Medizinische Fakultät

der
Universität Duisburg-Essen

Aus der Klinik für Neurologie,
Lehrstuhl für vaskuläre Neurologie,
Demenz und Altersforschung / NeuroScienceLab

Optimizing geriatric patient care via screening for risk of functional decline

I n a u g u r a l – D i s s e r t a t i o n
zur
Erlangung des Doctor of Philosophy (PhD)
durch die Medizinische Fakultät
der Universität Duisburg-Essen

Vorgelegt von
Dr. rer. nat. Janine Gronewold

aus
Ratingen
2021

DOI: 10.17185/duepublico/75910
URN: urn:nbn:de:hbz:465-20220609-090726-9

Dekan:	Herr Univ.-Prof. Dr. med. J. Buer
1. Gutachter/in:	Herr Univ.-Prof. Dr. med. D. M. Hermann
2. Gutachter/in:	Herr Prof. Dr. med. P. Heuschmann
3. Gutachter/in:	Herr Priv.-Doz. Dr. med. J. Benninghoff

Tag der mündlichen Prüfung: 26. April 2022

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1 INTRODUCTION

1.1 Overarching introduction of the research project

Due to advances in medical care and improved living and working conditions, life expectancy is increasing in Germany. According to the Federal Statistical Office of Germany, the current life expectation of newborns is 79 years for males and 83 years for females and is expected to increase.(Statistisches Bundesamt) In combination with lower birth rates, increased life expectancy leads to an aging population. The number of older people >65 years increased from 12 million in 1991 to currently about 18 million. Especially the number of very old people >85 years doubled from 1.2 million to 2.4 million.(Statistisches Bundesamt) Thus, older people come into focus of our health care system. The probability of becoming diseased increases with age. Both the number of diseased persons and the complexity of disease increases with age. According to the 2005 German microcensus, every 4th person ≥75 years was diseased or hurt due to trauma at that time.(Statistisches Bundesamt, 2006) Cardiovascular diseases,(Statistisches Bundesamt, 2008) musculoskeletal diseases and falls,(Statistisches Bundesamt, 2008) and psychiatric diseases like dementia and depression(Robert Koch-Institut, 2005; Weyerer and Bickel, 2007) are the most common diseases in older people. The latter also often suffer from multiple and especially chronic diseases (multimorbidity), which interact in a complex way leading to functional decline, lack of autonomy and reduced quality of life.(Bundesministerium für Familien, Senioren, Frauen und Jugend (BMFSFJ), 2002) According to the *Bundes-Gesundheitssurvey* 1998, men and women aged 60-79 years had on average 3 diseases.(Robert Koch-Institut, 2003) In the *Berliner Gesundheitsstudie*, 54% of all women and 41% of all men aged ≥85 years suffered from >1 disease.(Kruse and Schmitt, 2002) Older people and even medical staff without geriatric qualification often have problems to distinguish symptoms of normal aging from disease. Consequently, diseases are often overlooked in the older population. Medical and nursing interventions have different intentions and effects in older compared to younger persons. The major focus is often not healing the disease but restoring everyday functions to maintain autonomy in older persons. Older persons are characterized by restricted resources for recovery due to multimorbidity. Medical interventions thus need to consider interactions with other diseases and interventions. Beside restricted healing and recovery possibilities, physicians are confronted with restricted diagnostic possibilities.(Böhm *et al.*, 2009) Dementia patients, for example, poorly tolerate sleep laboratory diagnostics.(Hodgson and Safi, 2016) Consequently, reliable and valid screening methods to identify diseases that increase the risk of functional decline in older people are needed.

1.2 Introduction publication 1

Especially when entering the hospital environment due to an acute health event, older people are at a high risk of functional decline. The latter implies a decline in the ability to perform activities of daily living because of reduced physical, cognitive or emotional functioning during and after hospitalization, which may only be partly due to the acute illness.(Creditor, 1993; Sager *et al.*, 1996; Inouye *et al.*, 2000; Dendukuri *et al.*, 2004) Hospital routine care concentrates on diagnostic and therapeutic interventions targeting the acute illness, while comorbid geriatric problems leading to functional decline are often overlooked. Outcomes of older patients can be improved by comprehensive geriatric assessment (CGA) and subsequent intervention.(McCusker

et al., 2001; Ellis *et al.*, 2011) However, geriatric wards and geriatric counseling is still scarce in Germany. Because of these limited resources, careful selection of patients who will benefit from geriatric care is important. The Identification of Seniors at Risk (ISAR)(McCusker *et al.*, 1999) tool is the most frequently used screening to identify such people at risk of functional decline.(Warnier *et al.*, 2016) ISAR was developed in community-dwelling subjects ≥65 years who were admitted to the emergency departments of acute-care hospitals in Canada(McCusker *et al.*, 1999) and later adapted(Warburton *et al.*, 2004) to predict adverse health outcomes including death, admission to a nursing home or long-term hospitalization, or a clinically significant decrease in functional status. ISAR consists of 6 questions with yes/no answers assessing functional dependence (premorbid and acute change), recent hospitalization, impaired memory, impaired vision, and polypharmacy. In case of ≥2 “yes” answers, the screening is positive, indicating an increased risk for adverse health outcomes.(Sutton *et al.*, 2008) The Federal Association of Geriatrics, the German Society for Gerontology and Geriatrics, and the German Geriatrics Society suggested ISAR screening followed by CGA in case of positive screening for the emergency setting,(Thiem *et al.*, 2012) which was also recommended in the *Krankenhausplan NRW* 2015 by the *Ministerium für Gesundheit, Emanzipation, Pflege und Alter*.(Ministerium für Gesundheit, Emanzipation, Pflege und Alter, 2015) Although developed and validated for the emergency department, it was suggested to further test validity of ISAR screening in other settings such as internal medicine wards, which are less fast-paced and distressing for older patients probably increasing screening accuracy.(Hoogerduijn *et al.*, 2007; Beaton and Grimmer, 2013) To close this gap, we introduced ISAR screening followed by CGA conducted by a geriatric liaison service team consisting of a geriatrician, an occupational therapist and a psychologist, in older patients admitted to internal medicine departments of the University Hospital Essen.(Scharf *et al.*, 2019)

1.3 Introduction publication 2

There is still no consensus on the ideal content of geriatric assessments.(Krupp and Frohnhofen, 2019) The *Arbeitsgruppe Geriatrisches Assessment* suggested to assess the dimensions mobility, activities of daily living, cognition, and emotion with the Timed Up and Go, Barthel-Index, Mini-Mental State Examination (MMSE), and 15-item version of the Geriatric Depression Scale (GDS) or comparable tests.(Arbeitsgruppe Geriatrisches Assessment (AGAST), 1995) Recent studies revealing a high prevalence of sleep disorders and the utmost importance of sleep quality and quantity for physical and mental health undermine the necessity of including sleep assessment as a routine component of geriatric care and research.(Luyster *et al.*, 2015; Frohnhofen *et al.*, 2020) The Epworth Sleepiness Scale (ESS)(Johns, 1991; Johns and Hocking, 1997) is mostly used to assess excessive daytime sleepiness(Kendzerska *et al.*, 2014) as main symptom of sleep disorders such as sleep disordered breathing (SDB).(Slater and Steier, 2012) The ESS is a simple self-report questionnaire based on retrospective reports of the likelihood of dozing off or falling asleep from 0 (never) to 3 (high chance) in 8 different situations (sitting and reading, watching TV, sitting inactively in a public place like theatre or meeting, sitting in a car, lying down to rest, sitting and talking to someone, sitting quietly after lunch, driving a car). Since the ESS has been developed and validated in middle-aged community-dwelling subjects,(Johns, 1991; Johns and Hocking, 1997) especially older persons with physical or mental disabilities might face the problem that situations like sitting in a theatre or driving a car are not encountered any more. In line with this hypothesis, previous studies showed that questions regarding these situations are not answered by a high number of older, multimorbid

patients, leading to a high number of missing values(Frohnhofen *et al.*, 2009; Onen *et al.*, 2013) and possibly falsely low ESS sum scores which underestimate daytime sleepiness and prohibit further diagnostics to detect the cause of excessive daytime sleepiness. In a study by Frohnhofen et al., missing responses in the ESS were associated with higher functional and cognitive impairment.(Frohnhofen *et al.*, 2009) However, it remained elusive whether completing the ESS represents a valid response in geriatric subjects. So far, studies assessing the validity of the ESS for detecting SDB in geriatric patient samples are missing. Based on previous studies, especially physical and mental disabilities associated with ageing might represent the main reasons for missing ESS responses.(Spira *et al.*, 2011; Beaudreau *et al.*, 2012; Skibitsky *et al.*, 2012; Onen *et al.*, 2013; Ulander *et al.*, 2013; Frohnhofen *et al.*, 2020) Thus, we applied the ESS along with overnight polygraphy in a sample of geriatric in-patients suffering from mostly mild dementia and rather high functional impairment.(Gronewold *et al.*, 2019) Since SDB is an emerging risk factor for dementia and functional decline, but polysomnography diagnostics is timely, costly and often not feasible in the geriatric patient group, it is especially important to screen for SDB followed by innovative further diagnostics such as contactless sensors in case of positive screening.(Kagawa *et al.*, 2016)

1.4 Introduction publication 3

Despite the known negative consequences of sleep disorders for physical and mental health, a screening tool for daytime sleepiness as main symptom of many sleep disorders, is missing for older people. The ESS, which is most often used to screen for daytime sleepiness in clinical routine and research,(Kendzerska *et al.*, 2014) is not valid in older people, especially in those exhibiting physical and mental disabilities.(Frohnhofen *et al.*, 2009; Onen *et al.*, 2013; Gronewold *et al.*, 2019) Lacking validity is most probably caused by older people not encountering some of the situations described in the ESS anymore. The pediatric setting faced the same problem as the geriatric setting. Here, the problem was solved by developing a version for children and adolescents (ESS-CHAD), which better fits the everyday life of this population.(Janssen *et al.*, 2017) Since a specific version for geriatric patients, who often suffer from physical or mental disabilities, was lacking, we developed such an alternative version of the ESS (ESS-ALT) together with the developer of the original ESS, Dr. Murray Johns.(Gronewold *et al.*, 2021)

2 KEY RESEARCH FINDINGS

2.1 Key findings publication 1

ISAR screening has not been used and validated outside the emergency department setting. Of 547 patients admitted to internal medicine wards of the University Hospital Essen (78.1±6.0 years old, 54.7% males), 58.1% had a positive screening result (ISAR score≥2, ISAR+).(Scharf *et al.*, 2019) Subsequent CGA was abnormal (defined as impairment of activities of daily living plus impairment in at least one of the domains mobility, cognition, and emotion) in 40.1%. Regarding single ISAR items, more than half of the total cohort showed recent hospitalization and polypharmacy, whereas premorbid functional dependence, acute change in functional dependence, impaired vision, and impaired memory were reported less often (Fig. 1). Regarding single domains of CGA, 47.3% had impaired activities of daily living, 35.6% impaired mobility, 54.4% impaired cognition, and 11.6% presented signs of depression. Of note, 51.9% of patients without prior dementia diagnosis had impaired cognition in CGA, and 11.4%

of patients without prior diagnosis of depression showed signs of depression. For the analysis of validity to predict risk of functional decline, we analyzed the association of ISAR and CGA results with the length of hospital stay, nursing and physiotherapy hours, risk of falls, and discharge disposition. ISAR+/CGA abnormal patients and ISAR+/CGA normal patients had significantly increased length of hospital stay (17.4±18.8 and 11.0±11.9 days) compared with ISAR- patients (9.6±11.5 days, both $p<0.001$, Fig. 2). ISAR+/CGA abnormal patients further received significantly more hours of nursing care (3.0±2.3) and physiotherapy (2.2±3.2) compared with ISAR- patients (2.3±4.5 and 0.7±2.0, both $p<0.001$) and ISAR+/CGA normal patients (2.0±1.2 and 1.2±4.3, both $p<0.001$, Fig. 2). In line with thorough patient management, only very few people fell during their hospital stay (n=19, 4.0%) with a significantly higher number of falls in ISAR+/CGA abnormal patients (n=10, 10.1%) than in ISAR- (n=5, 2.2%, $p=0.002$) and ISAR+/CGA normal (n=4, 2.8%, $p=0.016$) patients. Although most patients terminated their treatment regularly with discharge back home, fewer ISAR+/CGA abnormal patients terminated their treatment regularly with discharge back home (59.6%) than ISAR+/ CGA normal (78.5%, $p=0.002$) and ISAR- (78.2%, $p=0.056$) patients.

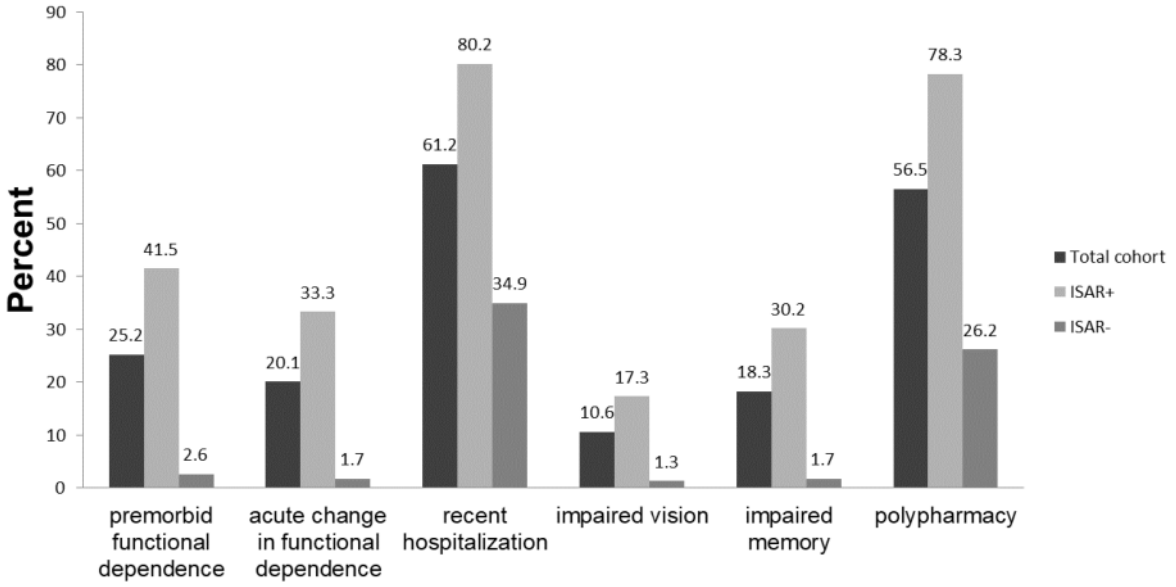

Figure 1. ISAR item responses for total cohort and separately for patients with positive (score≥ 2, ISAR+) and negative (score<2, ISAR-) screening result. ISAR, Identification of Seniors at Risk.

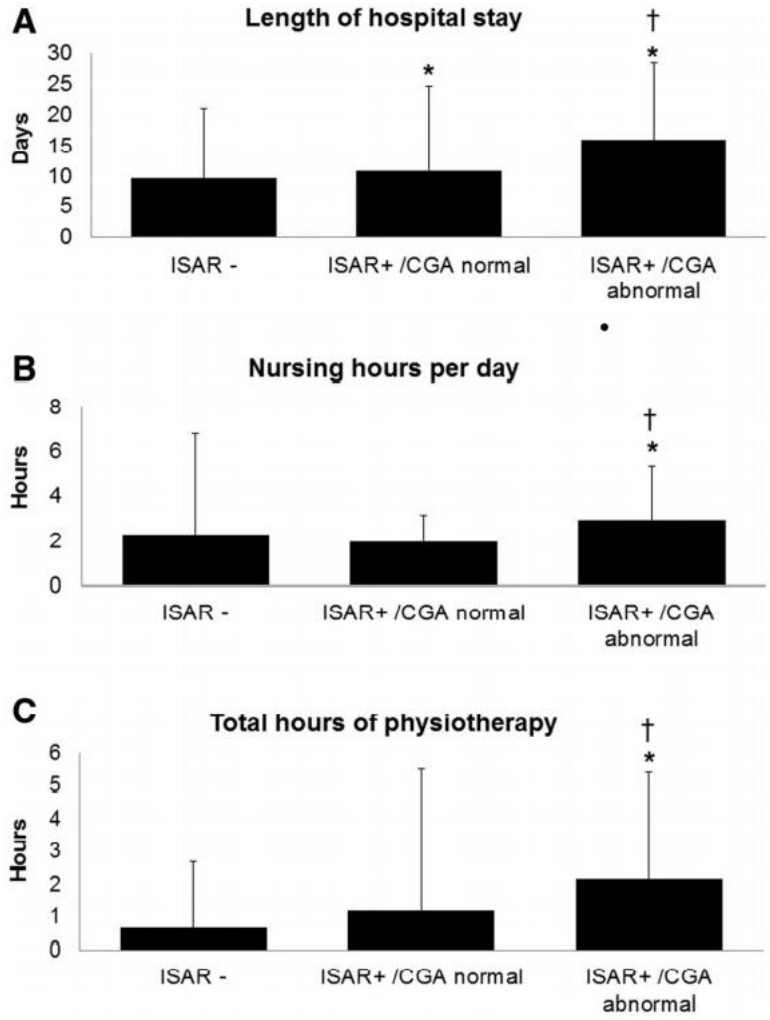

Figure 2. Association of ISAR and CGA results on length of hospital stay, nursing hours per day and total hours of physiotherapy during hospital stay. Data are shown as mean±standard deviation. CGA, Comprehensive Geriatric Assessment; ISAR, Identification of Seniors at Risk; ISAR+, positive ISAR screening (score≥2); ISAR-, negative ISAR screening (score<2); CGA abnormal, impairment of activities of daily living plus impairment in another domain of the CGA (mobility, cognition, emotion). *p≤0.05 compared to ISAR-, †p≤0.05 compared to ISAR+/CGA normal

2.2 Key findings publication 2

Screening for sleep disorders is not routinely included in geriatric risk assessments even though sleep disorders are frequent and lead to adverse health outcomes in older people. Especially SDB is an emerging risk factor for dementia. Overnight polygraphy in the patient room with a portable sleep apnea examination device and self-report questionnaires (ESS and *Essener Fragebogen Alter und Schläfrigkeit*), which were used to assess symptoms of SDB in 101 geriatric patients mostly with mild dementia recruited on German geriatric wards showed no significant association.(Gronewold *et al.*, 2019) When stratified by apnea-hypopnea index (AHI) category, the ESS score was similar in patients with AHI <5/h, indicating no SDB (median[Q1,Q3]=5.0[3.0, 9.0]), patients with 5/h≤ AHI <15/h, indicating mild SDB (median[Q1,Q3]=6.0[3.0, 9.0]) and patients with AHI≥15/h, indicating moderate to severe SDB (median[Q1,Q3]=6.0[2.0, 8.0]). Since excessive daytime sleepiness as main symptom of SDB is defined as ESS score >10, these results along with previous studies(Frohnhofen *et al.*, 2009; Onen *et al.*, 2013) indicate that the ESS is not suitable for geriatric patients. In addition to screening, further diagnostics of sleep disorders need to fulfill special requirements in

geriatric patients, especially those exhibiting cognitive deficits. Although polysomnography in the sleep laboratory is recommended for SDB diagnostics, it is often not tolerated in older people. This led to the recommendation that systems with a reduced number of channels should be used for screening purposes in geriatric patients at high SDB risk which are included in our cohort.(Netzer *et al.*, 2016; Mayer *et al.*, 2017) Even though we used a portable sleep apnea examination device in the patient room for overnight polygraphy, the nasal airflow sensor was not tolerated ≥6 hours, which is recommended for valid SDB diagnostics, in 72.3% of all patients. Patients who tolerated the nasal airflow sensor <6 hours were older (mean±SD=84.6±6.7 years), had worse cognition (MMSE score 21.0[16.5,24.5] and lower handgrip strength (12.5[9.0,20.5] kPa) than patients who tolerated the nasal airflow sensor for ≥6 hours (82.7±6.3, p=0.195; 23.5[18.3,25.0], p=0.210; 18.0[12.0, 24.8], p=0.014). Interestingly, the tolerant group showed more frequent nicotine abuse (10.7%) and coronary heart disease (39.3%), lower levels of folic acid (6.4[5.0, 7.7] µg/L), and more symptoms of depression (GDS score 5.0[3.5,7.5]) than the non-tolerant group (5.5%, p=0.051; 19.2%, p=0.070; 8.1[5.6,10.9] µg/L, p=0.021; 3.0[2.0,5.0], p=0.004). Higher levels of depressive symptoms and comorbidity in SDB could be associated with a higher motivation to tolerate diagnostic procedures to detect reasons for reduced emotional and physical well-being. Acceptance of pulse oximetry was higher than acceptance of nasal airflow sensor with about 38.6% tolerating measurement for ≥6 hours. Despite this low acceptance of SDB diagnostics, valid AHI calculation was possible in 81.2% of our study cohort by manual careful inspection and analysis of polygraphy data by an experienced sleep medicine expert. This analysis demonstrated a high prevalence of undetected SDB in our geriatric patient group with mostly mild dementia: only 12.2% had an AHI <5/h demonstrating absence of SDB (Fig. 3).

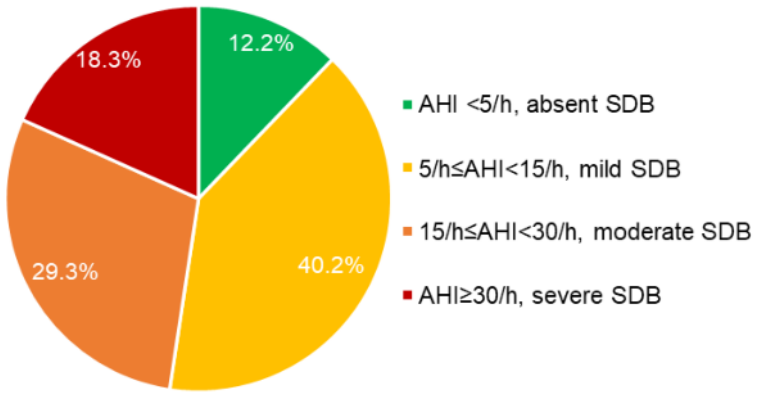

Figure 3. Prevalence and severity of SDB. SDB=sleep disordered breathing; AHI=apnea-hypopnea index

Positive airway pressure therapy improved cognitive performance in dementia patients in small preliminary studies(Ancoli-Israel *et al.*, 2008) and is generally suggested in case of at least moderate SDB (AHI ≥15/h), but can be considered in patients with mild SDB at high cardiovascular risk.(Netzer *et al.*, 2016; Mayer *et al.*, 2017) We therefore investigated associations of SDB severity (AHI<5/h, absent SDB; 5/h≤AHI<15/h, mild SDB; AHI≥15/h, moderate to severe SDB) with severity of impairment in cognitive function, observing modest associations with global cognitive function (Table 1 showing an excerpt of the cognitive tests results).

Table 1. Cognitive function also stratified by AHI category

Variables	Total (*n* = 101)	AHI<5/h (*n* = 10)	5/h≤AHI<15/h (*n* = 33)	AHI≥15/h (*n* = 39)	p
MMSE (score)	21.0(17.5;25.0)	23.5(20.8;26.0)	21.0(16.5;25.0)	21.0(19.0;25.0)	0.203
DemTect (score)	8.0(6.0;9.0)	11.0(7.0;14.0)	8.5(7.0;10.0)	7.0(6.0;9.0)	0.060
Clock drawing (score)	4.0(3.0;5.0)	3.5(2.0;4.3)	4.0(3.0;4.5)	4.0(3.0;5.0)	0.628
Trial Making Test (s)	90.0(51.5;159.8)	73.5(46.8;123.5)	82.5(52.0;176.3)	85.0(50.0;135.5)	0.824
Figural Memory Test (number of correct responses)	7.0(6.0;9.0)	8.0(7.0;9.5)	6.0(5.0;8.3)	8.0(7.0;9.0)	0.116
Timed Test of Money Counting (s)	34.0(13.0;70.5)	29.0(6.5;88.3)	23.0(12.0;55.5)	36.0(15.0;70.5)	0.510

All data are shown as median with 25th and 75th percentiles (median[Q1;Q3]). AHI=apnea-hypopnea index; MMSE=Mini-Mental State Examination; DemTect=Demenz-Detektions-Test

To sum up, our results show a high prevalence of SDB in geriatric patients with cognitive impairment. In combination with preliminary studies indicating that SDB treatment might prevent cognitive decline,(Bliwise, 2013) our results stress the need for valid screening and further diagnostic tools that match the specific requirements of older multimorbid patients often presenting with physical or mental disabilities.

2.3 Key findings publication 3

To meet the need of a valid screening tool for sleep disorders in geriatric patients, who often suffer from physical or mental disabilities, we adapted the ESS, which is the most often used screening questionnaire for daytime sleepiness, a main symptom of a variety of sleep disorders. Based on literature review and input from experts in sleep research and sleep medicine, as well as from nursing staff and patients, 9 alternative items to assess daytime sleepiness were identified.(Gronewold *et al.*, 2021) In a standardized expert survey including 35 participants of the 27th annual conference of the German Society for Sleep Research and Sleep Medicine (DGSM e.V.), these items were rated according to their adequacy to assess daytime sleepiness in older individuals (Table 2). Furthermore, the survey assessed problems experienced with the original ESS and asked for solutions.

Table 2. Expert opinion regarding alternative items to assess daytime sleepiness in older subjects

Item	Adequacy (%)				
	0 none	1 Slight	2 moderate	3 High	median
Sitting on a park bench	26.7	26.7	23.3	23.3	1
During lunch	16.1	12.9	22.6	48.4	2
During breakfast	12.9	16.1	22.6	48.4	2
Sitting and talking in a small group	3.3	10.0	20.0	66.7	3
During train ride	22.6	19.4	12.9	45.2	2
During restaurant visit	31.0	24.1	17.2	27.6	1
During family celebration	19.4	0.0	45.2	35.5	2
Sitting in a waiting room	3.1	6.3	15.6	75.0	3
Sitting and waiting for the bus	32.3	6.5	29.0	32.3	2

Based on the results of the expert survey, we selected the 8 original ESS and the 7 alternative items which received a median expert rating of at least moderate adequacy (median score ≥2; Table 2) for our pilot patient study. Additionally, we included an item referring to typical leisure activities of older individuals (crossword, Sudoku, parlor games) which was suggested by most of the expert survey participants. The pilot study with 52 in-patients ≥65 years of the geriatric department of the Alfried Krupp Hospital in Essen revealed that the original ESS item 3 “sitting inactively in a public place” and the original ESS item 8 “in a car while stopped” had a high number of missing responses (37% and 69%, respectively). These items were also identified as problematic in older patients in the expert survey. Consequently, we replaced these items by items that had a similar “somnificity”, that is a similar capacity to facilitate sleep onset in most persons, but less missing responses (Table 3). These items were “sitting in a waiting room” and “during lunch/during breakfast”. To match the ESS-CHAD and to have a set of ESS items as small as possible for different populations, we used the already validated ESS-CHAD item “sitting and eating a meal” instead of “during lunch/during breakfast”. Apart from showing similar somnificity, the items chosen for replacing the original ESS items also match by content: “sitting inactively in a public place” and “sitting in a waiting room” match because in both situations subjects sit passively, and “in a car while stopped” and “sitting and eating a meal” match because in both situations subjects engage in active motor behavior requiring high levels of alertness. The new version of the ESS with two original items replaced by new items (ESS-ALT) had fewer missing responses (23% vs. 73%) and higher internal consistency (Cronbach’s α = 0.64 vs. 0.23) than the original ESS, while keeping its original somnificity structure.

Table 3. Patient responses towards the original and new ESS items

Item	Chance of dozing off n(%)					Mean score (SD)
	0 never	1 slight	2 moderate	3 high	missing	
Original						
Sitting and reading	25(48.1)	6(11.5)	8(15.4)	8(15.4)	5(9.6)	0.98(1.19)
Watching TV	17(32.7)	13(25.0)	17(32.7)	4(7.7)	1(1.9)	1.16(0.99)
Sitting inactively in a public place	27(51.9)	3(5.8)	3(5.8)	0(0.0)	19(36.5)	0.27(0.63)
As a passenger in a car	36(69.2)	7(13.5)	5(9.6)	3(5.8)	1(1.9)	0.51(0.90)
Lying down to rest in the afternoon	8(15.4)	8(15.4)	12(23.1)	20(38.5)	4(7.7)	1.92(1.13)
Sitting and talking to someone	48(92.3)	3(5.8)	1(1.9)	0(0.0)	0(0.0)	0.10(0.36)
Sitting quietly after lunch	18(34.6)	15(28.8)	14(26.9)	4(7.7)	1(1.9)	1.08(0.98)
In a car while stopped	15(28.8)	1(1.9)	0(0.0)	0(0.0)	36(69.2)	0.06(0.25)
New						
During lunch	50(96.2)	2(3.8)	0(0.0)	0(0.0)	0(0.0)	0.04(0.19)
During breakfast	50(96.2)	2(3.8)	0(0.0)	0(0.0)	0(0.0)	0.04(0.19)
Sitting and talking in a small group	46(88.5)	5(9.6)	1(1.9)	0(0.0)	0(0.0)	0.13(0.40)
During train ride	12(23.1)	5(9.6)	8(15.4)	1(1.9)	26(50.0)	0.92(0.98)
During family celebration	49(94.2)	0(0)	1(1.9)	0(0.0)	2(3.8)	0.04(0.28)
Sitting in a waiting room	43(82.7)	4(7.7)	2(3.8)	0(0.0)	3(5.8)	0.16(0.47)
Sitting and waiting for the bus	28(53.8)	1(1.9)	1(1.9)	0(0.0)	22(42.3)	0.10(0.40)
During crossword, Sudoku or parlor games	32(61.5)	3(5.8)	3(5.8)	0(0.0)	14(26.9)	0.24(0.59)

3 DISCUSSION

3.1 Overarching discussion of the research project

In my research project, the need for screening for risk of functional decline to optimize geriatric patient care was revealed. In a sample of 557 older patients 78.1±6.0 years entering the internal medicine wards of the University Hospital Essen, more than half (58.1%) had a positive Identification of Seniors at Risk (ISAR) screening result. Of these patients screened for increased risk of functional decline, more than one third (40.1%) showed impairment of activities of daily living plus impairment in another domain (mobility, cognition, emotion) in the subsequent comprehensive geriatric assessment (CGA). As to patient health outcomes, patients with positive ISAR screening had a significantly longer stay in the hospital than patients with negative ISAR screening. Furthermore, patients showing impairment of activities of daily living plus impairment in another domain (mobility, cognition, emotion) of the CGA, which was defined as abnormal CGA, needed significantly more nursing care and physiotherapy. These patients less often terminated their hospital stay with a regular discharge back home compared to patients with a normal CGA.(Scharf *et al.*, 2019) Despite the acknowledged value of CGA for improving geriatric patient outcomes, there is still no consensus on what a CGA should include. In another sample including 101 geriatric patients with mostly mild cognitive but more advanced physical impairment, we observed a high prevalence of previously undetected sleep disordered breathing (SDB, 87.8%), which was not reproduced by results of subjective screening measures of daytime sleepiness as major symptom of SDB.(Gronewold *et al.*, 2019) Along with previous studies in geriatric patient samples, our results highlighted the need for a valid screening of daytime sleepiness in older patients. To meet this need, we developed an alternative version (ESS-ALT)(Gronewold *et al.*, 2021) of the Epworth Sleepiness Scale, which is the most often used screening questionnaire for excessive daytime sleepiness in clinical routine and research. In this alternative version, two original items with a high number of missing responses were replaced by items with similar capacity to facilitate sleep but lower number of missing responses. With the ESS-ALT, older multimorbid patients who often exhibit physical or mental disabilities and require further diagnostic workup for sleep disorders can be identified. Ideally, further diagnostics of sleep disorders are performed with novel contactless instruments in the patient's home for ambulatory patients or in the patient room in the hospital. This enables more valid diagnostics in a natural sleeping environment that is better tolerated and less costly. Currently, a variety of such devices is tested and will hopefully be available soon.

3.2 Discussion publication 1

The proportion of patients with positive ISAR screening in our study(Scharf *et al.*, 2019) is comparable to previous studies in emergency departments.(Edmans *et al.*, 2013; Asomaning and Loftus, 2014) To the best of our knowledge, this is the first study evaluating the predictive value of ISAR screening and CGA for hospitalized patients' health outcomes. Our findings indicate that ISAR screening alone may not be sufficient to identify the risk of functional decline in older hospitalized patients. Combining ISAR screening with CGA, however, enables the identification of patients who require longer hospital stay, more hours of nursing and physiotherapy, have a higher risk of falls and lower chances to terminate their treatment regularly. To conclude, ISAR could help to decide in a time-efficient and cost-efficient way, which patients should receive a CGA

and be targeted by geriatric interventions if needed.(Hoogerduijn *et al.*, 2010; van Loon *et al.*, 2017)

3.3 Discussion publication 2

The high prevalence of SDB observed in our study (88%)(Gronewold *et al.*, 2019) is in between the prevalence previously observed in a slightly younger population-based cohort (81%)(Ancoli-Israel *et al.*, 1991b) and a patient cohort with more severe dementia (89%).(Aoki *et al.*, 2014) Despite the high prevalence of SDB in our cohort, only 7% showed ESS scores >10 characterizing excessive daytime sleepiness, which indicates that the ESS may not be valid in patients with cognitive impairment.(Frohnhofen *et al.*, 2009) In contrast to previous studies, mostly observing a significant association between SDB severity and dementia severity,(Reynolds *et al.*, 1985; Hoch *et al.*, 1986; Ancoli-Israel *et al.*, 1991a; Aoki *et al.*, 2014) we only observed a low to moderate association which might be due to the inclusion of patient samples with more severe dementia in previous studies. Since SDB is often underdiagnosed in older multimorbid persons,(Lindberg and Gislason, 2000) our results in combination with previous literature suggest a potential role for SDB screening to detect a potentially reversible cause of cognitive impairment.(Yamout *et al.*, 2012; Emamian *et al.*, 2016)

3.4 Discussion publication 3

Similar to our study showing that only 27% of all geriatric inpatients were able to complete the ESS,(Gronewold *et al.*, 2021) a previous study with German geriatric inpatients showed that only 36% were able to complete the German version of the ESS.(Frohnhofen *et al.*, 2009) Also in geriatric outpatients, the French version of the ESS could be completed by only 40%.(Onen *et al.*, 2013) As in our study, both studies showed highest numbers of missing values for item 3 “sitting inactively in a public place” and item 8 “in a car while stopped”. Item 8 also showed inadequate psychometric properties in a large population-based study including women ≥70 years with an item-total scale correlation of only 0.26.(Beaudreau *et al.*, 2012) As a reaction, the ESS was also applied without item 8 in older individuals,(Kezirian *et al.*, 2009; Skibitsky *et al.*, 2012) or missing values were substituted by the median of subjects with the same sex and age.(Whitney *et al.*, 1998) When we replaced the two items showing low psychometric properties by two alternative items (“sitting in a waiting room” & “sitting and eating a meal”), which were identified in an expert survey and geriatric patient pilot study, this alternative version of the ESS (ESS-ALT) could be completed by 77% while keeping its original somnificity structure. Further studies assessing the validity of the ESS-ALT in different patient subsets like patients with obstructive sleep apnea and narcolepsy diagnosed in sleep laboratories have already begun. Additionally, we plan to study the improvement of predicting the risk of functional decline by the inclusion of the ESS-ALT into the comprehensive geriatric assessment.

4 ZUSAMMENFASSUNG

Aufgrund des demografischen Wandels ist das deutsche Gesundheitssystem mit einer steigenden Zahl älterer, multimorbider (geriatrischer) Patienten konfrontiert. Dieses Patientenklientel hat ein besonders hohes Risiko für negative Outcomes während und nach einem Krankenhausaufenthalt, welches nur bedingt mit der dem Krankenhausaufenthalt zugrundeliegenden Erkrankung zusammenhängt. Obwohl zunehmendes Interesse in der Identifizierung von Faktoren besteht, welche zu einem schlechten Outcome bei geriatrischen Patienten führen, gibt es nur wenig Evidenz, wie das Outcome dieser Patientengruppe durch optimiertes Risikoscreening verbessert werden kann. In meiner ersten Veröffentlichung konnte gezeigt werden, dass ein auffälliges Ergebnis im „Identification of Seniors At Risk“ (ISAR) Screening und im anschließenden umfassenden geriatrischen Assessment, welches die Bereiche Alltagsaktivitäten, Mobilität, Kognition, und Emotion beinhaltete, mit einem längeren Krankenhausaufenthalt, mehr Stunden an Pflege und Physiotherapie, höherer Anzahl an Stürzen und geringerem Anteil regulär beendeter Behandlungen bei älteren Patienten aus den Abteilungen für Innere Medizin am Universitätsklinikum Essen assoziiert war. Die genauen Inhalte des Risikoscreenings und geriatrischen Assessments sind jedoch bislang nicht festgelegt. In meiner zweiten Veröffentlichung konnten wir die Notwendigkeit identifizieren, bei geriatrischen Patienten auch auf Symptome von Schlafstörungen zu screenen. In einer Patientenstichprobe von den geriatrischen Stationen des Knappschaftskrankenhauses Essen hatten mehr als 80% Anzeichen für eine schlafbezogene Atmungsstörung, definiert durch einen Apnoe-Hypopnoe-Index ≥5/h. Allerdings waren die Maße zur Selbsteinschätzung von schlafbezogenen Atmungsstörungen nicht mit dem Apnoe-Hypopnoe-Index assoziiert, was darauf hinweist, dass valide Screeningfragebögen zu Schlafstörungen für geriatrische Patienten fehlen. Da die Epworth Schläfrigkeitsskala (ESS) am häufigsten verwendet wird, um subjektive Tagesschläfrigkeit als Symptom verschiedener Schlafstörungen zu erfassen, haben wurde die ESS in einer dritten Veröffentlichung an die Bedürfnisse von geriatrischen Patienten angepasst. In einer Expertenbefragung mit anschließender Pilotstudie an einer Patientenstichprobe der Station für Altersmedizin des Alfried Krupp Krankenhauses Essen identifizierten wir ungeeignete Items und ersetzten sie durch Items, die besser geeignet waren, Tagesschläfrigkeit bei geriatrischen Patienten zu erfassen. Item 3 „passiv in der Öffentlichkeit sitzen“ und Item 8 „als Fahrer eines Autos verkehrsbedingt einige Minuten halten müssen“ wurden in der Expertenbefragung als ungeeignet zur Erfassung von der Tagesschläfrigkeit bei geriatrischen Patienten identifiziert. Diese Items hatten auch die meisten fehlenden Antworten in der Patientenpilotstudie (37% bzw. 69%). Daher ersetzten wir diese Items durch Items, welche ähnliche schlafanstoßend bewertet wurden und weniger fehlende Antworten aufwiesen. In dieser finalen Version der alternativen ESS (ESS-ALT) wurde daher „passiv in der Öffentlichkeit sitzen“ durch „während Sie in einem Wartezimmer sitzen“ ersetzt und „als Fahrer eines Autos verkehrsbedingt einige Minuten halten müssen“ durch „Sitzen und eine Mahlzeit essen“. Die ESS-ALT konnte fehlende Antworten im Vergleich zur originalen ESS reduzieren (23% vs. 73%) und dabei die interne Konsistenz erhöhen (Cronbachs $\alpha = 0{,}64$ vs. 0,23). Zusammenfassend liefert mein Forschungsprojekt Hinweise für die Notwendigkeit eines geriatrischen Risikoscreenings, welches auch Symptome von Schlafstörungen umfassen sollte, um das Outcome geriatrischer Patienten zu verbessern.

5 SUMMARY

Due to demographic changes, the German health system is confronted with an increasing number of older, multimorbid (geriatric) patients. Even though there is increasing interest in understanding the role of geriatric problems for poor health outcomes, there is little information on how optimized geriatric risk screening can improve health outcomes of geriatric patients. In a first publication, we demonstrated that abnormal Identification of Seniors At Risk screening and Comprehensive Geriatric Assessment (including impairment of activities of daily living, mobility, cognition and emotion) results were associated with longer hospital stay, more hours of nursing and physiotherapy, higher number of falls and a lower percentage of regularly terminated treatments in older patients from internal medicine departments. However, the contents of geriatric risk screening and assessment are still a matter of debate. In a second publication, we identified the need to screen for symptoms of sleep disorders in a geriatric patient sample exhibiting mild mental and more advanced physical disabilities. Of note, more than 80% demonstrated some degree of sleep disordered breathing, defined by apnea-hypopnea index ≥5/h. However, self-report questionnaires of sleep disorders symptoms were not associated with apnea-hypopnea index, indicating that valid screening questionnaires of sleep disorders are lacking for geriatric patients. Since the Epworth Sleepiness Scale represents the most widely used self-report questionnaire to assess excessive daytime sleepiness, a major symptom of various sleep disorders, we adapted the ESS, which was developed and validated in community-dwelling adults, to better meet the needs of geriatric patients in a third publication. In an expert survey followed by a geriatric patient pilot study, we identified invalid items and replaced them by items better suited to assess daytime sleepiness in geriatric patients often exhibiting physical and mental disabilities. ESS item 3 “sitting inactively in a public place” and item 8 ”in a car while stopped” were identified as not adequate to assess daytime sleepiness in older multimorbid persons in the expert survey. These items also had the highest numbers of missing responses (37% and 69%, respectively). We replaced these items by items with a similar capacity to facilitate sleep but less missing responses in the patient pilot study. In the final version of this alternative ESS (ESS-ALT) to assess daytime sleepiness in geriatric persons, who often suffer from physical or mental disabilities, “sitting inactively in a public place” thus was replaced by “sitting in a waiting room” and “in a car while stopped” by “sitting and eating a meal”. The ESS-ALT had fewer missing responses (23% vs. 73%) and higher internal consistency (Cronbach’s $\alpha = 0.64$ vs. 0.23) than the original ESS in our sample while keeping its original somnificity structure. Conclusively, my research project provides evidence of the need for geriatric risk screening and assessment, which should also include symptoms of sleep disorders, to decrease the risk of adverse health outcomes and functional decline in geriatric patients.

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7 CURRICULUM VITAE

Der Lebenslauf ist in der Online-Version aus Gründen des Datenschutzes nicht enthalten

8 APPENDIX

8.1 Appendix 1. Publication 1

Scharf AC, Gronewold J, Dahlmann C, Schlitzer J, Kribben A, Gerken G, et al. Health outcome of older hospitalized patients in internal medicine environments evaluated by Identification of Seniors at Risk (ISAR) screening and geriatric assessment. BMC geriatrics. 2019;19(1):221.

8.2 Appendix 2. Publication 2

Gronewold J, Haensel R, Kleinschnitz C, Frohnhofen H, Hermann DM. Sleep-Disordered Breathing in Hospitalized Geriatric Patients with Mild Dementia and Its Association with Cognition, Emotion and Mobility. International journal of environmental research and public health. 2019;16(5).

8.3 Appendix 3. Publication 3

Gronewold J, Lenuck MCI, Gülderen I, Scharf AC, Penzel T, Johns MW, et al. Developing an Alternative Version of the Epworth Sleepiness Scale to Assess Daytime Sleepiness in Adults with Physical or Mental Disabilities. Gerontology. 2021;67(1):49-59.

Scharf et al. BMC Geriatrics (2019) 19:221
https://doi.org/10.1186/s12877-019-1239-3

BMC Geriatrics

RESEARCH ARTICLE Open Access

Health outcome of older hospitalized patients in internal medicine environments evaluated by Identification of Seniors at Risk (ISAR) screening and geriatric assessment

Anne-Carina Scharf[1*], Janine Gronewold[1], Christian Dahlmann[2], Jeanina Schlitzer[3], Andreas Kribben[4], Guido Gerken[5], Tienush Rassaf[6], Christoph Kleinschnitz[1], Richard Dodel[7], Helmut Frohnhofen[3,8] and Dirk M. Hermann[1*]

Abstract

Background: Hospitals are in need of valid and economic screening and assessment tools that help identifying older patients at risk for complications which require intensified support during their hospital stay.

Methods: Five hundred forty-seven internal medicine in-patients (mean age 78.14 ± 5.96 years; 54.7% males) prospectively received Identification of Seniors at Risk (ISAR) screening. If screening results were positive (ISAR score ≥ 2), a comprehensive geriatric assessment (CGA) was performed. We explored sensitivity and specificity of different ISAR and CGA cutoffs. Further, we analyzed the risk of falls and how patients got discharged from hospital.

Results: ISAR+/CGA abnormal patients spent more days in hospital (16.1 ± 14.5), received more nursing hours per day (3.0 ± 2.3), more hours of physiotherapy during their hospital stay (2.2 ± 3.2), and had more falls (10.1%) compared to ISAR+/CGA normal (10.9 ± 12.3, 2.0 ± 1.2, 1.2 ± 4.3, and 2.8%, respectively, all $p \leq 0.016$) and ISAR- (9.6 ± 11.5, 2.3 ± 4.5, 0.7 ± 2.0, and 2.2%, respectively, all $p \leq 0.002$) patients. ISAR+/CGA abnormal patients terminated their treatment regularly with being discharged back home less often (59.6%) compared to ISAR+/CGA normal (78.5%, $p = 0.002$) and ISAR- (78.2%, $p = 0.056$) patients. ISAR cutoff≥2 and CGA defined as abnormal in case of impairment of ADL plus another CGA domain achieved best sensitivity/specificity.

Conclusions: Abnormal geriatric risk screening and assessment are associated with longer hospital stay and higher amount of nursing and physiotherapy during hospital stay, greater risk of falling, and a lower percentage of successfully terminated treatment in older in-patients.

Keywords: ISAR, CGA, Older in-patients, Risk screening, Geriatrics, Internal medicine, Cutoff, Sensitivity, Specificity

Background

Due to ongoing demographic aging, hospitals face a constantly rising number of older patients with multimorbidity [1–3]. Although older people represent a challenge for the hospital setting, excellent medical attendance and high-quality care should be ensured. The use of screening tools allows for the identification of older patients at increased risk for poor health outcomes. Worldwide, geriatric societies demand the implementation of screening tools for the early identification of patients at increased risk for poor health outcomes [4–6]. The Identification of Seniors at Risk (ISAR) screening is one of the most commonly used tools with high sensitivity for the prediction of poor health outcomes in older patients entering emergency departments [7]. Created as a screening tool, ISAR requires a second-step diagnostic tool for patients with positive screening results. Comprehensive geriatric assessment (CGA) that evaluates impairments of activities of daily living (ADL), mobility, cognition, and mood as well

* Correspondence: anne-carina.scharf@uk-essen.de; dirk.hermann@uk-essen.de
[1]Department of Neurology, University Hospital Essen, University of Duisburg-Essen, Hufelandstraße 55, 45147 Essen, Germany
Full list of author information is available at the end of the article

as comorbidities is usually performed on patients with a positive screening result. Despite being only a diagnostic tool and not an intervention strategy, CGA preceded by ISAR screening has already been shown to reduce the risk for poor health outcomes in older patients attending emergency departments [8]. It further improves postoperative outcomes (mortality, delirium, and length of hospital stay) in older patients with colorectal carcinoma undergoing elective resection [9]. In addition, the probability of living at home one year after being released from hospital was about 16% higher in geriatric hospitalized patients undergoing CGA compared to those who received the usual care [1]. These data suggest that CGA leads to an improvement of individual patient health outcomes while lowering the costs associated with diseases, nursing, and health care [10].

