JGG 2017;65:238-247

Original Investigation

The implementation of a geriatric patients blood management program to monitor hemoglobin level in nursing homes

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Background and aims. In reference to the Resolution WHA63.12 of 21/05/2010 from the World Health Organization, the Italian National Blood Center has promoted an initiative encapsulated by the term Patient Blood Management (PBM). The aim of this study is to examine the relationships among the prevalence of genera-age-associated risk factors of anemia and hemoglobin level in geriatric patients with cognitive decline through CBA SIPCARplus software (medical records). Before this implementation, there was not the traditional blood management program in nursing homes.
Methods. The CBA database has been developed by a dedicated working group using Delphi process and PBM. It contains records on patient characteristics, and one set of biomarker laboratory.
Results. Between 2014 and 2015, 283 geriatric patients were enrolled at three Italian elderly nursing homes. Among these patients, 14% were men and 86% were women (mean age 79 years) and the overall prevalence of anemia was 55.9%; 32.6% of the geriatric patients were at risk of malnutrition and 11.5% were malnourished. Multivariate analysis determined that comorbidity was highly associated with malnutrition risk measured by Malnutrition Universal Screening Tool ≥ 2, cognitive decline measured by Mini-mental State Examination ≤ 19, functional independence in two or more basic activities of daily living, Hgb level of 69 g/L (p = 0.01) and Hgb level of 100 g/L (p = 0.02). Two variables were significantly associated with an increase of the transfusion threshold above 90 g/L: the poor tolerance of anemia (p = 0.001) and clinical risk situations (p = 0.03).
Conclusions. The appropriateness of results could be useful to better describe the role of PBM with CBA and biomarkers recorded in geriatric practice, transfusion thresholds, target hemoglobin levels after transfusion.

Key words: Anemia, Patient Blood Management, CBA outcome set, Cumulative Illness Rating Scale, Nursing Home

Abbreviations

WHA: World Health Organization
PBM: Patient Blood Management
CBA: Social Health Folder
CIRS: Cumulative Illness Rating Scale
CRS: Cricthon Rating Scale
MUST: Malnutrition Universal Screening Tool
MMSE: Mini-mental State Examination
CI: Confidence interval
CrCl: Creatinine Clearance
CGA: Comprehensive geriatric assessment
MLF: Multidimensional loss of function

INTRODUCTION

In reference to the Resolution WHA63.12 of 21/05/2010 from the World Health Organization, the Italian National Blood Center has promoted an initiative aimed at systematizing innovative and more effective methods and instruments for ensuring appropriate organizational and clinical management of blood use [1]. This initiative is a ground-breaking multiprofessional, multidisciplinary and multimodal project encapsulated by the term Patient Blood Management (PBM) and Geriatric anemia.
Anemia in the elderly (defined as people aged > 65

Received: September 26, 2016 - Accepted: October 6, 2017
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years) is common and increasing as the population grows. In older patients, anemia of any degree contributes significantly to morbidity and mortality and has a significant effect on the quality of life. Despite its clinical importance, anemia in the elderly is under-recognized and evidence-based guidelines on its management are lacking [2].

Causes of anemia in the elderly are divided into three broad groups: nutritional deficiency, anemia of chronic disease (ACD) and unexplained anemia (UA). These groups are not, however, mutually exclusive. In any given patient, several causes may co-exist and may each contribute independently to the anemia.

Other causes like Cancer or hematological malignancy related anemia were investigated for renal failure and/or inflammation (myelodysplastic syndromes, chronic leukemia or lymphoma and sarcopenia). Both types may cause anemia, mainly via erythropoiesis inhibition by cytokines, although the mechanisms of inflammatory anemia are incompletely elucidated. As a result, protracted elevation of interleukin (IL)-6 and tumor necrosis factor (TNF)-α in the plasma of elderly patients after exposure to inflammatory stimuli can be seen. This may be a common mechanism for the production of anemia in chronic illness unique to elderly patients [3].

Another approach is based on the definition of Hb concentrations that are optimal for the clinical outcome of elderly subjects [4].

Anemia of the elderly gives a challenge and a burden to them, the community, and the health care providers. All healthcare providers should be aware that anemia impacts a significant group within our societies. It is an entity that lies within our ability to diagnose and treat with PBM.

PBM is a holistic approach to the management of blood as a resource for each, single patient; it is a multimodal strategy that is implemented through the use of a set of techniques that can be applied to individual cases [5]. Indeed, the overall outcome resulting from the implementation of PBM cannot be fully appreciated and explained simply by summing up the effects of the single strategies and techniques used, since these can only produce the expected optimal outcome if used in combination [6]. PBM is, therefore, a patient-centered and multidisciplinary project which involves Hematology, Geriatrics, Physiotherapists, Nurses or just primary care.

