.11 (3.60)	7.07 (3.46)	0.925
Social	2.01 (1.11)	1.81 (0.89)	0.103
Recreational	4.50 (2.16)	4.58 (2.50)	0.772
Physical	6.30 (3.37)	5.58 (3.43)	0.068
Postoperative			
Intellectual	7.12 (3.56)	6.78 (3.25)	0.402
Social	4.79 (1.82)	4.09 (1.49)	< 0.001
Recreational	7.27 (3.00)	6.21 (2.43)	0.001
Physical	9.23 (4.41)	7.21 (3.78)	< 0.001

Table V. Satisfaction for patients who underwent primary THA and TKA.

	THA (n%)	TKA (n%)	P-value
Global satisfaction	91.90%	83.60%	0.028
Pain relief satisfaction	87.20%	77.40%	0.026
Functional improvement satisfaction	90.10%	83.08%	0.032

WOMAC AND QUALITY OF LIFE

Previous studies have shown that patients can obtain pains decrease and more body flexible after THA and TKA^{6 11 31}. In addition, THA resulted in better outcomes and greater satisfaction than TKA^{11 14 32}. Fortin et al.³³ found that contrasting with those who underwent TKA, patients who received primary THA treatment have gone more smoothly in SF-36 physical function, WOMAC pain, and WOMAC function outcomes. While this research operated 6 months after surgery, and the results did not reflect the actual differences between THA and TKA on account of clinically hip and knee replacement occurring among 6 to 12 month after surgery³⁴. Bourne et al.¹⁴ demonstrated that primary THA offered superior outcomes compared to primary TKA on several section, such as the willingness to undergo surgery again, WOMAC change scores, expectations met, and satisfaction. However, assessment of the quality of life was not carried out in this study. In addition, previous studies have included all patient ages; although the subjects averaged between 60 to 70 years old, the findings did not adequately reflect the actual situation of joint replacement in elderly patients. Our research aimed at the age group ≥ 65 years. We demonstrated that elderly patients who underwent primary THA had better WOMAC scores and improved quality of life (SF-12) compared with those treated with primary TKA, except the MCS.

LEISURE ACTIVITY

Taking part in leisure activities is strategic for patients

performing joint replacement, but still a quarter of patients after joint replacement cannot perform their valued leisure activities due to joint problems²¹, and patients' expectations of leisure activities are not met²². Our study demonstrated that patients treated with THA had greater participation in social, recreational, and physical leisure activity categories compared with those who underwent THK at 1-year follow-up. This finding was consistent with previous observations²¹. The social, recreational, and physical leisure activities are closely related to the lower limb joint function and status. Especially, physical leisure activities are closely associated with joint pain and function. We reasonably speculated that patients that underwent primary THA would have better outcomes than those treated with primary TKA: reduced pain, less stiffness, and improved functioning, which allow the THA patients to obtain greater participation in social, recreational, and physical leisure activities compared with individuals that received primary TKA.

Another finding was that there was not much significant difference in intellectual leisure activities. We believe that intellectual leisure activities, which mostly are sedentary (e.g. playing chess), hardly involve lower limb function, joint pain, or joint stiffness. Correlation analysis in this study also confirmed that intellectual leisure activities were not associated with joint status.

SATISFACTION

Patients that underwent THA presented a better overall satisfaction (91.90 *versus* 83.60%), pain relief

satisfaction (87.20 versus 77.40%), and functional improvement satisfaction (90 versus 83%) comparing with those suffering TKA, in agreement with previous findings¹⁴.

LIMITATIONS

Several limitations existed remains to be solved. First, the recruited patients had their surgery in academic, first-class tertiary hospitals. This may limit the generalizability of the results, especially for those treated in hospitals with different levels of service. However, it has been reported that no significant difference exists in functional outcomes of joint-replacement surgery among different types of hospital³⁵. Second, this study was a single-center retrospective study; the sample size needs to be expanded and further validation is required through a prospective multicenter study. Thirdly, the artificial joints used herein were not obtained from the same manufacturer, and different manufacturing settings might affect sample homogeneity. Almost 13% (44 patients) of all patients recruited have lost to trace, which may introduce a bias that the progression of those patients are often with poor prognosis, in keeping with previous reports³⁶.

CONCLUSIONS

Overall, this research demonstrated that elderly patients who underwent primary THA seem to have favourable prognosis, quality of life, satisfaction, participation in leisure activity than those treated with primary TKA at 1-year follow-up. Nevertheless, additional work are still necessary in evaluating the potential factors responsible for these differences such as patient, surgical, and implant-related parameters, and assess the factors that prevent elderly patients with joint replacement to participate in leisure activity.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Health status and functional profile at admission to nursing homes A population based study over the years 2003-2014: comparison between people with and without diabetes

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Background & Aims. Prevalence of diabetes in adults has been increasing in the last decades. Diabetes increases demand for nursing homes admission which is expensive for public and private finances. The aims of the study were to examine the prevalence of diabetes at admission to nursing homes in Iceland over 12 years, and to compare overall health, functioning, medication and medical diagnosis of residents with diabetes to those without diabetes.

Methods. A retrospective study of data obtained from the Minimum Data Set records at admission to nursing homes in Iceland during the years 2003-2014. Statistical analysis was carried out using a Chi-square-test, unpaired Student's t-test, linear regression and logistic regression.

Results. In total 5242 residents were assessed within 180 days from admission, 730 had diabetes (13.9%). Prevalence of diabetes increased from 9.4% in 2003 to 15% in 2014, with a peak of 19.1% in 2013. Mean age was 81.0 (SD 8.2) and 82.7 (SD 8.7) years for residents with and without diabetes, respectively ($p < 0.001$). Comorbidities like hypertension, congestive heart-failure, kidney-failure, arthritis, ulcers and amputations were more common among residents with diabetes, whereas cognitive diseases were more common in the other group.

Conclusions. The prevalence of diabetes in Icelandic nursing homes is increasing. Residents with diabetes are younger and have better cognitive performance, but suffer more physical disability and serious comorbidities than others. Nursing homes' staff need to be current in diabetes management to provide quality care.

Key words: Diabetes, Nursing homes, Health status, Minimum Data Set

INTRODUCTION

The epidemiology of diabetes is shifting toward older age, with the prevalence of diabetes being highest in the population ≥ 60 years ^{1,2}. Diabetes increases demand for nursing home admission ^{3,4} which is expensive in terms of public and private finances. In United States in the year 2002 the prevalence of diabetes in nursing homes ($n = 548,572$) was 26.4% ⁵, but in the years

2011-2012, ($n = 229,283$) the prevalence was 35.4% ⁶. In Europe, in a sample of 59 nursing homes in seven countries ($n = 4037$), the prevalence was estimated at 21.8% in the year 2009 to 2011 ⁷.

Physical disability and dementia are characteristics that affect admission to nursing homes ^{3,8} but this is also true for diabetes. Diabetes has been associated with risk of several, common clinical conditions of the geriatric population, such as functional decline, physical

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disability, falls, fractures, cognitive impairment and depression⁹, apart from the traditional long-term complications such as cardiovascular and renal diseases. This has been further shown in a systematic review and meta-analysis, where the authors found that diabetes enhanced deficits in mobility, as instrumental activities of daily living and activities of daily living (ADL)¹⁰. People admitted to nursing homes with diabetes have more comorbidities compared to other nursing homes residents, such as cardiovascular and kidney diseases^{5,7}. Diabetes treatment can be complicated in elderly persons, and the treatment of the disease presents additional challenges when symptoms of both hyper- and hypoglycaemia can be present⁹ and may need to be managed. Because diabetes is an increasing problem in nursing homes⁶ and is associated with escalating burden of care⁵, there is a need to recognise the scope of diabetes-related health issues of people with diabetes when admitted to nursing homes. The aim of this study was to examine the prevalence of diabetes at admission to nursing homes in Iceland over 12 years, as well as to compare health, functioning, medication use and medical diagnosis of residents with diabetes to those without diabetes.

MATERIAL AND METHODS

SUBJECTS

All admitted residents to nursing homes in Iceland during the years 2003-2014, who were assessed by the Minimum Data Set instrument (MDS) within 180 days from admission.

DESIGN AND DATA

A retrospective, descriptive study of data from the Minimum Data Set (MDS) instrument, which is a part of the Resident Assessment Instrument (RAI) and routinely assessed in clinical work at nursing homes. The RAI is designed to rate functioning and health care needs of nursing home residents¹¹, it is based on observation, clinical documentation and interviews with residents and or their family members. The MDS assessment was originally designed as a clinical tool intended to improve care but has also been used internationally for research purposes¹¹. The MDS instrument is considered a reliable and valid instrument¹² and adequate inter-rater reliability (Kappa > 0.6) has been reported for 85% of the MDS data elements¹³. Since year 2003 all nursing homes in Iceland have been required to assess residents with the MDS instrument at admission and thereafter at least 3 times a year. The MDS is then used as a basis for funding for the nursing home¹⁴.

For this study, data from the MDS for all nursing homes in Iceland conducted in the years 2003 through 2014 was obtained. The data set contains information on 8191 individuals but only MDS assessments completed within 180 days from admission were used. This applies to 5,242 assessments or 64% of all admission assessments for individuals in the dataset.

The MDS for nursing homes version 2.0, has 21 sections with about 350 clinical data elements and six scales. All six scales are used in this analysis (Tab. I).

In addition to the six measurement scales a further 29 medical conditions were reviewed. These include both diagnosed medical conditions, such as hypothyroidism and clinically relevant incidences, such as falls in past 30 days.

STATISTICAL ANALYSIS

Data analysis was performed using descriptive statistics (mean, standard deviation, percentages) and inferential statistics. Significant difference ($\alpha = 0.05$) between the background characteristics of the two groups (with and without diabetes) was tested using the unpaired Student's t-test and the chi-squared test, respectively, according to the nature of the data in question. To estimate differences between the two groups in the scores of the six assessment-scales, a linear regression analysis was performed, controlling for the effect of age and gender. To estimate differences between the groups on medical conditions and clinically relevant incidences, a binary logistic regression was applied, also controlling for the effect of age and gender.

ETHICAL CONSIDERATIONS

This research project was approved by the Icelandic National Bioethics Committee (VSNb2013030008/03.15), the Data Protection Authority of the Icelandic Ministry of Justice (2013030392HGK) and the Icelandic Directorate of Health (1303070/5.6.1/gkg).

RESULTS

Over the studied 12 years, the number of individual MDS admission assessments analysed was 5,242, whereof 730 residents were recorded as being diagnosed with diabetes, or 13.9%. In this cohort of new admission, 42% of the individuals were admitted from their homes, but 35.2% of the new admissions came from hospitals. Women made up 60% of these new admissions during the years 2003-2014. The mean age for all residents at admission over the 12 years varied from 82.2 to 83.9 years (Tab. II).