Besides emergency department patients and in-patients undergoing surgery, patients admitted to internal medicine departments also challenge healthcare professionals to identify needs and risks for poor health outcomes. Since ISAR was originally designed as a screening tool in emergency departments, we herein extended ISAR's utility and used the ISAR for defining the health outcome of older hospitalized internal medicine patients. We sought to determine the association between ISAR screening (with CGA if positive on screening) and length of stay, nursing and physiotherapy hours, risk of falls, and discharge disposition among older adults admitted to internal medicine departments. In sensitivity analyses, we explored the sensitivity and specificity of different ISAR and CGA cutoffs for identifying outcomes among older adults admitted to internal medicine departments.

Methods

Study cohort

Patients admitted to internal medicine wards of the University Hospital Essen via emergency departments or as selective inpatient admission or being transferred from another ward or hospital from July 2015 to February 2017 were included in the present study if they received ISAR screening and were (a) ≥75 years of age in the Department of Gastroenterology and Hepatology and the Department of Cardiology and Angiology or (b) aged ≥65 years in the Department of Nephrology. Nephrological patients were included based on a younger age criterion as their biological age appears to be higher than their chronological age [11, 12]. We decided to apply ISAR in these three departments because these departments cover all significant geriatric patient groups in our University Hospital within the internal medicine specialty. ISAR screenings were conducted by the nursing staff on admission and were only missed when there was a lack of time, language barriers or incompliant patients. Those who were not given ISAR were excluded from any further analyses. In case of a positive ISAR screening result, CGA was performed by a geriatric liaison service usually the day following ISAR screening and 3 days after admission the latest. The geriatric liaison service of the University Hospital Essen consisted of a geriatrician, an occupational therapist, and a psychologist. In all subjects, patient histories involving information about comorbidities and vascular risk factors were taken from the electronical Hospital Information System Cerner medico. The study was approved by the ethics committee of the University Duisburg-Essen and need for consent was waived.

Measurement methods

ISAR

In this study, we utilized a version of ISAR by Warburton [13] validated for patients aged ≥75 years which was a modification of the original test by McCusker et al. [14]. The ISAR consists of six items, each being a simple yes-no question about the following domains: Premorbid functional dependence, acute change in functional dependence within the last 24 h, recent hospitalization within the last 6 months, visual impairment, impaired memory and polypharmacy (≥6 medications). The ISAR score ranges from 0 to 6 points, with a cutoff ≥2 interpreted as positive (abbreviated as ISAR+) and indicating increased risk for poor health outcomes.

CGA

Since there is an ongoing discussion on which geriatric impairments are associated with deteriorated health condition, we analyzed different definitions of an abnormal CGA, which included the Barthel index for the assessment of impairment of ADL [15, 16], the Timed Up & Go [17] and the Tinetti Mobility Test [18] measuring impairment of mobility, the Mini-Mental State Examination Test (MMSE) [19] and the Clock-Drawing Test [20] assessing impairment of cognition, and the Geriatric Depression Scale (GDS) [21, 22] for the assessment of signs of depression. The Barthel index is a questionnaire assessing daily competences in which patients can reach a maximum score of 100 and scores < 90 are interpreted as abnormal [23]. Mobility was rated as impaired if Timed Up & Go was ≥20 s [24] or if patients had scores < 20 in the Tinetti Mobility Test [25]. Impaired cognition was defined as MMSE ≤27 [26, 27] or Clock-Drawing Test ≥3 [20] and a GDS score ≥ 6 [28] was interpreted as a sign of depression. If not noted differently, we interpreted CGA as abnormal in this study if Barthel index and one other domain (mobility, cognition, or signs of depression) were impaired (abbreviated as ISAR+/CGA abnormal) as suggested by Campbell et al. [29].

Health outcome variables

As indicators for poor health outcomes, we analyzed length of hospital stay, nursing hours per day, physiotherapy workload, falls during the hospitals stay, and type of discharge from hospital using data obtained from the electronical

Table 1 Characteristics of the total cohort also split by ISAR and CGA results

	Total ($n = 547$)	ISAR- ($n = 229$; 41.9%)	ISAR+/CGA normal ($n = 145$; 26.5%)	ISAR+/CGA abnormal ($n = 97$; 17.7%)	*p*-value ISAR+/ CGA normal vs ISAR-	*p*-value ISAR+/ CGA abnormal vs ISAR-	*p*-value ISAR+/CGA abnormal vs ISAR+/CGA normal
Age (years)	78.1 ± 6.0	77.9 ± 5.4	77.0 ± 5.9	80.5 ± 6.5	0.259	**0.001**	**<0.001**
Sex (male)	299 (54.7)	122 (53.3)	96 (66.2)	43 (44.3)	**0.013**	0.118	**<0.001**
Anemia	152 (27.8)	55 (24.0)	51 (35.2)	29 (29.9)	**0.019**	0.336	0.318
Chronic kidney disease	240 (43.9)	86 (37.6)	75 (51.7)	43 (44.3)	**0.007**	0.327	0.194
Heart failure	106 (19.4)	39 (17.0)	35 (24.1)	16 (16.5)	0.140	0.999	0.263
Coronary heart disease	213 (38.9)	90 (39.3)	51 (35.2)	45 (46.4)	0.511	0.329	0.142
Atrial fibrillation	174 (31.8)	62 (27.1)	47 (32.4)	37 (38.1)	0.293	**0.050**	0.412
Other cardiac arrhythmias	70 (12.8)	23 (10.0)	18 (12.4)	17 (17.5)	0.498	0.097	0.354
Valve insufficiency	196 (35.8)	78 (34.1)	53 (36.6)	39 (40.2)	0.738	0.213	0.423
Chronic obstructive pulmonary disease	69 (12.6)	25 (10.9)	17 (11.7)	15 (15.5)	0.867	0.277	0.448
Peripheral artery disease	76 (13.9)	27 (11.8)	22 (15.2)	21 (21.6)	0.348	**0.040**	0.237
Arterial hypertension	430 (78.6)	175 (76.4)	113 (77.9)	80 (82.5)	0.704	0.311	0.626
Diabetes	171 (31.3)	71 (31.0)	45 (31.0)	33 (34.0)	0.999	0.606	0.676
Hyperlipoproteinemia	269 (49.2)	96 (41.9)	79 (54.5)	55 (56.7)	**0.025**	**0.011**	0.694
Nicotine abuse	82 (15.0)	34 (14.8)	25 (17.2)	11 (11.3)	0.561	0.484	0.202
Obesity	116 (21.2)	46 (20.1)	29 (20.0)	23 (23.7)	0.999	0.463	0.427
History of myocardial infarction	56 (10.2)	23 (10.0)	9 (6.2)	13 (13.4)	0.255	0.443	0.073
History of pulmonary embolism	11 (2.0)	2 (0.9)	4 (2.8)	3 (3.1)	0.378	0.070	0.447
History of stroke	56 (10.2)	14 (6.1)	16 (11.0)	15 (15.5)	0.116	**0.006**	0.255
History of thrombosis	49 (9.0)	19 (8.3)	10 (6.9)	12 (12.4)	0.695	0.306	0.179
Hyperthyroidism	24 (4.4)	15 (6.6)	1 (0.7)	5 (5.2)	**0.007**	0.802	**0.042**
Hypothyroidism	84 (15.4)	30 (13.1)	30 (20.7)	11 (11.3)	0.081	0.859	0.118
Dementia	37 (6.8)	4 (1.7)	9 (6.2)	16 (16.5)	0.067	**<0.001**	**0.005**
Alcohol abuse	19 (3.5)	6 (2.6)	7 (4.8)	2 (2.1)	0.261	0.999	0.317
Depression	30 (5.5)	9 (3.9)	5 (3.4)	7 (7.2)	0.999	0.265	0.236
Anxiety disorder	2 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	0.999	0.999	0.999
Parkinson's disease	6 (1.1)	3 (1.3)	2 (1.4)	0 (0.0)	0.999	0.557	0.515
Polyneuropathy	40 (7.3)	13 (5.7)	10 (6.9)	14 (14.4)	0.825	**0.009**	**0.028**
Cancer	215 (39.3)	89 (38.9)	73 (50.3)	21 (21.6)	**0.041**	**0.003**	**<0.001**
Cataract	33 (6.0)	8 (3.5)	13 (9.0)	6 (6.2)	**0.036**	0.371	0.472
Presbycusis	21 (3.8)	8 (3.5)	4 (2.8)	7 (7.2)	0.773	0.161	0.128
Anal incontinence	3 (0.5)	1 (0.4)	2 (1.4)	0 (0.0)	0.562	0.999	0.515
Urinary incontinence	4 (0.7)	1 (0.4)	0 (0.0)	2 (2.1)	0.999	0.218	0.165
Pressure ulcers	24 (4.4)	1 (0.4)	4 (2.8)	14 (14.4)	0.075	**<0.001**	**0.002**
Rheumatism	24 (4.4)	11 (4.8)	5 (3.4)	4 (4.1)	0.609	0.999	0.999

CGA, comprehensive geriatric assessment; ISAR, Identification of Seniors at Risk; ISAR+, positive ISAR screening (score ≥ 2); ISAR-, negative ISAR screening (score < 2); CGA abnormal, impairment of ADL plus another domain of the CGA. In 318 ISAR+ patients, 242 CGAs were performed (76 missing due to transfer, discharge, foreign-language or incompliance of patients). Boldface values were significant at p <=0.05

Hospital Information System Cerner medico. Nursing hours were operationalized using the "Leistungserfassung in der Pflege", a scientifically valid tool documenting nursing workload (for further details see Gronewold et al. [30]).

We also reported the patients' type of hospital discharge. We classified if patients terminated their treatment regularly with being discharged back home or being transferred to further medical care. Further medical care was split into planned or unplanned subsequent readmission, transfer to other hospitals, and transfer to rehabilitation or nursing institution. We also indicated whether treatment was terminated against medical advice and if the patients died while in hospital.

Statistical analysis

Continuous data are presented as mean ± SD values, categorical data as counts (%). Comparisons between negative ISAR screening (ISAR-), ISAR+/CGA normal and ISAR+/CGA abnormal groups regarding demographic data, risk factors and comorbidities, number of falls, type of discharge, length of hospital stay, and nursing and physiotherapy hours were done with (1) one-way ANOVA followed by Games Howell post-hoc tests for normally distributed continuous data (age), (2) Kruskal-Wallis tests and post-hoc Mann-Whitney u test (corrected for multiple comparisons where needed) for not normally distributed continuous data (length of hospital stay, hours of nursing per day and physiotherapy during hospital stay) and (3) Pearson's chi-square or Fisher's exact tests for categorical data.

Since CGA is costly and time-consuming, screening instruments with high sensitivity and specificity for the identification of patients needing further risk assessment are needed. Thus, we analyzed the sensitivity and specificity of different ISAR cutoffs for the prediction of length of hospital stay (≥7 days), nursing (above median) and receiving physiotherapy (yes/no). Further, we used receiver operating characteristics (ROC) including the area under the curve (AUC) and confidence intervals as well as Youden's J statistics [sensitivity + specificity − 1]. Since there is no agreement on which tests a CGA should include and when a CGA should be interpreted as abnormal, we analyzed different definitions of an abnormal CGA. In line with published suggestions [31, 32], abnormal CGA was first defined as significant impairment of ADL combined with impairment of one other CGA test domain (cognition, mobility or signs of depression). In sensitivity/specificity analyses, we also evaluated alternative definitions. Again, we used these different alternative definitions of abnormal CGA for the prediction of length of hospital stay (≥7 days), nursing (above median) and receiving physiotherapy (yes/no) and calculated the Youden's J statistics.

P values ≤0.05 indicate statistical significance and are shown in bold in the tables. All statistics were performed using Statistical Packing for Social Science 22 (SPSS 22) for Windows (SPSS, Chicago, IL, U.S.A.).

Results

Study cohort

Demographic and medical data

Of 1329 patients fulfilling the above inclusion criteria (76.62 ± 6.3 years, 55.7% males), 547 patients (41.2%) received ISAR screenings. Patients receiving ISAR screenings were 78.1 ± 6.0 years old (54.7% males) and stayed in hospital for 11.22 ± 13.9 days, patients not receiving ISAR screening were slightly younger (75.66 ± 6.40 years, 56.5% males) and stayed in hospital considerably shorter for 8.96 ± 11.9 days. Of the 547 screened patients, 318 (58.1%) had a positive screening result (ISAR score ≥ 2). Of these patients, 242 (76.1%) received a subsequent CGA, which was abnormal in 97 (40.1%) patients. The 76 ISAR+ patients who did not receive CGA did not differ significantly from ISAR+ patients who received CGA on patients' characteristics in Table 1. Reasons for not performing a CGA despite positive screening results were transfer to another hospital or ward, discharge, foreign-language barriers or incompliance of patients.

Demographic and medical data including comorbidities and risk factors for the total cohort and split by ISAR and CGA results are shown in Table 1. Various diseases were coded as main medical diagnoses leading to hospital admission (Table 2). Nearly 80% of the cohort suffered from comorbid arterial hypertension and about half of the cohort suffered from hyperlipoproteinemia. Clinical diagnosis of dementia and depression known before the CGA had a rather low prevalence of 7 and 6% in the total cohort.

ISAR screening and CGA results

More than half of the total cohort showed recent hospitalization (61.2%) and polypharmacy (56.5%) whereas premorbid functional dependence (25.2%), acute change in functional dependence (20.1%), impaired vision (10.6%) and impaired memory (18.3%) were reported less often (Fig. 1). Looking at the domains affected, 47.3% of the total cohort had impaired ADL, 35.6% impaired mobility, 54.4% impaired cognition, and 11.6% showed signs of depression. Interestingly, even in patients without prior dementia diagnosis, 51.9% had impaired cognition in CGA and in patients without prior diagnosis of depression we found signs of depression in 11.4% in CGA.

Sensitivity and specificity analyses of different ISAR cutoffs for the prediction of length of hospital stay, nursing hours and physiotherapy

The ROC results for the ISAR screening for the prediction of a hospital stay ≥7 days, i.e., the precondition for geriatric rehabilitation in several countries including Germany, revealed an AUC = 0.593 (95% CI = 0.545–0.640), indicating poor discriminating ability of ISAR. Yet, compared to other cutoffs, the Youden's J index still revealed best performance for the ≥2 cutoff as suggested in the literature [33], with a

Table 2 Main medical diagnosis leading to hospital admission of the total cohort also split by ISAR and CGA results

	Total ($n = 547$)	ISAR- ($n = 229$)	ISAR+/CGA normal ($n = 145$)	ISAR+/CGA abnormal ($n = 97$)
Liver cancer	71 (13.0)	30 (13.1)	25 (17.2)	5 (5.2)
Renal transplantation	55 (10.1)	15 (6.5)	24 (16.6)	9 (9.3)
CKD (not dialysis-dependent)	38 (6.9)	17(7.4)	10 (6.9)	4 (4.3)
Peripheral artery disease	30 (5.5)	16 (7.0)	7 (4.8)	6 (6.2)
Aortic valve stenosis	25 (4.6)	6 (2.6)	4 (2.8)	9 (9.3)
CKD requiring dialysis	21 (3.8)	11 (4.8)	8 (5.5)	0 (0.0)
Arterial hypertension	19 (3.5)	12 (5.2)	3 (2.1)	2 (2.1)
Acute renal failure	19 (3.5)	7 (3.1)	3 (2.1)	5 (5.2)
Heart failure	17 (3.1)	6 (2.6)	3 (2.1)	5 (5.2)
Neoplasia of the gastrointestinal tract	14 (2.6)	9 (3.9)	4 (2.8)	0 (0.0)
Cholangiocarcinoma	13 (2.4)	6 (2.6)	3 (2.1)	1 (1.0)
Liver cirrhosis	10 (1.8)	3 (1.3)	5 (3.4)	1 (1.0)
Cholangitis	8 (1.5)	4 (1.7)	1 (0.7)	1 (1.0)
ST-segment elevation myocardial infarction	8 (1.5)	3 (1.3)	1 (0.7)	2 (2.1)
Aneurysm	8 (1.5)	8 (3.5)	0 (0.0)	0 (0.0)
Angina pectoris	8 (1.5)	5 (2.2)	1 (0.7)	0 (0.0)
Vasculitides	8 (1.5)	1 (0.4)	4 (2.8)	1 (1.0)
Infectious diseases	7 (1.3)	0 (0.0)	3 (2.1)	3 (3.1)
Diverticulosis	7 (1.3)	3 (1.3)	1 (0.7)	3 (3.1)
Non-ST-segment elevation myocardial infarction	7 (1.3)	4 (1.7)	0 (0.0)	2 (2.1)
Mitral valve stenosis or insufficiency	7 (1.3)	2 (0.9)	1 (0.7)	4 (4.3)
Bile duct strictures	6 (1.1)	3 (1.3)	1 (0.7)	0 (0.0)
Aortic dissection	6 (1.1)	2 (0.9)	1 (0.7)	2 (2.1)
Cholelithiasis	5 (0.9)	3 (1.3)	1 (0.7)	1 (1.0)
Gastrointestinal bleeding	5 (0.9)	4 (1.7)	0 (0.0)	0 (0.0)
Pancreatic cysts	5 (0.9)	3 (1.3)	1 (0.7)	0 (0.0)
Urinary tract infection	4 (0.8)	0 (0.0)	1 (0.7)	2 (2.1)

Data are total numbers complemented in brackets by frequencies. CGA, comprehensive geriatric assessment; ISAR, Identification of Seniors at Risk; ISAR+, positive ISAR screening (score ≥ 2); ISAR-, negative ISAR screening (score < 2); CGA abnormal, impairment of ADL plus another domain of the CGA; CKD, chronic kidney disease

true positive rate (sensitivity) of 0.643 and false positive rate (1-specificity) of 0.520 (Fig. 2).

The analysis of the predictive value for the ISAR in predicting nursing hours split by the median (≥2 h) exposed an AUC of 0.632 (95% CI = 0.583–0.682). The Youden's J index revealed a similar performance for an ISAR cutoff ≥2 and ISAR cutoff ≥3. However, sensitivity of the ISAR cutoff ≥3 was low, which is undesirable for a screening tool (Fig. 2). For the ISAR cutoff ≥2, the sensitivity was 0.696 with a false positive rate of 0.502.

Since only about one quarter of the total cohort (28.7%) received physiotherapy, we analyzed the predictive value of the ISAR score for receiving physiotherapy (yes/no) which resulted in an AUC of 0.603 (95% CI = 0.550–0.657), again with best performance for the ISAR cutoff ≥2 with a sensitivity of 0.691 and a false positive rate of 0.539.

Sensitivity and specificity analyses of different CGA abnormal definitions for the prediction of needs (length of hospital stay, nursing hours and physiotherapy)

The definition of an abnormal CGA in case of impairment of ADL plus one other test of the CGA was present in 40.9% of patients. This definition resulted in the best trade-off between sensitivity and false positive rate for the prediction of an increased length of hospital stay and receiving physiotherapy (Tables 3, 5). Only for the prediction of increased nursing, the definition of impairment of ADL plus impairment of cognition or signs of depression (alternative definition A, present in 33.1% of patients) achieved the best performance (Table 4). The definition of impairment of ADL plus impairment of mobility (alternative definition B, present in 28.5%) achieved the lowest performance for all outcomes (Tables 3, 4 and 5).

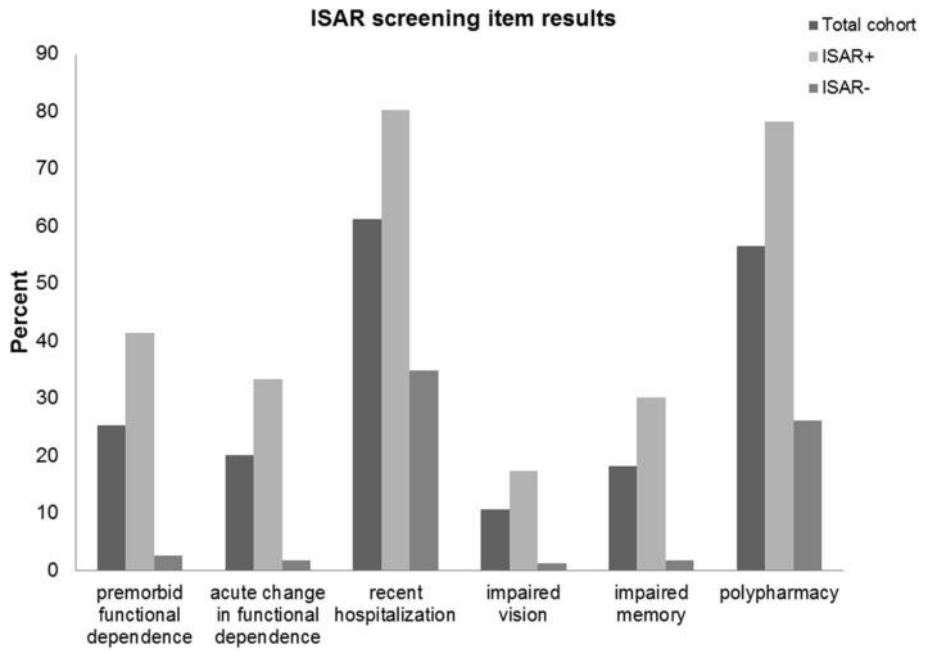


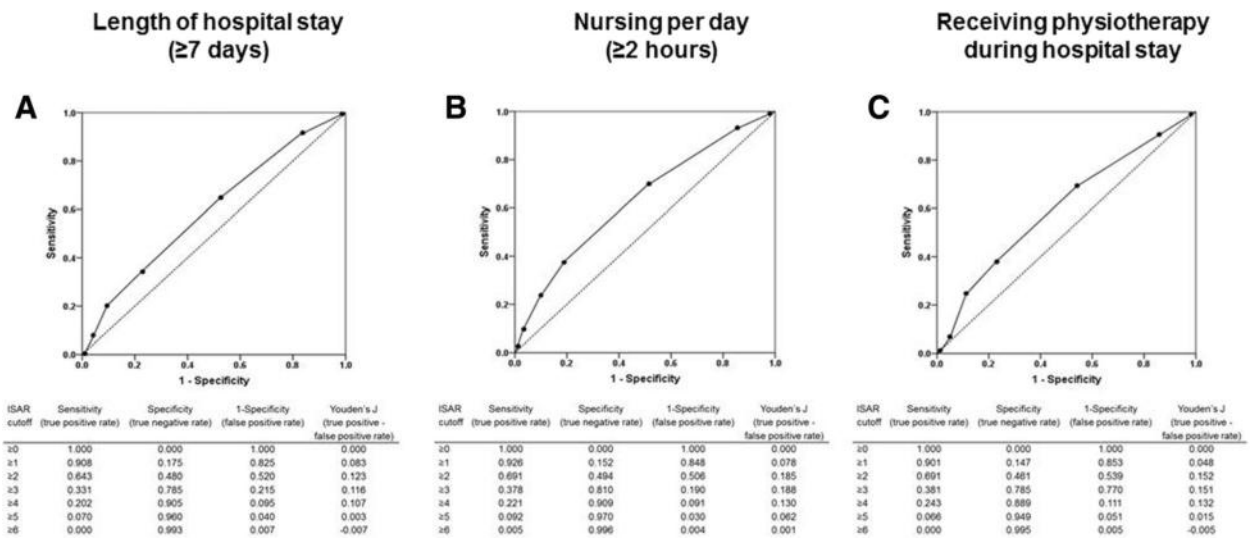
Fig. 1 "Identification of Seniors at Risk" items for total cohort and separately for patients with positive and negative ISAR screening result. ISAR, Identification of Seniors at Risk; ISAR+, positive ISAR screening (score ≥ 2); ISAR-, negative ISAR screening (score < 2)

Associations of ISAR and CGA results with health outcome (length of hospital stay, nursing and physiotherapy hours, incident fall and type of discharge)

Using the ISAR ≥2 cutoff and definition of abnormal CGA as impairment of ADL plus another domain, ISAR+/CGA abnormal patients and ISAR+/CGA normal patients stayed significantly longer in hospital (17.35 ± 18.80 and 10.95 ± 11.85 days) than ISAR- patients (9.60 ± 11.46 days, both comparisons $p < 0.001$, Fig. 3).