It is, also, a multimodal approach to the optimal management of anemia and haemostasis, to limiting allogeneic transfusion needs, and to use the blood components appropriately and, when relevant, plasmaderived medicinal products [7].

The concept of PBM is not centered on a specific pathology or procedure, nor on a specific discipline or sector of medicine, but is aimed at managing a resource, "the patient's blood", shifting attention from the blood component to the patient who, therefore, acquires a central and preeminent role [8].

PBM combines the dual purposes of improving the outcomes of patients and reducing costs, being based on the patient rather than on allogeneic blood as the resource. For this reason, PBM goes beyond the concept of appropriate use of blood components and plasma-derived medicinal products, since its purpose is to avoid or significantly reduce their use, managing, in good time, all the modifiable risk factors that can lead to the need for transfusion [9].

These aims can be achieved through the so-called "three pillars of PBM", which are crucial for making the paradigmatic shift that characterizes the innovative, patient-centered approach: (i) optimizing the patient's erythropoiesis; (ii) minimizing bleeding; and (iii) optimizing and exploiting an individual's physiological reserve to tolerate anemia. Each of these three key points are a strategic response to clinical circumstances that can cause adverse outcomes and necessitate the use of allogeneic transfusion therapy, namely anaemia, blood loss and hypoxia, respectively [10].

PBM is, therefore, intended to guarantee all patients a series of personalized programs, based on clinical requirements and the characteristics of the patients themselves, with the dual purposes of using allogeneic transfusion support appropriately and reducing the need for this resource. For this reason, PBM requires multidisciplinary and multimodal strategies to systematically identify, evaluate and manage anemia (boosting, if necessary, individual physiological reserves) and to avoid or minimize blood losses. It seems necessary to produce specific national standards [11].

The aim of this study is to examine the relationships among the prevalence of genera-age-associated risk factors of anemia and hemoglobin level in geriatric patients with cognitive decline through CBA SIPCARplus (medical records).

Before this implementation, there was not a traditional blood management program to evaluate risk factors of anemia and hemoglobin concentration associated with age and sex. It used a protocol for massive bleeding without monitoring the prevention of risks in this structured way.

MATERIALS

The CBA database has been developed by a dedicated working group using Delphi process and PBM.

It contains records on patient characteristics called health-assessment-delivery-warnings-analysis area, and one set of biomarker laboratory data identified in several variables

(the hemoglobin level, iron, ferritin, transferrin saturation, folate, vitamin B12, C-reactive protein, thyroid-stimulating hormone-TSH, albumin, and haptoglobin). It was categorized into normal and abnormal values according to standard laboratory norms.

The three pillars of the PBM with CBA are:

1) Optimization of erythropoiesis: detect anemia; identify and treat its underlying causes; re-evaluate the patient, if necessary; treat iron deficiency and iron-deficiency anemia, anemia of chronic disease and functional iron deficiencies, so-called ironrestricted erythropoiesis; treat deficiencies of other haematinics;
2) Minimization of blood losses: identify and manage bleeding risk, minimize iatrogenic bleeding, plan the procedure carefully and prepare well in very selected cases;
3) Optimization of the tolerance of anemia: assess and optimize the patient's physiological reserve to tolerate anemia and risk factors; compare estimated blood loss with the individual patient's tolerable blood loss; formulate a personalized blood management program that includes patient specific blood-conservation techniques; adopt restrictive blood transfusion thresholds.

Descriptive and inferential statistics were applied to describe and compare patients' demographic and epidemiological characteristics in Nursing Home. The IBM SPSS version 21 statistical software was used to perform data analysis. The data analysis was concluded in January 2014.

METHODS

Researchers responsible for recruitment from three nursing homes informed management and potential participants about the study. Inclusion criteria were as follows: age, availability of a venous blood sample result including hemoglobin (Hb) concentration collected during the current nursing home stay, possibility of verbal communication with the patient or a proxy, and informed consent to participate by the patient or legal guardian.

Exclusion criteria were as follows: non-correctable visual or hearing impairment, severe pain, sedation, or clinical depression. Blood samples were taken for laboratory biomarker assays of Hb level, iron, ferritin, transferrin saturation, folate, vitamin B12, C-reactive protein, TSH, albumin, and haptoglobin.

The comprehensive geriatric assessment (CGA) for this study consisted of six tools and their ranking methodologies to evaluate the following functional domains: cognition, mobility, transfer skills, competence in performing basic activities of daily living (BADLs), and swallowing ability [12].