The proportion of residents with the diagnosis of diabetes at admission increased significantly over the

Table I. Overview of the six MDS scales, names, scoring of the scales and properties.

Name of scales	Scoring of scales	Properties
The ADL (Activities of Daily Living) long scale	Scores 0-28 Higher score indicates greater need for assistance ¹²	The ADL scale is sensitive to change ¹⁵
The CHESS Scale (Changes in Health, End-stage disease and Signs and Symptoms)	Scores 0-5 0, stable health, 5, unstable health, risk of mortality, hospitalization, pain, caregiver stress and poor self-rated health ¹⁶	The CHESS Scale is a strong predictor of mortality ¹⁶
The CPS (Cognitive Performance Scale)	Scores 0-6 0, cognitively intact 6, severe cognitive impairment ¹⁷	The CPS correlates moderately well with the Mini-Mental State Examination ¹⁷
The DRS (Depression Rating Scale)	Scores 0-14 0, no indication of depression 3, mild depression 14, very severe depression ¹⁸	The DRS scale is reported to have excellent sensitivity and acceptable specificity ¹⁸
The ISE Scale (Index of Social Engagement)	Scores 0-6 0, severe withdrawal from social engagement 6, considerable initiative and participation in social activities ¹²	Score 0-2 indicates low social engagement, compared to scores 3-6 which demonstrate better social engagement ¹²
The PS (Pain Scale)	Scores 0-3 0, no pain 3, severe (horrible /excruciating) pain ¹⁹	The PS scale is valid in detecting pain in nursing home residents ¹⁹

research period, from 9.4% in the year 2003 to 15% in 2014, with a peak of 19.1% in 2013 (Fig. 1).

More women than men were admitted to nursing homes in the studied period, but among the residents with diabetes, the gender ratio was nearly equal (Tab. III).

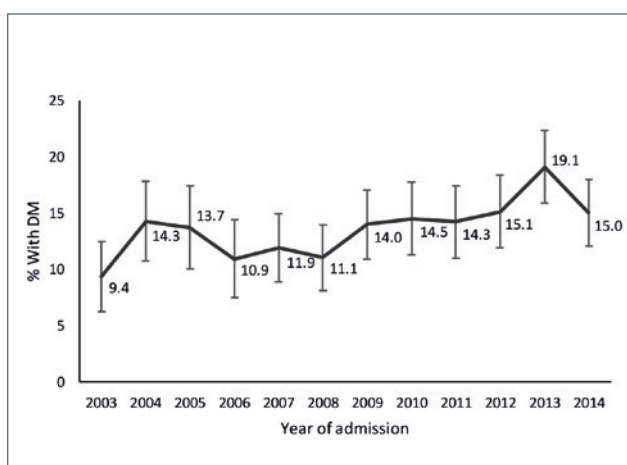


Figure 1. Prevalence (%) of diabetes at admission to nursing homes according to years 2003- 2014, $Y = 10.3 + 0.50X$ ($p < 0.001$, for an overall increase in diabetes).

Residents with diabetes were younger at admission and the proportion of residents at the age of 75 years or younger was higher in their group than in residents without diabetes. Those with diabetes also had higher BMI and used more medications compared to residents without diabetes. A vast majority of residents with diabetes used more than nine medications (Tab. III).

COMORBIDITIES

Newly admitted nursing home residents with diabetes had increased odds of having comorbidities as arteriosclerotic heart disease, hypertension, congestive heart disease, peripheral vascular disease, amputation, kidney failure, but less odds of having osteoporosis compared to new residents without diabetes (Tab. IV). There was no difference between the two groups (with and without diabetes) in cerebrovascular accidents as stroke, hemiparesis or TIA, but diabetes increased the risk of kidney failure by 24% and bladder incontinence by 14%. Residents with diabetes had more skin problems as ulcers, and almost double the risk of being admitted with stage 3 ulcers compared to other residents. Pressure ulcers were also more common in the group with diabetes at admission, that is 11% compared to

Table II. Number of admissions to nursing homes according to year, gender distribution, age at admission (mean and standard deviation) and where from the new residents were admitted.

Year	Admission (n =)	Admission (%)	Women (%)	Mean age (SD), years	Living at home (%)	Admitted from a hospital (%)
2003	342	6.5	56.7	82.7 (6.9)	45.3	33.6
2004	371	7.1	56.8	81.6 (7.9)	42.3	36.4
2005	335	6.4	60.3	81.2 (8.0)	49.9	33.4
2006	311	5.9	61.4	81.9 (7.8)	49.8	29.3
2007	437	8.3	57.0	82.8 (7.8)	48.5	35.5
2008	443	8.5	62.1	82.5 (8.6)	37.5	38.8
2009	493	9.4	57.8	82.3 (8.6)	39.8	33.3
2010	455	8.7	58.0	82.8 (8.7)	38.9	32.3
2011	449	8.6	58.4	82.5 (9.2)	39.4	38.1
2012	482	9.2	62.4	82.7 (8.4)	35.5	40.2
2013	565	10.8	54.9	83.1 (8.6)	43.7	36.8
2014	559	10.7	56.5	83.0 (8.9)	39.5	32.0
Total	5,242	100	58.4	82.5 (8.4)	42.0	35.2

Table III. Number of residents, mean age, percentage admitted at or below 75 years, gender distribution, Body Mass Index, use of medications and percentage of residents using nine or more types of medications in residents with and without diabetes over the years 2003-2014, at admission to nursing homes.

	With DM (n = 730)	Without DM (n = 4512)	Total (n = 5242)	P-value*
Age (years) at admission (mean and SD)	81.0 (8.2)	82.7 (8.4)	82.5 (8.4)	< 0.001
Admitted ≤ 75 years (%)	19.9	15.3	16	< 0.001
Women (%)	50.8	59.6	58.4	< 0.001
Body Mass Index (mean and SD)	26.1 (6.7)	23.8 (5.6)	24.1 (5.8)	< 0.001
Medications (mean and SD)	11.6 (4.0)	9.5 (4.1)	9.8 (4.2)	< 0.001
Using ≥ 9 medications (%)	91.1	75.5	77.7	< 0.001

*p-value for difference between groups obtained with a t-test for age, BMI and number of medications but a Chi-square test for % admitted ≤ 75 years, women and using 9 or more medications.

9% in the group without diabetes. Fewer residents with diabetes were diagnosed with Alzheimer disease and osteoporosis than those without diabetes. No difference was found between the groups regarding medical diagnoses of depression, falls or fractures in the last 180 days (Tab. IV).

MDS SCALES

The scores from the six MDS- scales are shown in Table V. There was a significant difference between the groups in the CHESS-, CPS- and ISE-scales, revealing that residents with diabetes had significantly more unstable health status (CHESS-scale), but less cognitive impairment (CPS-scale) compared to residents without diabetes and were capable of more social engagement (ISE) than the latter group. The scores from the DRS-scale, the ADL-long scale and the Pain-scale demonstrated no difference between residents with and without diabetes (Tab. V).

DISCUSSION

Our findings over the studied 12 years demonstrate that the prevalence of diabetes has increased in nursing homes in Iceland, similar to other countries^{6,7}. Although our results show a lower prevalence rate than observed in many other countries, the upward trend is the same. A study from US claims that over a period of 10 years the prevalence of diabetes in nursing homes increased from 16.3% in 1995 to 23.4% in 2004²⁰. Others report 26.4 to 35.4% prevalence of diabetes in nursing homes in US, using data from the MDS instrument^{5, 6}. In Norway, however, the prevalence of diabetes in 19 randomly selected nursing homes was assessed to be 16% in 2012²¹, which is quite similar to the prevalence found in Iceland in the current study. However, a study found that medical diagnosis of diabetes was documented for 75% of residents with diabetes in medical records in eight nursing homes in Norway, but the

Table IV. Comparisons of residents with and without diabetes at admission, percentage, odds ratio and p-values.

	With DM (n = 730)	Without DM (n = 4512)	OR*	P-value*
Hyperthyroidism	1	1	1.37	0.40
Hypothyroidism	13	10	1.54	< 0.001
Arteriosclerotic heart disease	40	27	1.86	< 0.001
Arrhythmias	31	26	1.40	< 0.001
Congestive heart failure	32	19	2.20	< 0.001
Hypertension	65	47	2.31	< 0.001
Peripheral vascular disease	12	7	1.84	< 0.001
Other cardiovascular disease	19	14	1.51	< 0.001
Alzheimer disease	23	28	0.80	0.02
Cerebrovascular accident [stroke]	19	17	1.03	0.76
Hemiparesis	8	7	1.02	0.90
TIA	5	5	0.87	0.47
Amputation	2	0	4.85	< 0.001
Arthritis	43	38	1.35	< 0.001
Osteoporosis	15	22	0.70	< 0.001
Kidney failure	17	8	2.36	< 0.001
Depression	38	36	1.08	0.36
Falls in past 30 days	19	18	1.06	0.56
Hip fractures in past 180 days	3	4	0.80	0.30
Other fractures	4	5	0.87	0.46
Ulcers stage 1	16	10	1.59	< 0.001
Ulcers stage 2	14	11	1.34	0.01
Ulcers stage 3	3	2	1.77	0.01
Ulcers stage 4	1	0	2.23	0.07
Pressure ulcers	11	9	1.30	0.04
Bladder incontinence	79	75	1.27	0.01
Bowel incontinence	59	56	1.09	0.31
Urinary tract infections past 30 days	16	16	1.10	0.39
Respiratory infections	5	4	1.24	0.25

* Odds Ratio and p-value obtained with a binary logistic regression measuring the effect of diabetes while controlling for age and gender.

medical diagnoses was documented in medical records for all residents with diabetes in four nursing homes in Iceland²². The increased diabetes prevalence in nursing homes in Iceland is in line with the results from a recent study that shows that the prevalence of type 2 diabetes among Icelanders aged 50-69 increased rapidly during the first decade of this millennium, especially among males²³. The higher prevalence of diabetes found among middle-aged and elderly males, compared to women in the study by Andersen et al.²³ probably explains the difference in gender distribution between the two groups in our results.

