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Association between hematologic parameters and functional impairment among geriatric inpatients: Data of a prospective cross-sectional multicenter study ("GeriPrävalenz2013")

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ABSTRACT

Objectives: Objective of this study was to analyse the association between impairment of Barthel Index items and hematologic parameters in geriatric inpatients.
Methods: Patient recruitment of the "GeriPrävalenz2013" study has been described before. Inclusion criteria: in-patient aged > = 70 years; exclusion criteria: actual cancer disease or cancer associated treatment. Anemia was defined according to WHO criteria. Physical impairment was assessed by Barthel Index (BI). Association between all 10 items of the BI and hematologic parameters was statistically evaluated.
Results: Anemia prevalence was 55.1% (319/579) with BI impairment in 96.2% patients. T-test revealed significant lower BI in anemic patients (47.9 vs 54.3; p = 0.004). Binary logistic regression revealed that growing age, reduced MCV, reduced iron levels and reduced Hb levels were associated with increased impairment of several items of the Barthel-Index. Interestingly, increased levels of albumin and folic acid (FA) were associated with increased impairment of BI items.
Conclusion: Anemia and lower levels of anemia related parameters showed a negative impact on ADL and physical performance based on BI items. An impaired total BI should result in an analysis of BI subitems, particularly if anemia related laboratory parameters are deviant. Reasons for the negative impact of elevated FA and albumin levels on BI remain speculative.

1. Introduction

Anemia is a frequent finding in older patients and association with functional deficits has been described [1,2]. Data of physical impairment in anemic German geriatric inpatients, however, is scarce [3]. Most of the study groups evaluating association between functionality and anemia in older patients apply Barthel Index (BI) for assessment of physical impairment [4]. "Functional evaluation: the Barthel Index". Md Med J 14: 61–65. The BI is part of the comprehensive geriatric assessment (CGA) and an established assessment tool, measuring the performance of activity of daily living. Ten performance items are used describing mobility and activity of daily living. Every item is rated and assigned a number of points. A high number of points (maximum 100 points) is associated with more independence in everyday life and less dependence on assistant help [4]. As the original version of BI had shown some weaknesses [5], several modified versions were developed. The Hamburg Classification Manual is a standardized and consensus-based oper-

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ationalization of the BI and has been developed for application in German geriatric medicine [6]. Assessment of functional impairment in this study is based on the Hamburg Classification Manual for the BI.

As numerous previous studies have revealed significant impairment of overall results of BI score in anemic patients, this study analyses every single item of BI for impairment by anemia associated hematologic parameters. Primary objective of this study was to evaluate the impact of Hb values on impairment of the ten items. Secondary objective of this study was to evaluate impacts of several hematologic variables on impairment of the ten BI items.

Data derives from the cross-sectional multicenter study "GeriAnämie2013", which has been issued by the German Geriatric Society to evaluate hematologic findings in German geriatric inpatients. It is registered in the German Clinical Trials Register (DRKS, Freiburg) with No. DRKS00004617. The local Ethics Committee of the University Hospital Cologne approved of the study (No. 12-322; 13.2.2013). The study was carried out in accordance with the current version of the Declaration of Helsinki of 2013.

2. Patients and methods

Recruitment of patients for "GeriAnämie2013" has been described before [7]: Between June 2013 and December 2014 a number of 598 geriatric inpatients were consecutively recruited on admission in six participating German study centers (5 geriatric centers and 1 general emergency department of a university hospital). Recruitment interval was 4–6 weeks in every study center. Included were patients > 70 years admitted to the geriatric department or – in case of the general emergency department – purposed to be admitted to a geriatric department. All study patients gave informed consent. Patients with actual cancer disease or actual cancer associated treatment were not included in the study.Nineteen patients were excluded due to age <70 years or no written informed consent. The remaining 579 patients met with study criteria. Anemia associated hematologic parameters were analysed in every center-associated laboratory department on admission. The blood draw was part of a routine blood draw for standard of care at admission in every study center. The parameters included: hemoglobin (Hb) (g/dl), erythrocyte count (ery) (mio/μl), hematocrit (%), mean corpuscular volume (MCV) (fl), serum iron (μg/dl), ferritin (μg/l), folic acid (FA) (ng/ml), creatinine (mg/dl), vitaminB12 (vitB12) (ng/l), serum albumin (g/dl) and transferrin saturation (TSAT) (%). Additional data was gathered concerning patients' sex and age. Anemia was defined according to WHO criteria (females <12 g/dl, males <13 g/dl); severity of anemia was defined according to NCI scale (>10 g/dl mild, 8–9.9 g/dl moderate, 6.5–7.9 g/dl severe, <6.5 g/dl very severe). Based on MCV, anemia was classified microcytic (MCV < 78 fl), normocytic (78 fl < MCV < = 94 fl) or macrocytic (MCV > 94 fl); deficiency of serum albumin was defined <3.5 g/dl, deficiency of VitB12 was defined < 200 ng/l, folic acid was defined <3 ng/ml; drug intake was elevated if > = 5 drugs/day were taken.