The Barthel Index (BI) assesses BADL functionality using a rating scale from 0 (totally dependent) to 100 (maximal independence). An abnormal outcome was defined as 90 points or less [13]. The mini mental state examination (MMSE) measures the global cognitive state with a rating ranging from 0 (severe cognitive impairment) to 30 (normal cognitive function) [14]. Results of 27 points or less were considered abnormal. The clock-drawing test (CDT) covers cognitive domains incompletely tested for by the MMSE, such as executive function and spatial visualization skills. It uses a scale from 1 (perfect) to 6 (no reasonable representation of a clock), with a result of 3 or higher rated as abnormal. The timed up and go (TUG) test was used to assess mobility status. For methodical reasons, it uses five ranks according to the time needed to finish the test: ≤ 15 s, 1; > 15 to ≤ 25 s, 2; > 25 to ≤ 35 s, 3; > 35 s, 4; and TUG test not realizable, 5. Results of 3 or higher were considered abnormal. The Esslinger Transfer Scale (ETS) refers to the degree of independence while changing position in bed and transferring oneself from bed to chair, and it ranges from 0 (no assistance needed) to 4 (more than one professional assistant required). Ranks from 2 upwards were regarded as a functional limitation. Daniels test was used to detect dysphagia and was rated abnormal (positive) or normal. Multidimensional loss of function (MLF) as an aggregated outcome was diagnosed when three or more CGA tests showed an abnormal result [15].

In order to adjust for possible confounding factors in the relationship between anemia and MLF, this study collected information on 12 major comorbidities directly from patients by studying their medical histories. Renal and thyroid functions were assessed on the basis of laboratory results: serum creatinine concentration with a standard of 0.5-0.9 mg/dL in women and 0.5-1.1 mg/dL in men, and TSH with a standard of 0.27 and 4.20 μIU/mL, respectively). Multimorbidity was defined as the non-specific presence of more than one major disease [16].

This study was approved by the Internal Review Board of the university hospital, Bergamo. Informed consent was procured, and the protection and confidentiality of data was guaranteed according to applicable privacy laws.

RESULTS

Epidemiological studies consistently show an increase in the prevalence of anemia with advancing age, despite differences across studies in patient characteristics such as age and comorbidities [17].

Perhaps of greater significance, anemia has been

shown to impact mortality in elderly patients with other co-morbid conditions. For example, Esekowitz and colleagues have shown an increase in mortality in elderly patients with congestive heart failure as compared with their non-anemic cohorts [18].

Improvement in hemoglobin levels can also lead to improvements in end-organ function. Hayashi and colleagues have shown that the left ventricular function improves in chronic renal failure patients treated with erythropoietin. These data begin to address the important question of the relative roles of the anemia and the co-morbid condition in the excess morbidity and mortality experienced by the anemic elderly [19].

In this study 283 geriatric patients at three Italian nursing homes for the elderly were enrolled during 2014 and 2015. The mean age of enrolled patients was 79 years, with 14% male and 86% female. The overall prevalence of anemia was 55.9%. 32.6% of patients were at risk for malnutrition and 11.5% were malnourished. Comorbidities were weighed with the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) ≥ 4 [20] (Figg. 1-2).

The mean total CIRS-G score was 9 ± 3.7 and the mean composite CIRS-G score was 3.7 ± 1.5 (Fig. 3). The mean Creatinine Clearance (CrCl) was 40.9 ± 16.5 mL/min (Normal values was: 56 to 131 mL/min). The mean Hb level was 122 g/L. The Hb level was < 120 g/L in 110 (61.1%) patients and ≥ 120 g/L in 173 (38.9%) patients. In the group with severe anemia, the mean Hb level was 105 ± 11 g/L [21].

Anemia was multifactorial in most patients: the mean number of potential causes per patient was 1.85 ± 1, and 65.4% of patients had two to four concomitant causes [22 23]. Anemia prevalence was 2.12-fold higher in patients at risk for malnutrition than the malnourished groups. When the study compared age, sex, CrCl, and comorbidity scores in the groups with and without anemia, the total CIRS-G score was the only variable significantly and independently associated with anemia ($p < 0.001$) [24]. The total CIRS-G score was also the only variable significantly associated with the Hb level in the multivariate analysis ($p < 0.001$). Multivariate analysis determined that comorbidity was highly associated with malnutrition risk as measured by the Malnutrition Universal Screening Tool ≥ 2 (Fig. 4); cognitive decline as measured by the MMSE ≤ 19; functional dependence in two or more basic activities of daily living; Hb level of 69 g/L ($p = 0.01$); and Hb level of 100 g/L ($p = 0.02$) (Tab. I).