In the current study, residents with diabetes were younger, had higher BMI and used more medications than their counterparts. The BMI in our residents with diabetes was considerably lower than the mean BMI of 30.0 kg/m² in 81,087 nursing home residents with diabetes in the US as reported by Zarowitz et al.⁶. That

reflects the difference in BMI between the two nations on the whole²⁴. Diabetes is a predictor of early nursing home admission⁴ and this was clearly reflected in our results. The Icelandic residents with diabetes in our study were slightly younger than found in European nursing homes in 2009-2011, where Szczerbinska et al.⁷ reveal residents with diabetes to be on average 82.3 years and those without diabetes to be 84.6 years. In the US, the mean age of residents with diabetes is found to vary, from being reported by Resnick et al.²⁵ to be 81.7 years and 84.9 years for those without diabetes in the year 2004, to the results of Zarowitz et al.⁶ who found that residents with diabetes were on average 75.7 years in the years 2011 and 2012. Zarowitz et al.⁶ also report in their recent study that 20% of nursing homes residents with diabetes in US are younger than 65 years and Dybicz et al.²⁶ demonstrate that residents with diabetes are younger males with increased

Table V. Mean score and standard deviation (SD) of rating scales; activity of daily living (ADL), Changes in Health, End-stage disease and Signs and Symptoms (CHESS), cognitively performance scale (CPS), depression rating scale (DRS), index of social engagement (ISE) and pain scale (PS), according to residents with and without diabetes, over the years 2003-2014.

Scale	With DM (n = 730)		Without DM (n = 4512)		B*	P-value
	Mean	SD	Mean	SD		
ADL [0-28]	14.3	8.2	14.0	8.5	0.1	0.69
CHESS [0-5]	1.9	1.4	1.7	1.4	0.2	<0.001
CPS [0-6]	2.8	1.7	2.9	1.8	-0.2	0.03
DRS [0-14]	2.0	2.6	2.1	2.6	-0.2	0.10
ISE [0-6]	2.6	2.0	2.5	2.0	0.2	0.03
Pain [0-3]	1.2	1.0	1.1	1.0	0.1	0.17

* Mean difference estimated with linear regression, controlled for age and gender.

BMI. The results in our study are quite concurrent with the findings of these two studies. Luppá et al.³ demonstrated through a systematic review of 36 studies regarding factors predicting admission to nursing homes that diabetes, high number of medications and impaired ADL increase the risk of admission. Younger diabetic residents can be expected to have complex physical problems, with heavy care burden, indicating the need to try to prevent development of diabetes and its complications.

Our results from the CHESS scale confirmed that residents with diabetes had more unstable physical health condition compared with other residents. This was supported by the findings that the residents with diabetes had more comorbidities, and were more than two times likely to have hypertension and congestive heart failure than other new residents. Russell et al.²⁷ estimate that diabetes alone is responsible for 52.1% of nursing home admissions, and diabetes plus related cardiovascular conditions are responsible for 57.1% of nursing home admissions. Dybicz et al.²⁶ and Zhang et al.²⁰ report heart and circulatory comorbidities to be the most common diseases in residents with diabetes. Our findings that no difference was demonstrated in cerebrovascular accidents as stroke, hemiparesis or TIA in residents with and without diabetes are in conflict with the results from Dybicz et al.²⁶. The lack of difference in cerebrovascular accidents between the groups in our material, in spite of higher prevalence of hypertension among those with diabetes, might indicate that modern treatment with blood pressure lowering medication is effectively protective, although information regarding blood pressure measurement is lacking in the MDS data base.

Kidney failure, skin problems as ulcers, and amputations are more common in Icelandic new residents with diabetes compared to new residents without diabetes, similar to other studies^{5,26}. No newly admitted resident

was found to have a stage 4 ulcer, but one third of new residents with diabetes had ulcers at stages 1 and 2, and 3% at stage 3, which is higher than in the study by Feldman et al.²⁸. Using the MDS instrument to assess 302 residents with diabetes, Feldman et al.²⁸ found 10.8% ulcers at stages 1 and 2 and 3% had infected wounds. Pressure ulcers were 1.3 times more common in the Icelandic residents with diabetes than in the residents without diabetes. To prevent skin and foot problems and if they occur, early and aggressive treatment should be undertaken. Residents with diabetes commonly have peripheral neuropathy and or peripheral arterial disease, as here, contributing to foot ulcers or infections²⁹.

At admission the Icelandic nursing home residents with diabetes used slightly more medication than Travis et al.⁵ report in a study from US, where the mean medication use was 10.9. Our results confirm the results by others^{5,26}, that residents in nursing homes with diabetes use more medication compared to those without diabetes. Medication that induces hypoglycaemia has been associated with increased emergency department visits³⁰ and hypoglycaemia is found to be common in nursing homes³¹. Among older people with diabetes, symptoms of both hyper- and hypoglycaemia have often changed with ageing and cognitive impairment makes recognizing and interpreting symptoms even more challenging⁹. Administering many medications can be burdensome both for the resident and the staff and the risk for drug interaction increases. Therefore, careful attention must be paid to adapt medication use to the requirement of each resident.

The CPS scale scores revealed a better cognitive functioning of the residents with diabetes, supported by the fact that fewer in that group were diagnosed with Alzheimer disease. Although the difference in ADL performance was not significant between the groups, the level of impairment was considerable, which is in

line with the findings of Zarowitz et al.⁶. No difference was found between residents with and without diabetes according to medical diagnoses of depression or scoring of the depression rating scale (DRS), which is not in agreement with the study by Travis et al.⁵, who found that more residents with diabetes (30%) were diagnosed with depression compared to those without diabetes (27.5%), using MDS data.

Diabetes in nursing home residents might be more difficult to manage because of their complex health status as found here. Evidence-based guidelines^{9,32} for frail old people with diabetes highlight the importance of individual treatment goals for blood glucose measurements and regulation. Regular assessment of HbA1c is also emphasized and recommendation for HbA1c treatment goals, in frail old people with diabetes³², has also changed in recent years. This fact requires good inter-professional cooperation and knowledgeable staff. Also, the increasing prevalence of diabetes in nursing homes indicates need for qualified staff that is knowledgeable in caring for residents with unstable health conditions and able to address the residents' special needs³³.

There are several limitations of this study. Firstly, this is a retrospective analysis of data that were collected for clinical use. The MDS instrument has been deemed a valuable resource for research³⁴ and has moderate to high reliability as a research tool¹³. In addition, the MDS scales have shown to be valid and reliable in research³⁴. However, many factors outside the scope of this study, such as staffing and staff mix may have influenced the quality of the MDS assessments and may therefore be considered a limitation. As we acknowledge this limitation, it must also be clarified that the instrument comes with a detailed manual and all the registered nurses who did the assessments in the nursing homes had been trained and qualified to conduct the assessments. We decided to use in our analyses all first assessments at admission that were done within 180 days from admission to the nursing homes. This time frame, however, could be criticised, as it might have resulted in the health profile of the residents possibly being in better or worse health than in a timeframe closer to the admission date. We did a special analysis to investigate if and how it affected the results to use 180 days instead of 90 days from admission, as reported by others³⁵. No significant difference was found between the outcomes of the analysis between the two different time frames, but the chosen time frame allowed us to include 1416 more residents than if we had only included assessments done within 90 days from admission. Over the study period the percentage of MDS assessments conducted within 90 days from admission increased, and in the last 6 years of the analysed period, between 76 and 81% of the MDS assessments were conducted within 90 days from admission.

The main strengths of this study are that it covers all the nursing homes in the whole country for a period of 12 years and admission data covers 5,242 nursing home residents. This means that 72% of all new Icelandic nursing home residents' MDS admission tests over the 12 years were included in the study. Thus, it should be noted that as the data contains information on such a large proportion of the target population this can be considered to limit substantially the risk of random statistical error in the findings.

The results of this study add important knowledge about the health status and functional profile of residents with and without diabetes at admission to nursing homes. Residents with diabetes are younger and have better cognitive performance, but more physical disability and serious comorbidities than others, implicating that residents with diabetes need more complex care in nursing homes, an area where more research is needed in. Nursing homes' staff need to be current in diabetes management to provide quality care. These results also confirm the need for activities and strategy to prevent or delay the development of type 2 diabetes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTIONS

AKS, KO, RHA and IH designed the study. KO worked on the data analysis in cooperation with other authors. AKS coordinated the study and drafting of the manuscript. Critical revisions for important intellectual content: KO, RHA and IH.

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ETHICAL APPROVAL

This research project was approved by the Icelandic National Bioethics Committee (VSNb2013030008/03.15), the Data Protection Authority of the Icelandic Ministry of Justice (2013030392HGK) and the Icelandic Directorate of Health (1303070/5.6.1/gkg).

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The relationship between spiritual well-being and life orientation in elderly people with type 2 diabetes

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Background. Diabetes is accompanied by multi-dimensional physical, mental, and family-related consequences. For this reason, exploring levels of spiritual well-being and life orientation among elderly people and designing learning intervals to improve their spiritual well-being and optimism can improve quality of life, increase treatment-regimen adherence, and reduce complications in this vulnerable group. This study aims to determine the relationship between spiritual well-being and life orientation in elderly people with type 2 diabetes.

Methods. This correlational descriptive study was carried out in 2016. The convenience method was used for sampling and the participants were 145 elderly people who attended a healthcare center. The data were gathered using the Functional Assessment of Chronic Illness Therapy – Spiritual Well-Being Scale (FACIT-Sp) and the Revised Life Orientation Test (LOT-r) questionnaires. The data entry and analysis were conducted using SPSS, version 21.

Results. The participants' total scores for spiritual well-being and the FACIT-Sp questionnaire were 31.37 ± 7.95 and 130.66 ± 31.74 , respectively. The results of the Pearson correlation coefficient indicated an inverse statistical correlation between spiritual well-being and life orientation ($r = .612$, $p = 0.001$).

Conclusions. The results of this study show that spirituality may play the main role in creating an optimistic life orientation. Educational learning intervals that focus on spiritual well-being are recommended to improve elderly people's quality of life.

Key words: Spiritual well-being, Life orientation, Elderly people, Type 2 diabetes

List of abbreviations

FACIT-Sp: Functional Assessment of Chronic Illness Therapy – Spiritual Well-Being Scale

LOT-R: Life Orientation – Revise

BACKGROUND

Old age is an important life stage that is rapidly expanding and will account for a high percentage of the earth's population in the near future. In 2015, older adults made up 12.5% of the world's population, according to the World Health Organization (WHO) ¹. According to official

national statistics, elderly people accounted for 8.20% of Iran's population in 2011 ². As people grow older, they become more likely to contract chronic illnesses; most people over 60 have at least one chronic illness ³. Among elderly people, the prevalence of diabetes is high, in comparison to other chronic illnesses, accounting for 25% of all chronic illnesses in the U.S. ⁴ and 49.5% in Iran ⁵.

