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Original Research

Alterations in comprehensive geriatric assessment decrease survival of elderly patients with cancer

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Abstract ***Introduction:*** A comprehensive geriatric assessment (CGA) evaluating several domains of health is recommended for elderly patients with cancer. Effects of altered domains on the risk of death in this population need to be clarified. The aim of this study was to estimate the independent association of each CGA domain to overall survival (OS).
Method: Patients included in the ONCODAGE cohort completed a CGA at baseline. Cox models (one per domain) estimated the hazard ratio (HR) of death for each CGA domain. Directed Acyclic Graphs (DAGs) selected specific sets of adjustment factors for each model.
Results: The analysis included 1264 patients (mean age: 78 years, women: 70%). Median follow-up was 5.2 years, and 446 patients died. Each altered domain had a detrimental effect on survival, sometimes dependent on gender, age, education or time from inclusion. Nutritional status had a time-varying effect, with higher mortality rates if altered only within the first 3 years of follow-up. In case of altered mobility, the risk of death was higher only for the youngest patients and, in case of altered autonomy, only for the youngest women. An altered neurological state led to higher mortality rates; this effect increased with the level of education. Patients with altered psychological status or more than four comorbidities at baseline had also higher mortality rates.

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Conclusions: Patients with an altered CGA domain have a higher risk of death than those without any alteration. The effect of some alterations is different in some subgroups or at a given time of the treatments.

1. Introduction

In 2017, 19.2% of the French population was 65 years and older, which corresponds to a 2.4% increase over the past 10 years [1]. Cancer affects older adults disproportionately, and patients over the age of 65 constitute nearly 60% of new cancer diagnoses in the United States of America (USA) and central Europe [2,3]. As a result, there is a growing demand for care services in the elderly population with cancer.

Many studies have investigated factors associated with survival in this population. Age, malnutrition, number of comorbidities, metastatic status or advanced stage have been described as prognostic factors [4,5]. Most of these are associated to domains of health involving frailty. In oncology setting, this multidimensional set of comorbidities related to age may allow identifying patients at risk of complications due to cancer treatment. According to international recommendations, a comprehensive geriatric assessment (CGA) should be performed for all elderly cancer patients in order to detect frailty [6]. CGA assesses six domains of health (nutritional state, autonomy, mobility, cognitive state, psychological state, comorbidity) and geriatric syndromes such as pressure ulcers, incontinence or falls [7,8]. A decrease in overall survival (OS) in elderly patients with cancer may be associated with one or more altered domains of the CGA.

Most of the studies investigating survival in this population focus on survival at 12 months or 3 years. However, the 5-year survival rates reach up to 79% for breast cancer, 67% for prostate cancer and 46% for colorectal cancer patients over the age of 65 [9]. Long-term survival is therefore a relevant criterion to describe risk of death even in the elderly patients with cancer and a longer follow-up is necessary.

Studies analysing the association between frailty and survival often use a single model including all domains of CGA. However, each domain may have potentially different confounding factors that can explain some or all of their association with death. For example, while education level may confound the relationship between neurological state and death, it may not affect the relationship between nutritional state and death. Yet, adjusting for unnecessary covariates may impair statistical efficiency and even produce biased results [10]. Directed Acyclic Graph (DAG) may help identify the minimally sufficient adjustment sets of covariates, in order to minimise confusion and collision biases and to limit loss of power [11]. To our knowledge, there are no publications on the use of such an approach to identify adjustment variables for investigating the effect of each CGA domain on mortality.

The main objective of this study was to assess the effect of each CGA domain at the beginning of treatment on survival, while carefully adjusting for specific potential confounders.

2. Methods

2.1. Population

Our population included patients from the ONCODAGE cohort. Patients were recruited in 23 health care facilities from 2008 to 2010. They were older than 70 years with a histologically confirmed cancer and included either before first-line treatment, or between two steps of a first-line treatment. Persons with psychological disorders that would prevent data collection were not included [12]. Only patients with a complete CGA at baseline were included in the survival analysis. The study was approved by the regional ethics committee (Comité de Protection des Personnes Sud-Ouest et Outre Mer III), and was conducted in accordance with the Declaration of Helsinki, and Good Clinical Practices.

3. Materials

3.1. Comprehensive Geriatric Assessment

All patients were required to have a complete CGA at baseline. CGA comprises seven instruments for the six domains of health: Mini Nutritional Assessment (MNA) for nutritional state, Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) for autonomy, Timed Up and Go test (TUG) for mobility, Mini-Mental State Examination (MMSE) for cognitive state, Geriatric Depression Scale-15 (GDS-15) for psychological state and Cumulative Illness Rating Scale-Geriatric (CIRS-G) for comorbidities.

Domains of CGA were considered altered if an abnormal score was obtained. Abnormal scores were established according to published cut-offs (MNA $\leq$ 23.5/30, ADL $\leq$ 5/6, IADL $\leq$ 7/8, TUG $>$ 20 s, MMSE $\leq$ 23/30, GDS15 $\geq$ 6/15) [13]. For the purpose of this analysis,