Overall, 61% of patients were presented with three or more abnormal results in the six tests of the CGA and were thus diagnosed with MLF. Logistic regression identified a significant association of both anemia and low Hb concentrations with abnormal outcomes in five tests of the CGA and therefore with functional deficits like mobility limitation, impaired cognition, and dysphagia. Furthermore, being anemic increased the odds of MLF more than fourfold [25]. The significance of this relationship persisted after adjustment for various major comorbidities.

Table I. Multivariate Analyses of Geriatric test score, comorbidity score and biomarkers laboratory.

Comorbidity	MUST ≥ 2 p	MMSE ≤ 19 p	Barthel Index ≤ 50 p
Hb>69 g/L_cod	0.105	0.013	0.001
Hb>100 g/L_cod	0.035	0.021	0.194
CIRS_SCORE ≥ 4	0.495	0.029	0.535

Test score: MUST, MMSE, Barthel Index; biomarkers laboratory Anemia severity: Hb > 69 g/L, Hb > 100 g/L; comorbidity: CIRS_SCORE ≥ 4.

Given the association of anemia with MLF, Hb level might serve as a useful geriatric screening marker to identify frail older people at risk for adverse outcomes; such a screening should contain indicators of functional deterioration [26].

This study also evaluated anemia treatment to gain insights into Hb threshold for transfusion [27].

The mean hemoglobin level before red blood cell transfusion was 84.5 ± 9.4g/L. There was a significant inverse relationship between the baseline Hb and the Hb response to treatment ($p = 0.007$) [28]. Hb loss after treatment decreased from 38 (29-49) g/L at baseline to 31 (26-40) g/L after algorithm implementation ($p < 0.001$). The mean number of red blood cell units prescribed for each transfusion was 1.88 ± 0.55, with the only predictive factor being the hemoglobin level ($p < 0.001$). Two variables were significantly associated with an increase of the transfusion threshold above 90 g/L: the poor tolerance of anemia ($p = 0.001$) and the clinical situations at risk for poor tolerance of anemia ($p = 0.03$) [29]. The most frequent symptoms of poor tolerance of anemia were cardiovascular symptoms and acute neuropsychiatric symptoms that could be considered as specific criteria for red cell transfusion in the elderly [30].

DISCUSSION

The results confirm that anemia is prevalent and often multifactorial in the elderly: 55.9% of study participants were anemic and 65.4% of anemic patients had two to four concomitant potential causes of anemia. Anemia increases the risk of mortality and morbidity and adversely affects quality of life, self-sufficiency, and cognitive function [31].