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By 2030, rates of diabetes will have doubled worldwide (based on 2000 levels), primarily affecting people aged 65 or older⁶. Diabetes is therefore predicted to become a huge problem for societies with aging populations and changing lifestyles, afflicting a high proportion of people aged 75 or older. This condition will damage both health systems and society, causing early complications, health problems, and death for many people⁷. Diabetes is a disabling illness for elderly people, bringing numerous other diseases, including cardiovascular conditions and physical and cognitive aging syndromes. It increases the probability that an elderly individual will end up in a nursing home by up to three times⁶. It is also one of the most psychologically onerous disorders, as it tends to be accompanied by associated mental disorders⁸.

The complications of diabetes can lead to depression and sleep disorders among elderly people⁹. Diabetics can trigger emotional problems that affect treatment outcomes, leading to treatment non-adherence, an unwillingness to control glycemic levels, and an inability to pay treatment costs; all of these can increase the death toll¹⁰. Previous studies have shown that people with diabetes suffer more from mental disorders and have a lower quality of life than non-diabetics in society¹¹. In addition, the symptoms of diabetes can lead to stigmatization and negative responses from others, affecting personality and generating negative emotions¹². This illness is known to cause crises related to multiple psychological and family problems. For this reason, it drives some sufferers to search for coping strategies, one of which is spirituality¹³. Spirituality represents the basic values that guide a person to search for answers to existential questions, such as the purpose and meaning of life, reality, love, good and evil, disease, and death¹⁴. Spiritual well-being is a key domain of health for older people, closely related to beliefs and religions. It provides goals and a sense of direction for older people, helping them live healthy, satisfying lives¹⁵. It can also help people cope with chronic diseases, improve their mental health, reduce anxiety, and achieve a better quality of life¹⁶.

In addition, spirituality can alleviate the negative mental effects of chronic illness and increase adherence to treatment regimens by creating a sense of objectivity¹⁷. Several studies have explored the role of spirituality in helping diabetic patients; most of these studies have reported a positive relationship between spiritual health and better management of diabetes, including glycemic control, general self-control, and an improvement in self-caring activities^{18 19}.

An "optimistic life orientation" is another concept that can be useful in controlling chronic diseases. According to the Scheier and Carver model (1985), optimism and

pessimism are the two main aspects of life orientation. When younger and older people are assessed, their life orientation results are expected to be meaningfully related to psychological adaptability²⁰. In a diabetic patient, optimism increases dietary adherence, physical activity, treatment, and insulin therapy adherence. It improves physiologic processes (reducing inflammation, increasing parasympathetic activities, and decreasing sympathetic activities) and ultimately improves glycemic control, reducing both complications of diabetes and mortality rates²¹. A study conducted in Iran has shown that optimistic patients with diabetes experience positive outcomes, including lifestyle changes, improved interpersonal interactions, and a feeling of health during the treatment process²².

Within the health system of Iran, diabetes is a costly disease, using up more than 8.69% of the nation's health budget²³. Spiritual well-being and religious beliefs act as facilitators in helping diabetic patients to become less pessimistic²⁴. Enhancing the spiritual well-being and life orientation of elderly people can improve their quality of life, increase treatment adherence, and decrease complications of diabetes. The present study therefore aims to identify the relationship between spiritual well-being and life orientation among elderly people with type 2 diabetes; the results can provide a basis for further studies of spiritual well-being and optimistic beliefs.

METHOD

PARTICIPANTS

The study population included the elderly who referred to a diabetes treatment center where they entered the treatment process and educational programs like insulin therapy, exercising, diets and self-care in Varamin City, Iran, 2016 (as the Authors stated in the abstract, otherwise modify the year in the abstract in 2017).

The participation criteria were having diabetes, having no other chronic diseases, and having unaffected cognitive abilities. Potential participants were first given the Mini Mental State Examination (MMSE) questionnaire to assess their cognitive abilities. Elderly receiving the score of 21 or higher could enter the study²⁵.

The convenience method was used to develop a sample: all diabetic patients registered with the diabetes center were eligible and invited to participate.

SAMPLE SIZE

The sample size was based on the findings of a previous study on the prevalence of diabetes among elderly people. That study estimated that 145 participants were

needed, based on the following parameters ($\alpha = 0.05$, $\beta = 0.2$, $d = 1$ and $\alpha = 3$).

MEASUREMENTS

1. The first set of data collected included 14 items of personal, social, and disease-related information.

2. The second set of data was obtained using the FACIT-Sp questionnaire, designed in 1990. This tool has five sections: physical well-being (7 items), social/family well-being (6 items), emotional well-being (6 items), functional well-being (7 items), and spiritual well-being (12 items). All of these items are rated using a five-point Likert scale, with responses ranging from strongly disagree to strongly agree. The final score is obtained by adding together the scores of all four parts²⁶.

The spiritual well-being questionnaire has 12 items, including three sub-scales of peace, meaning, and faith; the scoring domain for each sub-scale ranges from 0 to 16 and the total scoring domain ranges from 0 to 48. A higher score signifies a higher level of spiritual well-being²⁷.

The spiritual well-being aspect of the FACIT-Sp tool has high internal consistency across all three sub-scales (the Cronbach's alpha for the whole scale is 0.81; for the peace and meaning sub-scales it is 0.81; and for the faith sub-scale, it is 0.88)²⁸.

The FACIT-Sp questionnaire is used to assess the well-being among the diabetic adults according to Jafari et al. study, which is an example of using this questionnaire for chronic illnesses patients²⁹.

The validity of FACIT-Sp questionnaire for elderly patients is assessed by Monod in 2015³⁰.

3. The third set of data was provided by the Revised Life Orientation Test (LOT-r) scale designed by Scheier and Carver (1994)³¹. This 10-item scale evaluates an individual's expectations about life consequences; it has three positive and three negative items. All of the items mentioned above were rated using a five-point Likert scale (from strongly disagree to strongly agree). Items 1, 4, and 10 were positive and directly scored; items 3, 7, and 9 were negative and reversely scored. Items 2, 5, 6, and 8 were filler questions, intended not to further the goals of the test but to stop participants from overanalyzing the main items. The scoring domain varied from 0 to 24, with higher scores signifying a greater expectation of positive results³¹.

The reliability of this tool has been demonstrated in a study of 59 women with breast cancer; the alpha factor in this study was 0.87. A retest was carried out after 12 months and the result was: $r = 0.74$ ³². The convergent and discriminant validity of the tool can also be confirmed by applying Rosenberg's self-esteem scale and comparing results derived from the control-source scale method³². In Iran, the tool's reliability has been proven

via a study of 27 pre-university students, in which the retest was carried out after 10 days ($r = 0.70$)³³.

The convergent reliability of the test is acceptable in relation to the 5 factors of disappointment³⁴.

The FACIT-Sp and the Revised Life Orientation Test (LOT-r) scales were first translated from English into Persian by an expert. Their accuracy was then confirmed by another English language expert for use in this study. The translated questionnaires were checked by 10 faculty members and all of the recommended changes were made. In addition, the reliability of the tool was tested using an initial study of 30 diabetic patients; when the Cronbach's alpha was applied, the results were $\alpha = 0.89$ and $\alpha = 0.70$.

STATISTICAL ANALYSIS

Data were analyzed using SPSS (Version 21) for Windows. Descriptive statistics, including the mean, standard deviation, frequency, and percentage were applied to describe each variable. Kolmogorov-Smirnov test was used to examine normal distribution of the population. A Pearson's correlation coefficient (r) and t-test were used to measure the strength of the association between spiritual well-being and life orientation variables. All statistical tests used a significance level of $p < 0.05$.

ETHICAL CONSIDERATIONS

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Ethics Committee of Babol University of Medical Sciences. Before the study began, we presented a brief explanation of its aims and research processes and obtained informed consent.

RESULTS

The mean duration of disease and the duration of treatment were 74.08 ± 68.52 and 2.13 ± 0.66 , respectively; 63.4 percent of the patients had complications of diabetes (Tab. I).

The results of a t- test showed that the mean total score for spiritual well-being was 31.37 ± 7.95 and that the highest score was related to faith, with a mean of 11.68 ± 3.33 . The total FACIT-Sp score was 130.66 ± 31.74 and the highest score involved the emotional subdomain, with a mean of 14.60 ± 9.52 (Tab. II).

According to this data analysis, the mean score for life orientation was 13.16 ± 3.90 . This result indicates that most participants tended toward optimism. The Pearson's correlation coefficient showed a significant

Table I. The demographic characteristics of elderly people with type 2 diabetes.

Frequency (percent)	Demographic Information
	Gender
110 (75.9)	Female
35 (24.1)	Male
	Education
114 (78.6)	High school
31 (21.4)	University
	Occupation
103 (71.0)	Housewife
11 (7.6)	Employee
15 (10.3)	Self-Employed
16 (11.0)	Retired
	Marital status
9 (6.2)	Single
122 (84.1)	Married
14 (19.7)	Widowed
	Monthly income
23 (15.9)	High
79 (54.5)	Average
43 (29.7)	Low
	Treatment regimen
39 (26.9)	Oral treatment
17 (11.7)	Insulin
8 (5.5)	Insulin and oral treatment
9 (6.2)	Diet
65 (44.8)	Diet and oral treatment
7 (4.9)	Diet and insulin
	Complications of diabetes
4 (2.8)	Foot damage
38 (26.2)	Eye damage
9 (6.2)	Kidney damage

positive relationship between spiritual well-being and life orientation: $r(145) = .612, p = 0.001$. "Peace" had a stronger relationship with life orientation than other spiritual well-being approaches ($r(145) 0.517, p = 0.001$) (Tab. III).

DISCUSSION

The present study was designed to assess relationship between spiritual well-being and life orientation in elderly people with type 2 diabetes and to explore possible associations. The results showed that participants had good levels of spiritual well-being. As elderly people with diabetes have to manage crises, including diagnosis and treatment challenges, the progression of the disease, loneliness, and loss of freedom, they do tend to adopt spirituality, religion, and religious traditions as

Table II. The FACIT-Sp and spiritual well-being subdomain scores of elderly people with type 2 diabetes.

Mean (SD)	Subdomain
	FACIT-Sp
17.62 (6.26)	Physical well-being
17.40 (5.99)	Social/family well-being
14.60 (9.52)	Emotional well-being
18.27 (5.62)	Functional well-being
31.37 (7.95)	Spiritual well-being
130.66 (31.74)	Total score
	Spiritual well-being
10.8 (3.61)	Meaning
3.95 (3.27)	Peace
11.68 (3.33)	Faith
31.37 (7.95)	Total score

Table III. The relationship between spiritual well-being and life orientation in elderly people with type 2 diabetes (n. 145).