ISAR+/CGA abnormal patients also received significantly more hours of nursing care (2.98 ± 2.32) and physiotherapy (2.19 ± 3.19) than ISAR- patients (2.30 ± 4.46 and 0.67 ± 2.02, both $p < 0.001$) and ISAR+/CGA normal patients (1.97 ± 1.18 and 1.19 ± 4.30, both $p < 0.001$, Fig. 3).

Incident falls occurred in 4.0% ($n = 19$) of the total cohort with a significantly higher number of falls in ISAR+/CGA abnormal patients (10.1%, $n = 10$) than in



ISAR cutoff	Sensitivity (true positive rate)	Specificity (true negative rate)	1-Specificity (false positive rate)	Youden's J (true positive - false positive rate)
≥0	1.000	0.000	1.000	0.000
≥1	0.908	0.175	0.825	0.083
≥2	0.643	0.480	0.520	0.123
≥3	0.331	0.785	0.215	0.116
≥4	0.202	0.905	0.095	0.107
≥5	0.070	0.960	0.040	0.003
≥6	0.000	0.993	0.007	-0.007

ISAR cutoff	Sensitivity (true positive rate)	Specificity (true negative rate)	1-Specificity (false positive rate)	Youden's J (true positive - false positive rate)
≥0	1.000	0.000	1.000	0.000
≥1	0.926	0.152	0.848	0.078
≥2	0.691	0.494	0.506	0.185
≥3	0.378	0.810	0.190	0.188
≥4	0.221	0.909	0.091	0.130
≥5	0.092	0.970	0.030	0.062
≥6	0.005	0.996	0.004	0.001

ISAR cutoff	Sensitivity (true positive rate)	Specificity (true negative rate)	1-Specificity (false positive rate)	Youden's J (true positive - false positive rate)
≥0	1.000	0.000	1.000	0.000
≥1	0.901	0.147	0.853	0.048
≥2	0.691	0.461	0.539	0.152
≥3	0.381	0.785	0.770	0.151
≥4	0.243	0.889	0.111	0.132
≥5	0.066	0.949	0.051	0.015
≥6	0.000	0.995	0.005	-0.005

Fig. 2 Receiver operating characteristics of ISAR score for the prediction of **a**) hospital stay ≥7 days, **b**) nursing hours above the median in the cohort (≥2 h) and **c**) receiving physiotherapy during hospital stay. ISAR, Identification of Seniors at Risk

Table 3 Receiver operating characteristics of different CGA abnormal definitions for the prediction of increased length of hospital stay (≥7 days)

	Sensitivity (true positive rate)	Specificity (true negative rate)	1-Specificity (false positive rate)	Youden's J (true positive - false positive rate)
Impairment of ADL plus another domain	0.493	0.730	0.270	0.223
Alternative definition A: Impairment of ADL plus cognition impairment or signs of depression	0.415	0.790	0.210	0.205
Alternative definition B: Impairment of ADL plus mobility impairment	0.364	0.818	0.182	0.182

CGA comprehensive geriatric assessment

ISAR- (2.2%, $n = 5$, $p = 0.002$) and ISAR+/CGA normal (2.8%, $n = 4$, $p = 0.016$) patients.

Although in the total cohort most of the patients terminated their treatment regularly with discharge back home, fewer ISAR+/CGA abnormal patients terminated their treatment regularly with discharge back home (59.6%) compared to ISAR+/ CGA normal (78.5%, p = 0.002) and ISAR- (78.2%, $p = 0.056$) patients (see Table 6).

Discussion

While there is a growing interest in understanding the role of geriatric problems for poor health outcomes, there is little information on how geriatric risk screening followed by CGA affects health outcomes of patients hospitalized in internal medicine environments. We demonstrated that abnormal ISAR screening and CGA results were associated with longer hospital stay, more hours of nursing and physiotherapy, higher number of falls and a lower percentage of regularly terminated treatments. In line with previous suggestions [33], an ISAR cutoff ≥2 and the definition of an abnormal CGA as impairment of ADL plus impairment of another CGA domain best predicted patient health outcomes (length of hospital stay, nursing, and physiotherapy hours).

Almost 60% of our patient cohort had a positive ISAR screening, which is comparable to previous studies using similar patient cohorts from emergency departments. In 667 patients aged ≥70 years from emergency departments in the United Kingdom (mean age 80 years), 69% had a positive ISAR screening [34]. In 258 patients aged ≥65 years (mean age: 79 years) from a Canadian emergency department 61.2% screenings were positive [35]. About 40% of our cohort receiving CGA due to positive ISAR screening had an abnormal CGA defined as impairment of ADL plus another domain of the CGA.

In data from the Department of Orthopedics and Trauma Surgery of the University Hospital Essen, we observed a higher proportion of positive ISAR screenings and abnormal CGA results [30]. However, this study revealed similar associations of ISAR and GCA with length of hospital stay and amount of nursing hours indicating suitability of ISAR and CGA in different clinical specialties.

Our ROC results indicated a low discriminating ability of the ISAR tool for length of hospital stay, nursing hours and physiotherapy. This is in line with previous studies demonstrating that ISAR lacks sufficient prognostic validity for various short- and long-term outcomes [7] in contrast to the original development and validation study stating fair performance [36]. A Dutch study including 177 patients aged ≥65 years admitted to internal medicine departments, who were subjected to ISAR, showed sensitivity, specificity and AUC for functional decline measured by self-reported Katz ADL index of 92.9, 39.3% and 0.67, respectively [37, 38]. The different values, specifically for sensitivity, indicate that ISAR may be more suitable for predicting functional decline than length of hospital stay, nursing hours and physiotherapy. Since the present study is based on data available during hospital stay, information about long-term outcomes after the hospital stay including mortality, readmission to hospital or not being able to live at home independently is not available.

We must consider that we applied ISAR screening in internal medicine wards and not in emergency department

Table 4 Receiver operating characteristics of different CGA abnormal definitions for increased nursing per day (≥2 h)

	Sensitivity (true positive rate)	Specificity (true negative rate)	1-Specificity (false positive rate)	Youden's J (true positive - false positive rate)
Impairment of ADL plus another domain	0.556	0.731	0.269	0.286
Alternative definition A: Impairment of ADL plus cognition impairment or signs of depression	0.741	0.798	0.202	0.539
Alternative definition B: Impairment of ADL plus mobility impairment	0.364	0.818	0.182	0.182

CGA comprehensive geriatric assessment

Table 5 Receiver operating characteristics of different CGA abnormal definitions for receiving physiotherapy during hospital stay

	Sensitivity (true positive rate)	Specificity (true negative rate)	1-Specificity (false positive rate)	Youden's J (true positive - false positive rate)
Impairment of ADL plus another domain	0.651	0.730	0.270	0.381
Alternative definition A: Impairment of ADL plus cognition impairment or signs of depression	0.566	0.792	0.208	0.358
Alternative definition B: Impairment of ADL plus mobility impairment	0.457	0.797	0.203	0.254

CGA comprehensive geriatric assessment

setting, representing the original and validated setting. Including patients who were already hospitalized, we created a more homogenous patient cohort compared to emergency department setting. In the original studies by McCusker's group [8, 14, 36], only 35% of the tested emergency department patients were subsequently admitted to the hospital. Further, ISAR was designed for patients aged ≥65 years. In our study cohort inclusion criterion was in most cases an age of ≥75 years, again creating a more homogenous patient group. The low performance of ISAR in ROC analyses could therefore lead to a misclassification which could result in over- or underuse of medical resources.

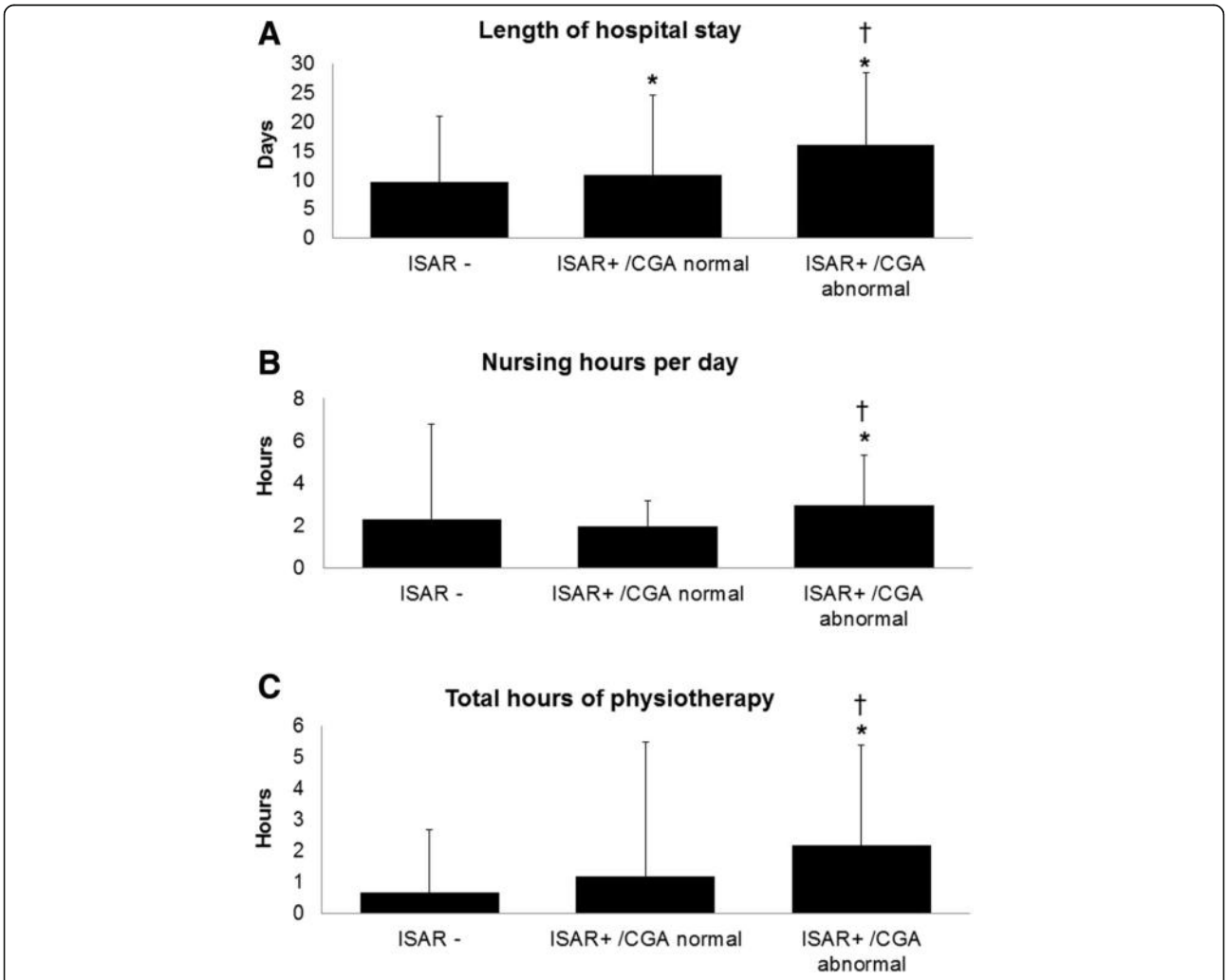


Fig. 3 Effects of ISAR and CGA results on length of hospital stay, nursing hours per day and total hours of physiotherapy during hopital stay. CGA, Comprehensive Geriatric Assessment; ISAR, Identification of Seniors at Risk; ISAR+, positive ISAR screening (score ≥ 2); ISAR-, negative ISAR screening (score < 2); CGA abnormal, impairment of ADL plus another domain of the CGA. *$p \leq 0.05$ compared to ISAR-, †$p \leq 0.05$ compared to ISAR+/ CGA normal

Table 6 Type of hospital discharge in the total internal medicine cohort

	ISAR- ($n = 229$; 48.6%)	ISAR+/CGA normal ($n = 143$; 30.4%)	ISAR+/CGA abnormal ($n = 99$; 21.0%)	*p*-value ISAR+/ CGA normal vs ISAR-	*p*-value ISAR+/ CGA abnormal vs ISAR-	*p*-value ISAR+/CGA abnormal vs ISAR+/CGA normal
Treatment terminated regularly	179 (78.2%)	113 (78.5%)	59 (59.6%)	0.056	0.133	**0.002**
Treatment terminated regularly, post-treatment planned	34 (14.8%)	17 (11.8%)	19 (19.2%)	0.097	0.715	0.073
Treatment terminated against medical advice	2 (0.9%)	0 (0.0%)	2 (2.0%)	0.999	0.999	0.438
Transfer to another hospital	6 (2.6%)	7 (4.9%)	10 (10.1%)	0.753	0.086	0.280
Death	4 (1.7%)	2 (1.4%)	3 (3.0%)	0.531	0.592	0.190
Discharge to rehabilitation institution	0 (0.0%)	3 (2.1%)	2 (2.0%)	0.137	0.098	0.999
Discharge to nursing institution	0 (0.0%)	0 (0.0%)	2 (2.0%)	0.999	0.315	0.438
Discharge or transfer with subsequent readmission	4 (1.7%)	1 (0.7%)	2 (2.0%)	0.999	0.677	0.999

Data are total numbers complemented in brackets by frequencies. CGA, comprehensive geriatric assessment; ISAR, Identification of Seniors at Risk; ISAR+, positive ISAR screening (score ≥ 2); ISAR-, negative ISAR screening (score < 2); CGA abnormal: impairment of ADL plus another domain of the CGA. Boldface values were significant at $p <= 0.05$

Of course, older patients with higher risk require the provision of a sufficient amount and quality of care which a relevant and indispensable cost factor in hospital and health management [39]. However, since medical resources are valuable but limited, ISAR, alone or combined with CGA, can only be a single element in a process leading to the allocation of patient support.

To the best of our knowledge, this is the first study evaluating the predictive value of ISAR screening and CGA for hospitalized patients' health outcomes in internal medicine departments. Based on our results, ISAR screening alone may not be suitable for identifying the needs of older hospitalized patients, whereas combination with CGA may allow for the detection of patients requiring longer hospital stay, requiring more hours of nursing and physiotherapy, exhibiting higher risk of falls and having a lower percentage of regularly terminated treatments. Thus, ISAR could help to decide time- and cost-efficiently, which patients should receive a CGA and subsequently be targeted by geriatric interventions [37, 40]. Our findings emphasize that ISAR screenings and CGA should be applied at the time point of a patient's hospitalization since positive screening and abnormal CGA was associated with more falls during the subsequent hospital stay. The initial use of screening tools is in line with previous recommendations of international geriatric societies [41, 42].

As major limitation, only 41.2% of all eligible patients in our cohort received ISAR screening which, although comparable to other screening implementation trials [35], may not allow truly representative statements for older patient populations, which raises the need for cautious data interpretation. Further limitations are intrinsic to the nature of the ISAR and CGA instruments. It needs to be questioned whether ISAR can reliably be applied to patients with cognitive impairment, which is a common phenomenon in older patient cohorts, since these patients may not answer the ISAR item about memory problems correctly. Furthermore, our CGA did not differentiate the nature of cognitive deficits, which in the setting of acute hospitalized patients may either be related to mild cognitive impairment, dementia or delirious states. Additional influencing factors, such as nutritional status, psychosocial factors or lack of social support, were not assessed. Patients with short hospital stays were under-represented in the cohort receiving ISAR screening followed by CGA. The low ISAR completion rate of 41.2% mirrors some key barriers in the implementation of new screening procedures which requires the compliance of both, patients and staff.

Conclusions

Abnormal geriatric risk screening and assessment are associated with longer hospital stay and higher amount of nursing and physiotherapy during hospital stay, greater risk of falling, and a lower percentage of successfully terminated treatment in older in-patients. An ISAR cutoff ≥2 and the definition of an abnormal CGA as impairment of ADL plus impairment of another CGA domain best predicted patient health outcomes in our study. Further efforts are urgently needed to optimize geriatric patient management. By increasing the awareness of health professionals, we should be able to establish improved health support procedures that may prevent unfavorable patient outcomes.

Abbreviations

ADL: Activities of daily living; AUC: Area under the curve; CGA: Comprehensive geriatric assessment; CI: Confidence interval; GDS: Geriatric Depression Scale; ISAR: Identification of Seniors at Risk screening; ISAR-: ISAR screening negative < 2; ISAR+: ISAR screening positive ≥ 2; ISAR+/CGA abnormal: ISAR screening positive ≥ 2, but abnormal results in CGA; ISAR+/CGA normal: ISAR screening positive ≥ 2, but normal results in CGA; MMSE: Mini Mental State Examination; SD: Standard deviation; SPSS 22: Statistical Packing for Social Science 22

Acknowledgements

We thank Mrs. Nickel-Gögel for her contribution to CGA. We also thank the nursing staff of the Department of Cardiology and Angiology, Department of Gastroenterology and Hepatology, and Department of Nephrology for conducting ISAR screenings upon hospital admission. We thank Mrs. Lucie Winkler for language editing the paper.

Authors' contributions

All authors read and approved the final version of the manuscript. ACS Data curation, Formal analysis, Methodology, Project administration, Visualization, Writing-original draft. JG Data curation, Formal analysis, Methodology, Project administration, Supervision, Visualization, Writing-original draft. CD Conceptualization Software, Project administration, Writing-review & editing. JS Data curation, Writing-review & editing. HF Conceptualization, Project administration, Writing-review & editing. AK Conceptualization, Project administration, Writing-review & editing. GG Conceptualization, Project administration, Writing-review & editing. TR Conceptualization, Project administration, Writing-review & editing. CK Conceptualization, Writing-review & editing. RD Conceptualization, Project administration, Writing-review & editing. DMH Conceptualization, Investigation, Methodology, Project administration, Supervision, Writing-original draft.

Funding

The authors receive no specific funding for this work.

Availability of data and materials

All relevant data are within the paper. If additional data is needed it can be made available from the ethical committee of the University Duisburg-Essen (ethikkommission@uk-essen.de) for researchers who meet the criteria for access to confidential data by contacting the corresponding author.

Ethics approval and consent to participate

The study was approved by the ethics committee of the University Duisburg-Essen, need for consent was waived and the study was performed in accordance to the Declaration of Helsinki.

Consent for publication

Since there are no details on individuals reported within the manuscript consent for publication was waived.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Neurology, University Hospital Essen, University of Duisburg-Essen, Hufelandstraße 55, 45147 Essen, Germany. [2]Nursing Headquarters, University Hospital Essen, University of Duisburg-Essen, Hufelandstraße 55, 45147 Essen, Germany. [3]Department of Nephrology, Geriatric and Internal Medicine, Alfried Krupp Hospital Ruettenscheid-Essen, Alfried-Krupp-Straße 21, 45131 Essen, Germany. [4]Department of Nephrology, University Hospital Essen, University Duisburg-Essen, Hufelandstraße 55, 45147 Essen, Germany. [5]Department of Gastroenterology and Hepatology, Faculty of Medicine, University Hospital Essen, University of Duisburg-Essen, Hufelandstraße 55, 45147 Essen, Germany. [6]Department of Cardiology and Vascular Medicine, West German Heart and Vascular Center, University Hospital Essen, Hufelandstraße 55, 45147 Essen, Germany. [7]Department of Geriatrics, University Hospital Essen, Germaniastraße 1-3, 45356 Essen, Germany. [8]Faculty of Health, Department of Medicine, University Witten-Herdecke, Witten, Germany.

Received: 18 March 2019 Accepted: 31 July 2019
Published online: 14 August 2019

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Publisher's Note

International Journal of
Environmental Research and Public Health

MDPI

Article

Sleep-Disordered Breathing in Hospitalized Geriatric Patients with Mild Dementia and Its Association with Cognition, Emotion and Mobility

Janine Gronewold [1], Robert Haensel [1,2], Christoph Kleinschnitz [1], Helmut Frohnhofen [2,3] and Dirk M. Hermann [1,*]

1 Department of Neurology, University Hospital Essen, University of Duisburg-Essen, Hufelandstraße 55, 45147 Essen, Germany; janine.gronewold@uk-essen.de (J.G.); robert-haensel@gmx.net (R.H.); christoph.kleinschnitz@uk-essen.de (C.K.)
2 Department of Nephrology, Geriatric and Internal Medicine, Alfried Krupp Hospital Ruettenscheid-Essen, Alfried-Krupp-Straße 21, 45131 Essen, Germany; helmut.frohnhofen@krupp-krankenhaus.de
3 Faculty of Health, Department of Medicine, University Witten-Herdecke, Alfred-Herrhausen-Straße 50, 58448 Witten, Germany
* Correspondence: Dirk.Hermann@uk-essen.de; Tel.: +49-201-723-2814

Received: 17 January 2019; Accepted: 5 March 2019; Published: 9 March 2019

Abstract: Sleep-disordered breathing (SDB) is an emerging dementia risk factor. Data on the prevalence of SDB in dementia patients and its association with cognitive impairment is so far only based on patients with severe dementia. In 101 geriatric patients mostly with mild dementia recruited on German geriatric wards, SDB was assessed during overnight polygraphy in the patient room with a portable sleep apnea examination device and associations of SDB severity with severity of impairment in cognitive and emotional function as well as mobility were investigated. We also elucidated which factors influence compliance of SDB diagnostics. In 82 of the 101 dementia patients (81.2%), SDB could be assessed. Of those, only 12.2% had an apnea-hypopnea index (AHI) < 5/h demonstrating the absence of SDB. 40.2% exhibited 5/h $\leq$ AHI < 15/h representing mild SDB, and 47.6% revealed an AHI $\geq$ 15/h representing moderate/severe SDB. Patients in these three AHI categories did not significant differ from each other in demographical and clinical characteristics. Patients with an AHI $\geq$ 15/h particularly often presented with heart failure and vitamin D deficiency. We observed a low to moderate association between severity of SDB and severity of dementia. Tolerance of the nasal airflow sensor of at least 6 h was present in less than one third of all patients. The tolerant group exhibited more symptoms of depression and higher physical fitness compared to the non-tolerant group. We observed a high prevalence of SDB also in geriatric patients with mild dementia underlining the importance of SDB screening in the elderly.