This study showed that low Hb levels were associated

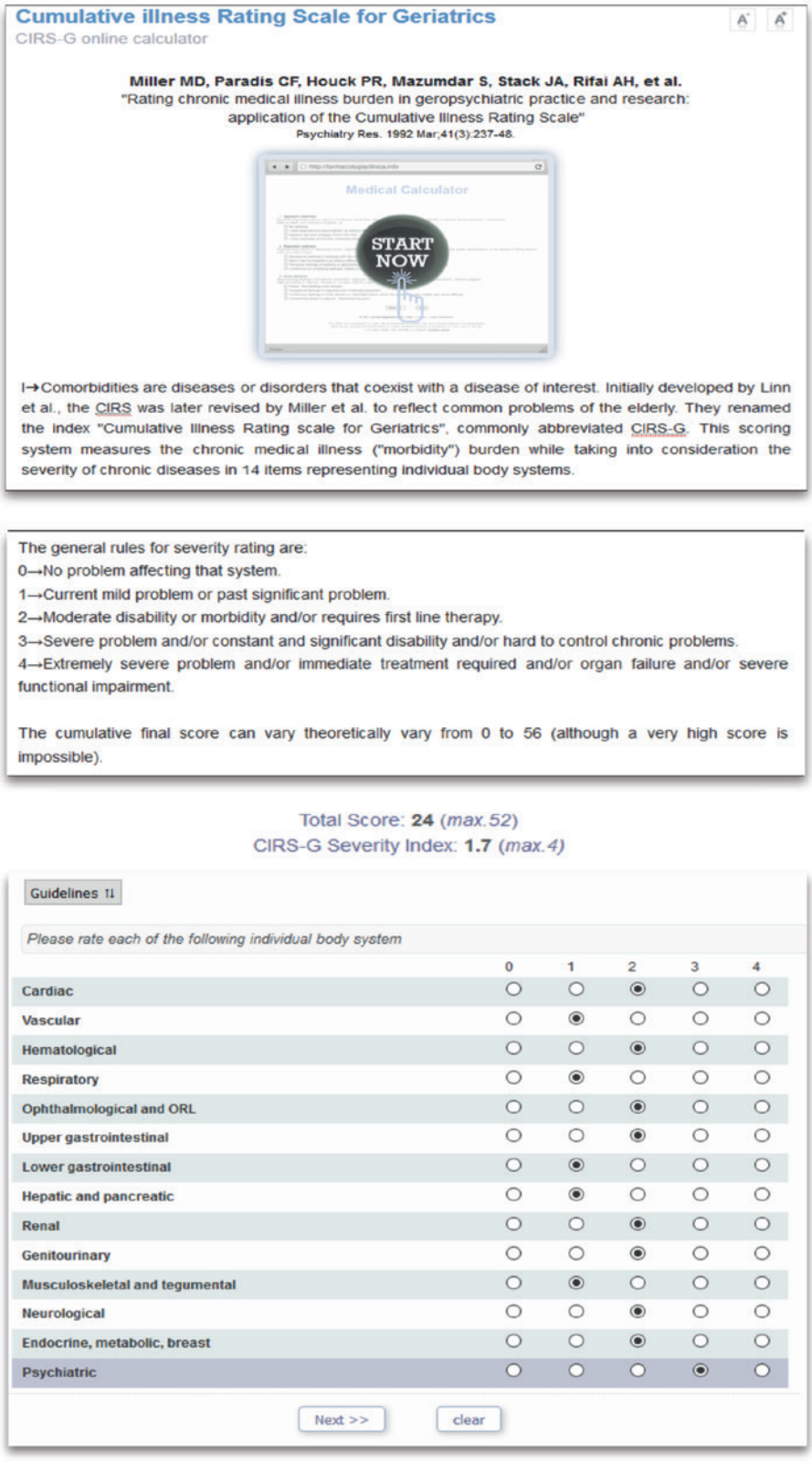

Figure 1. CIRS and their respective point scores. This scoring system measures the chronic medical illness ("morbidity") burden while taking into consideration the severity of chronic in 14 items representing individual body systems (Available on: http://farmacologiaclinica.info/scales/CIRS-G/).

Section A

Systems	Description	Scores				
Cardiac	-Any cardiac problem (angina, myocardial infarction, arrhythmia, valve problems)? -If affirmative, any medication taken for these problems? -Any heart surgery in the past?	0	1	2	3	4
Vascular	-Any circulatory problem (includes peripheral atherosclerotic disease, aneurysm of the abdominal aorta...), hypertension, or cholesterol problem? -If affirmative, any medication taken for these problems? -Any vascular surgery in the past (bypass graft surgery of lower limbs, carotid endarterectomy...)?					
Hematological	-Any blood problem (anemia, leukemia, hypercoagulability or any other problem affecting the blood, the blood cells, the spleen, or the lymphatic system)? -If affirmative, any medication taken for these problems (such as iron)? Note: Patients taking anticoagulants belong to this system if the main problem is hypercoagulability (thrombosis or recurrent embolism). If anticoagulants were taken for arrhythmias, rate the problem in *Cardiac*.					
Respiratory	-Any respiratory problem (asthma, emphysema, bronchitis, pulmonary embolism)? -If affirmative, any medication taken for these problems (such as pressurized aerosols)? -Any lung surgery? -Cigarette smoking? How many packs per day? For how long? Pack years = number of packs per day x the number of years smoked (example: 1 pack per day for 20 years = 20 pack years) Smoker up to 20 pack years: Rated 1 Smoker from 21 to 40 pack years: Rated 2 Smoker over 40 pack years: Rated 3					
Ophthalmological and otorhinolaryngology	-Any problem with eyes (glaucoma, cataract, important lost of vision), ears (includes important hearing impairment), nose, throat, voice? -Any medication taken for these problems (such as eye drops)? Note: Vertigo and dizziness are included in this section, unless they are of neurological origin.					
Upper gastrointestinal	-Any problem with stomach or digestion (includes the esophagus, the stomach, and the duodenum)? -If affirmative, any medication taken for these problems? -Any surgery for the stomach or the esophagus?					
Lower gastrointestinal	-Any intestinal problem (includes intestinal hernias, constipation, anal problems, incontinence...)? -If affirmative, any medication taken for these problems? -Any surgery for the abdomen?					