Assessment of physical ability was carried out based on BI on admission. The ten performance items of the BI check for [8]

1. Presence of impairment with feeding (<10 points).
2. Presence of impairment with transfers (<15 points).
3. Presence of impairment with grooming (<5 points).
4. Presence of impairment with use of toilet (<10 points).
5. Presence of impairment with bathing (<5 points).
6. Presence of impairment with walking/wheel chair use (<15 points).
7. Presence of impairment with climbing stairs (<10 points).
8. Presence of impairment with dressing (<10 points).
9. Presence of fecal incontinence (<10 points).
10. Presence of urinary incontinence (<10 points).

Table 1
Barthel Index and anemia associated hematologic study parameters (metric) (n = number of patients, mean value and standard deviation (SD)).

	N	Mean or median	Standard deviation (SD) or quartiles
Barthel Index	579	51.33	26.53
Erythrocytes Mio/μl	579	3.94	0.63
Hemoglobin g/dl	579	11.90	1.90
Hematocrit%	579	35.60	5.57
MCV fl	579	90.83	6.50
Iron μg/dl	461	53.0	37.0–75.0
Ferritin μg/l	445	157.0	83.2–291.8
Transferrin-saturation%	426	21.0	14.0–29.0
Folic acid ng/ml	468	5.8	4.2–8.9
Creatinine mg/dl	574	1.1	0.8–1.4
Vitamin B12 ng/l	469	433	311–655
Albumin g/dl	462	3.19	0.60

Database was created by means of Research Electronic Data Capture (REDCap®). Statistical analysis was carried out by means of the IBM SPSS Statistics Version 22.

Groups were compared by *t*-test for normally distributed data, Mann Whitney *U* test for not normal distributions and nominal data by Chi-Square test. Descriptive numbers are mean ± standard deviation, median (inter quartile range) or frequencies, accordingly. Predictors for the outcome of the 10 BI items were analyzed by multivariable binary logistic regression. Additionally to all examined blood parameters gender and age were considered. Potential predictors with a p-value < = 0.05 in a Spearman (Pearson for gender) correlation analysis were selected for the respective BI item regression model. The final models were calculated by stepwise backward selection, calculating adjusted odds ratios (OR).

3. Results

Anemia was found in 319 of 579 (53.3%) patients (205 female, 114 male). Anemic patients were between 70 and 97 years old, with a mean age of 81.9 years (standard deviation (SD) 6.23).52.4% of women and 60.6% of men were anemic according to WHO criteria. Anemia was mainly mild and normocytic. BI was evaluated in all 579 patients with a mean value of 51.33 points (SD 26.53). Description of Barthel Index and items as well as the 11 metric and 5 nominal anemia associated hematologic study parameters are shown in Tables 1 and 2.

The most frequent impairment seen in this study group was impaired stair climbing (42.7%), followed by impaired bathing (40.6%). The least prevalent impairment was seen in connection with feeding (18%) and fecal continence (15.4%).

Student's *t*-test revealed that anemic patients have a significant lower BI than not-anemic patients (47.9 and 54.3, respectively; p = 0.004).

In the multivariable regression analyses for BI items gender was not included because no association was found with any item at all. Overall in the final models age and five anemia related parameters were associated with impairment of BI items: growing age was associated with increased impairment of feeding (1.07 (1.03; 1.12)), impairment of dressing (OR 1.03 (0.99; 1.06)) and with fecal incontinence (OR 1.05 (1.00; 1.09)); although for impairment of dressing age failed to be a significant predictor (p = 0.055), it was considered due to better model accuracy.