Keywords: sleep-disordered breathing; obstructive sleep apnea; dementia; cognition; emotion; mobility; sleep quality; geriatrics

1. Introduction

Sleep-disordered breathing (SDB) is an emerging dementia risk factor [1] but often remains undetected because patients report no subjective complaints like daytime sleepiness [2]. Although a causal relationship between SDB and dementia is not yet established, SDB is known to induce neurodegenerative changes as a consequence of sleep fragmentation and intermittent hypoxia [3]. In prospective population-based studies SDB was associated with increased risk for cognitive decline and dementia [4,5]. In small preliminary studies, positive airway pressure therapy, the gold standard for the treatment of obstructive sleep apnea, improved cognitive performance in dementia patients

with SDB [6]. Such empirical evidence supports the hypothesis that SDB might be a reversible cause of cognitive decline and that treatment of SDB, especially in the early stages of dementia when patients are still largely independent, may slow dementia progression [7]. From a clinical perspective, it is thus important to know the prevalence of SDB in patients with dementia in order to plan resources and treatment. Even though a high prevalence of dementia [8] and SDB [9] has been consistently shown in the general elderly population, their overlap remains poorly understood. Only a few studies have analyzed SDB prevalence in dementia patients as well as the association between cognitive impairment and SDB in dementia. So far, research was mostly conducted by a single research group within the San Diego nursing home studies [10]. These studies showed that 70% of 235 institutionalized dementia patients showed SDB (defined by five or more respiratory disturbances per hour of sleep in portable sleep recording) and that SDB severity was significantly associated with dementia severity. Additional studies recruited smaller sample sizes and also included only patients with severe dementia of mostly Alzheimer's pathology. In the majority of those studies, SDB severity was associated with dementia severity [10–13]. Only in one study including multiinfarct dementia patients, who were younger and exhibited lower levels of dementia than Alzheimer's disease patients [14], and in a subgroup of patients with both cognitive impairment and depressive symptoms [12], SDB severity was not significantly associated with dementia severity. SDB detection and treatment would however be especially important in the early dementia stages since SDB is suggested to further decrease cognitive function via intermittent hypoxemia. Consequently, we analyzed the prevalence and severity of SDB in mild dementia patients treated in a German geriatric unit and investigated associations with severity of cognitive impairment and additionally with impairments in emotional function and mobility, which are highly prevalent in the elderly. Since SDB is often underdiagnosed and instrumental laboratory diagnostics especially of obstructive sleep apnea has been shown to be difficult in dementia patients, we also elucidated which factors influence compliance of nasal airflow sensor as a central part for the detection of obstructive sleep apnea.

2. Materials and Methods

2.1. Subjects

One hundred and one (101) patients (70% women, age range 66–97 years, mean 84.1 years and SD 6.5 years) with a dementia diagnosis according to ICD10 (F00-03) and Mini-Mental state examination test scores $\leq$27, were recruited on the geriatric wards of the Knappschafts-Krankenhaus in Essen, Germany between November 2015 and April 2016. The study was approved by the ethical committee of the medical faculty of the University Duisburg-Essen and all participants or their legal representatives gave written informed consent.

2.2. Data Collection

2.2.1. Sleep Disordered Breathing

SDB was evaluated during overnight polygraphy in the patient room with a portable sleep apnea examination device (ApneaLink AirTM, ResMed Germany Inc., Martinsried, Germany). Apnea-hypopnea index (AHI) was calculated as mean number of all apnea classes (unclassified, central, mixed, obstructive) and hypopneas per hour in the evaluation period. Apneas were defined as reduction of airflow to 0–20% that lasts 10 s or longer up to 80 s using an average of the last five breath cycles in accordance with the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and associated Events [15]. Consistent with the AASM definition for the scoring of patients qualifying for positive airway pressure therapy reimbursement, hypopneas were scored when a flow reduction of at least 30% that lasts 10 s or longer up to 100 s was detected with a corresponding desaturation event of at least a 4% drop [15]. When no oximetry data was available, or was missing for a significant portion of the recording, ApneaLink software (ApneaLink AirTM, ResMed Germany Inc.,

Martinsried, Germany) scored hypopneas in case of a reduction in airflow of 50% lasting longer than 10 s. Average and lowest blood oxygen saturation (SpO2) were evaluated. (https://airview.resmed.com/resources/welcome-page/pdf/Apnealink-Air_clinical_guide_glo_eng.pdf) Screening results offered by the ApneaLink software were carefully checked by a certified sleep medicine physician with years of experience in sleep apnea screening in the geriatric setting (H.F.) and corrected if necessary using raw data.

2.2.2. Daytime Sleepiness

Daytime sleepiness was assessed by the self-report Epworth Sleepiness Scale (ESS) [16], and the German "Essener Fragebogen Alter und Schläfrigkeit" (EFAS) [17], which is designed as observational scale and completed by the nursing staff. The ESS describes eight activities people frequently engage in, and respondents rate their usual chances of dozing off or falling asleep in these situations on a scale from 0–3. ESS sum scores >10 indicate excessive daytime sleepiness. Since the ESS is not well suited for elderly frail people and people with serious cognitive impairment, we additionally used the German EFAS. The EFAS describes ten situations in which people usually should not be asleep and the nursing staff assessed how often persons were asleep in these situations as well as the severity of daytime sleepiness meaning the degree of impairment in everyday life in these situations on a scale from 0–3. EFAS score is created by multiplying the score of frequency and severity for the item with the highest scores in frequency and severity. EFAS scores >2 indicate at least moderate daytime sleepiness.

2.2.3. Demographic and Medical Characteristics

Education was assessed by interview of the patient or their legal representatives and classified as primary school, secondary school, or baccalaureate graduation. Information about hypertension, diabetes, hyperlipoproteinemia, smoking, renal insufficiency, coronary heart disease, heart failure, peripheral artery disease, history of stroke, and medication prescription was prospectively collected from patient records. Blood and urine samples were collected, which were analyzed in the hospital's central laboratory. Noninvasive tests included the measurement of systolic and diastolic blood pressure, and standardized height and weight measurement to calculate body mass index (BMI [kg/m^2]), overweight being defined as BMI $\geq$ 30 kg/m^2.

2.2.4. Cognitive and Emotional Function

Cognitive function was assessed by Mini-Mental state examination test (MMSE) [18], DemTect [19], clock-drawing test [20], Alzheimer's disease assessment scale–cognitive subscale (ADAS-cog) [21], trail making test (ZVT-G) and figural memory test (FT) from the German "Nürnberger Altersinventar" [22], Timed Test of Money Counting (TTMC) [23], and the German "Alters-Konzentrations-Test" (A-K-T), which measures the ability to concentrate in the elderly [24].

Emotional function was assessed by WHO-5 Well-Being Index [25], a score $\leq$50 indicates reduced well-being and can be regarded as sign of depression [26]. Depression was further assessed by the short form of the Geriatric Depression Scale (GDS) [27], a score $\geq$6 in the German version being interpreted as a hint towards depression [28].

2.2.5. Mobility

Mobility was assessed by Barthel index, which is a simple clinical index measuring the extent of independence in activities of daily living [29], by instrumental activities of daily living scale, which measures the extent of independence in more complex activities of daily living [30], timed Up & Go, a test of basic functional mobility [31], test of standing balance including side-by-side, semi-tandem and tandem stands [32], Tinetti mobility test, which measures static and dynamic balance [33], walking speed (meter per second during 10 s of walking), hand grip strength of the left and right hand measured with an hydraulic hand dynamometer (Saehan Corporation, Masan, South Korea), and number of frailty criteria fulfilled [34].

2.3. Statistical Analysis

Continuous data are presented as mean±SD values for normally distributed data and median (Q1; Q3) for non-normally distributed data, categorical data are presented as counts (%). Comparisons between AHI categories (AHI < 5/h, representing absent SDB, 5/h ≤ AHI < 15/h, representing mild SDB and AHI ≥ 15/h representing moderate/severe SDB) regarding demographic data, risk factors and comorbidities, daytime sleepiness, cognitive and emotional function, and mobility were done with (a) one-way ANOVA followed by Bonferroni post-hoc tests for continuous normally distributed data, and (b) Kruskal-Wallis-Test followed by Mann-Whitney-U-Test post-hoc tests for non-normally distributed data, and (c) Chi-square or Fisher's exact test for categorical data. In a sensitivity analysis, we also used an alternative AHI categorization focusing more on severe SDB (AHI < 5/h, representing absent SDB, 5/h ≤ AHI < 30/h, representing mild/moderate SDB and AHI≥30/h representing severe SDB). Comparisons between patients tolerating the nasal airflow sensor for at least vs less than 6 h were done with (a) *t*-test for continuous normally distributed data, and (b) Mann-Whitney-U-Test post-hoc tests for non-normally distributed data, and (c) Chi-square or Fisher's exact test for categorical data. Correlation between AHI and MMSE was calculated with Pearson correlation coefficient. *p*-values ≤0.05 indicate statistical significance. All above-mentioned statistics were performed using Statistical Package for the Social Science 22 (SPSS 22) for Windows (SPSS, Chicago, IL, USA). Based on the significant correlation of −0.37 between the Mattis Dementia Rating Scale and the respiratory disturbance index observed by the research group around Ancoli-Israel et al. within the San Diego nursing home studies [10], our power calculation showed that we needed a sample size of n = 52 to detect a correlation between cognitive function and SDB of this strength with a two-sided 5% significance level and a power of 80%. Power calculation was done with G*Power [35].

3. Results

In 82 of the 101 dementia patients (81.2%), AHI could be determined during overnight polygraphy according to the manufacturer's suggestions (https://airview.resmed.com/resources/welcome-page/pdf/Apnealink-Air_clinical_guide_glo_eng.pdf). Of those 82 patients, 10 patients (12.2%) had an AHI < 5/h, representing absent SDB, 33 patients (40.2%) had a 5/h ≤ AHI < 15/h, representing mild SDB, and 39 patients (47.6%) had an AHI ≥ 15/h representing moderate/severe SDB. Patients in those three AHI categories did not significant differ from each other in demographical and clinical characteristics (Table 1).

Descriptively, patients with an AHI ≥ 15/h more often suffered from heart failure, had lower levels of vitamin D, and were more often women. Even though nearly half of our cohort had at least moderate SDB, levels of daytime sleepiness were rather low with no significant differences between AHI categories (Table 2).

With most patients in the study cohort exhibiting mild dementia, there were no significant differences between AHI categories in neuropsychological tests (Table 3). Descriptively, patients with absent SDB showed better performance in the MMSE, DemTect, trail making test, and ADAS-cog memory subscale compared to patients with mild SDB and patients with moderate/severe SDB. When split by SDB severity (AHI < 5/h representing absent SDB, 5/h ≤ AHI < 15/h representing mild SDB, and AHI ≥ 15/h representing moderate/severe SDB) and dementia severity (MMSE ≥ 20 representing mild dementia, 10 ≤ MMSE < 20 representing moderate dementia, and MMSE < 10 representing severe dementia) as it was done in a previous study by Aoki et al. [11],we observed a low to moderate [36] but statistically non-significant association between severity of SDB and severity of dementia ($\chi^2(4) = 3.33$, $p = 0.521$, Cramer's V = 0.14, Figure 1). Since only few patients in our cohort showed moderate or severe levels of dementia ($n = 22$ with moderate dementia and $n = 5$ with severe dementia), we additionally did a correlation analysis using continuous AHI and MMSE scores, observing a low to moderate association (r = −0.214, $p = 0.054$).

Table 1. Demographic and clinical characteristics of the study cohort also split by AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h $\leq$ AHI < 15/h (n = 33)	AHI $\geq$ 15/h (n = 39)	p-Value
Age (years), mean ± SD	84.1 ± 6.5	84.7 ± 8.6	83.5 ± 5.4	84.1 ± 5.8	0.855
Male sex, n (%)	32 (31.7)	5 (50.0)	8 (24.2)	14 (35.9)	0.113
Academic degree, n (%)					0.289
Primary school	52 (52.0)	6 (60.0)	19 (59.3)	16 (41.0)	
Secondary school	42 (42.0)	4 (40.0)	10 (31.3)	21 (53.9)	
Baccalaureate	6 (6.0)	0 (0.0)	3 (9.4)	2 (5.1)	
Body mass index (kg/m^2), mean±SD	25.3 ± 5.7	23.9 ± 4.0	25.5 ± 6.1	27.0 ± 5.8	0.251
Overweight, n (%)	14 (13.9)	1 (10.0)	3 (9.1)	10 (25.6)	0.205
Smoking, n (%)	7 (6.9)	3 (30.0)	1 (3.2)	2 (5.1)	0.101
Systolic blood pressure (mmHg), mean ± SD	140.3 ± 22.1	145.4 ± 20.5	135.1 ± 23.6	140.7 ± 23.7	0.389
Diastolic blood pressure (mmHg), mean ± SD	77.6 ± 34.7	75.9 ± 15.0	72.1 ± 10.9	75.5 ± 13.2	0.471
Antihypertensive medications, n (%)	73 (72.3)	6 (60.0)	27 (81.8)	26 (72.2)	0.230
Arterial hypertension, n (%)	75 (74.3)	7 (70.0)	28 (84.8)	27 (69.2)	0.281
HbA1c (%), (median [Q1; Q3])	6.8 (5.6; 7.4)	7.1 (6.9; 7.1)	6.9 (5.4; 7.8)	6.5 (5.5; 7.4)	0.649
Antidiabetic medications, n (%)	19 (18.8)	2 (20.0)	8 (24.2)	5 (12.8)	0.478
Diabetes mellitus, n (%)	28 (27.7	2 (20.0)	11 (33.3)	9 (23.1)	0.684
Hyperlipoproteinemia, n (%)	2 (2.0)	0 (0)	0 (0)	2 (5.1)	0.582
Antihyperlipidemic medications, n (%)	22 (21.8)	1 (10.0)	8 (24.2)	6 (15.4)	0.265
eGFR (mL/min/1.73 m^2), mean±SD	58.7 ± 24.6	70.8 ± 22.6	57.3 ± 26.8	59.2 ± 21.9	0.332
Renal insufficiency, n (%)	31 (30.7)	1 (10.0)	13 (39.4)	9 (23.1)	0.174
Coronary heart disease, n (%)	25 (24.8)	3 (30.0)	10 (30.3)	7 (17.9)	0.424
Heart failure, n (%)	31 (30.7)	0 (0)	8 (24.2)	14 (35.9)	0.070
Stroke, n (%)	12 (11.9)	0 (0)	2 (6.1)	5 (20.5)	0.540
Peripheral artery disease, n (%)	2 (2.0)	0 (0)	1 (3.0)	1 (2.6)	0.999
Anticoagulant medications, n (%)	52 (51.5)	8 (80.0)	12 (36.4)	23 (59.0)	0.208
Natrium (mmol/L), mean ± SD	140.0 ± 5.3	143.3 ± 4.3	140.2 ± 5.4	139.7 ± 4.6	0.190
NT-pro BNP (pg/mL), (median [Q1; Q3])	598.3 (266.4; 1357.8)	296.0 (168.8; 631.1)	588.6 (214.0; 1559.5)	633.1 (330.2; 1177.5)	0.280
Vitamin B12 (pg/mL), (median [Q1; Q3])	434.0 (318.0; 645.0)	467.0 (238.5; 860.5)	392.0 (324.0; 710.0)	410.0 (310.5; 614.5)	0.989
Vitamin D (ng/mL), (median [Q1; Q3])	10.8 (6.1; 24.0)	12.0 (7.7; 27.5)	13.5 (8.7; 31.2)	7.9 (5.3; 22.6)	0.082
TSH (mU/L), (median [Q1; Q3])	1.3 (0.9; 2.2)	0.9 (0.8; 1.7)	1.2 (0.9; 2.2)	1.4 (0.8; 1.8)	0.569
Folic acid (µg/L), (median [Q1; Q3])	7.3 (5.2; 10.1)	5.3 (3.9; 11.5)	7.9 (5.4; 10.3)	7.1 (5.3; 9.2)	0.772
Hemoglobin (g/dL), (median [Q1; Q3])	12.2 (10.5; 13.8)	13.0 (10.8; 14.1)	11.0 (10.1; 14.5)	11.6 (10.7; 13.2)	0.426

AHI = Apnea-hypopnea index; eGFR = estimated glomerular filtration rate; HbA1c = Glycated hemoglobin; NT-pro BNP = N-terminal pro-brain natriuretic peptide; TSH = Thyroid-stimulation hormone.

Table 2. Sleep-related characteristics of the study cohort also split by AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h ≤ AHI < 15/h (n = 33)	AHI ≥ 15/h (n = 39)	p-Value
AHI, (median [Q1; Q3])	14.0 (7.0; 25.3)	3.0 (2.0; 3.0)	8.0 (6.0; 11.0)	26.0 (19.0; 35.0)	<0.001
Nasal airflow sensor ≥6 h, n (%)	28 (27.7)	3 (30.0)	10 (30.3)	15 (38.5)	0.761
Nasal airflow sensor ≥3 h, n (%)	48 (47.5)	6 (60.0)	20 (60.6)	22 (56.4)	0.950
Pulse oximetry ≥ 6 h, n (%)	39 (38.6)	6 (60.0)	17 (51.5)	16 (41.0)	0.477
Pulse oximetry ≥ 3 h, n (%)	62 (61.4)	10 (100.0)	23 (69.7)	28 (71.8)	0.131
Average saturation (%), (median [Q1; Q3])	92.0 (90.0; 94.0)	93.5 (89; 95)	92 (90; 95)	92 (90; 94)	0.638
Lowest saturation (%), (median [Q1; Q3])	77.0 (71.0; 82.0)	82.0 (79.8; 82.3)	77.0 (71.8; 82.8)	74 (64.8; 81.3)	0.055
Epworth Sleepiness Scale (score), (median [Q1; Q3])	5.0 (2.0; 8.0)	5.0 (3.0; 8.5)	6.0 (3.0; 8.5)	6.0 (2.0; 8.0)	0.972
"Essener Fragebogen Alter und Schläfrigkeit" (score), (median [Q1; Q3])	1.0 (0.0; 4.0)	3.0 (0.0; 7.0)	1.0 (0.0; 3.5)	1.0 (0.0; 5.0)	0.515

AHI = Apnea-hypopnea index.

Table 3. Cognitive and emotional function also split by AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h ≤ AHI < 15/h (n = 33)	AHI ≥ 15/h (n = 39)	p-Value
MMSE (score)	21.0 (17.5; 25.0)	23.5 (20.8; 26.0)	21.0 (16.5; 25.0)	21.0 (19.0; 25.0)	0.203
DemTect (score)	8.0 (6.0; 9.0)	11.0 (7.0; 14.0)	8.5 (7.0; 10.0)	7.0 (6.0; 9.0)	0.060
Clock drawing (score)	4.0 (3.0; 5.0)	3.5 (2.0; 4.3)	4.0 (3.0; 4.5)	4.0 (3.0; 5.0)	0.628
Trial Making Test (s)	90.0 (51.5; 159.8)	73.5 (46.8; 123.5)	82.5 (52.0; 176.3)	85.0 (50.0; 135.5)	0.824
Figural Memory Test (number of correct responses)	7.0 (6.0; 9.0)	8.0 (7.0; 9.5)	6.0 (5.0; 8.3)	8.0 (7.0; 9.0)	0.116
Timed Test of Money Counting (s)	34.0 (13.0; 70.5)	29.0 (6.5; 88.3)	23.0 (12.0; 55.5)	36.0 (15.0; 70.5)	0.510
"Alters-Konzentrations-Test" (number of correct responses)	20.0 (18.5; 20.0)	20.0 (17.8; 20.0)	20.0 (19.0; 20.0)	20.0 (18.5; 20.0)	0.893
WHO-5 Well-Being Index (%-score)	56.0 (40.0; 72.0)	34.0 (19.0; 58.0)	56.0 (38.0; 68.0)	62.0 (44.0; 76.0)	0.065
Geriatric depression scale (score)	3.0 (2.0; 6.0)	5.5 (3.3; 10.5)	3.0 (2.0; 6.0)	3.0 (2.0; 5.0)	0.144
ADAS-cog total (score)	19.0 (13.0; 24.0)	19.0 (12.0; 22.0)	19.0 (12.0; 23.5)	18.5 (13.3; 23.0)	0.859
ADAS-cog memory (score)	12.0 (10.0; 16.0)	14.0 (9.0; 17.0)	12.0 (9.5; 16.0)	11.5 (10.0; 14.0)	0.703
ADAS-cog praxis (score)	5.0 (2.0; 8.3)	5.0 (1.0; 5.0)	5.0 (2.0; 8.0)	6.0 (2.0; 9.0)	0.444
ADAS-cog language (score)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)	0.860

All data are shown as median with 25th as well as 75th percentile (median [Q1; Q3]). MMSE = Mini-Mental state examination; DemTect = Demenz-Detektions-Test; ADAS-cog = Alzheimer's Disease Assessment Scale-cognitive subscale.

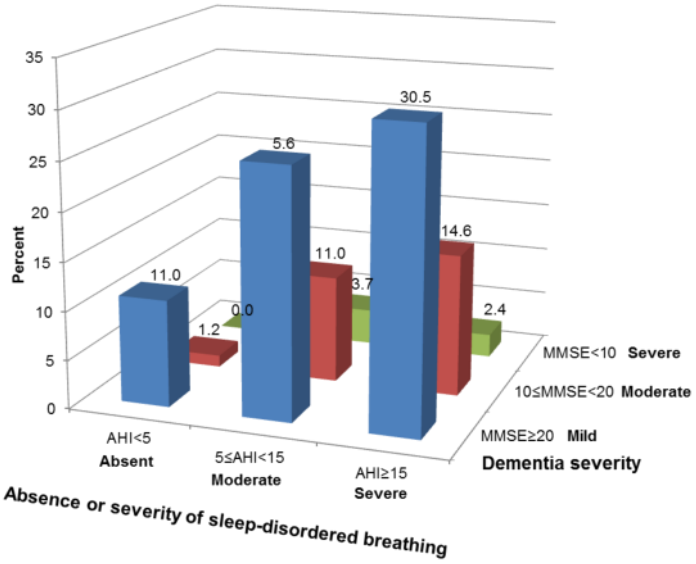

Figure 1. Association between severity of sleep-disordered breathing and severity of dementia. Chi-square test revealed no significant association $\chi^2(4) = 3.33$, $p = 0.521$, Cramer's V = 0.14. MMSE = Mini-Mental state examination.

Since Hoch et al. observed a significant association between SDB severity and dementia severity only in dementia patients without depression but not in patients with both cognitive impairment and depressive symptoms [12], we additionally evaluated the association between SDB severity and dementia severity in non-depressed dementia patients by excluding patients with a geriatric depression score of 6 or more which is in indicator of depressive symptoms [28]. However, also in this subgroup of non-depressed dementia patients we observed no significant association between SDB severity and dementia severity (Table A4).

With overall rather high impairment in activities of daily living and physical functioning including mobility, which represents the typical pattern of geriatric patients, there were no significant differences between AHI categories (Table 4).

Table 4. Mobility also split by AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h ≤ AHI < 15/h (n = 33)	AHI ≥ 15/h (n = 39)	p-Value
Barthel index (score)	47.5 (30.0; 65.0)	60.0 (27.5; 65.0)	50.0 (30.0; 67.5)	50.0 (30.0; 60.0)	0.924
IADL scale (score)	4.0 (2.0; 6.0)	4.0 (1.8; 5.0)	4.0 (3.0; 6.0)	4.0 (3.0; 5.0)	0.335
Timed Up & Go (s)	24.0 (14.0; 39.3)	27.0 (11.5; 92.0)	21.0 (12.0; 31.5)	24.0 (14.0; 39.0)	0.873
Tinetti mobility test (score)	17.0 (11.8; 22.0)	17.0 (13.0; 23.0)	17.5 (12.0; 22.0)	16.0 (8.0; 22.0)	0.821
Test of standing balance (score)	1.0 (0.0; 2.0)	1.0 (0.0; 3.0)	2.0 (0.0; 3.0)	1.0 (0.0; 2.0)	0.814
Walking Speed (m/s)	0.50 (0.30; 0.80)	0.50 (0.35; 1.00)	0.60 (0.33; 0.88)	0.50 (0.30; 0.90)	0.895
Hand grip strength right (kPa)	14.0 (10.0; 21.5)	18.0 (10.0; 31.5)	12.0 (9.0; 20.0)	16.0 (10.0; 22.0)	0.538
Hand grip strength left (kPa)	12.0 (8.0; 20.0)	15.0 (6.0; 27.5)	12.0 (8.0; 20.8)	14.0 (10.0; 20.0)	0.412
Frailty criteria (number)	4.0 (3.0; 4.0)	3.0 (2.3; 4.8)	3.5 (3.0; 4.0)	3.0 (2.0; 4.0)	0.956

All data are shown as median with 25th as well as 75th percentile (median [Q1; Q3]). IADL = Instrumental activities of daily living.

