Comprehensive Geriatric Assessment in Infectious Diseases

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Comprehensive geriatric assessment (CGA) is a multidimensional, interdisciplinary diagnostic process to determine the medical, psychological and functional capabilities of a frail elderly person in order to develop a coordinated and integrated plan for treatment and long-term follow-up [1, 2]. The clinical basis for the development of CGA was primarily the heterogeneity of the ageing population. Indeed, the ageing process manifests itself in a wide variety of ways, affecting a large spectrum of capacities and functions, due to the complex interplay of genetics, biology, disability, disease, cognitive status, psychosocial conditions, income, family, cohabitation, etc. In order to be able to perform an assessment, all these different variables need to be measured and integrated into a unique parameter, i.e. CGA.

From a clinical point of view, in addition to medical clinical evaluation, a range of other aspects need to be assessed, including functional and cognitive performance, and mood, using appropriate tools, in order to calculate the overall biological risk in terms of nutrition and then perform social evaluation, covering home life, social network, income and available resources. The ultimate objective is to characterize the clinical profile, the pathological risk and the residual skills, with a view to developing an individualized care plan.

CGA has demonstrated its efficacy in a range of settings, as shown in a recent review of three decades of trials from different healthcare settings and conditions [3]. In this review, it was shown that CGA was significantly useful in reducing such outcomes as mortality, functional decline, institutionalization or readmission, both in-hospital and long-term, and in different clinical settings including solid cancers, orthogeriatrics, preoperative assessment and patients with cognitive impairment [3]. Both home CGA programmes and CGA performed in-hospital were shown to be

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consistently beneficial for several health outcomes and in specific clinical conditions with tailored programmes for frail older patients.

Frailty is a state of vulnerability to external stressor events resulting from a cumulative decline in various physiological systems over a lifetime [4]. It is the most problematic expression of population ageing and is a known risk factor for various negative outcomes. Indeed, frail patients who experience a stressor event may be more prone to falls, delirium or fluctuating disability, ultimately resulting in increased care needs and admission to hospital or long-term care. CGA has become the internationally established method to assess elderly people in clinical practice, because it is sensitive to the reliable detection of degrees of frailty. CGA is the gold standard to detect frailty and should be used more widely in this context.

In several infectious diseases, there are risk factors related to functional disability. One study of modifiable risk factors for pneumonia requiring hospitalization in community-dwelling older adults found that by attributable fraction analysis, 11.5% of cases of pneumonia could be attributed to incident mobility limitation [5]. In another study of 90 hospitalized older adults with severe *Clostridium difficile* infection, poor functional status assessed by Katz's activities of daily living (ADL) was found to be associated with severity of infection [6]. A clinical review of urinary tract infections in older women found that functional disability was a risk factor for recurrent symptomatic urinary tract infection [7]. Furthermore, geriatric syndromes are common in older HIV-infected adults, particularly pre-frailty, difficulty with instrumental activities of daily living (IADLs) and cognitive impairment [8], and clinical care of older HIV-infection adults should include geriatric principles. So clearly, there is a compelling need to incorporate CGA into the management approaches whenever older adults are concerned.

After three decades of use, CGA is facing new challenges. From a methodological point of view, informatics, robotics and self-assessment present new horizons to which CGA needs to adapt. There are also continuing challenges in terms of evaluation, with the need to compare different methods in terms of discrimination, generalizability, feasibility and clinimetric properties. In terms of its clinical use, CGA needs to move from risk assessment to outcome measures and also needs to be incremented with quality of life evaluation and patient preferences [9].

In this regard, a CGA-based prognostic tool for clinical decision-making has been developed, combining the eight different domains of standard CGA (namely, ADL, IADL, cognitive, nutrition, motility, comorbidity, polypharmacy, cohabitation status) into one single cumulative index called the multidimensional prognostic index (MPI). The MPI yields a score that is a continuous number ranging from 0 (indicating lowest risk) to 1 (highest risk) [10]. From clinical practice, with appropriate cutoffs, the MPI identifies three risk categories, namely, low, moderate and severe risk of short-term (1 month) and long-term (1 year) mortality. This index has been used over the last 10 years in many clinical situations. In a study of 134 hospitalized patients with community-acquired pneumonia (CAP), mean age 78.7 ± 8.8 years, the MPI was found to be a sensitivity measure of the multidimensional risk assessment that might be useful in identifying elderly patients with CAP at different risk of mortality who probably need a different intensity of clinical