Section B

Systems	Description	Scores				
Hepatic and pancreatic	-Any problem in the liver or the pancreas? -Any medication taken for these problems? -Any surgery for the liver or the pancreas? Note: Cholecystectomy is rated in this section.					
Renal	-Any problem in the kidneys (impairment in function, infection...)? -If affirmative, any medication taken for these problems? -Any surgery for the kidneys?					
Genitourinary	-Any urinary problem (lithiasis, incontinence...)? -If affirmative, any medication taken for these problems? -Any surgery for the urinary bladder, for renal lithiasis?					
Musculoskeletal and tegumental	-Any problem in the skin, the joints, the bones, the muscles (includes arthrosis, osteoporosis, carpal tunnel, and any other skin or musculoskeletal problem)? -Any medication, anti-inflammatory drugs? Infiltrations? Creams prescribed by a doctor? Note: Fibromyalgia is rated in this section, but it may also be rated in *Psychiatric* if necessary.					
Neurological	-Any neurological problem (cerebrovascular accident, peripheral neuropathy, headaches...)? -If affirmative, any medication taken for these problems? -Any surgery for these problems?					
Endocrine, metabolic, breast	-Any problem of the thyroid gland, obesity, diabetes, or any other hormonal problem? -For obesity: Body mass index (BMI) ≥30: Rated 1 BMI ≥30 + medication or moderate disability: Rated 2 BMI ≥45: Rated 3 -Any medication? Surgery for any of these problems? -Any problem with breasts (dysplasia, cancer....)? -Surgery for these problems? -Menopause (or andropause in men)? Any hormone (the same for men in andropause)? Menopause or andropause: Without hormonotherapy or symptoms: Rated 0 Symptomatic or with hormonotherapy: Rated 1					
Psychiatric	-Any problem of depression, anxiety, alcohol, drug abuse, or other problems? -Any medication taken for these problems? Note: Personality problems are rated in this section, but the patient's chart should be checked.					
Total score						

Figure 2 [Section A]. CIRS and their respective point scores. [Section B]. CIRS and their respective point scores.

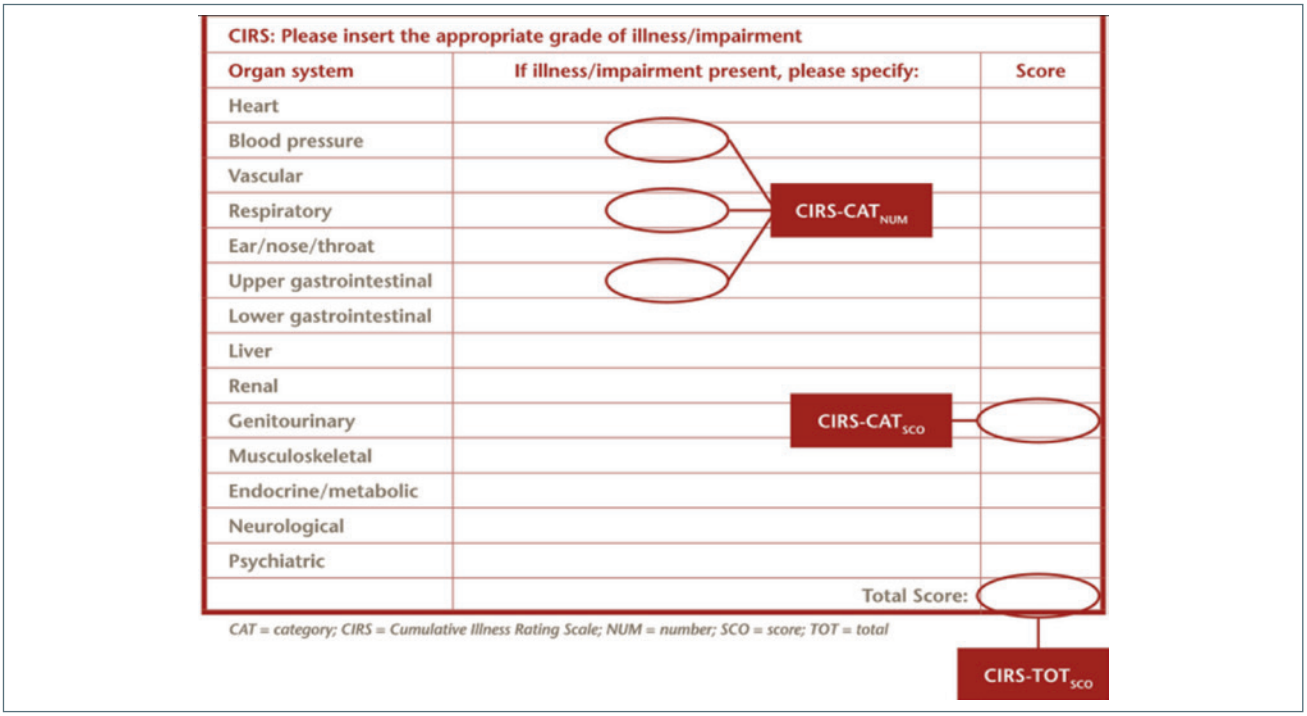

Figure 3. CIRS and their respective point scores with Italian CBA software (medical records).