Test	Spiritual well-being	Meaning	Peace	Faith
R	0.612	0.416	0.517	0.146
P-value	0.001	0.001	0.001	0.08

coping mechanisms³⁵. Livnen et al. (2004) believe that aging can enhance spiritual well-being and that spirituality plays an important role in elderly people's ability to cope with stressful situations and chronic illnesses³⁶. In addition, numerous studies have mentioned the role of spiritual well-being as an important cultural factor in coping with physical problems^{37,38}.

The elderly people in our study had good levels of spiritual well-being, due to the cultural, traditional, and religious atmosphere of Iranian society. The other benefit of high spiritual well-being scores is that they help people face the reality of death, as they grow older. Younger people do not have such high levels of spiritual well-being because they use non-spiritual methods to relieve stress.

Our results are similar to those of Bastane et al.³⁹ and Shahdadi et al.⁴⁰ but do not support those of Jafari et al.²⁹. Jafari's study found that patients with diabetes did not experience good spiritual well-being²⁹. Since spiritual well-being is a fundamental requirement for elderly people, educational programs and consulting services should be used to support and improve patients' spiritual or religious condition and to encourage much stronger relationships. Such connections seem both advantageous and effective in improving health and the quality of life within this vulnerable group in society⁴¹. In the present study, the faith aspect of spiritual

well-being received the highest score. The fact that the elderly participants were Muslim and believed in God is likely to be the main reason for this result. The patients spent time praying every day and participated in religious traditions that are common in Iranian religious culture. These actions affected all aspects of their lives and health. In addition, applying religious rules to life was a shared moral value. It is therefore easy to understand why faith and religion would receive the highest score; other studies have also emphasized various aspects of the impact of religious values on health³⁷.

The participants' life orientation scores showed a tendency toward optimism. The belief that age makes life less meaningful; the feeling that aging threatens perfection, sophistication, and independence; the difficulty to tolerate problems and not having enough time to perfect oneself; the absence of religious beliefs and support of family members – all of these factors – can be key reasons for a pessimistic life orientation. By contrast, a positive self-concept can support daily routines and also help people adapt to stressful events⁴². People with a more positive life orientation have better psychological health and experience more positive emotions (including happiness, vitality, and volition) and fewer negative ones (depression and anxiety)⁴³.

Among elderly people, pessimism has consequences, affecting treatment regimen adherence²¹, the management of complications of chronic illness⁴⁴ and the ability to maintain self-care⁴⁵. Group education can generate a sense of optimism, happiness, and hope among elderly people⁴⁶.

The results of this study confirm that higher levels of spiritual well-being increase a sense of optimism. Spiritual well-being does help patients navigate life by increasing their motivation and giving them the ability to evaluate their activities and develop meaning and goals, despite being ill. The peace they derive from their relationship with God can reduce disease-related stress. On the other hand, the hope created by meaning and life goals is an energetic and motivating feeling, which can improve treatment adherence and change patients' perspective on health improvements^{36 37}. The sense that life is meaningful helps people feel effective, valuable, and able to control routines. It also makes them better able to manage failures, disasters, life conflicts, and even positive events and improvements⁴³.

Spirituality can help patients evaluate negative events in an optimistic way⁴⁷. Anandarajah and Gupta (2014) believe that having individuals with higher levels of spiritual well-being expect more positive events because they believe in a strong God who always responds to human needs⁴⁸. These findings reflect those of Gheinaghi et al.⁴⁹, Asgari et al.⁵⁰, Brown et al.⁵¹ and McFarland et al.⁵².

CONCLUSIONS

These results show that spirituality is effective in fostering an optimistic life orientation. We therefore recommend educational learning intervals that focus on improving spiritual well-being to enhance quality of life. Additional research on the spiritual needs of elderly people and other potential solutions for improving well-being are also recommended.

CLINICAL IMPLICATIONS

If nurses are convinced that spiritual well-being can improve other aspects of health, they may be willing to apply spiritual-well-being assessments to patients in their care. Such assessments can be carried out during the care process to support better diagnoses and interventions. The use of programs that develop spiritual well-being could help patients with chronic diseases to better adapt to illness, find aims and meanings in life, and look toward a brighter future as they follow their treatment regimens.

LIMITATIONS

Since the sampling for this study was carried out using the convenience method and the participants were elderly people attending a diabetes center, its methods are generalizable to similar studies using random sampling in other parts of Iran. The FaCIT-Sp questionnaire is not limited to diabetic patients. All of the participants were Shia Muslims; no other religious groups were included because they are very small minority populations in Iran.

The value of the study will be substantially improved if authors can show that spiritual well-being is associated with better lifestyle and glycemic control. Therefore, it is recommended that a study be conducted to determine the relationship between spiritual well-being and lifestyle and glycemic control in patients with type 2 diabetes.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTIONS

S F participated in writing the paper and interpreting the results. F Gh and A Sh participated in the design of the study and carried out the statistical analysis. N

Y participated in data collection. All of the authors read and approved the final manuscript.

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REVIEW

Obstructive sleep apnea and cardiovascular risks in the elderly population

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Sleep disorder breathing (SDB) is a group of diseases common in the elderly population which are strongly associated with development of cardiovascular comorbidities including stroke, heart failure, hypertension and atrial fibrillation. Age-related anatomical and functional changes in upper airways are partially responsible for increasing prevalence of SDB in the elderly. Full-night polysomnogram remains the gold standard in diagnostic workup; symptoms assessment using validated scoring system such as Epworth Sleepiness Scale may underestimate the severity of disease in the elderly population. Therapeutic approach for SDB depends on symptoms and disease severity in addition to the presence of cardiovascular or metabolic disorders. CPAP and NIV treatment in the elderly with associated OSA and cardiovascular disease improves quality of life and may reduce incidence of future cardiovascular events.

Key words: Obstructive Sleep Apnea, Sleep Disorder Breathing, Cardiovascular Risk, CPAP

INTRODUCTION

Sleep disturbances (insomnia, sleep disordered breathing, restless leg syndrome and periodic movement of sleep, REM sleep behavior disorder) are common in older adults¹. Obstructive Sleep Apnea (OSA) is characterized by frequent episodes of total and/or partial collapse of upper airways (respectively causing apnea and hypopnea) during sleep, for a time longer than ten seconds, in presence of thoracic and abdominal movements. The prevalence of OSA in general population is estimated from 9 to 38%^{2,3} and is higher in men than in women. However, the gender gap decreases with age; prevalence of OSA among women shows a sharp increase after the age of 50, catching up with the males⁴. In a large population-based sample, age has been reported to be a central epidemiological factor associated with sleep-disordered breathing⁵. The authors found that moderate-to-severe sleep-disordered breathing increased significantly in participants aged 60

or older compared with younger age group. However, elderly patients are often under-represented in clinical sleep studies and specific knowledge in frail patients is still lacking, even in other respiratory diseases⁶⁻⁹. The increased OSA prevalence among older subjects could be primarily related to aging. In murine model, age-related upper airway muscle function impairment has been proved to be a major risk factor for sleep apnea¹⁰. Likewise, similar results have been reported in humans¹¹. Furthermore, in the elderly patients the instable ventilatory control is associated to obstructive and central respiratory events¹². OSA causes systemic adverse consequences and is associated to different comorbidities arising from different biological pathways including those involved in metabolic dysregulation¹³⁻²⁸.

Several researches have highlighted that OSA is an independent risk factor for cardiovascular and metabolic diseases, involving an increased risk to develop systemic and/or pulmonary hypertension, arrhythmias, heart failure,

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coronary heart disease, stroke and diabetes though different molecular pathways not fully elucidated²⁹⁻³².

Sunnetcioglu et al.³³ showed that increased oxidative stress and failure in antioxidant mechanisms have been observed in obstructive sleep apnea.

An integrated approach in older patients harbouring these co-morbid respiratory disorders may result in better outcomes when compared to standard therapies³⁴⁻³⁹.

This review investigates the principal features of OSA pathogenesis and cardiovascular consequences among older subjects. Thus, we debate the management and therapeutic strategies in this subgroup of patients.

SLEEP DISORDERED BREATHING EPIDEMIOLOGY

A growing body of research have documented that SDB prevalence increases with age. According to the World Health Organization, the number of people aged 65 years or older is projected to grow to nearly 1.5 billion in 2050 and the amount of older people affected by SDB is expected to increase similarly. In view of these considerations, it should not be surprising that untreated SDB in older adults is associated with significant medical costs⁴⁰. SDB is an umbrella term including obstructive sleep apnoea (OSA), primary or secondary Central sleep apnoea (CSA), high-altitude periodic breathing, Cheyne-Stokes respiration and hypoxemia disorders secondary to various pulmonary and chest pathologies. OSA is the most common SDB and it is characterized by a distinctive snoring pattern caused by intermittent airway collapse, resulting in drowsiness, as the most common symptom. The count of apnoea and hypopnea episodes per hour of sleep is known as apnea hypopnea index (AHI).

The prevalence of SDB in people aged 65 years or older has been reported above 20% in various epidemiological studies⁴⁰. In frail elderly patients, prevalence rates reach as high as 60%⁴¹.

In large sleep cohort clinical study^{42 43}, the prevalence of SDB in older adults has been assessed stratifying the study population into two age categories, younger than 60 years and 60 years or older patients. Moderate-to-severe sleep-disordered breathing increased significantly in older participants compared with those in the younger age group⁴⁴.

The known risk factors for SDB in older adults, include male gender, positive family history, smoking, several craniofacial abnormalities, central obesity⁴⁵. Data from Miner et al.¹ reported that the difference in prevalence of SDB between men and women seemed to diminish in participants aged 60 years or older, probably because of the increased proportion of postmenopausal women in this age category. Although women and men with an AHI of 15 or more had a similar BMI, women had a lower

neck circumference and waist-to-hip ratio compared with men. This finding confirms that not only central obesity but also hormonal status affects the prevalence of sleep-disordered breathing in women. Many studies aim to determine whether sleep apnea in the elderly constitutes a specific entity. Many studies investigate several mechanisms proposed to account for the higher prevalence of sleep apnea in elderly. They include the increased upper airway resistance during sleep with advancing age and upper airway diameter narrow in older people due to increased pharyngeal wall fat deposit and bony structure changes.

Edwards et al.⁴⁶ showed that collapsibility of the pharyngeal airway worsens with aging, whereas the sensitivity of the ventilatory control system. In younger adults, dominant traits likely to contribute to the pathogenesis of OSA may be the reduced upper airway collapse and a higher ventilatory response to the disturbance of ventilation together with greater ventilatory demand. By the contrast OSA in older adult could be considered as a unique phenotype due to a worsening of the upper airway anatomy/collapsibility, mitigated by a reduced ventilatory demand and feedback control sensitivity. Although the age related reduction in ventilatory drive should protect against OSA, any reduction in the predisposition toward OSA is balanced by worsening anatomy with age⁴⁶.