Table 5. Demographic and clinical characteristics split by tolerance of the nasal airflow sensor ≥6 h vs. <6 h.

Variables	Nasal Airflow Sensor < 6 h (*n* = 73)	Nasal Airflow Sensor ≥ 6 h (*n* = 28)	*p*-Value
Age (years), mean ± SD	84.6 ± 6.7	82.7 ± 6.3	0.195
Male sex, *n* (%)	22 (30.1)	9 (32.1)	0.845
Academic degree, *n* (%)			0.351
Primary school	41 (56.2)	11 (40.7)	
Secondary school	28 (38.3)	14 (51.8)	
Baccalaureate	4 (5.5)	2 (7.4)	
Body mass index (kg/m^2), mean ± SD	25.0 ± 5.9	26.2 ± 5.4	0.358
Overweight, *n* (%)	9 (12.3)	5 (17.9)	0.522
Nicotine abuse, *n* (%)	4 (5.5)	3 (10.7)	0.051
Systolic blood pressure (mmHg), mean ± SD	139.5 ± 21.0	142.1 ± 24.9	0.537
Diastolic blood pressure (mmHg), mean ± SD	79.6 ± 44.3	74.6 ± 78.7	0.602
Antihypertensive medications, *n* (%)	53 (72.6)	19 (67.9)	0.958
Arterial hypertension, *n* (%)	55 (75.3)	20 (71.4)	0.872
HbA1c (%), (median [Q1; Q3])	6.9 (5.7; 7.5)	6.8 (5.2; 7.0)	0.333
Antidiabetic medications, *n* (%)	14 (19.2)	6 (21.4)	0.777
Diabetes mellitus, *n* (%)	21 (28.8)	8 (28.6)	0.984
Hyperlipoproteinemia, *n* (%)	2 (2.7)	0 (0.0)	0.999
Antihyperlipidemic medications, *n* (%)	13 (17.8)	5 (17.9)	0.977
eGFR (mL/min/1.73 m^2), mean±SD	58.4 ± 25.2	59.6 ± 23.5	0.833
Renal insufficiency, *n* (%)	26 (35.6)	6 (21.4)	0.329
Coronary heart disease, *n* (%)	14 (19.2)	11 (39.3)	0.070
Heart failure, *n* (%)	24 (32.9)	7 (25.0)	0.629
Stroke, *n* (%)	10 (13.7)	2 (7.1)	0.505
Peripheral artery disease, *n* (%)	2 (2.7)	0 (0.0)	0.999
Anticoagulant medications, *n* (%)	36 (49.3)	16 (57.1)	0.799
Natrium (mmol/L), mean ± SD	140.1 ± 4.9	140.2 ± 5.5	0.949
NT-pro BNP (pg/mL), (median [Q1; Q3])	627.8 (280.3; 1546.8)	421.7 (236.2; 1173.3)	0.282
Vitamin B12 (pg/mL), (median [Q1; Q3])	433.0 (280.0; 661.0)	408.5 (329.0; 593.5)	0.924
Vitamin D (ng/mL), (median [Q1; Q3])	10.2 (5.6; 25.0)	11.9 (7.7; 17.3)	0.585
TSH (mU/L), (median [Q1; Q3])	1.3 (0.9; 2.2)	1.2 (0.9; 1.8)	0.436
Folic acid (µg/L), (median [Q1; Q3])	8.1 (5.6; 10.9)	6.4 (5.0; 7.7)	0.021
Hemoglobin (g/dL), (median [Q1; Q3])	12.2 (10.5; 13.9)	11.7 (10.6; 13.4)	0.723

AHI = Apnea-hypopnea index; eGFR = estimated glomerular filtration rate; HbA1c = Glycated hemoglobin; NT-pro BNP = N-terminal pro-brain natriuretic peptide; TSH = Thyroid-stimulation hormone.

Although in our cohort valid AHI measurement was possible in 82 of the 101 dementia patients (81.2%), we observed that acceptance of the nasal airflow sensor of at least 6 h, which is requested for the billing of the diagnostic procedure for health insurance companies in Germany, was present in less than one third of all patients (Table 2). Since literature on the minimal recording time required for valid SDB diagnostics is lacking, we also examined acceptance of the nasal airflow sensor of at least 3 h, which we observed as an acceptable compromise between patient acceptance and still adequate validity for SDB determination and which was already present in half of the study sample. Acceptance of pulse oximetry was higher with about 40% tolerating measurement for 6 h and 60% for 3 h (Table 2). When comparing patients tolerating the nasal airflow sensor for 6 or more hours with those tolerating the nasal airflow sensor for less than 6 h, the tolerant group exhibited a higher frequency of nicotine abuse and coronary heart disease, lower levels of folic acid (Table 5), more symptoms of depression (Table 6), and higher physical fitness (Table 7).

Table 6. Cognitive and emotional function split by tolerance of the nasal airflow sensor ≥6 h vs. <6 h.

Variables	Nasal Airflow Sensor < 6 h (n = 73)	Nasal Airflow Sensor ≥ 6 h (n = 28)	p-Value
MMSE (score)	21.0 (16.5; 24.5)	23.5 (18.3; 25.0)	0.210
DemTect (score)	8.0 (6.0; 9.0)	7.0 (5.0; 9.0)	0.695
Clock drawing (score)	4.0 (3.0; 5.0)	4.0 (3.0; 5.0)	0.983
Trial Making Test (s)	85.0 (55.0; 163.0)	95.0 (45.0; 175.5)	0.670
Figural Memory Test (number of correct responses)	7.0 (6.0; 8.0)	7.5 (5.8; 9.0)	0.928
Timed Test of Money Counting (s)	33.0 (13.0; 61.8)	36.0 (12.0; 90.0)	0.896
"Alters-Konzentrations-Test" (number of correct responses)	20.0 (18.0; 20.0)	20.0 (19.0; 20.0)	0.934
WHO-5 Well-Being Index (%-score)	56.0 (41.0; 76.0)	52.0 (24.0; 64.0)	0.089
Geriatric depression scale (score)	3.0 (2.0; 5.0)	5.0 (3.5; 7.5)	0.004
ADAS-cog total (score)	19.5 (13.0; 25.0)	18.0 (14.5; 22.0)	0.437
ADAS-cog memory (score)	12.0 (10.3; 16.0)	11.5 (9.8; 15.0)	0.404
ADAS-cog praxis (score)	5.0 (2.0; 9.0)	5.5 (2.0; 8.0)	0.613
ADAS-cog language (score)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)	0.714

All data are shown as median with 25th as well as 75th percentile (median [Q1; Q3]). MMSE = Mini-Mental state examination; DemTect = Demenz-Detektions-Test; ADAS-cog = Alzheimer's Disease Assessment Scale-cognitive subscale.

Table 7. Mobility split by tolerance of the nasal airflow sensor ≥6 h vs. <6 h.

Variables	Nasal Airflow Senor < 6 h (n = 73)	Nasal Airflow Senor ≥ 6 h (n = 28)	p-Value
Barthel index (score)	45.0 (25.0; 61.3)	50.0 (30.0; 68.8)	0.332
IADL scale (score)	4.0 (2.0; 6.0)	3.0 (2.0; 6.0)	0.823
Timed Up & Go (s)	24.5 (14.8; 61.0)	23.5 (12.3; 34.0)	0.358
Tinetti mobility test (score)	16.5 (10.5; 21.0)	17.5 (12.3; 23.5)	0.351
Test of standing balance (score)	1.0 (0.0; 2.0)	2.0 (1.0; 3.0)	0.040
Walking Speed (m/s)	0.60 (0.28; 0.90)	0.50 (0.40; 0.90)	0.813
Hand grip strength right (kPa)	12.5 (9.0; 20.5)	18.0 (12.0; 24.8)	0.014
Hand grip strength left (kPa)	11.5 (8.0; 16.3)	16.5 (10.5; 21.8)	0.022
Frailty criteria (number)	4.0 (3.0; 5.0)	3.0 (3.0; 4.0)	0.391

All data are shown as median with 25th as well as 75th percentile (median [Q1; Q3]). IADL = Instrumental activities of daily living.

In a sensitivity analysis we divided AHI in the alternative categories AHI < 5/h, representing absent SDB, 5/h ≤ AHI < 30/h, representing mild/moderate SDB and AHI ≥ 30/h, representing severe SDB, and observed similar results compared to the previous classification (Tables A1–A3 and A5, Figure A1).

4. Discussion

In a cohort of 101 consecutive hospitalized geriatric patients mostly exhibiting mild dementia, we observed that the detection of SDB by overnight polygraphy using a portable sleep apnea examination device in the patient room was possible in 81.2% of all patients. About half of all patients with valid SDB evaluation showed at least moderate SDB with about one fifth exhibiting even severe SDB. This prevalence matches the results of a slightly younger American population-based cohort (mean age 73 ± 6 years) which observed a respiratory disturbance index ≥5/h in 81% of the cohort [37] whereas we observed an AHI ≥ 5/h in 88% of our cohort. Further, it matches the prevalence previously observed in elderly dementia patients (80.3 ± 8.6 years) with 89.2% of patients exhibiting a respiratory disturbance index ≥5/h [11]. Despite the high prevalence of SDB in our cohort, levels of daytime sleepiness were rather low and were not significantly associated with SDB severity. In our total cohort, only 7% showed ESS scores >10, which matches previously reported minimal daytime sleepiness levels in people with at least moderate SDB, even though it has to be considered that ESS might not be valid for assessing daytime sleepiness in patients with severe dementia [4].

In line with previous literature [38], we observed that vitamin D deficiency became more pronounced with increasing SDB severity with already moderate SDB patients exhibiting vitamin D deficiency. The mechanisms underlying the relation between SDB and vitamin D level and the direction of effect are however not known so far. The interplay between SDB, cognition and vitamin D is suggested to be further influenced by individual patients' comorbidity profile. One possible explanation for the positive association between Vitamin D and SDB observed in our study might be that vitamin D levels are reduced by a hypoxia-induced mechanism, since a study in 90 patients with severe obstructive sleep apnea (AHI > 30/h) could show that short-term positive airway pressure therapy was able to recover vitamin D homeostasis in males [39]. Moreover, vitamin D deficiency has been associated with vascular risk factors and events [40], matching our observation of a high stroke and heart failure frequency in patients with moderate or severe SDB which also exhibited vitamin D deficiency. Further studies are needed to determine the clinical relevance of the vitamin D insufficiency observed in SDB patients, especially since the effect of vitamin D on cognition is still not clear with observational cross-sectional and longitudinal data showing that low vitamin D level was associated with worse cognitive performance and cognitive decline whereas intervention studies showed no significant benefit of vitamin D supplementation on cognition [41].

Since SDB is often underdiagnosed and instrumental laboratory diagnostics especially of obstructive sleep apnea has been shown to be difficult in dementia patients, we also elucidated which factors influence compliance of nasal airflow sensor as a central part for the detection of obstructive sleep apnea. In our total cohort of geriatric patients with mild dementia, less than one third tolerated nasal airflow sensor diagnostics for 6 or more hours. We observed higher levels of depressive symptoms in those patients tolerating nasal airflow diagnostics for at least 6 h compared to those not tolerating nasal airflow diagnostics for this time period. Higher levels of depressive symptoms could be associated with a higher motivation to tolerate diagnostic procedures in order to detect reasons for reduced emotional well-being and improve emotional well-being. This pattern matches the descriptively higher education level, younger age, higher MMSE scores and higher physical fitness in the tolerant group. Especially when comparing patients where SDB diagnostic was not possible (n = 19) with patients where AHI could be determined and which were included in the present analyses of SDB prevalence and its association with cognition (n = 82), it has to be noted that patients where SDB diagnostic was not possible had significantly worse cognition (MMSE median = 18.0, Q1 = 14, Q3 = 24) compared with patients where AHI could be determined and which were included in the present analyses (MMSE median = 22.0, Q1 = 19.0, Q3 = 25.0, p = 0.034). Thus, the low compliance of SDB diagnostics in our geriatric dementia patient cohort represents a considerable limitation of our study but emphasizes the need for alternative SDB diagnostics in dementia patients. The selective inclusion of patients with higher mental and physical fitness might have biased our results towards a lower prevalence of SDB and a weaker association between SDB and functional patient outcomes such as

cognition, emotion and mobility. However, as already shown above, our SDB prevalence was very similar to the prevalence observed by Aoki et al. which was based on a diagnostic procedure tolerated by all patients [11].

In contrast to previous studies, which mostly observed a significant association between SDB severity and dementia severity [10–13], we only observed a low to moderate statistically not significant association between SDB severity and dementia severity. Reasons for these inconsistent results might be differences in patient cohorts. The research group around Ancoli-Israel et al. for example recruited institutionalized nursing home patients, which had a similar age than our cohort but exhibited severe dementia [10]. Hoch [12] and Reynolds [13] recruited in- and outpatients from a geriatric unit of a psychiatric institute and a geriatric center which again exhibited higher levels of dementia (MMSE = 18) compared to our patients (MMSE = 21). In the most recent analysis, Aoki et al. recruited dementia patients in a psychiatric Japanese hospital, which also exhibited severe dementia (MMSE = 11) but less comorbid conditions since patients with comorbid conditions were not treated in psychiatry [11]. Further, previous studies used less extensive neuropsychological test batteries to assess cognitive function like the Mattis Dementia Rating Scale [10], Blessed Dementia Rating Scale [12,13], or MMSE and Hasegawa dementia scale [11], even though especially vigilance and executive function is influenced by SDB [42]. Our results more resemble the picture seen in healthy elderly cohorts, which also demonstrated no significant association between SDB severity (defined by AHI) and cognitive performance (assessed by a comprehensive neuropsychological test battery) [2].

Due to the cross-sectional design we cannot answer the question whether SDB increases the risk of dementia due to hypoxic brain damage or whether dementia leads to lesions in brain areas associated with breathing, and perhaps both processes take place. Evidence for the mechanism of increases in dementia risk due to hypoxic brain damage exists from (a) preliminary studies showing improvement in cognition in dementia patients with obstructive sleep apnea after positive airway pressure therapy [6], (b) prospective population-based studies showing that SDB predicted incident dementia/cognitive decline in community-dwelling elderly [4,5], and (c) prospective population-based studies showing that SDB increases cardiovascular risk which then mediates increased risk of cognitive decline [43]. Since SDB is often underdiagnosed due to lack of clinical symptoms and lack of tolerance of sophisticated diagnostic procedures including sleep laboratory in the elderly [44], our results in combination with previous literature suggests a potential role for SDB screening in the elderly to uncover a potentially reversible cause of cognitive impairment [45,46]. SDB in the elderly might exert different mechanism than SDB in the middle-aged since elderly, often multimorbid patients, have less reserve to compensate for SDB [9,47]. Especially elderly patients with early dementia pathology might suffer from devastating effects of SDB since additional hypoxemia can aggravate dementia pathology. Detection of SDB in the elderly, especially those suffering from comorbid dementia, is a particular challenge due to reduced acceptance of diagnostic procedures. Although polysomnography in the sleep laboratory with recording of sleep electroencephalography, electrooculography, electromyography, electrocardiography, oronasal airflow, snoring, respiratory effort, oxygen saturation and video of behavior is recommended for SDB diagnosis [15], systems with a reduced number of channels should be used for screening purposes even in ambulatory settings in patients at high SDB risk like in elderly patients with high levels of comorbidity, which are included in our cohort. Positive airway pressure therapy is generally suggested in case of moderate or severe SDB (AHI >15/h) and could be considered in patients with mild SDB (AHI $\leq$ 15/h) and additionally high cardiovascular risk and/or daytime fatigue also in case of comorbid mild or moderate dementia [48,49]. In our cohort, the majority of patients (84%) showed obstructive sleep apnea and would thus qualify for positive airway pressure therapy. It is estimated that about 15% of Alzheimer's disease may be attributable to long-term SDB with obstructive sleep apnea being the main risk factor [1,49], suggesting that SDB screening should be incorporated in clinical routine also in the elderly.

5. Conclusions

Sleep-disordered breathing (SDB) is an emerging dementia risk factor but literature on the association between SDB and cognitive impairment is still scarce. For the first time we showed that SDB is highly prevalent in elderly geriatric patients suffering from mild dementia (87.8% with AHI $\geq$ 5/h), with more than half of these patients exhibiting moderate/severe SDB. We observed a low to moderate association between severity of SDB and severity of dementia. Since preliminary studies already showed that positive airway pressure therapy improved cognition in dementia patients, our data underline the importance of SDB screening in the elderly, especially those with mild dementia. SDB is often underdiagnosed and instrumental laboratory diagnostics and treatment especially of obstructive sleep apnea has been shown to be difficult in dementia patients. We also experienced that less than one third of our cohort of geriatric patients with mild dementia tolerated nasal airflow sensor diagnostic for 6 or more hours. Further studies are needed to develop innovative valid SDB diagnostic and treatment devices which are better tolerated by dementia patients. Additionally, larger studies analyzing the benefit of such innovative SDB screening and subsequent treatment as well as the influence of further comorbidities in geriatric patients have to be conducted.

Author Contributions: Conceptualization, J.G., R.H., C.K., H.F. and D.M.H.; Methodology, J.G., H.F. and D.M.H.; Software, J.G. and R.H.; Validation, J.G. and R.H.; Formal analysis, J.G. and R.H.; Investigation, R.H. and H.R.; Resources, C.K., H.F. and D.M.H.; Data curation, J.G., R.H., H.F.; Writing—original draft preparation, J.G. and R.H.; Writing—review and editing, J.G., R.H., C.K., H.F., D.M.H.; Visualization, J.G.; Supervision, H.F. and D.M.H.; Project administration, H.F. and D.M.H.; Funding acquisition, H.F. and D.M.H.

Funding: Supported by Paul Kuth Foundation.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

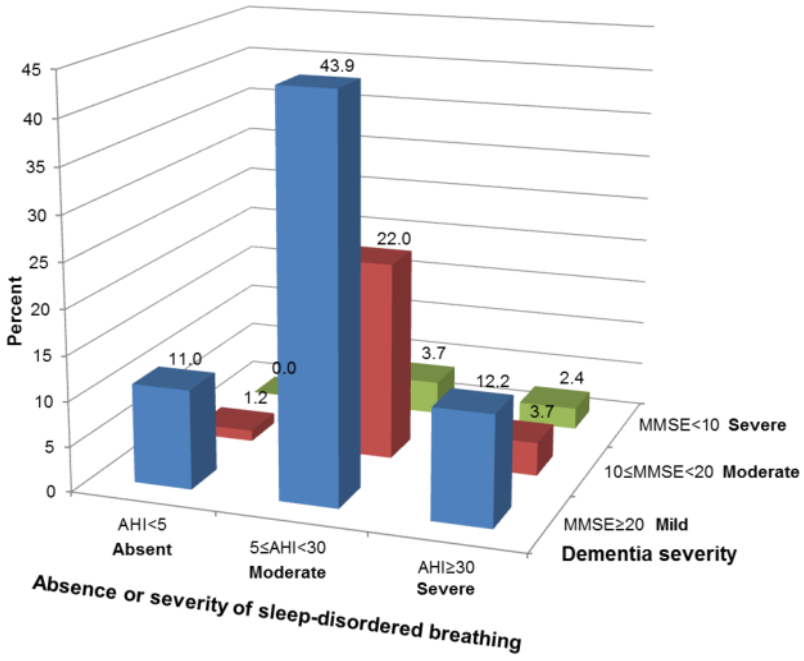

Figure A1. Association between severity of sleep-disordered breathing and severity of dementia. Chi-square test revealed no significant association $\chi^2(4) = 4.67$, $p = 0.313$, Cramer's V = 0.17. MMSE = Mini-Mental state examination.

Table A1. Demographic and clinical characteristics of the study cohort also split by alternative AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h $\leq$ AHI < 30/h (n = 57)	AHI $\geq$ 30/h (n = 15)	p-Value
Age (years), mean ± SD	84.1 ± 6.5	84.7 ± 8.6	83.9 ± 5.5	83.3 ± 6.2	0.856
Male sex, n (%)	32 (31.7)	5 (50.0)	15 (26.3)	7 (46.7)	0.133
Academic degree, n (%)					0.338
Primary school	52 (52.0)	6 (60.0)	28 (50.0)	7 (46.7)	
Secondary school	42 (42.0)	4 (40.0)	23 (41.1)	8 (53.4)	
Baccalaureate	6 (6.0)	0 (0.0)	5 (8.7)	0 (0)	
Body mass index (kg/m^2), mean ± SD	25.3 ± 5.7	23.9 ± 4.0	25.7 ± 5.7	28.6 ± 6.3	0.105
Overweight, n (%)	14 (13.9)	1 (10.0)	8 (14.0)	5 (33.3)	0.221
Smoking, n (%)	7 (6.9)	3 (30)	1 (1.8)	2 (13.3)	0.035
Systolic blood pressure (mmHg), mean ± SD	140.3 ± 22.1	145.4 ± 20.5	138.4 ± 22.9	136.9 ± 22.9	0.641
Diastolic blood pressure (mmHg), mean ± SD	77.6 ± 34.7	75.9 ± 15.0	73.4 ± 10.5	75.9 ± 17.7	0.721
Antihypertensive medications, n (%)	73 (72.3)	6 (60.0)	40 (70.2)	13 (86.7)	0.317
Arterial hypertension, n (%)	75 (74.3)	7 (70.0)	42 (73.7)	13 (86.7)	0.548
HbA1c (%), (median [Q1; Q3])	6.8 (5.6; 7.4)	7.1 (6.9; 7.1)	6.9 (6.0; 7.4)	5.5 (5.5; 7.1)	0.488
Antidiabetic medications, n (%)	19 (18.8)	2 (20.0)	13 (22.8)	1 (6.7)	0.421
Diabetes mellitus, n (%)	28 (27.7	2 (20.0)	17 (29.8)	4 (26.7)	0.928
Hyperlipoproteinemia, n (%)	2 (2.0)	0 (0)	1 (1.8)	1 (6.7)	0.433
Antihyperlipidemic medications, n (%)	22 (21.8)	1 (10.0)	10 (17.5)	4 (26.7)	0.390
eGFR (mL/min/1.73 m^2), mean ± SD	58.7 ± 24.6	70.8 ± 22.6	57.2 ± 24.9	62.2 ± 21.3	0.272
Renal insufficiency, n (%)	31 (30.7)	1 (10.0)	19 (33.3)	4 (26.7)	0.404
Coronary heart disease, n (%)	25 (24.8)	3 (30.0)	14 (24.6)	3 (20.0)	0.853
Heart failure, n (%)	31 (30.7)	0 (0)	17 (29.8)	5 (33.3)	0.102
Stroke, n (%)	12 (11.9)	0 (0)	3 (5.3)	4 (26.7)	0.039
Peripheral artery disease, n (%)	2 (2.0)	0 (0)	1 (1.8)	1 (6.7)	0.525
Anticoagulant medications, n (%)	52 (51.5)	8 (80.0)	27 (47.4)	8 (53.3)	0.350
Natrium (mmol/L), mean ± SD	140.0 ± 5.3	143.3 ± 4.3	140.2 ± 5.1	138.9 ± 4.5	0.129
NT-pro BNP (pg/mL), (median [Q1; Q3])	598.3 (266.4; 1357.8)	296.0 (168.8; 631.1)	617.6 (263.6; 1368.5)	690.7 (295.9; 1289.3)	0.491
Vitamin B12 (pg/mL), (median [Q1; Q3])	434.0 (318.0; 645.0)	467.0 (238.5; 860.5)	392.0 (321.0; 604.0)	400.5 (300.5; 914.5)	0.941
Vitamin D (ng/mL), (median [Q1; Q3])	10.8 (6.1; 24.0)	12.0 (7.7; 27.5)	12.4 (7.2; 26.0)	7.0 (4.6; 11.8)	0.059
TSH (mU/L), (median [Q1; Q3])	1.3 (0.9; 2.2)	0.9 (0.8; 1.7)	1.3 (0.9; 2.2)	1.2 (0.9; 1.8)	0.560
Folic acid (µg/L), (median [Q1; Q3])	7.3 (5.2; 10.1)	5.3 (3.9; 11.5)	7.3 (5.6; 9.5)	7.0 (4.6; 10.2)	0.504
Hemoglobin (g/dL), (median [Q1; Q3])	12.2 (10.5; 13.8)	13.0 (10.8; 14.1)	11.2 (10.2; 13.2)	12.7 (11.1; 14.7)	0.173

AHI = Apnea-hypopnea index; eGFR = estimated glomerular filtration rate; HbA1c = Glycated hemoglobin; NT-pro BNP = N-terminal pro-brain natriuretic peptide; TSH = Thyroid-stimulation hormone.