with worse outcomes in several CGA tests and thus with multidimensional loss of function, with MLF still significant after adjustment for comorbidity. Against the backdrop of an aging society, these findings highlight the relevance of identifying low Hb level in elderly patients at risk for adverse outcomes during nursing home stays [32]. This study also shows that anemia is associated with a higher total CIRS-G score, with comorbidities adversely impacting anemic prevalence and outcomes [33]. The association with the CIRS-G score supports the usefulness of this score as an additional marker for frailty, whose pathogenic factors include several causes of anemia (mainly nutritional deficiencies and chronic diseases) [34].

Protein malnutrition is usually not considered to be a cause of anemia, and its role is difficult to evaluate because malnutrition is often associated with vitamin deficiencies and comorbidities that can contribute to anemia [35].

However, some proteins are essential for blood cell production, so protein deficiency may indeed contribute directly to the development of anemia [36].

The comprehensive nature of the laboratory screen performed in all of this study's anemic patients may help to explain this difference (Malnutrition *vs* Comorbidity related anemia).

Complementing indicators of anemic risk, effective treatment of anemia can result in lower mortality and morbidity rates in the elderly.

However, few studies have focused specifically on anemia in the elderly or on its underlying causes. In this study, severe renal impairment was found in nearly one-third of patients and was a possible cause of anemia in almost half of the anemic patients. Although advanced age is associated with a poor response of the erythropoietic system to stress, this itself does not cause anemia [37]. It is suggested that cytokines may inhibit erythropoiesis and thus lead to inflammatory anemia, but the precise causal mechanisms are not completely understood [38]. It is clear, however, that renal failure must be looked for routinely as a cause of anemia in the elderly, both because renal failure is common after 80 years of age and because recombinant erythropoietin is a simple and effective, albeit underused, treatment [39].

The implementation of CBA SIPCARplus (medical records) allows to analyze the correlation between the variables set out to increase the traceability of the information communicated and written to inter-levels.

The advantages of using this software are: current data on anemic geriatric patients, evaluating the prevention of hemorrhage, assessing blood loss, monitoring and rapid laboratory assessment of coagulopathy in the setting and team work, simulation (monitoring Skill-Rule-Knowledge based errors).

The disadvantages of using this software: understanding the physiology of coagulopathy in geriatric hemorrhage and Potential Adverse Events (High-volume