Among the anemia related parameters a reduction of MCV, iron levels and Hb levels was associated with increased impairment: reduced MCV impaired feeding (OR 0.94 (0.90;0.98)), grooming

Table 2
Barthel Index items and anemia associated hematologic study parameters (nominal) (n = number of patients, frequency in%).

	n	Frequency (%)
Barthel Index	579	100
Impaired feeding	104	18.0
Impaired transfers	212	36.6
Impaired grooming	150	25.9
Impaired use of toilet	206	35.6
Impaired bathing	235	40.6
Impaired walking/use of wheelchair	218	37.7
Impaired stair climbing	247	42.7
Impaired dressing	184	31.8
Fecal incontinence	89	15.4
Urinary incontinence	148	25.6
Anemia	319	55.1
Total	579	
Anemia severity		
Mild	260	44.9
Moderate	232	40.1
Severe	76	13.1
Very severe	11	1.9
Total	579	
MCV based cytology		
microcytic	10	1.7
Normocytic	413	71.3
Macrocytic	156	26.9
total	579	
Deficiency of folic acid	28	4.8
Total	469	
Deficiency of VitB12	27	4.7
total	469	
Deficiency of albumin	328	56.6
total	462	
Drug intake/day > = 5	487	84.1
total	579	

(OR 0.95 (0.92;0.99)), bathing (OR 0.95 (0.92;0.98)), use of toilet (OR 0.95 (0.92;0.99)) and was associated with fecal incontinence (OR 0.94 (0.90;0.98)); reduced iron levels were associated with impaired grooming (OR 0.98 (0.97; 0.99)) and urinary incontinence (OR 0.98 (0.97;0.99)); reduced Hb levels were associated with impaired walking (OR 0.79 (0.70; 0.90)).

Interestingly, increased levels of the anemia related parameters albumin and folic acid were associated with increased impairment: an elevation of serum albumin levels affects all 10 items, increasing patients' chance of impairment from 1.8-fold (impaired feeding, OR = 1.87 (1.22; 2.86)) to 5-fold (impaired use of toilet, OR = 5.22 (3.37;8.07)). An elevation of folic acid levels by one unit increases patients' chance to be impaired in transfers only slightly (OR = 1.05 (1.00;1.10)) (Table 3).

4. Discussion

Aim of this study was to analyse an association between anemia related parameters and functional impairment assessed by BI items among geriatric inpatients. To our knowledge this is the first study to evaluate BI items and anemia related parameters in geriatric inpatients. Our finding of anemic patients having significantly lower BI scores than not-anemic patients is in accordance with previous findings of a Spanish study [2]. In our study multivariable analysis further revealed that reduced levels of hemoglobin were associated with impaired walking (OR = 0.79), which is in accordance with findings of the Octabaix study group [1]: even though they did not subanalyse BI items, they revealed an OR = 0.99 for dependence of anemia from BI values. MCV, iron and Hb are anemia related parameters. Reduced levels of serum iron are seen in iron deficient anemia (IDA) with absolute iron deficiency due to empty iron stores as well as in anemia of chronic inflammation (ACI) with functional iron deficiency due to impaired iron release from iron stores. Although MCV has been shown to be an inappropriate parameter for anemia assignment in older patients [9,7], low MCV is often associated with iron deficiency anemia [9,7]. Our finding that reduced levels of MCV, iron and Hb are associated with impairment of several BI items endorses previous findings of anemia being associated with functional impairment based on BI [1–3,10]. The association of older age with increasing impairment of several BI items confirms previous findings: Impairment of feeding in older age has been shown to be due to swallowing problems [11] or to impaired oral health [12,13,]; due to its association with further impairments, impaired dressing in growing age is a red flag for affected activity of daily living (ADL) and has to be taken seriously by health care workers [14]; a US study on the change of ADL impairment before and after hospital admission revealed a decline of ADL after hospital admission, associated with an age-related incapacity to recover the lost ADL function [15]. Fecal incontinence in older patients has been shown to be associated with age-related changes of gut function with increasing susceptibility to intestinal problems like malnutrition, constipation or incontinence [16].

In this study, analysis of BI items with albumin and FA showed an unexpected association: the OR for impairment of ADL is increased if albumin levels or FA levels increase by one unit. Literature on the association between impairment and FA mainly refers to an association between low FA levels and cognitive impairment. In connection with physical performance, FA substitution remains controversial. A recently published study by Swart et al. revealed that a 2-year- supplementation of folic acid in older patients did neither prevent falling nor the decline of physical performance [17]. However, indications for a positive effect on gait were provided, but underlying mechanisms remain unclear. Further research is needed to assess if FA supplementation might be equally beneficial to cognitive as to physical decline. Low serum albumin has been associated with risk of morbidity and mortality in older patients [18,19] as well as risk of malnutrition [20,21], Findings of our present study with elevated albumin levels increasing OR for impairment of ADL seems to be contradictory. However, in recent years there is growing evidence that glycated serum albumin is associated with adverse outcome. Lu et al. (2007) revealed that increased serum levels of glycated albumin in diabetes type 2 patients > 52 years were associated with increased prevalence and severity of coronary artery disease and renal impairment [22]. A recent review by Vetter [23] underlines the association between glycated serum albumin and diabetic complications, neurodegeneration and vascular disease [23]. Glycated serum albumin (GSA) is a physiologic finding in human metabolism independent of sex and race [24]. Elevated levels of GSA are found in patients with diabetes mellitus. In contrast to glycated proteins like HbA1c, glycated albumin is more sensitive to changes in blood glucose and might be an effective parameter for glycemic control in diabetic patients [24].