Table A2. Sleep-related characteristics of the study cohort also split by alternative AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h ≤ AHI < 30/h (n = 57)	AHI ≥ 30/h (n = 15)	p-Value
AHI, (median [Q1; Q3])	14.0 (7.0; 25.3)	3.0 (2.0; 3.0)	12.0 (8.0; 19.5)	42.0 (33.0; 46.0)	<0.001
Nasal airflow sensor ≥6 h, *n* (%)	28 (27.7)	3 (30.0)	23 (40.4)	2 (13.3)	0.169
Nasal airflow sensor ≥3 h, *n* (%)	48 (47.5)	6 (60.0)	37 (64.9)	5 (33.3)	0.084
Pulse oximetry ≥6 h, *n* (%)	39 (38.6)	6 (60.0)	28 (49.1)	5 (33.3)	0.404
Pulse oximetry ≥3 h, *n* (%)	62 (61.4)	10 (100.0)	39 (68.4)	12 (80.0)	0.078
Average oxygen saturation (%), (median [Q1; Q3])	92.0 (90.0; 94.0)	93.5 (89.0; 95.0)	92.0 (90.0; 94.0)	92.0 (89.0; 93.0)	0.660
Lowest oxygen saturation (%), (median [Q1; Q3])	77.0 (71.0; 82.0)	82.0 (79.8; 82.3)	75.0 (69.0; 82.0)	76.0 (66.0; 81.0)	0.119
Epworth Sleepiness Scale (score), (median [Q1; Q3])	5.0 (2.0; 8.0)	5.0 (3.0; 8.5)	6.0 (2.0; 8.0)	5.0 (2.5; 10.5.0)	0.477
"Essener Fragebogen Alter und Schläfrigkeit" (score), (median [Q1; Q3])	1.0 (0.0; 4.0)	3.0 (0.0; 7.0)	1.0 (0.0; 4.0)	1.0 (0.0; 6.0)	0.664

AHI = Apnea-hypopnea index.

Table A3. Cognitive and emotional function also split by alternative AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h ≤ AHI < 30/h (n = 57)	AHI ≥ 30/h (n = 15)	p-Value
MMSE (score)	21.0 (17.5; 25.0)	23.5 (20.8; 26.0)	21.0 (17.5; 24.5)	24.0 (19.0; 25.0)	0.122
DemTect (score)	8.0 (6.0; 9.0)	11.0 (7.0; 14.0)	8.0 (6.0; 9.0)	8.0 (6.3; 9.0)	0.143
Clock drawing (score)	4.0 (3.0; 5.0)	3.5 (2.0; 4.3)	4.0 (3.0; 4.5)	4.0 (3.0; 5.0)	0.669
Trial Making Test (s)	90.0 (51.5; 159.8)	73.5 (46.8; 123.5)	89.0 (50.0; 172.5)	80.0 (52.0; 111.0)	0.808
Figural Memory Test (number of correct responses)	7.0 (6.0; 9.0)	8.0 (7.0; 9.5)	7.0 (6.0; 9.0)	7.5 (7.0; 9.0)	0.266
Timed Test of Money Counting (s)	34.0 (13.0; 70.5)	29.0 (6.5; 88.3)	32.0 (12.5; 70.5)	34.0 (13.5; 42.0)	0.970
"Alters-Konzentrations-Test" (number of correct responses)	20.0 (18.5; 20.0)	20.0 (17.8; 20.0)	20.0 (19.0; 20.0)	20.0 (20.0; 20.0)	0.318
WHO-5 Well-Being Index (%-score)	56.0 (40.0; 72.0)	34.0 (19.0; 58.0)	56.0 (43.0; 72.0)	62.0 (46.0; 75.0)	0.089
Geriatric depression scale (score)	3.0 (2.0; 6.0)	5.5 (3.3; 10.5)	3.0 (2.0; 6.0)	4.0 (2.0; 5.0)	0.155
ADAS-cog total (score)	20.0 (15.0; 26.5)	20.0 (14.0; 24.0)	20.0 (15.0; 26.3)	21.0 (14.0; 29.0)	0.829
ADAS-cog memory (score)	19.0 (13.0; 24.0)	19.0 (12.0; 22.0)	19.0 (13.0; 23.0)	19.0 (13.8; 25.5)	0.749
ADAS-cog praxis (score)	12.0 (10.0; 16.0)	14.0 (9.0; 17.0)	11.0 (9.0; 16.0)	12.0 (10.8; 14.3)	0.592
ADAS-cog language (score)	5.0 (2.0; 8.3)	5.0 (1.0; 5.0)	6.0 (2.0; 8.0)	5.0 (1.8; 11.3)	0.560

All data are shown as median with 25th as well as 75th percentile (median [Q1; Q3]). MMSE = Mini-Mental state examination; DemTect = Demenz-Detektions-Test; ADAS-cog = Alzheimer's Disease Assessment Scale-cognitive subscale.

Table A4. Cognitive and emotional function also split by AHI category in non-depressed patients (geriatric depression scale score ≤5) *.

Variables	Gesamt (n = 69)	AHI < 5 (n = 4)	5 ≤ AHI < 15 (n = 21)	AHI ≥ 15 (n = 29)	p-Value
MMSE (score)	21.0 (18.0; 25.0)	22.0 (20.3; 24.5)	22.0 (18.0; 25.0)	21.0 (19.0; 25.0)	0.948
DemTect (score)	7.0 (5.0; 9.0)	8.0 (8.0; 8.0)	8.5 (7.0; 10.0)	7.0 (5.0; 9.0)	0.355
Clock drawing (score)	4.0 (3.0; 5.0)	3 (2.3; 4.5)	3.0 (2.0; 4.0)	3.5 (3.0; 4.8.)	0.490
Trial Making Test (s)	90.0 (53.5; 145.3)	101.0 (52.3; 177.5)	82.5 (50.0; 180.0)	90.0 (51.5; 111.75)	0.867
Figural Memory Test (number of correct responses)	7.0 (6.0; 8.0)	7.0 (5.5; 9.3)	6.5 (5.3; 8.8)	8.0 (6.5; 8.5)	0.438
Timed Test of Money Counting (s)	34.5 (13.8; 63.5)	40.0 (14.0; 40.0)	32.0 (13.0; 51.0)	35.5 (15.0; 102.8)	0.702
"Alters-Konzentrations-Test" (number of correct responses)	20.0 (18.0; 20.0)	20.0 (17.0; 20.0)	20.0 (18.5; 20.0)	20.0 (19.0; 20.0)	0.996
WHO-5 Well-Being Index (%-score)	64.0 (52.0; 79.0)	54.0 (34.0; 74.0)	56.0 (48.0; 72.0)	68.0 (52.0; 80.0)	0.352
Geriatric depression scale (score)	3.0 (1.5; 4.0)	3.5 (2.3; 4.0)	3.0 (1.0; 3.6)	3.0 (1.0; 4.0)	0.750
ADAS-cog total (score)	22.5 (16.8; 27.5)	24.0 (22.0; 24.0)	20.0 (13.6; 27.0)	23.0 (17.0; 27.0)	0.640
ADAS-cog memory (score)	20.0 (14.0; 24.0)	22.0 (19.0; 22.0)	20.0 (13.0; 23.0)	16.0 (16.0; 24.0)	0.646
ADAS-cog praxis (score)	12.0 (11.0; 16.0)	15.0 (12.0; 16.0)	12.0 (11.0; 16.0)	12.0 (10.0; 15.0)	0.303
ADAS-cog language (score)	6.0 (3.0; 9.0)	5.0 (5.0; 5.0)	5.0 (2.0; 8.0)	7.0 (2.0; 11.0)	0.726

* 8 patients had missing data on the geriatric depression scale. All data are shown as median with 25th as well as 75th percentile (median [Q1; Q3]). MMSE = Mini-Mental state examination; DemTect = Demenz-Detektions-Test; ADAS-cog = Alzheimer's Disease Assessment Scale-cognitive subscale.

Table A5. Mobility also split by alternative AHI category.

Variables	Total (n = 101)	AHI < 5/h (n = 10)	5/h ≤ AHI < 30/h (n = 57)	AHI ≥ 30/h (n = 15)	p-Value
Barthel index (score)	47.5 (30.0; 65.0)	60.0 (27.5; 65.0)	50.0 (30.0; 67.5)	50.0 (35.0; 60.0)	0.955
IADL scale (score)	4.0 (2.0; 6.0)	4.0 (1.8; 5.0)	3.0 (2.0; 6.0)	4.0 (2.0; 5.0)	0.786
Timed Up & Go (s)	24.0 (14.0; 39.3)	27.0 (11.5; 92.0)	18.5 (12.0; 36.5)	29.0 (24.0; 150.0)	0.089
Tinetti mobility test (score)	17.0 (11.8; 22.0)	17.0 (13.0; 23.0)	17.0 (9.0; 23.0)	15.0 (13.0; 20.0)	0.763
Test of standing balance (score)	1.0 (0.0; 2.0)	1.0 (0.0; 3.0)	2.0 (0.0; 3.0)	1.0 (0.0; 2.0)	0.407
Walking Speed (m/s)	0.50 (0.30; 0.80)	0.50 (0.35; 1.00)	0.55 (0.33; 1.00)	0.50 (0.20; 0.70)	0.481
Hand grip strength right (kPa)	14.0 (10.0; 21.5)	18.0 (10.0; 31.5)	14.0 (10.0; 21.0)	14.0 (10.0; 22.0)	0.767
Hand grip strength right (kPa)	12.0 (8.0; 20.0)	15.0 (6.0; 27.5)	12.0 (8.3; 20.8)	14.0 (10.0; 20.0)	0.854
Frailty criteria (number)	4.0 (3.0; 4.0)	3.0 (2.3; 4.8)	3.5 (3.0; 4.0)	3.0 (2.0; 4.5)	0.976

All data are shown as median with 25th as well as 75th percentile (median [Q1; Q3]). IADL = Instrumental activities of daily living.

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Gerontology

Clinical Section: Research Article

Gerontology 2021;67:49–59
DOI: 10.1159/000511361

Received: June 23, 2020
Accepted: September 5, 2020
Published online: December 3, 2020

Developing an Alternative Version of the Epworth Sleepiness Scale to Assess Daytime Sleepiness in Adults with Physical or Mental Disabilities

Janine Gronewold[a] Michelle Chantal Isidora Lenuck[a] Isra Gülderen[a] Anne-Carina Scharf[a] Thomas Penzel[b] Murray W. Johns[c] Helmut Frohnhofen[d] Dirk M. Hermann[a]

[a]Department of Neurology, University Hospital Essen, University Duisburg-Essen, Essen, Germany; [b]Centre for Sleep Medicine, Charité – Universitätsmedizin Berlin, Berlin, Germany; [c]Epworth Sleep Centre, East Melbourne, VIC, Australia; [d]Department of Medicine, Faculty of Health, University Witten-Herdecke, Witten, Germany

Keywords
Sleepiness · Epworth Sleepiness Scale · Geriatric assessment · Psychometrics · Diagnostic techniques and procedures

Abstract
Introduction: Excessive daytime sleepiness (EDS) is a frequent symptom with many possible causes, and many of these can be treated. EDS and its underlying causes have been associated with various negative health consequences. Recognition of EDS is thus an important public health concern. The concept of EDS is, however, not yet well defined, and different measures are used to diagnose EDS. The Epworth Sleepiness Scale (ESS) is the most widely used tool to assess daytime sleepiness in a broad range of populations. Its applicability in patients exhibiting physical or mental disabilities, like older multimorbid patients, is limited, since the ESS was not developed and validated in this patient group. ***Methods:*** Within an expert study with 35 sleep medicine experts and a pilot study with 52 geriatric in-patients, who frequently exhibit physical or mental disabilities, and patients' close relatives, we adapted the original ESS to develop an alternative version to assess daytime sleepiness in adults with physical or mental disabilities (ESS-ALT). ***Results:*** In this adapted version, items 3 (sitting inactively in a public place) and 8 (sleepy in traffic) were replaced by 2 new items (sitting in a waiting room, sitting and eating a meal) and an interview format was used. This ESS-ALT achieved fewer missing responses (23 vs. 73%) and a higher level of internal consistency (Cronbach's $\alpha = 0.64$ vs. 0.23) than the original ESS while keeping its somnificity structure. ***Conclusion:*** The ESS-ALT achieves better psychometric properties than the original ESS for individuals with physical or mental disabilities.

Introduction

Excessive daytime sleepiness (EDS) and frequent napping represent a major symptom of sleep disorders (such as obstructive sleep apnea-hypopnea syndrome, restless legs syndrome, narcolepsy, and idiopathic hypersomnia) and many diseases (e.g., cardiovascular illnesses, infections), and a frequent medication side effect [1]. EDS has been associated with a variety of serious health conse-

H.F. and D.M.H. contributed equally to this work.

karger@karger.com
www.karger.com/ger

Janine Gronewold
Department of Neurology
University Hospital Essen
Hufelandstrasse 55, DE–45122 Essen (Germany)
janine.gronewold@uk-essen.de

quences, such as falling [2], deficits in general health, functional status and quality of life [3–5], cognitive decline [6, 7], depression [8–10], stroke [11], cardiovascular morbidity and mortality [12, 13], and all-cause mortality [13–15]. Identification of EDS is an important public health concern because early treatment of its underlying causes can improve patient outcome [16]. Still, EDS is often neglected in the clinical routine, most probably because a clear definition of EDS is lacking [17, 18].

The Epworth Sleepiness Scale (ESS) is the most widely used tool to assess daytime sleepiness [19]. Although the ESS has been developed and validated in middle-aged white community-dwelling subjects [20, 21], it is routinely used in a variety of populations, including older persons and different ethnicities [19]. In older individuals, especially item 8 of the ESS asking for sleepiness in traffic (in a car while stopped for a few minutes in the traffic) shows insufficient psychometric properties, such as low item-total scale correlation, low convergent validity, and frequent missing responses [22–25].

A validated German version of the ESS is available [26], which also suffered from inadequate psychometric properties for item 8 in older individuals [27]. Children had similar problems with the ESS as older subjects because of limitations in their comprehension of the questions and limitations in their life experiences. These were overcome by the development of the ESS for children and adolescents (ESS-CHAD) [28, 29]. Previous research suggests that daytime sleepiness is a multidimensional phenomenon, composed of chronobiological, homeostatic, psychological, medical, and possibly other aspects including age. The various methods and questionnaires available measure different aspects of daytime sleepiness and it seems appropriate to use more than 1 method to assess daytime sleepiness [30].

Due to the demographic aging in Western societies and the increasing prevalence of physical and mental disabilities with age, simple and valid tools for the assessment of EDS in patients exhibiting physical or mental disabilities are needed. Except the three-item ODSI (Observation and Interview-Based Diurnal Sleepiness Inventory) [31] such tools are lacking. In order to offer an additional comprehensive questionnaire to assess EDS in older patients, we now developed, in a 2-step model, a modified version of the ESS suitable for patients exhibiting physical or mental disabilities. In an expert survey, we evaluated difficulties when using the ESS in older persons and identified alternative items, which were rated as more adequate for the assessment of EDS in older patients often exhibiting physical or mental disabilities. In a pilot study with 52 geriatric in-patients and close relatives, we assessed the reliability and validity of the original and alternative items to construct a modified version of the ESS for the assessment of EDS in patients exhibiting physical or mental disabilities (ESS-ALT).

Expert Survey

Expert Survey Methods

In the formal item-generation phase, 9 alternative items were identified by literature review and input from experts in sleep research and sleep medicine, as well as from nursing staff and patients. These items were rated according to their adequacy to assess daytime sleepiness in older individuals, who often suffer from physical or mental disabilities, in a standardized expert survey which was conducted at the 27th annual conference of the German Society for Sleep Research and Sleep Medicine (DGSM e.V.) in November 2019. Additionally, this standardized interview evaluated problems experienced with the original ESS in the clinical routine and asked for possible solutions. A total of 35 sleep medicine experts took part in the survey.

Expert Survey Results

Of the 35 sleep medicine experts, 30 (86%) regularly used the ESS in their clinical routine. No alternative questionnaire was used to assess daytime sleepiness. According to the expert opinion (free response format, thus >1 answer possible), the ESS was difficult to administer, especially in older patients (37%), foreign patients (14%), patients with cognitive deficits (11%), and patients without a driver's license/patients not using a car (9%); 34% of the experts reported having no difficulties to administer the ESS in their clinical routine. Regarding single items of the ESS, especially item 8 caused problems due to frequent missing responses and queries (Table 1). More than 30% of the experts rated this item as not adequate to assess daytime sleepiness because driving a car does not apply to a broad range of persons. Also sitting in a car (item 4) and sitting in a public place (item 3) was judged not to apply to a considerable proportion of people (Table 1). The experts furthermore stated that item 5 (lying down to rest in the afternoon) was often not answered by older patients because they consider it normal to take a nap in the afternoon and experts also fear that this item does not discriminate sleepy from non-sleepy older subjects because it is rare for older individuals not to sleep in the afternoon. Item 2 (watching TV) was criticized because it is not formulated precisely enough since

Table 1. Expert opinion regarding items of the ESS with frequent missing responses, frequent queries, and evaluation as "not adequate" to assess daytime sleepiness

Item	Frequent missing responses, %	Frequent queries, %	"Not adequate," %
ESS1 Sitting and reading	3	0	0
ESS2 Watching TV	9	6	9
ESS3 Sitting inactively in a public place	11	0	9
ESS4 As a passenger in a car	9	3	11
ESS5 Lying down to rest in the afternoon	14	6	9
ESS6 Sitting and talking to someone	0	0	0
ESS7 Sitting quietly after lunch	3	3	0
ESS8 In a car while stopped	46	14	31
No problematic items	43	71	60

Data represent the percentage of expert responses given in a free response format, thus more than one answer was possible and percentages may not add up to 100%.

Table 2. Expert opinion regarding patient/relative feedback on the ESS as well as feedback from medical staff directly applying the ESS

Patients/relatives		Medical staff	
+	–	+	–
Short	Version for relatives lacking	Simple to administer	High number of missing responses
Simple		Good patient acceptance	Often disagreement between patient and relative
Assesses symptoms of daytime sleepiness		Assesses symptoms of daytime sleepiness	Does not measure daytime sleepiness in a reliable way
		Adequate as self-report	Patients often need assistance

no time of the day is fixed and patients sometimes ask which TV program is meant since different programs differ in their somnificity. Taking everything into account, based on the expert survey items 1 (sitting and reading), 6 (sitting and talking to someone), and 7 (sitting quietly after lunch) were found most suitable, and item 8 (in a car while stopped for a few minutes in the traffic) least suitable to assess daytime sleepiness.

According to the experts, the feedback from patients and their relatives regarding the adequacy of the ESS to assess daytime sleepiness was rather positive. The ESS was rated as short, and a simple tool which assesses symptoms of daytime sleepiness (Table 2). However, the feedback from persons who directly apply the ESS was mixed, also revealing difficulties for some patients in answering all questions on their own, which leads to a high number of missing responses and reduced reliability to assess daytime sleepiness (Table 2).

Of the 9 alternative items which were identified by literature review and input from expert sleep researchers and sleep medical specialists, nursing staff, and patients, the expert survey identified 7 items which received a median rating of at least moderate adequacy to assess daytime sleepiness in older individuals. Alternative item 8 (sitting in a waiting room) was rated as most adequate, alternative item 6 (during restaurant visit) as least adequate, and alternative item 9 (sitting and waiting for the bus) had the highest variability (Table 3).

Suggestions of the experts to improve the assessment of EDS in older subjects included an interview format and a format to be able to question close relatives/other people with insight into the patient's sleepiness, an item with a free response format, items assessing sleep propensity during leisure activities commonly performed by older persons such as playing with grandchildren, as well as items assessing actual sleep time during the night and

Table 3. Expert opinion regarding alternative items to assess daytime sleepiness in older subjects

Item	Adequacy				
	0 none, %	1 slight, %	2 moderate, %	3 high, %	median
ALT1 Sitting on a park bench	26.7	26.7	23.3	23.3	1
ALT2 During lunch	16.1	12.9	22.6	48.4	2
ALT3 During breakfast	12.9	16.1	22.6	48.4	2
ALT4 Sitting and talking in a small group	3.3	10.0	20.0	66.7	3
ALT5 During a train ride	22.6	19.4	12.9	45.2	2
ALT6 During a restaurant visit	31.0	24.1	17.2	27.6	1
ALT7 During a family celebration	19.4	0.0	45.2	35.5	2
ALT8 Sitting in a waiting room	3.1	6.3	15.6	75.0	3
ALT9 Sitting and waiting for the bus	32.3	6.5	29.0	32.3	2

day. An interview format and a format to be able to question close relatives/other people with insight into the older patient's sleepiness as well as items assessing actual sleep time during the day were methods previously used in the 3-item ODSI [31, 32]. Most experts (42%) suggested a maximum of 10 items for a screening tool to assess daytime sleepiness in older persons, 8 items, like in the original ESS, was suggested as the maximum by 19% of all experts.

Discussion Expert Survey

In line with previous studies which applied the ESS in the older general population [22, 25, 33] or older patient samples [24, 27, 34], the expert survey identified problems in administering the ESS in older individuals, especially regarding the items assessing sleep propensity in a car, since such situations are not encountered any more.

Patient Study

Patient Study Methods

Based on the results of the expert survey, we tested the original ESS and the 7 alternative items which received a median expert rating of at least moderate adequacy (median score ≥2; Table 3) to assess daytime sleepiness in older persons in a pilot patient study. We included 1 additional item assessing sleep propensity during typical leisure activities of older individuals (crossword, Sudoku, parlor games) which was suggested by most of the expert survey participants. We tested the 8 original ESS items and 8 new items in the interview form in a sample of 52 in-patients ≥65 years of the geriatric department of the Alfried Krupp Hospital in Essen, Germany, and their close relatives. Patients exhibiting an unstable clinical condition, palliative condition, or severe frailty (entirely dependent on nursing care, life expectancy <6 months) were not included. To better clarify the concept of sleep propensity, we introduced the following short example before administering the 8 original ESS items and 8 new items: "I would never doze off while I am talking to you, but there is a high chance of dozing off when I am listening to a relaxing CD after work in the evening."

