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#### Review

# The anorexia of ageing: Physiopathology, prevalence, associated comorbidity and mortality. A systematic review\*

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#### ABSTRACT

The physiological processes of ageing and factors prevalent in the elderly such as comorbidities and polypharmacy often cause loss of appetite in the elderly, which we call anorexia of ageing. Social factors, together with changes in the sensory organs, can be important causes of a reduction in both appetite and ingestion. This review assesses the regulation of appetite in the elderly and the development of anorexia of ageing. It also examines the prevalence of this type of anorexia, its associated comorbidities and mortality rates. We have reviewed 27 studies, with a total of 6208 patients. These reported changes in the secretion and response of both central and peripheral hormones that regulate appetite. Anorexia, very prevalent among hospitalized and institutionalized elderly people, is associated with comorbidity and represents a predictive factor for mortality. No treatment for it has been proved to be effective. The mechanism regulating ingestion in elderly people is complex and difficult to resolve. Comorbidity as a cause or a consequence of anorexia of ageing has become a research field of great interest in geriatrics. A correct nutritional evaluation is a fundamental part of an integrated geriatric assessment.

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#### 1. Introduction

The changes in the regulation of appetite and the lack of hunger frequently observed in association with ageing have been described as anorexia of ageing (AA) [1].

The main factors associated with the onset of AA can be split into three main groups: (1) physiological; (2) psychological and social; and (3) medical. Among the physiological factors, we may list those related to the process of ageing itself, including: (a) loss of acuity in taste, smell and sight; (b) changes in the secretion and peripheral action of the hormones that regulate the wish to eat, hunger and satiation; (c) changes in gastrointestinal motility; (d) changes to the central control of ingestion; and (e) chronic low-grade inflammation [2,3]. Poverty, isolation and changes to a person's environment are the main psychological and social causes. The third group comprises medical causes, among which we can list certain pathologies and drugs [4].

Fig. 1 is a simplified and schematic representation of the appetite regulation system.

The importance of knowledge and, especially, diagnosis of AA is related to the fact that it represents a major cause of loss of weight and malnutrition, as well as of sarcopenia and fragility [5,6].

The main aim of this review is to describe and summarize the physiopathological factors at the root of AA. Secondary aims are to assess the prevalence of AA, to report on associated comorbidities and mortality rates, and to assess possible treatments for AA.

#### 2. Methods

We performed this review in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines [7,8]. The protocol of the present review was registered with PROSPERO, which is an international database of prospectively registered systematic reviews in health and social care. PROSPERO is funded by the UK National Institute for Health Research. See http://www.crd.york.ac.uk/PROSPERO/display\_record.asp?ID=CRD 42012002893.

### 2.1. Search strategy

A search was carried out in PubMed, limited to the title or the abstract and using the following terms and term associations: anorexia, ageing/aging/older person/elderly/senile, loss/regulation of appetite, dietary intake, feeding, nutrient/food/fluid intake, gastrointestinal hormones, treatment, megestrol acetate/loxiglumide/dronabinol. We limited the search to articles published between January 1987 and June 2012. We then reviewed the bibliographies of all the papers identified from the search, as another bibliographical source.

#### 2.2. Inclusion and exclusion criteria

We included studies on people above 65 years of age that assessed the physiopathology, prevalence, comorbidities, mortality or treatment of AA. As regards physiopathology, we included articles that studied the secretion of the hormones related to appetite, the regulation of ingestion or intestinal motility. We discarded studies on anorexia nervosa or on anorexia secondary to acute pathologies. