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Peripheral neuropathy in elderly patients

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Abstract
Background: Among others, a peripheral polyneuropathy lead to an increased risk for fall in elderly frail patients.
Aims: Therefore, we aimed to investigate the frequency of a polyneuropathy in elderly patients treated in a specialized geriatric unit with a selected neurological expertise.
Methods: Patients hospitalized for comprehensive geriatric care in our geriatric unit were selected for the analysis. For proving the presence of a polyneuropathy, we performed extended electrophysiological examinations in patients with a current fall event or at risk for falling.
Results: We included in the final analysis 378 patients (median age was 82.1 years (IQR: 77.2 - 87.6 years, 64.6%were female). The diagnosis of polyneuropathy was identified in 340 patients (89.9%); in patients with a current fall event (n=173) a polyneuropathy was identified in 154 subjects (89%); in 31.5% of the cases the polyneuropathy was caused by diabetes mellitus, in 47.6% no etiology could be identified.
In patients with polyneuropathy higher rates of individuals aged ≥80 years (67.1% versus 50%; p=0.038), with heart insufficiency (26.5% versus 7.9%; p=0.038) and renal insufficiency (45.6% versus 18.4%; p=0.001) were detected. The diagnosis of a polyneuropathy was associated with the factor renal insufficiency (OR: 2.680; CI: 1.100 - 6.529; p=0.03).
Conclusion: Applying specific electrophysiological examinations in the particular setting of a specialized geriatric unit, we detected in a high proportion of patients a polyneuropathy (90%). Our results underline the benefit considering this approach in elderly patients at risk for fall hospitalized for comprehensive geriatric care.

Keywords: polyneuropathy, frailty, geriatric unit, risk for fall

Introduction
Different factors are responsible for the increased risk for fall in elderly [1-4]. On the one hand, the frail status with a generalized loss of muscles may lead to gait instability, on the other hand, factors such as osteoporosis, polypharmacy, cognitive impairment or neurodegenerative diseases may facilitate the occurrence of falls in older patients [5, 6]. It is important to know the underlying cause for falls when developing prevention strategies or toileted rehabilitation programs after a fall event. Therefore, a neurological work up for proving the diagnosis of a polyneuropathy including an electrophysiological examination appears in elderly frail patients with risk for fall a useful measure. However, despite the increasing number of specialized geriatric units limited information exists on polyneuropathy in elderly frail patients treated in such departments. This might be due to the fact neurologists joined the genuine geriatric field in recent years, so this particular knowledge shortly became broadly available in the geriatric care. In the so-called comprehensive geriatric care (CGC), patients undergo a treatment according to standardized protocols focusing on medical requirements but also taking into account the potential functional outcome [7, 8]. Unveiling a damage of peripheral nerves, which may lead to disturbed proprioceptive function and consecutive gait imbalance seem in the setting of a CGC an appropriate amendment. For this reason, we aimed to study the occurrence of a polyneuropathy in elderly patients at risk for fall treated in a specialized geriatric unit with a selected neurological expertise.

Methods
Patients and Measures
All patients hospitalized between May 2018 and May 2019 in our geriatric department with 50 beds were selected for the present analysis. Patients were assigned from the in-house emergency, other in-house departments, external hospitals or patients' resident doctors. Admitted patients received a detailed assessment and were allocated to CGC if appropriate. A geriatric assessment regarding patients' mobility and ability to cope with daily tasks was standardized performed on hospital admission. Each patient at risk for fall underwent a standardized electrophysiological examination for proving the presence of a polyneuropathy.
All relevant data from patients' care and medical treatment were documented and recorded systematically and used regularly as background for interdisciplinary discussions, quality assurance measures and also for billing calculations. For the current analysis demographic parameters as well as information regarding patients' co-morbidities and information regarding a

current fracture. Additionally diagnoses potentially related to the development of a polyneuropathy were recorded as well as the differentiation between an axonal versus demyelinating type of the polyneuropathy was documented.

Eletrophysiological examination for proving the presence of a polyneuropathy

In our department, as a standard procedure all patients with a current fall or at risk for fall are selected for an eletrophysiological examination. In case patients were suitable for the procedure, the examination was performed by an experienced neurologist in the same laboratory. For investigating the motor and sensoric nerve conduction velocities the Dantec Natus Keypoint system (Natus Europe GmbH, Robert-Koch-Str. 1, 82152 Planegg, Germany) was used. For establishing the electrophysiological diagnosis of polyneuropathy, we considered reference values Bischoff and co-workers established [9].

Statistical analyses

Data for continuous variables are expressed as median and interquartile range. Categorical variables are reported as frequencies and percentages. A normal distribution was verified by the Kolmogorov-Smirnov's one-sample test. Nonparametric data were compared by applying a two-tailed Mann-Whitney U-test. For comparing relative frequencies, the Fisher's exact test was used. For proving associations between parameters in the equation, factors were entered into a logistical regression analysis. For statistical analysis the SPSS software, (version 22.0, IBM Corporation, Armonk, NY, USA) was used.

Ethical approval

For the offline analysis of data obtained in the clinical care delivery, we obtained ethical approval from the local ethical committee (protocol number: 2019-517-f-S).

Results

We included in the final analysis 378 patients who underwent the electrophysiological examination (figure 1); the median age was 82.1 years (IQR: 77.2 - 87.6 years), 244 were female (64.6%). Male patients were younger (median 80.5 versus median 82.3 years) and had lower rates of hypertension (males: 76.9% versus females: 87.3%, p=0.009) and obesity (males: 11.9% versus females: 20.5%, p=0.009) (table 1). The diagnosis of polyneuropathy was established in 340 patients (89.9%) (table 1); in patients with a current fall event a polyneuropathy was identified in 89% of the subjects (154/173); in 31.5% of the cases the polyneuropathy was caused by diabetes mellitus, in 47.6% no aetiology could be identified (figure 2).

In patients with polyneuropathy higher rates of individuals aged ≥80 years (67.1% versus 50%; p=0.038), heart insufficiency (26.5% versus 7.9%; p=0.038) and renal insufficiency (45.6% versus 18.4%; p=0.001) were detected. Entered into a logistical regression analysis the diagnosis of a polyneuropathy was associated with the factor renal insufficiency (OR: 2.680; CI: 1.100 - 6.529; p=0.03) (table 2).

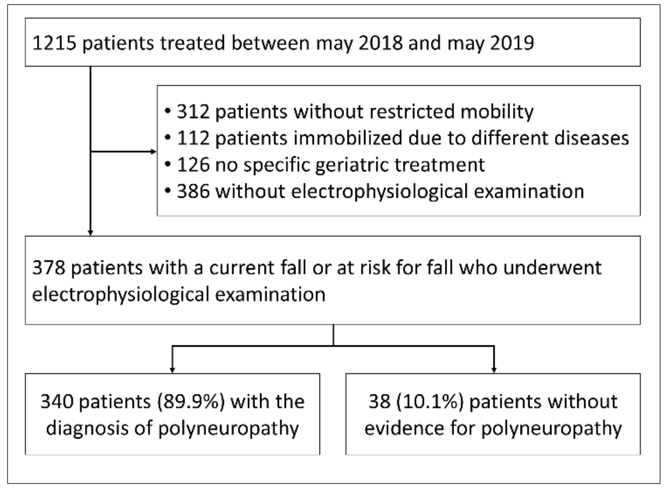

Fig 1: Patient's selection for the analysis

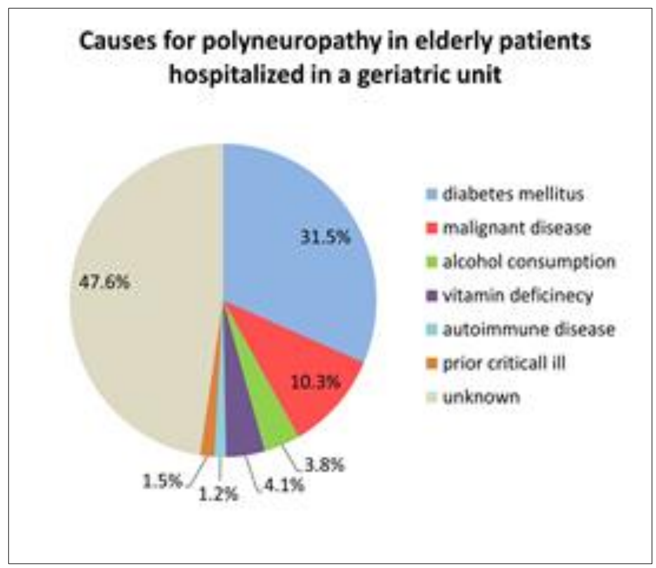

Fig 2: Distribution of pathologies responsible for causing a polyneuropathy in elderly patients treated in structured geriatric setting (n=340).

Table 1: Differences between elderly male and female patients with a neurological electrophysiological work up for diagnosing a polyneuropathy

	Total group (n=378)	**Females (n=244)**	**Males (n=134)**	***p****
Age (median, IQR, years)	82.1 (77.2-87.6)	82.3 (78.4-87.3)	80.5 (73.4-86.7)	0.003
Co-morbidities				
Hypertension	316 (83.6%)	213 (87.3%)	103 (76.9%)	0.009
Diabetes mellitus	132 (34.9%)	86 (35.2%)	46 (34.3%)	0.858
Obesity	66 (17.5%)	50 (20.5%)	16 (11.9%)	0.036
Heart failure	93 (24.6%)	65 (26.6%)	28 (20.9%)	0.215
Renal insufficiency	160 (42.9%)	102 (41.8%)	60 (44.8%)	0.576
Dementia	46 (12.2%)	30 (12.3%)	16 (11.9%)	0.920
Fall	n=173 (45.8%)	n=122 (50.0%)	n=51 (38.1%)	0.026

Bruise	46 (26.6%)	32 (26.2%)	14 (27.5%)	0.868
Brain injury[l]	19 (11.0%)	11 (9.0%)	8 (15.7%)	0.201
Fractures	110 (64.0%)	79 (64.8%)	31 (62.0%)	0.733
Fractures	n=112 (29.6%)	n=81 (33.2%)	n=31 (23.1%)	0.040
Upper Extremities	12 (10.7%)	11 (13.6%)	1 (3.2%)	0.174
Lower Extremities	52 (46.4%)	39 (48.1%)	13 (41.9%)	0.555
Spinal column	18 (16.1%)	9 (11.1%)	9 (29.0%)	0.021
Fractures of the pelvis	20 (17.9%)	18 (22.2%)	2 (6.5%)	0.057
Thorax (ribs)	7 (6.3%)	2 (2.5%)	5 (16.1%)	0.017
Polyneuropathy	n=340 (89.9%)	n=219 (89.8%)	n=121 (90.3%)	0.866
Axonal damage	308 (90.6%)	205 (93.6%)	103 (85.1%)	0.010
Demyelinating damage	16 (4.7%)	8 (3.7%)	8 (6.6%)	0.284
Combined damage	16 (4.7%)	6 (2.7%)	10 (8.3%)	0.031
Etiologies				
Diabetes mellitus	107 (31.5%)	73 (33.3%)	34 (28.1%)	0.320
Malignant disease	35 (10.3%)	17 (7.8%)	18 (14.9%)	0.061
Alcohol consumption	13 (3.8%)	4 (1.8%)	9 (7.4%)	0.016
Vitamin deficiency	14 (4.1%)	10 (4.6%)	4 (3.3%)	0.777
Autoimmune disease	4 (1.2%)	0 (0%)	4 (3.3%)	0.015
Prior critical ill	5 (1.5%)	0 (0%)	5 (4.2%)	0.005
Unknown	162 (47.6%)	115 (52.5%)	47 (38.8%)	0.016

[l]includes intracerebral haemorrhages, subarachnoid haemorrhages, subdural haemorrhages and unspecified head injuries
*refers to p-value calculated in the univariate analysis

Table 2: Differences in elderly patients with versus without the diagnosis of polyneuropathy

	Total group (n=378)	**PNP+ (n=340)**	**PNP- (n=38)**	***p****	***p*****
Age (median, IQR)	82.1 (77.2-87.6)	82.6 (78.4-87.1)	79.5 (71.6-82.3)	0.001	
Age ≥80 years	247 (65.3%)	228 (67.1%)	19 (50.0%)	0.036	0.120
Sex					
females	244 (64.6%)	219 (64.4%)	25 (65.8%)	0.866	
males	134 (35.4%)	121 (35.6%)	13 (34.2%)		
Co-morbidities					
Hypertension	316 (83.6%)	284 (83.5%)	32 (84.2%)	0.914	
Diabetes mellitus	132 (34.9%)	120 (35.3%)	12 (31.6%)	0.722	
Obesity	66 (17.5%)	60 (17.6%)	6 (15.8%)	0.775	
Heart insufficiency	93 (24.6%)	90 (26.5%)	3 (7.9%)	0.012	0.141
Renal insufficiency	160 (42.9%)	155 (45.6%)	7 (18.4%)	0.001	0.030[$]
Dementia	46 (12.2%)	43 (12.6%)	3 (7.9%)	0.395	
Fall	173 (45.8%)	154 (45.3%)	19 (50.0%)	0.581	
Bruise	47 (12.4%)	41 (12.1%)	6 (15.8%)	0.509	
Brain injury[l]	20 (5.3%)	16 (4.7%)	4 (10.5%)	0.128	
Fractures	112 (26.9%)	99 (29.1%)	13 (34.2%)	0.514	
Upper Extremities	15 (4.0%)	11 (3.2%)	4 (10.5%)	0.053	
Lower Extremities	54 (13.2%)	49 (14.4%)	5 (13.2%)	0.834	
Spinal column	21 (5.6%)	20 (5.9%)	1 (2.6%)	0.407	
Fractures of the pelvis	21 (5.6%)	19 (5.6%)	2 (5.3%)	0.999	
Thorax (ribs)	8 (2.1%)	7 (2.1%)	1 (2.6%)	0.575	

[l]includes intracerebral hemorrhages, subarachnoid hemorrhages, subdural hemorrhages and unspecified head injuries
*refers to p-value calculated in the univariate analysis
**refers to p-value calculated in the logistical regression analysis
[$]OR for Renal insufficiency: 2.680 with CI: 1.100 - 6.529

Discussion

Our study represents an attempt to prove the diagnosis of polyneuropathy in patients hospitalized in a specialized geriatric unit with extended neurological expertise. Of 378 geriatric patients with a fall event or risk of falling, we established the electrophysiologic diagnosis of polyneuropathy in nearly 90% of cases.

While risk factors for falls in the elderly such as polypharmacy, vitamin D deficiency, multimorbidity, sarcopenia/fracture, or environmental factors have been well studied, fewer publications address this in the context of underlying polyneuropathy [2, 3, 10-13]. Some studies likely refer to the role of polyneuropathy causing falls in the elderly, outlining associated symptoms in the form of balance disorders [2, 10, 14, 15]. Since the incidence of neurological disorders increases with age and falls are common in neurological disorders, falls could be expected to be a common event in elderly patients with polyneuropathy [13, 16]. In a study conducted by Richardson et al. in a group of 82 subjects (with electrophysiologically proven polyneuropathy), the authors identified a history of at least one fall in 49% of the participants

[10]. In a small series of 32 elderly patients with a fall event, Aktas et al. identified polyneuropathy as a possible underlying cause in 25% of cases [12]. In light of this literature review, our results may provide valuable information about the involvement of polyneuropathy in the pathomechanism of falls in elderly patients. In contrast to the results presented by Aktas et al, we identified 89% of individuals with polyneuropathy in a much larger group and in participants of older age (median: 82.1 years versus mean age 78 years) [12]. When considering the subgroup of patients with a recent fall event with a consecutive fracture (n=154), the proportion of patients with a diagnosis of polyneuropathy remained the same (89%).

Although diagnosis of this condition does not ensure a definitive link between the fall event or fall risk and the underlying polyneuropathy, knowledge alone could facilitate further diagnostic as well as other therapeutic strategies. The comorbidity of polyneuropathy would allow different approaches to the rehabilitation process in these patients [4, 17-19]. Moreover, it could determine further investigations to verify the underlying cause of the neuropathy.

The cause of polyneuropathy even in the elderly population are diverse. The etiology may be metabolic, immune-mediated, hereditary, or an infectious one.

As expected, in our work, many polyneuropathies are associated with diabetes mellitus, since diabetes mellitus is common in the elderly population and is causative for diabetic neuropathy [20]. The other etiologies of polyneuropathy tend to be diminished in the elderly population [21].

The high incidence of cryptogenic polyneuropathy is striking in our study. Despite intensive diagnosis of the cause, the etiology of polyneuropathy is cryptogenic in almost half of the patients (47.6%), i.e., no known risk factors were found. In electrophysiological examination, we also found an axonal type in the majority of cryptogenic polyneuropathy. This is consistent with others [22] Mathis et al., 2015 [20, 23]. Visser et al. found that with increasing age, the chance of a confirmed etiology of polyneuropathy decreases [20]. These polyneuropathies are referred to as cryptogenic or chronic idiopathic axonal neuropathy [CAP or CIAP] [23, 24, 25]. For example, Visser et al [20] found that 1/7 patients between 40 and 49 years of age have CIAP, but this is already increased to 1/3 in patients around 80 years of age. However, the data is thin in this regard.

It is shown that chronic idiopathic axonal polyneuropathy is frequently associated with metabolic syndrome, such as obesity, hypertension, and diabetes mellitus [26]. This is also found in our study, but in addition, we demonstrated that CIAP is significantly associated with renal insufficiency. It is known that patients with chronic kidney disease have a higher risk of developing polyneuropathy [27, 28, 29]. Renal insufficiency is characterized by a lack of energy production, enzymatic activity, and dysfunction of mitochondria due to uremic toxins, and leads to premature damage of the large myelinated sensory fibers, resulting in paresthesia and numbness in the lower limbs [30].

Older age together with increasing proportions of vascular risk factors are characteristic of geriatric multimorbid patients, but these factors are also associated with the development of renal disease and renal insufficiency [31]. Therefore, in our case, the renal insufficiency parameter could also be interpreted as a surrogate for multimorbidity in elderly patients.

CIAP leads to muscle atrophy and decreased sensitivity, among others, and is a cause of gait disturbances. Many elderly patients reported that they are afraid of falling. This can contribute to further loss of function in elderly frail patients. They become less mobile and weaker, leading to loss of activities of daily living [32, 33].

Considering the comprehensive and multidisciplinary approach of specialized geriatric departments and the interpretation of our results, systematic screening for polyneuropathy in the setting of comprehensive geriatric care seems appropriate and an important measure. It allows further diagnostic procedures with direct consequences for treatment. It also highlights the specific nature of the geriatric specialty by linking different disciplines to develop the best treatment strategies for elderly patients. In addition, our results suggest that the addition of specific neurological expertise to the geriatric field appears to be of outstanding benefit to patient care.

The strength of the presented study is the attempt to use data from electrophysiological studies of peripheral nerves in elderly patients treated in a specific geriatric unit. In addition to the extended neurological expertise in our department, the detailed documentation of all relevant parameters in the clinical course according to standardized protocols underlines the reliability of the collected data. However, limitations must also be considered. The main limitation of the study is that a control group with regular specialist treatment was not available. Furthermore, a selection bias has to be mentioned, because in a geriatric pre-assessment especially those patients were selected for treatment in the geriatric department who could be expected to benefit the most.

Conclusion

Applying specific electrophysiological examinations in the particular setting of a specialized geriatric unit, we detected in a high proportion of patients a polyneuropathy (90%). Our results underline the benefit considering this approach in elderly patients at risk for fall. The environment of a comprehensive geriatric care appears suitable for screening for polyneuropathy and for applying specific electrophysiological diagnostic procedures.

Author contributions

CT and SS contributed to the development of the original protocol. MM, TS, UN, AA, RI, DB, RAG and KK contributed to the study design. TS, AA, UN and RAG acquired the data; CT, SS and KK performed the statistical analysis and wrote the initial draft. All authors critically reviewed the manuscript for important intellectual content and approved the final version submitted for publication. CT is the guarantor for the article.

Data availability

All authors had full access to the study data (including statistical reports and tables) and can take responsibility for the data integrity and the accuracy of the analysis.

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We received no funding for this study.

Compliance with ethical standards
Conflict of interest
All authors report to have no conflicts of interest or competing interests related to the current manuscript.

Ethical approval
The Medical Ethical Committee of the Landesärztekammer Westfalen-Lippe and Wilhelms-University of Münster approved the study.

Informed consent
For this analysis including data obtained in the clinical routine, informed consent from subjects was not necessary.

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