For each of the 16 items in total we assessed: (1) sleep propensity (0 = never to 3 = high chance), (2) whether patients needed help from the nursing staff to answer the item, (3) if patients needed help why they needed help, (4) whether patients could not answer the items, (5) if patients could not answer the item why they could not answer, (6) time needed to answer the item, (7) the adequacy to assess daytime sleepiness (0 = not at all to 3 = well suited). In 2 additional questions with a free response format, we evaluated points of criticism and ideas for improvement.

Patient Study Measures

Epworth Sleepiness Scale

The ESS is an 8-item self-report measure of EDS [20, 21]. Respondents indicate on a 4-point Likert-type scale (0 = never, 3 = high chance) how likely they would be to doze off or fall asleep in 8 different situations based on their usual way of life in recent times. By asking for the likelihood of dozing off or falling asleep in a specific situation instead of how often they do so, the ESS tries to overcome the fact that people have different daily routines. Furthermore, respondents are asked to distinguish dozing behavior from feeling tired. If a person has not been in some of the situations recently, he/she is asked to

estimate how each situation might affect him/her. Of note, we used the 1997 version of the ESS in the present study, which included an extra sentence of instructions to respondents – "it is important that you answer each question as best you can" to reduce the frequency of missing responses [21]. A person's likelihood of dozing off or falling asleep in one situation (situational sleep propensity) does not necessarily relate to that in other situations. The 8 situations of the ESS are often part of daily life and were chosen on a priori grounds to vary in their somnificity. Somnificity is defined as the general characteristic of a posture, activity, and environmental situation that reflects its capacity to facilitate sleep onset in a majority of persons. For example, item 5 (lying down to rest) represents a situation with a high somnificity, whereas item 6 (sitting and talking) is characterized usually by low somnificity [18]. Responses to the 8 items are summed to yield a total score from 0 to 24. The ESS total score represents a person's average sleep propensity in daily life with scores of >10 indicting EDS, that is, the tendency to doze off in situations that seldom facilitate dozing in normal individuals [21]. This longer-term, persistent component of daytime sleepiness may be influenced by several factors such as inherently different levels of sleep propensity or the presence of chronic sleep disorders such as obstructive sleep apnea, narcolepsy, or periodic limb movement disorder. It is suggested that a person's general sleep propensity becomes incorporated into everyday life and determines the likelihood of dozing off or staying awake in various situations [18]. The ESS, ESS-CHAD, and ESS-ALT are subject to copyright (© M.W. Johns 1990, 1997, 2015, 2020). Authorized versions of these questionnaires are made available in various formats, including electronic versions, and in many different languages from Mapi Research Trust, as described in www.epworthsleepinessscale.com.

New Items

Based on the above-mentioned results of the expert survey (Table 3), the following 8 new items were tested in the patient study: NEW1 during lunch, NEW2 during breakfast, NEW3 sitting and talking in a small group, NEW4 during a train ride, NEW5 during a family celebration, NEW6 sitting in a waiting room, NEW7 sitting and waiting for the bus, NEW8 during crossword, Sudoku, or parlor games.

Additional Measures

Demographic and medical characteristics were collected from patient records. Standardized height and weight measurements were used to calculate body mass index (BMI; kg/m^2). Mobility was assessed by the Barthel index [35] and De Morton mobility index [36]. Frailty was assessed by the Clinical Frailty Scale [37]. Cognitive function was assessed by the Mini-Mental State Examination [38]. Depressive symptoms were assessed by the short form of the Geriatric Depression Scale [39].

Patient Study Statistical Analysis

Continuous data are presented as the mean (SD) for normally distributed data or median (Q1–Q3) for non-normally distributed data; categorical data are shown as the number (%). Statistical comparisons between patients with missing and complete responses in the original ESS or the ESS-ALT were performed by Student *t* test for normally distributed data, by Mann-Whitney test for non-normally distributed data, and by χ^2 test or Fisher's exact test for categorical data. Statistical comparisons between scores of the original and new ESS items were performed by Wilcoxon signed-rank test. Internal consistency of the scales was assessed by calculating the item to total correlation and the Cronbach's α coefficient. All hypothesis tests used two-sided tests, and p values <0.05 were considered statistically significant. Missing values were excluded listwise. All analyses were done with IBM SPSS Statistics 21 for Windows (IBM Corporation, Armonk, NY, USA).

Patient Study Results

Patient Characteristics

Fifty-two patients aged 65 years or older (mean 84.0, SD 6.4, range 66–96, 32.7% males) admitted to the Geriatrics Department of the Alfried Krupp Hospital in Essen, Germany, in November and December 2019 were included. The clinical characteristics of the patient cohort are presented in Table 4. Most patients were admitted electively (75%) and orthopedic problems were the most frequent reason for hospital admission (58%). Patients exhibited a high level of comorbidities (median number of diseases = 11, Q1–Q3 = 7–13). Frailty and mobility impairment characterizing physical disability was moderate, cognitive deficits characterizing mental disability were rather mild. None of the patients regularly took sleep medication, only 1 patient had a history of sleep disorders. Most patients lived alone without external help so that it was difficult to obtain close relative responses regarding the patients' daytime sleepiness: a close relative could be recruited for only 7 patients.

Table 4. Characteristics of the patient study cohort (n = 52)

Variables	Patient cohort characteristics	Missing responses
Age, years	84.0±6.4	0 (0.0)
Sex, male	17 (32.7)	0 (0.0)
Emergency admission	13 (25.0)	0 (0.0)
Elective admission	39 (75.0)	
Main diagnosis at admission		0 (0.0)
Cardiovascular	10 (19.2)	
Neurological	6 (11.5)	
Pulmonary	3 (5.8)	
Gastroenterological	2 (3.8)	
Nephrological	1 (1.9)	
Orthopedic	30 (57.7)	
Number of diseases	11.0 (7.3–13.8)	0 (0.0)
Number of medications	7.4±2.8	0 (0.0)
Hypnotics	11 (21.2)	0 (0.0)
History of stroke	4 (7.7)	0 (0.0)
History of coronary heart disease	32 (61.5)	0 (0.0)
NYHA classes of heart failure		0 (0.0)
I	25 (48.1)	
II	10 (19.2)	
III	11 (21.2)	
IV	6 (11.5)	
Arrhythmia	24 (46.2)	0 (0.0)
Anemia	37 (71.2)	0 (0.0)
Dementia	14 (26.9)	0 (0.0)
Thyroid dysfunction	7 (13.5)	4 (7.7)
Cancer	10 (19.2)	0 (0.0)
Osteoporosis	19 (36.5)	5 (9.6)
Arthrosis	17 (32.7)	0 (0.0)
Chronic obstructive pulmonary disease	7 (13.5)	0 (0.0)
Arterial hypertension	44 (84.6)	0 (0.0)
Diabetes mellitus	16 (30.8)	0 (0.0)
Hypercholesterolemia	9 (17.3)	10 (19.2)
Current smoking	0 (0.0)	1 (1.9)
Former smoker	7 (13.5)	
Never smoked	44 (84.6)	
BMI	24.4 (22.2;26.8)	1 (1.9)
Renal insufficiency	34 (65.4)	0 (0.0)
Hearing loss		1 (1.9)
None	2 (3.8)	
Slight	47 (90.4)	
Moderate	1 (1.9)	
Deaf	1 (1.9)	
Visual impairment		1 (1.9)
None	4 (7.7)	
Slight	44 (84.6)	
Moderate	1 (1.9)	
Blind	2 (3.8)	
Barthel index	41.0±16.7	0 (0.0)
De Morton mobility index	35.0 (26.0–44.0)	7 (13.5)
Mini-Mental State Examination	27.5 (23.8–29.0)	2 (3.8)
Geriatric depression scale	3.0 (2.0–5.0)	1 (1.9)
Clinical frailty scale	6.0 (5.0–6.0)	2 (3.8)
Fall during the last 3 months	27 (51.9)	0 (0.0)
Housing situation		0 (0.0)
With partner/family	12 (23.1)	
Alone, with external support	4 (7.7)	
Alone, without external support	31 (59.6)	
Nursing home	4 (7.7)	
Assisted living	1 (1.9)	

Data are presented as the mean ± SD, n (%), or median (Q1–Q3).

Table 5. Responses and scores of the original ESS items based on patient's self-report (n = 52)

Item	Chance of dozing off, n (%)					Median score (Q1–Q3)	Mean score (SD)
	0 never	1 slight	2 moderate	3 high	missing		
ESS1 Sitting and reading	25 (48.1)	6 (11.5)	8 (15.4)	8 (15.4)	5 (9.6)	0 (0–2)	0.98 (1.19)
ESS2 Watching TV	17 (32.7)	13 (25.0)	17 (32.7)	4 (7.7)	1 (1.9)	1 (0–2)	1.16 (0.99)
ESS3 Sitting inactively in a public place	27 (51.9)	3 (5.8)	3 (5.8)	0 (0.0)	19 (36.5)	0 (0–0)	0.27 (0.63)
ESS4 As a passenger in a car	36 (69.2)	7 (13.5)	5 (9.6)	3 (5.8)	1 (1.9)	0 (0–1)	0.51 (0.90)
ESS5 Lying down to rest in the afternoon	8 (15.4)	8 (15.4)	12 (23.1)	20 (38.5)	4 (7.7)	2 (1–3)	1.92 (1.13)
ESS6 Sitting and talking to someone	48 (92.3)	3 (5.8)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0–0)	0.10 (0.36)
ESS7 Sitting quietly after lunch	18 (34.6)	15 (28.8)	14 (26.9)	4 (7.7)	1 (1.9)	1 (0–2)	1.08 (0.98)
ESS8 In a car while stopped	15 (28.8)	1 (1.9)	0 (0.0)	0 (0.0)	36 (69.2)	0 (0–0)	0.06 (0.25)
ESS Total					38 (73.1)	5 (3–7)	5.14 (2.28)

Patient and Close Relative Responses to the 8 Original ESS Items

Many of the geriatric patients were not able to answer item 3 (sitting inactively in a public place, 37%) and item 8 (in a car while stopped, 69%). Complete responses for all 8 original ESS items allowing a valid calculation of the total score were only obtained for 14 of the 52 patients (27%; Table 5). Patients reported that they were not in these situations as reason for the missing responses, which was confirmed by the responses of their close relatives (n = 7; online suppl. Table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000511361). Patients with missing responses in the original ESS differed from those with complete data mainly by being more often female, suffering more often from tumor, exhibiting more often osteoporosis and dementia, and showing lower levels of mobility (online suppl. Table 2). Consequently, both limited experience due to mental or physical disability and limited cognitive capacity due to mental disability might contribute to missing responses for the original ESS items.

Patients did not need a lot of help from the interviewer to answer the items (online suppl. Table 3). Only at the beginning with item 1 (sitting and reading) 12% needed help: the response format had to be repeated, the situation had to be repeated, and the situation had to be described in more detail (patients asked which literature because their sleepiness depends on the content of the literature). Furthermore, patients did not need a lot of time to answer the questions, most being answered within 2 s (online suppl. Table 3). Patients rated the adequacy of the ESS items to assess their daytime sleepiness mostly as moderate or high except for items 3 (sitting inactively in a public place), 6 (sitting and talking to someone), and 8 (in a car while stopped), which were rated as only slightly adequate (item 3) or not adequate (items 6 and 8; online suppl. Table 3). Close relative adequacy evaluations agreed with patient adequacy evaluations (online suppl. Table 4).

Patient and Close Relative Responses to the 8 New Items

As with the original ESS items, we observed missing responses for items covering situations where geriatric patients reported that they no longer experience these situations, like riding a train (item 4, 50%), taking the bus (item 7, 42%), or doing a crossword, Sudoku, or playing parlor games (item 8, 27%; Table 6). All new items were very economic because none of the patients needed help to answer the items and all items were answered very quickly (online suppl. Table 5). Patients rated the new items mostly as inadequate to assess their daytime sleepiness (online suppl. Table 5). Close relative responses agreed with patient responses (online suppl. Tables 6, 7).

Adaptation of the ESS to Assess Daytime Sleepiness in Older Subjects Often Exhibiting Physical or Mental Disabilities (ESS-ALT)

Responses from experts, patients, and close relatives (Tables 1, 5; online suppl. Table 1) showed that item 3 (sitting inactively in a public place) and item 8 (in a car while stopped) of the original ESS were not adequate to assess daytime sleepiness in older individuals who often exhibit physical or mental disabilities. We decided to replace these with new items with similar somnificity and a low number of missing responses. In the present study, the rankings of somnificity (from highest to lowest: items 5, 2, 7, 1, 4, 3, 6, 8; Table 5) for the original ESS items were

Table 6. Responses and scores of the new items based on patient's self-report (n = 52)

Item	Chance of dozing off, n (%)					Median score (Q1–Q3)	Mean score (SD)
	0 never	1 slight	2 moderate	3 high	missing		
NEW1 During lunch	50 (96.2)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0–0)	0.04 (0.19)
NEW2 During breakfast	50 (96.2)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0–0)	0.04 (0.19)
NEW3 Sitting and talking in a small group	46 (88.5)	5 (9.6)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0–0)	0.13 (0.40)
NEW4 During a train ride	12 (23.1)	5 (9.6)	8 (15.4)	1 (1.9)	26 (50.0)	1 (0–2)	0.92 (0.98)
NEW5 During a family celebration	49 (94.2)	0 (0)	1 (1.9)	0 (0.0)	2 (3.8)	0 (0–0)	0.04 (0.28)
NEW6 Sitting in a waiting room	43 (82.7)	4 (7.7)	2 (3.8)	0 (0.0)	3 (5.8)	0 (0–0)	0.16 (0.47)
NEW7 Sitting and waiting for the bus	28 (53.8)	1 (1.9)	1 (1.9)	0 (0.0)	22 (42.3)	0 (0–0)	0.10 (0.40)
NEW8 During crossword, Sudoku, or parlor games	32 (61.5)	3 (5.8)	3 (5.8)	0 (0.0)	14 (26.9)	0 (0–0)	0.24 (0.59)

similar as described before for different samples, ranging from patients with sleep disorders to healthy students [18]. Only item 7 (sitting quietly after a lunch without alcohol) received higher somnificity ratings in our cohort of geriatric patients, most probably due to routine afternoon napping often observed in older people [18].

The somnificity ratings for the original ESS item 3 (sitting inactively in a public place) did not significantly differ from those for the new item 6 (sitting in a waiting room, z = –0.58, p = 0.564). It also matches by content because in both situations subjects sit passively. The somnificity ratings for the original ESS item 8 (in a car while stopped) did not significantly differ from those for the new item 1 (during lunch) or new item 2 (during breakfast, z = –1.00, p = 0.317). It also matches by content because in all situations subjects engage in active motor behavior and need high levels of alertness. The new item 8 is very similar to the ODSI item 1 [31]: "Do you fall asleep or do you feel sleepy during basic activities of daily living (washing, dressing, eating, talking, driving or similar conditions …)?"

Our proposed changes to the original ESS items are comparable to those performed for the construction of the ESS-CHAD, which offers the possibility to take advantage of the previously validated items of the ESS-CHAD [28, 29]. Item 3 of the original ESS (sitting inactive in a public place, e.g., a theatre or a meeting), was changed to "in a classroom at school" in the ESS-CHAD. Similarly, we changed item 3 of the original ESS to "sitting in a waiting room" because older, often multimorbid individuals with physical or mental disabilities more often sit in a waiting room than in a theatre or meeting. Item 8 of the original ESS (in a car, while stopped for a few minutes in the traffic) was changed to "sitting and eating a meal" in the ESS-CHAD to overcome the problem that children and adolescents do not drive a car. Since our new ESS items "during lunch" and "during breakfast" achieved the same somnificity ratings, which were similar to the somnificity ratings for the original ESS item 8 (in a car, while stopped for a few minutes in the traffic), we decided to change the original ESS item 8 into "sitting and eating a meal" as was done in the ESS-CHAD [28, 29]. With that change, we put an emphasis on the posture of "sitting," rather than which meal they are having.

For the ESS-ALT total score, only 12 of our 52 patients (23%) had missing values (online suppl. Table 9) whereas for the original ESS this proportion was much higher (73%, n = 38; Table 5). This lower number of missing responses was also observed for close relatives (29 vs. 57%; online suppl. Tables 1, 8). The ESS-ALT total score ranged from 0 to 14, measures of central tendency were higher (median = 5.5, Q1–Q3 = 3.3–8.8, mean = 6.0, SD = 3.7) than for the total score of the original ESS (median = 5.0, Q1–Q3 = 3.0–7.0, mean = 5.1, SD = 2.3). In contrast to the original ESS, missing responses in the ESS-ALT were similarly frequent in males and females. As for the original ESS, patients with missing responses in the ESS-ALT more often suffered from dementia and lower levels of mobility than those with complete data (online suppl. Table 9). However, the level of mobility and frequency of dementia differed to a lesser degree between participants with incomplete versus complete data for the ESS-ALT than for the original ESS (online suppl. Tables 2, 9), implying the ESS-ALT is now more adequate for women and those with physical or mental disabilities than the original ESS.

All ESS-ALT item scores are moderately correlated with the ESS-ALT total score (Table 7) and the ESS-ALT shows a considerably higher level of internal consistency (Cronbach's α = 0.64) compared with the original ESS

Table 7. Adapted version of the ESS (ESS-ALT) based on patient's self-report (n = 52)

Item	Reliability and validity			
	missing responses, *n* (%)	difficulty, %	corrected item, total correlation	Cronbach's α[3]
ESS-ALT1 Sitting and reading	5 (9.6)	32.6	0.47	0.56
ESS-ALT2 Watching TV	1 (1.9)	38.6	0.40	0.59
ESS-ALT3 Sitting in a waiting room[1]	3 (5.8)	5.4	0.36	0.61
ESS-ALT4 As a passenger in the car	1 (1.9)	17.0	0.16	0.66
ESS-ALT5 Lying down in the afternoon	4 (7.7)	63.9	0.54	0.53
ESS-ALT6 Sitting and talking	0 (0.0)	3.2	0.28	0.63
ESS-ALT7 Sitting quietly after a lunch	1 (1.9)	35.9	0.34	0.61
ESS-ALT8 Sitting and eating a meal[2]	0 (0.0)	1.3	0.36	0.63
ESS-ALT Total	12 (23.1)			0.64

[1] ESS3 (sitting inactively in a public place), was replaced by NEW6 (sitting in a waiting room).
[2] ESS8 (sleepy in traffic) was replaced by NEW2 (during breakfast, now termed "sitting and eating a meal").
[3] If the item was deleted.

Table 8. Final English version of the ESS-ALT approved by M.W. Johns

ESS-ALT items
1. Sitting and reading
2. Watching TV or a video
3. Sitting in a waiting room
4. As a passenger in a car or a bus for about half an hour
5. Lying down to rest in the afternoon
6. Sitting and talking to someone
7. Sitting quietly by yourself after lunch
8. Sitting and eating a meal

(Cronbach's α = 0.23), even though high internal consistency and unidimensionality are no prerequisite for the reliability and validity of the ESS since it comprises situations which differ in their capacity to facilitate sleep onset (somnificity).

In a personal communication with M.W. Johns, we discussed our above-mentioned study results achieved in a sample of German geriatric patients using a German adaptation of the ESS as an alternative to assess daytime sleepiness in patients with physical and mental disabilities (ESS-ALT). We agreed on using the following items as the final translated English version of the ESS-ALT (Table 8) to integrate our novel findings, that is replace the third item of the original ESS (sitting inactive in a public place, e.g., a theatre or a meeting) with the item "in a waiting room," incorporating the validated changes previously made in the ESS-CHAD. This English version of the ESS-ALT, like the original ESS and ESS-CHAD, is subject to copyright (© M.W. Johns 1990, 1997, 2015, 2020). Authorized versions of these questionnaires are made available from Mapi Research Trust, as described in www.epworthsleepinessscale.com.

Discussion

Principal Findings

Via a systematic analysis of responses from sleep researchers and sleep medical specialists, nursing staff, geriatric patients and their close relatives, we were able to adapt the original ESS to make it a more adequate alternative for the assessment of daytime sleepiness in adults with physical or mental disabilities. This new ESS-ALT achieves better psychometric properties than the original ESS, including a lower number of missing responses (23 vs. 73%) and higher level of internal consistency (Cronbach's α = 0.64 vs. 0.23), while keeping the somnificity structure of the original ESS, including situations with low, moderate, and high probability of dozing off or falling asleep.

Comparison with Other Studies

In a previous study with geriatric in-patients, the German version of the ESS was shown to be inadequate to assess daytime sleepiness since only 36% were able to complete it [27]. In that study, as in our current work, physical disability and dementia were associated with

missing responses. Item 8 (in a car while stopped) had an especially high number of missing responses (60%), but also items 1 (sitting and reading), 3 (sitting inactively in a public place), and 4 (passenger in a car) were not answered by a considerable number of geriatric patients (13, 21, and 14%, respectively) [27]. Similarly, for the French version of the ESS it has been shown that only 40% of patients from 2 university-based geriatric outpatient clinics were able to answer all items [23]. Missing values occurred mostly for items 1 (11%), 3 (22%), and 8 (41%). The authors suggested that missing responses might be explained by the fact that patients were generally not in these situations anymore [23]. We have confirmed this by the evaluation of reasons for missing responses in our study. Also for the original English version of the ESS, item 8 had inadequate psychometric properties: in a large sample of the population-based Study of Osteoporotic Fractures, the item-total scale correlation was only 0.26 in 2,662 white women aged ≥70 years [22]. Based on such problems with item 8, the ESS was also applied without this item in older individuals [24, 33] or missing values were substituted by the median of subjects with the same sex and age [4]. However, a methodologically sound construction of a scale to assess daytime sleepiness in older persons exhibiting physical or mental disabilities was missing, which we have now realized with the ESS-ALT. Despite this novel methodologically sound construction it has to be considered that the participants of the expert survey were limited to attendees at a single conference in a single country, and there were no clear mechanisms for selection and consensus. In addition, it is only possible to generalize our results to a limited extent because our sample was composed only of older adults. Reliability and validity in younger adults with physical or mental disabilities need to be established. In the future, the ESS-ALT will be validated against measures of sleep such as polysomnography and pupillometry in subjects and patients with sleep disorders at different ages.

Acknowledgements

The authors express their gratitude to all study participants. We thank Mrs. Nickel-Gögel for her contribution to the geriatric assessment.

Statement of Ethics

The present study complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The study was approved by the Ethics Committee of the University of Duisburg-Essen, Germany (19-8875-BO). All participants gave their written informed consent.

Conflict of Interest Statement

Dr. Johns is the owner of the copyright of ESS, ESS-CHAD, and ESS-ALT. All other authors declare no potential conflicts of interest.

Funding Sources

This work was supported by the Paul Kuth Foundation. The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Author Contributions

J.G., A.-C.S., and H.F.: study conception. M.C.I.L., I.G., A.-C.S., and H.F.: data acquisition. M.C.I.L. and J.G.: data analysis. J.G., M.C.I.L., H.F., M.W.J., D.M.H., and T.P.: data interpretation. J.G. wrote the manuscript. All authors revised the manuscript critically for important intellectual content, gave final approval of the version to be published, and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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