SDB, in older populations as in younger ones, is associated with serious outcomes including stroke, occult nocturnal hypertension, open angle glaucoma, falls with fractures, impaired quality of life decreased, pain tolerance frailty and mortality⁴⁰.

The combination of sleep and ventilatory instability is likely to account for the high occurrence of central events in the elderly, a situation that is not observed in younger subjects with sleep instability. Untreated SDB in the elderly appears to have a lesser impact on mortality than in middle-aged adults. The milder clinical impact of OSA in older adults could be based on the underlying mechanism of worsening upper airway anatomy and reduction in ventilatory drive, supporting the concept of redefining OSA as a different phenotype in young versus old individuals, not based purely on AHI⁴⁶.

SLEEP-DISORDERED BREATHING PATHOPHYSIOLOGY

Several mechanisms have been proposed to clarify the increased prevalence of sleep breathing SDB in older subjects. Firstly, the parapharyngeal fat pads deposition increases significantly in the elderly population and regardless the BMI. Thus, the ratio of antero-posterior to lateral length of the bony shape become progressively lower with aging and can be associated

to soft palate length increase. Finally, the genioglossus nerve has been showed to be less responsive to negative pressure⁴⁷. Central events in the elderly are more frequent than middle age population because of increasing sleep fragmentation and ventilatory instability⁴⁸. Several studies have investigated the correlation between sleep breathing disorders and cardiovascular risk, with contrasting results. While in the young middle age population severe untreated OSA is related to higher risk due to cardiovascular mortality, in the elderly this association is not so clear. Punjabi and colleagues⁴⁹ in a multicentric prospective community based cohort study – The Sleep Heart Health Study – investigated the cardiovascular effects of SDB in subjects aged 70 or older. They did not observe a significant increase of all cause mortality related to sleep breathing disorders. Conversely, Martinez Garcia and colleagues⁵⁰ in their prospective, observational study have found that untreated severe OSA is associated with an higher risk of mortality from stroke and from heart failure, but not from ischemic heart disease compared with patients that did not suffer from OSA. CPAP treatment compliant patients reduced risk of cardiovascular mortality to levels similar to mild-moderate OSA untreated group or non OSA subgroup⁵¹. The ischemic preconditioning hypothesis suppose that intermittent hypoxia in SDB could trigger collateral neovascularization genesis, giving a sort of protection versus cardiovascular ischemic accidents⁵². SDB are also associated with heart rhythm disorders onset and particularly with Atrial Fibrillation (AF). Tung et al.⁵³ performed a subgroup analysis in the cohort of patients affected by AF in the population of The Sleep heart Health study in order to assess the linkage between obstructive sleep apnea, central sleep apnea and AF. Mean age of this of this group was 62.8 years at baseline. Results of the study showed that atrial fibrillation was more common in severe obstructive sleep apnea than in mild OSA but no statistical significant association between OSA and incident atrial fibrillation has been demonstrated. Conversely, Central sleep apnea, defined by CAI \geq 5/h by Cheyne stokes respiration or by a combination of them, was associated with a significant increase in the odds of developing AF. Periodic arousals and intermittent variation in PaCo₂ as occurs with CSA, may predispose to arrhythmia by enhancing sympathetic activation, changing the sensitivity of central chemoreceptors to PaCo₂ and causing structural and electrical remodeling of the heart⁵³. The Wisconsin Sleep cohort study was designed to evaluate the relationship between obstructive sleep apnea during REM sleep and prevalent and incident hypertension, comparing apnea-hypopnea events during non rem sleep and rem sleep and their correlation with blood pressure. Conclusions of the study underlined

that only REM-OSA group was associated with a significantly higher prevalence of hypertension⁵⁴. Further prospective studies are needed to evaluate the correlation between REM OSA and hypertension in the elderly population.

DIAGNOSIS AND TREATMENT

RESULTS IN THE ELDERLY POPULATION

OSA is characterized by a distinctive snoring pattern caused by intermittent airway collapse; there are periods of snoring or brief gasping followed by cessation of respiration lasting at least 10 seconds. Patients are not aware of snoring and nighttime arousals, but often they complain excessive daytime sleepiness. These patients present apneas (complete cessation of respiration) and/or hypopneas (30% reduction in airflow associated with 4% oxygen desaturation) both lasting more than 10 seconds and occur several times during the night, leading to frequent arousals and fall in oxygen saturation. Physical examination findings that supports OSA include: neck circumference $>$ 40 cm in males and 37 cm in females, body mass index (BMI) $>$ 25 kg/m², low-lying soft palate, elongated uvula, large tongue, or large tonsils or narrow distance between the tonsillar pillars. In elderly, an additional risk factor is an edentulous state, as this leads to a reduction in the vertical dimension that increases the occurrence of upper airway obstructive events⁴⁵. The impact of OSA may be more severe in older people, including increases in the risk of falls and fractures and in overall fragility and mortality. OSA can also affect cognitive function and quality of life⁵⁵. Epworth Sleepiness Scale may be used to document day-time sleepiness and it is significant if the total score of the evaluation items is 11 or higher, but in elderly patients it could underestimate the disorder because of other causes of insomnia (i.e. depression or medications) or nocturia (i.e. prostate adenoma in men or urinary incontinence in women), the under-report of nocturnal symptoms (snoring, choking etc.) in who do not have a bed partner, and the fact they may not drive. Periodic leg movements (PLM) have high prevalence in elderly subjects and may co-exist with SDB contributing to sleep fragmentation and daytime symptoms⁵¹.

The “gold standard” for the diagnosis of SDB is full-night polysomnogram (PSG). The total number of apnea and hypopnea episodes per hour of sleep is known as apnea/hypopnea index (AHI) and is considered significant in presence of 5 or more events per hour of sleep in patients with symptoms or comorbidities, and \geq 15 events per hour in patients without symptoms or comorbidities. Staging of OSA is the following: mild AHI 6-15, moderate AHI 16-30, and severe AHI $>$ 30.

Management of sleep disorders includes a careful respiratory functional assessment coupled with comorbidities diagnostic evaluation⁵⁶⁻⁶⁴.

Treatments for SDB depend on the symptoms and disease severity, and the presence of cardiovascular or metabolic disease. In mild-to-moderate SDB, positional measures and oral mandibular advancement splints are used. Oral appliances, prescribed by a qualified dentist, are helpful in improving respiration and sleep quality in patients with mild-to-moderate OSA. The mouthpiece is prepared so that the lower jaw and tongue are pushed forward during sleep. The effectiveness of the use of oral appliances is not specifically studied in older adults mainly because of incidence of their edentulous state. Although there is no full remedy for OSA, in moderate-to-severe OSA (associated with other comorbidities) continuous positive airway pressure devices (CPAP) are considered the most cost-effective treatment and the gold standard treatment. During sleep, these devices remove apnoeas by continuously running air from a mask and applying pressure so the airway obstruction is prevented. Manual CPAP device is usually preferred. Bilevel PAP device is advisable when the patient is not able to tolerate CPAP pressure or when PAP pressure requirement is > 20 cmH₂O. Several meta-analysis showed that CPAP is the most effective treatment for OSA. In patients with severe OSA who cannot tolerate CPAP therapy, behavioral modification and oral appliances may be used.

In elderly patients with severe OSA, CPAP treatment results in an improvement in quality of life, including daytime and night-time symptoms, as choking, nocturia and daytime sleepiness, depression, anxiety and memory⁵⁵. Some reports have shown that severe OSA was a high-risk factor for cardiovascular mortality in elderly patients⁶⁵. Some authors showed good results on improvement in hypertension and heart failure that are considered severe complications related to OSA.

Evidence for the effectiveness of CPAP treatment for the secondary prevention of cardiovascular events (CVEs) in elderly patients are scarce^{40 66}. Martinez-Garcia et al.⁵¹ reported that not treated severe OSA in elderly patients was associated with a twofold increase in cardiovascular mortality compared with elderly patients without OSA. Other evidence shows that in elderly patients, severe OSA not treated with CPAP was associated with an increase in cardiovascular mortality due to stroke and heart failure, whereas treatment with CPAP reduced CVEs, including re-hospitalization due to heart failure, acute coronary syndrome, arrhythmia, stroke, and aortic dissection⁶⁷. CPAP treatment seems to inhibit the development of CVD, directly reducing intrathoracic negative pressure and venous return. Moreover, it reduces the intramural pressure, lowers pulmonary capillary wedge pressure, and increases cardiac output in

patients with heart failure. Furthermore, CPAP indirectly reduces sympathetic nervous activity, oxidative stress, and inflammation. These effects may contribute to the prevention of coronary plaque rupture, thrombotic formation, arrhythmias, and cardiac dysfunction⁶⁷.

SLEEP-DISORDERED BREATHING AND FRAILITY

CURRENT KNOWLEDGE AND PERSPECTIVE

Frailty impacts negatively on long-term outcomes and intrinsically increases mortality risk. Frailty is generally considered as “primary” when it is independent from specific clinical disorders or “secondary” when underlying chronic comorbid conditions are present. In a cross-sectional study including subjects aged 74.2 ± 6.3 years, Galizia et al. showed that both COPD (HR = 1.34; 95% CI = 1.02-1.81; $p = 0.042$) and frailty score (HR = 1.69 for each unit of increase of frailty; 95% CI = 1.42-2.00; $p < 0.001$) were predictive of long-term mortality in a 12-years follow-up. Interestingly, influence of frailty on mortality was higher in presence of COPD⁶⁸.

Similar results have been reported in chronic cardiovascular and metabolic diseases^{62 69 70}.

Sleep breathing disorders may influence both prevalence and severity of age-related chronic comorbidities as well frailty of older subjects. Ensrud et al.⁷¹ reported a strong correlation between frailty status and prevalence of sleep disturbances, including poor sleep quality, excessive daytime sleepiness, short sleep duration, nocturnal hypoxemia and sleep fragmentation; however there are several multiparametric indexes to measure frailty and there is not general consensus on standard definition⁷². Future researches in sleep disordered breathing should include the two principal tools to evaluate the frailty, “Fried’s frailty” and “frailty index” to best define phenotype of elderly subject⁷³.

CONCLUSIONS

Identification of causes of sleep disordered breathing in the elderly is crucial to provide, for clinicians, appropriate treatments.