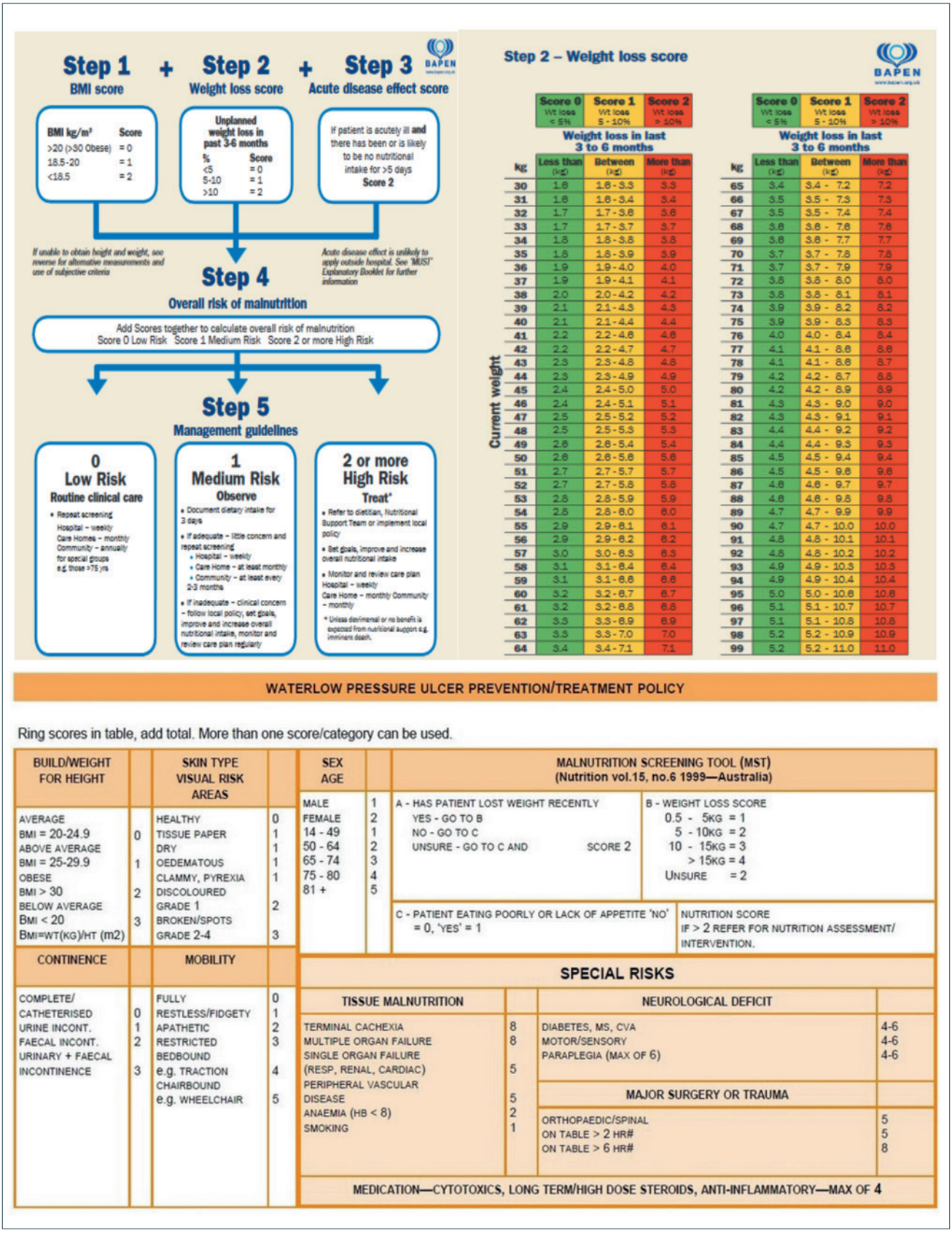

Figure 4. MUST point scores with Italian CBA software (medical records).

transfusions are associated with a risk of complications and Platelet Administration), evaluating indirect causes of anemia.
Strong aspects of this study include the training for data collectors, the overall size of the study sample, the use of an explicit conceptual framework on PBM, and the use of international, standardized tools to evaluate and describe patient characteristics.
The subgroups' sample sizes, convenience sampling and the difficulty of generalization beyond the study population represent some limitations of the research.

CONCLUSIONS

Multimorbidity is naturally prevalent in nursing home settings, particularly for those patients in whom severe renal and cardiovascular diseases are present. Therefore, the high burden of comorbidities must be taken into account when considering the high anemia prevalence in this study population.
Nevertheless, this study's results could be applied to better understand the role of PBM with CBA and biomarkers recorded in geriatric practice, transfusion thresholds, and target hemoglobin levels after transfusion. The identification of risk factors and screening markers could help notice the risk for adverse outcomes of frail elderly [40].
With regard to functionality, in this study, Hb concentration and anemia prevalence were all significantly associated with CGA test outcomes. It is possible that the association between anemia and MLF result from a direct independent deteriorating effect of anemia. With regard to cognitive function, previous studies have found anemia to be associated with cognitive impairment in specific domains as well as related to dementia and delirium [41]. In this study only MMSE results were significantly related to anemia, whereas group differences in CDT scores were not related.
There are many possible mechanisms by which anemia can contribute to cognitive impairment.
One, a synergistic direct vascular effect on cardiovascular diseases. Two, neuroprotection due to Erythropoietin (EPO) deficiency in the elderly. Three, an indirect effect on cognitive function which influences physical fitness and cardiac function [42].
Questions regarding the influence of low Hb levels on distinct cognitive domains exceed the objectives of this study and should be addressed by future research. Future interventional studies could be conducted to evaluate the clinical relevance of specific geriatric criteria in transfusion indications that seem related to comorbidities. Studies are also needed to define optimal hemoglobin levels and to confirm the causal link between anemia and laboratory test abnormalities [43]. Finally, further studies could evaluate therapeutic interventions for anemia in the elderly, including cost effective therapeutic services aligning with multidisciplinary recommendations for pharmacy benefit management in nursing homes.
A parallel, significant restriction of healthcare costs is also predicted. Indeed, the great interest currently shown in PBM, not only in North America, has firm financial roots. According to a recent report from a Chicago-based healthcare analysis company, the "Huron Healthcare Consulting Group", PBM is one of the ten "overlooked opportunities" that could enable healthcare systems to improve the quality of their performance. PBM could reduce the cost of blood use by 10-20%, precisely through better management of this resource [44].
In this context, the multidisciplinary recommendations for the implementation of PBM in Nursing Homes are a useful instrument for healthcare staff and management in public and private structures, supporting the provision of cost-effective therapeutic services [45].

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