Epidemiologic data among German policyholders of statutory health insurance revealed an age-associated increase of diabetes prevalence of 18% to 25% among patients > 60 years, with a considerable number of unreported cases [25]. In our study, neither prevalence of diabetes mellitus was assessed, nor the levels of GSA determined. GSA and serum albumin are usually measured by immunoassay with an additional measurement of the glycation sites in GSA [24]. Our study results are based on serum albumin levels without any information about glycation. Therefore, the idea, that the finding of increasing OR for ADL impairment associated with the rise of serum albumin levels reflects a potentially negative effect of GSA is purely hypothetic and cannot be proven by our data.

For clinicians providing care for geriatric patients, results of this study may imply clinical relevance: Barthel subitems appear to be impaired by different factors including age and laboratory param-

Table 3
Results of binary logistic regression analyses of anemia related parameters on BI items. Adjusted odds ratios (OR) for a one-unit-change of the influencing variable.

	variables	adjusted OR (CI)	n
Impaired feeding	Albumin (g/dl)	1.77 (1.17; 2.68)	462
	MCV (fl)	0.94 (0.90;0.98)	
	age	1.07 (1.03; 1.12)	
Impaired transfers	Albumin (g(dl)	3.50 (2.32;5.26)	433
	Folic acid (ng/ml	1.05 (1.00;1.10)	
Impaired grooming	Albumin (g/dl)	2.80 (1.82; 4.31)	429
	Iron (μg/dl)	0.98 (0.97; 0.99)	
	MCV(fl)	0.95 (0.92;0.99)	
Impaired use of toilet	Albumin (g/dl)	5.22 (3.37; 8.07)	433
	MCV (fl)	0.95 (0.92;0.99)	
		0.91 (0.87; 0.95)	
Impaired bathing	Albumin (g/dl)	3.35 (2.28;4.92)	462
	MCV (fl)	0.95 (0.92;0.98)	
Impaired walking/use of wheelchair	Albumin (g/dl)	2.11 (1.49;3.00)	462
	Hemoglobin	0.79 (0.70; 0.90)	
Impaired stair climbing	Albumin (g/dl)	3.59 (2,45; 5,26)	462
Impaired dressing	Albumin (g/dl)	2.11 (1.48; 3.02)	462
	age (failed to be significant, but increased model accuracy)	1.03 (0.99; 1.06)	
Fecal incontinence	Albumin (g/dl)	2.05 (1.31;3.20)	462
	age	1.05 (1.00; 1.09)	
	MCV	0.94 (0.90;0.98)	
Urinary incontinence	Albumin (g/dl)	2.32 (1.51;3.57)	429
	Iron (μg/dl)	0.98 (0.97;0.99)	

eters. Bearing in mind the geriatricians' endeavor to strengthen patient resources and eliminate – as far as possible – functional deficits to maintain activity of daily living, consideration of BI subitems will provide the clinician with more precise information about the kind of functional impairment than the usually considered total BI. This consideration will allow an even more focussed treatment of functional deficits. Results of this study suggest a distinct analysis of BI subitems particularly if anemia related parameters are deviant.

This study has a number of shortcomings: study parameters like vitamin B12 and folic acid and albumin were not available in all study centers and GSA was not analysed. Due to this lack of data, results only have a limited informative value. The lack of consistent laboratory analysis for all study centers may also be responsible for result variability. Due to the cross sectional design of the study, changes in functional impairment and hematologic parameters during hospital stay could not be evaluated serially.

5. Conclusion

Results of this study underline the idea of a negative impact of anemia and anemia related parameters on ADL and physical performance based on BI items. An impaired total BI should result in an analysis of BI subitems, particularly if anemia related laboratory parameters are deviant.

Contributors

Gabriele Röhrig, contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data and writing the article. Ingrid Becker contributed to the statistical analysis and interpretation of data as well as drafting the article. Ralf-Joachim Schulz, Romana Lenzen-Großimlinghaus, Peter Willschrei, Sybille Gebauer, Mirja Modreke and Martin Jäger contributed to the acquisition of data and drafting the article. Rainer Wirth contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data and revising the article critically for important intellectual content.

Conflict of interest

None declared.

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Ethics

The Ethics Committee of the University Hospital Cologne approved of the study (No. 12-322; 13.2.2013) and informed consent was obtained from participants.

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