Management of sleep disordered breathing includes a multidimensional evaluation of cardiovascular and metabolic associated disorders. CPAP and NIV treatment in this age group with OSA and cardiovascular diseases improves quality of life and could be associated with prevention of future cardiovascular events, though further studies in this subgroup are required. Finally, the implementation of adherence to CPAP is an

urgent need and specific strategies should be carefully evaluated in the clinical setting.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Hyponatremia initial presenting feature of normal pressure hydrocephalus in elderly patient: a rare case report

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A 70 year old male presented with unsteadiness, declining cognitive functions and urinary incontinence, with serum sodium level of 108 meq/L and serum osmolality of 268 mosm/kg. His computerized tomography scan of Brain showed ventriculomegaly which made us to keep the possibility of Normal Pressure Hydrocephalus (NPH). This case report highlights about suspecting syndrome of inappropriate antidiuretic hormone secretion (SIADH) due to hyponatremia as an important differential in a case of Normal Pressure Hydrocephalus. Theoretically, hyponatremia may occur in NPH, but only three associated cases of SIADH have previously been reported in the literature and first in India.

Key words: Hyponatremia, Normal Pressure Hydrocephalus, Elderly, SIADH

INTRODUCTION

Normal pressure hydrocephalus is a rare condition which is clinically characterized by triad of gait disturbance, incontinence of urine and decline in cognitive function resulting from ventriculomegaly without elevated CSF pressure. Etiology of NPH is unknown; current theory suggests there is diminished vascular compliance¹. The disorder of SIADH is due to non physiological release of hormone from the neurohypophysis due to low plasma osmolality. Theoretically hyponatremia may occur in NPH, but till late only three associated cases of SIADH has been reported in literature¹⁻³. Here a case of elderly male with typical clinical features and brain imaging consisting with NPH accompanied by hyponatremia due to SIADH is presented.

CASE REPORT

A 70 year old male patient was admitted in medicine intensive care unit of our hospital with complaint of urinary incontinence since 6 month, generalized weakness, unsteadiness and giddiness. Patient's relatives also gave

history of forgetfulness on and off. There was no history of swelling in lower limbs. There was no history of head trauma, cerebrovascular episodes and chronic illness like hypertension or diabetes. There was no history of chronic urinary tract infection, benign prostatic hypertrophy and diuretic use. He was non smoker and non alcoholic.

On examination, the patient was conscious, disoriented to time, place and person. His BP was 110/70 mmHg, pulse of 110 beat per minute, normal Jugular Venous Pressure, and respiratory rate of 20 per minute. There was no edema in lower limb. His pupils reacted appropriately to light and there was no papilledema on fundus examination. There was no postural hypotension. Rest of the systemic examination was normal. Neurological examination showed mild cognitive function impairment with ataxic gait. His speech was normal and there was no evidence of any sensory deficit.

On routine investigations his Complete blood count was within normal limit. Renal function test was done which showed blood urea of 40 mg/dl, serum creatinine of 0.9 mg/dl, serum sodium levels of 108 mmol/L, potassium of 4.5 mmo/L. His thyroid and hepatic profile was within normal limits. His chest X-ray was normal. In view of low

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serum sodium, we investigated for serum Osmolality which was 268 mOsm/kg, urine Osmolality was 158 mOsm/kg and urine sodium was 24 mmol/L. In this patient, hyponatremia associated with decreased osmolality with inappropriately increased urine osmolality, natriuresis, normal thyroid and adrenal function, absence of renal, hepatic, or cardiac disease makes the diagnosis of SIADH.

His computerized tomography scan of Brain revealed disproportional enlargement of the temporal horns of the lateral ventricles with diffuse periventricular and confluent white matter signal changes (Fig. 1).

His sodium was corrected with 3% and normal saline infusion in due course. He became oriented, as well as unsteadiness and giddiness also improved. He did not undergo neurosurgical intervention due to financial constraint, hence was subjected to therapeutic lumbar puncture where 20 ml of CSF was drained which was under normal pressure after which there was subjective improvement in the patient's symptoms. There was no recurrence of hyponatremia after treatment with 3% and normal saline along with CSF drainage by lumbar puncture. Patient had partial improvement in cognition, his gait and urinary incontinence also improved. Blood chemistry became normal.

DISCUSSION

This patient developed hyponatremia because of SIADH which was part of NPH, a relatively rare form of hydrocephalus especially in elderly. The temporal profile of symptomatology of this patient like forgetfulness, ataxia and urinary incontinence in the presence of characteristic ventriculomegaly from the brain imaging was diagnostic of NPH.

Essential diagnostic criteria for the diagnosis of SIADH are:

- serum sodium < 135 mmol/L;
- decreased measured plasma osmolality (< 275 mOsm/kg);
- urinary osmolality > 100 mOsm/kg during Hypotonicity;
- clinical euvolemia;
- no clinical signs of contraction of extracellular fluid (e.g. no orthostasis, tachycardia, decreased skin turgor or dry mucous membranes);
- no clinical signs of expansion of extracellular fluid (e.g. no edema or ascites);
- increased urinary sodium excretion > 30 mmol/L with normal dietary salt and water intake;
- normal thyroid and adrenal function determined by both clinical and laboratory assessment;
- no recent use of diuretic agents.

Supporting diagnostic criteria are:

- plasma uric acid < 4 mg/dL;

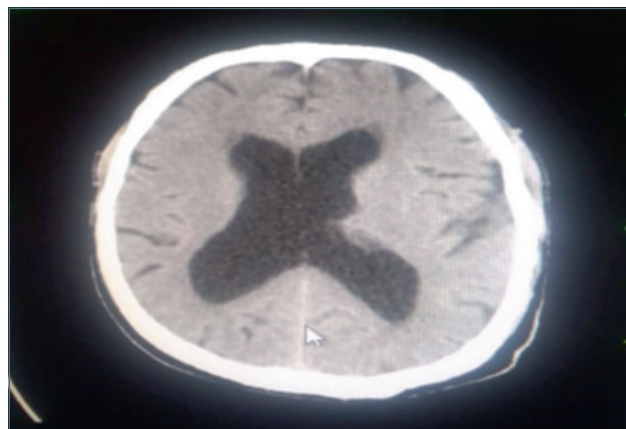


Figure 1. Computerized tomography scan of Brain showing disproportional enlargement of the temporal horns of the lateral ventricles.

- blood urea nitrogen < 10 mg/dL;
- fractional sodium excretion > 1%;
- fractional urea excretion > 55%;
- failure to improve hyponatremia after 0.9% saline infusion;
- improvement of hyponatremia with fluid restriction⁴.

In this patient hyponatremia was accompanied by decreased osmolality with inappropriately increased urine osmolality, natriuresis, normal thyroid function, absence of renal cardiac and hepatic disease, a classical feature of SIADH and NPH was tenable.

Hyponatremia due to SIADH in a patient with NPH is thought to be result from the mechanical pressure on the hypothalamus from the third ventricle. Possible explanation for this hypothesis is that many patients with NPH show response to CSF shunting¹³.

In conclusion SIADH, an extremely rare metabolic manifestation of NPH should be considered whenever a hyponatremia is considered especially in elderly.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Drug hypersensitivity cutaneous diseases in the elderly

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The worldwide increase of life expectancy, changes in immunological capacity, comorbidities and polytherapy are responsible for the increasing prevalence of geriatric drug related allergic skin diseases. In the elderly other factors contribute to the onset of these phenomena, such as changes in the structure of the skin and mucous tissues. The integrity of the epithelial barrier in old people is compromised by the loss of its constituents, that predisposes to alterations of the hydrolipidic film with dryness, xerosis and pruritus. Also at the skin level are frequently found abnormal immunological reactions towards new antigens and a chronic inflammatory state that predisposes to a response oriented towards the Th2 cytokinic pattern, allowing allergens to penetrate into tissues. Nevertheless, in the elderly drug related allergic disorders, in particular at the skin level, are often underdiagnosed and difficult to treat.

Among the IgE mediated cases, urticaria and angioedema are frequent. However, there are also cell-mediated mechanisms; in particular delayed type reactions to drugs often arise in the elderly for the reiterate use of topical medications (anesthetic, antibiotic and anti-inflammatory creams).

A detailed anamnestic history is essential to establish the causal link between an adverse drug reaction and the specific drug. Moreover, in some cases it is necessary the specific knowledge of the histological picture.

Key words: Drug allergy, Drug hypersensitivity, Elderly

INTRODUCTION

During senescence important changes contribute to the fragility of the elderly skin. In particular, the production of type 1 collagen is reduced during senescence; its reduction is responsible for the skin thinning and for the worsening of skin functions. Fibroblasts present an alteration in the spread due to the fragmentation of the collagen fibers, secondary to an increase in the synthesis of prostaglandin E2¹.

The decrease in the activity of fibroblasts can also be responsible for the elasticity rupture of the elderly skin that appears atrophic, with thinning of the dermal papillae, also due to the loss of hydration and to the changes in the blood flow; it can also lead to the reduced production of

sebum, sweat glands atrophy and immune responses modification².

Therefore aged skin appears atrophic, with notes of dryness, fragility, alterations in pigmentation, roughness and greater tendency to xerosis. These factors affect the health conditions of the elderly skin, with a marked increase in infectious, autoimmune or neoplastic diseases. In addition, these anatomical and functional changes in the skin district predispose to the appearance of cutaneous drug allergic diseases^{3,4}.

In the elderly the skin becomes particularly sensitive to the action of the sun rays with consequent increase of erythema, photo-dermatitis or photo-contact dermatitis and neoplastic skin lesions.

Photosensitivity phenomena in the elderly are particularly

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relevant for the frequent use of drugs. In fact, phototoxic reactions may occur after intake of common orally administered drugs such as diuretics, cardiac agents and antidiabetics. Photo-contact dermatitis is due to perfumes and other agents contained in topical medications used by the elderly. Actinic dermatitis, the most disturbing disorder of this type, should be reported⁵.

Hypersensitivity drug reactions (type B) can be classified, depending on the timing of the reaction, as immediate and delayed. Conventionally, immediate drug reactions occur within one hour after drug intake but may occur also several hours after the exposure. Delayed reactions occur more than 24 hours after exposure. The different time of onset generally implies different pathogenic mechanisms. Non-life-threatening cutaneous adverse drug reactions are frequent and include allergic contact dermatitis (ACD), urticaria, macopapular exanthema/morbilliform eruptions, photo-distributed drug reactions, fixed drug eruptions⁶.