interventions. Importantly, the accuracy of the MPI in terms of sensitivity and specificity is significantly higher than that of the pneumonia severity index, enabling the MPI to identify patients at higher risk that warrant more intensive interventions [11]. In another study of 49 consecutive patients aged over 65 years with CAP (mean age 86.6 ± 7 years), mean MPI score was measured at admission and discharge in combination with procalcitonin serum levels, and MPI at discharge was found to be a significant predictor of 1-month mortality [12]. The addition of procalcitonin levels significantly improved the accuracy of MPI at admission in predicting 1-month mortality [12]. Similar efficacy of the MPI for predicting short- and long-term mortality has been demonstrated in the context of acute gastrointestinal bleed [13], transient ischemic attack [14], chronic kidney disease [15], cancer [16], heart failure [17] and dementia [18]. The evaluation of tools to identify frailty showed that the MPI and modified MPI had the highest quality score, as critically appraised using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) [19]. Another review of frailty measurements in research and clinical practice showed that only three tools are actually based on the CGA, namely, the Frailty Index of Accumulated Deficits [21]; the Fatigue, Resistance, Ambulation, Illness, Loss of Weight (FRAIL) Index [22], which is a screening tool; and the MPI, which is the only one developed and validated in Europe [20].

In this context, an ongoing project called MPI-Age, in conjunction with the European Commission and the EUGMS, will use the MPI to improve cost-effectiveness of interventions in multimorbid frail older persons. To date, this project has investigated the relation between the use of various drugs including statins, anticoagulants and anti-dementia drugs and mortality in older adults.

Regarding statin use, the majority of randomized controlled trials do not include patients aged older than 80 years, and, therefore, it may be hard to know whether the benefits of these drugs observed in younger adults can also be yielded by their older counterparts. Beyond the age of 80, people are very heterogeneous, with varying life expectancy, and regardless of whether they are frail or not, the decision to treat is not evidence-based. In a retrospective observational cohort study of 1712 community-dwelling older subjects, ≥65 years with diabetes mellitus who underwent a CGA evaluation to establish accessibility to homecare services or nursing home admission showed that 3-year mortality increased with increasing MPI, but statin prescription declined with risk groups [23]. After adjustment for propensity score quintiles (for the propensity to be treated with statins), statin treatment was significantly associated with lower 3-year mortality, irrespective of MPI group [23]. Thus, statin treatment appears to be useful in older frail people with comorbidities, regardless of multidimensional impairment, although the frailest patients are those least likely to be treated with statins [23]. Similar results were reported in a cohort of 2597 older subjects with coronary artery disease (CAD) confirming that statin treatment was significantly associated with reduced 3-year mortality independently of age and multidimensional impairment, although the frailest were less likely to be treated with statins [24]. The results are somewhat different for anti-dementia drugs. In a retrospective analysis of 6818 community-dwelling older people who underwent a Standardized Multidimensional Assessment Schedule for

Adults and Aged Persons (SVaMA) in Italy, the same authors found that anti-dementia treatment was significantly associated with lower mortality only in subjects with low or moderate mortality risk as assessed by the CGA-based MPI-SVaMA, but not in the high mortality risk group [25]. This finding is interesting because MPI grade was previously found to be associated with a metabolic signature [26], whereby the concomitant elevation of markers of inflammation, associated with a simultaneous reduction in multiple metabolic and hormonal factors, predicts mortality in hospitalized elderly patients.

There is therefore compelling evidence to suggest that the MPI is now poised to become a key parameter in infectious diseases and vaccination discussions. Indeed, a special interest group on infectious disease and CGA was formed at the EUGMS meeting held in Lisbon in 2016 to initiate a cross-national, observational, non-interventional survey of older patients with infectious diseases to evaluate in a "real-world" population of older hospitalized patients at different mortality risks as assessed by the MPI, the prevalence of various infectious (including vaccine-preventable) diseases.

In conclusion, the ageing of the world population calls for an innovative perspective. To this end, clinicians need to consider the prognostic information obtained through well-validated, accurate and calibrated prognostic indices to identify those patients who may benefit from interventions given with the aim of increasing survival.

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