CUTANEOUS ADVERSE DRUG REACTIONS

ALLERGIC CONTACT DERMATITIS

The alteration of the barrier function is responsible for the onset of ACD, an inflammatory dermatitis, intensely itchy, characterized by erythemato-vesicular lesions with a tendency to desquamation or to lichenification. Controversial is the datum concerning the number of Langerhans cells, although, more frequently in the literature it is reported that their percentage would not decrease in senile age. Above all CD4+ and CD8+ lymphocytes seem to contribute to the immune response immunology in the ACD with IL-17 production and lymphocytic infiltrate at the site of the lesion. In the elderly the main haptens responsible for ACDs are nickel, perfume and balsam of Peru in addition to topical medications, including antibiotics, anti-inflammatory ointments, anesthetics and corticosteroids, frequently used for the treatment of skin ulcers or other skin diseases. It is always advisable to perform targeted allergy tests using patch test indicated by national or regional medical societies (e.g. SIDAPA series). Differential diagnosis must be addressed to other dermatology diseases including scabies, seborrheic dermatitis, psoriasis, stasis dermatitis and atopic dermatitis^{7,8}.

URTICARIA

Few studies have examined the prevalence of hives in the elderly and the causes that more frequently support the appearance of urticaria. Furthermore, nowadays there are no specific protocols for the diagnosis and the treatment of urticaria in the subjects over 65 years old. With particular reference to EAACI/GA2LEN/EDF/WAO guidelines hives are distinct as “acute” and “chronic” and classified

as “spontaneous” or “induced” depending on whether it manifests itself spontaneously or it is caused by inducible stimuli. Cutaneous lesions are characterized by the transient appearance of smooth, slightly elevated plaques (wheals), intensely itchy and sometimes associated with angioedema. When etiology is not identified, diagnosis of chronic spontaneous urticaria (CSU) is made.

In general, the pathogenesis of CSU is difficult to detect, also if a percentage between 0.5 and 1% suffers from CSU and at least a quarter of the population has experienced hives during its lifetime. It occurs more frequently in the female sex with an incidence equal to about double. In turn, acute urticaria is a clinical manifestation of immediate drug hypersensitivity reactions.

Some authors^{9,10} take into consideration the possible correlation between urticaria-angioedema syndrome, comorbidity and polypharmacy in elderly population and reports that in this range of age urticaria is more tied to some internist pathologies including autoimmune diseases, neoplasms, immune-proliferative diseases, diabetes and thyroid disorders. Moreover, in the elderly population the incidence of urticaria is greater if patients take a number of drugs higher than three. This last aspect is related to the degranulation of mast cells induced by drugs, both with immunological and non-immunological mechanisms and to the changes in pharmacokinetics related to age, especially in patients who take drugs that block angiotensin receptors¹¹⁻¹³.

Non-steroidal anti-inflammatory drugs (NSAIDs) are responsible for a large spectrum of hypersensitivity reactions and are considered the first or second cause of hypersensitivity reactions to drugs. Acute skin diseases induced by NSAIDs comprise: i) NSAIDs-exacerbated cutaneous disease (NECD) induced by aspirin or other NSAIDs manifesting as wheals and/or angioedema occurring in patients with a history of chronic spontaneous urticaria; ii) NSAIDs-induced urticaria/angioedema (NIUA); induced by NSAIDs manifesting as wheals and/or angioedema occurring in subjects without history of chronic spontaneous urticaria; iii) Single-NSAID-induced urticaria/angioedema or anaphylaxis (SNIUAA) that is an immediate hypersensitivity reactions to a single NSAID or to several NSAIDs belonging to the same chemical group, manifesting as urticaria, angioedema and/or anaphylaxis. NECD and NIUA are determined by ciclo-oxygenase 1 inhibition while SNIUAA is considered an IgE-mediated reaction¹⁴ (Fig. 1).

ANGIOEDEMA

Regarding angioedema, also defined as Quincke's angioneurotic angioedema, it is generally drug-dependent in the elderly patients. There are many drugs that can play a role, including NSAIDs, angiotensin converting enzyme inhibitors (ACEis), radiocontrast means, angiotensin II



Figure 1. Generalized urticaria induced by ibuprofen intake.

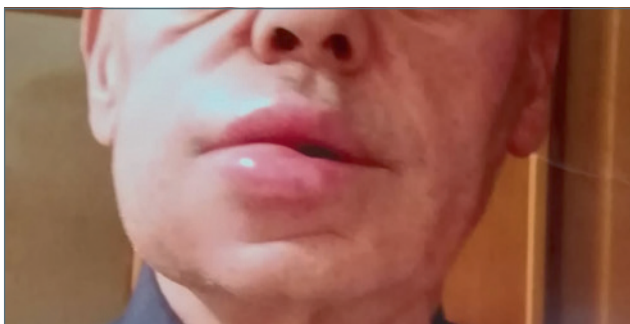


Figure 2. Angioedema of the lips induced by enalapril intake.

receptor antagonists, antibiotics, proton pump inhibitors, statins, fibrinolytic agents, estrogens, diuretics, calcium antagonists, beta blockers and psychotropic drugs (serotonin reuptake inhibitors).

Angioedema may occur in 0.1 to 0.7% of treated patients. It affects the head, neck, face, lips, tongue and larynx with potentially lethal upper airway edema. It can also be resistant to treatment and be fatal (Fig. 2).

The mechanism in patients taking ACEi is due to ACE inhibition, which blocks the conversion of angiotensin, reduces the bradykinin catabolism and increases its activity. The decreased activity of aminopeptidase P and dipeptidyl peptidase P in the degradation pathways of substance P also seems to play a role.

Acquired C1 inhibitor deficiency (AAE-C1-INH) can occur in older patients and it is due to the activation of the classic pathway of the complement system accelerated by the catabolism of C1-INH due to neoplasms of lymphatic tissue or autoimmune diseases.

The prevalence of angiotensin converting enzyme inhibitor of angioedema (AE-ACEi) is relatively high, between 0.1-2.2% and should be suspected in all patients with AE who are receiving ACEi. Normal levels of complement factors help to strengthen the clinical suspicion and to exclude the possibility of AE with C1-INH deficiency. These data suggest that in these cases a careful evaluation of the patient's drug therapy should be encouraged (especially for aspirin and ACEi), besides the evaluation of autoimmune or neoplastic diseases ¹⁵.

EXANTEMATOUS, MORBILLIFORM OR MACULOPAPULAR ERUPTIONS

These clinical entities represent 95% of all cutaneous drug eruptions. Their clinical features consist of erythematous papules and macules than can become confluent and widespread. Low fever, mild eosinophilia and pruritus can be present. It generally occurs 4-14 days after drug discontinuation. The onset may be faster in previously sensitized patients.

FIXED DRUG ERUPTION

The clinical presentation is an unique itchy, round, well-circumscribed, erythematous macule or dusky plaque on the skin or on the mucosal surfaces (Fig. 3). Infrequently a small number of macules can be present. The lesions recur on the same area in case of re-exposure to the same offending drug. It is generally benign with the exception of the uncommon severe generalized bullous subtype ⁶.

SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS)

SCARs encompass several hypersensitivity drug reactions and are mediated by type IV reactions according to Gell and Coombs classification. They include Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), drug reactions with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP).

Most common offenders are allopurinol (the highest agent in Europe, China and USA), aromatic anticonvulsivants, antibiotics, sulphonamides and oxicam NSAIDs ⁶.

Stevens-Johnson syndrome/toxic epidermal necrolysis This spectrum of conditions is one of the most common among SCARs (prevalence 1-7 per million) and is associated with high mortality (up to 40%). It is characterized by cutaneous detachment, blisters, necrosis and erosive



Figure 3. Fixed drug eruption.

mucositis of more than 2 districts. It can be preceded by macules and widespread flat target lesions. Early painful erythema of palms and feet is a typical feature. Fever and influenza-like symptoms may be present. In SJS the affected skin area is less than 10%, in TEN the detachment involves more than 30%. In between lies the SJS/TEN overlap syndrome^{6,16}. The onset is usually 4-28 days after the start of the offending drug¹⁷.

Erythema multiforme mayor is usually associated to viral infections and only a minority of cases seems to be associated with drug reactions. It differs from SJS/TEN for the distribution of target lesions which affect acral areas (Figs. 4-5). Chronic kidney disease and the use of diuretics is associated with an increased risk of allopurinol-induced SJS/TEN. Liver disease and HIV infection may be a risk factor of SJS/TEN. A recent Portuguese study observed a significant association between in-hospital mortality consequent to SJS/TEN and advanced age and liver disease. In this study the median age of the affected patients was 63 years and the main drug classes responsible of SJS/TEN were antibiotics, uric metabolism drugs, anticonvulsants and antivirals. Moreover, advanced age is a risk factor included in SCORTEN (SCORE of Toxic Epidermal Necrosis) severity scale¹⁶.

DRUG REACTIONS WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS

DRESS is one of the most common SCARs with an estimated prevalence of 1-4 per million. The eruption is most commonly urticaria-like or an exanthema. The onset is usually 2-6 weeks after the initiation of drug therapy. Fever, facial and acral edema, lymphadenopathy, leucocyte abnormalities (leukocytosis, eosinophilia and/or atypical lymphocytosis), hepatitis, non erosive mucositis, nephritis, pancreatitis, pneumonitis and myocarditis have been reported. It can be associated with reactivation of human herpesvirus-6 and -7 and Epstein-Barr virus. Advanced age and renal failure are risk factors for DRESS. Mortality rate is estimated at 10%⁶.



Figure 4. Erythema multiforme mayor associated to viral infections.

ACUTE GENERALIZED EXANTEMATOUS PUSTULOSIS

Non-follicular, sterile pustules and erythema are typical clinical signs of AGEP. Mucosal surfaces are also involved in 20-25% of patients with AGEP. It may include fever, leukocytosis, neutrophilia, eosinophilia and hypocalcemia, hepatitis, renal insufficiency and respiratory distress. The onset is typically 1-2 days after the start of the offending drug. Its prevalence is estimated 0.35-5 per million. Mortality is lower than 5%¹⁷.

CONCLUSIONS

In conclusion, drug allergic reaction at skin level is an emerging problem in geriatric age. The structural changes in old cutaneous physiology can favor the onset of atopic dermatitis, ACD, urticaria and angioedema. Furthermore,



Figure 5. Target lesions induced by drug intake.

the use of numerous drugs and immune system modifications predispose to drug-induced adverse reactions, the incidence of which is directly correlated with the number of pathologies that elderly people are suffering from¹⁸. “Danger signs” of delayed cutaneous drug reactions are intense facial involvement, atypical target or bullous lesions, epidermolysis, hemorrhagic necrotizing lesions, purpura, widespread dark-red erythema, extensive pustulosis, painful skin, mucosal involvement, generalized lymphadenopathy, epatopathy, nephropathy¹⁹. Management of drug hypersensitivity reactions include prompt diagnosis, removal of the culprit drug and early treatment.

CONFLICT OF INTEREST

All authors have no conflict of interest according to the content of this manuscript.

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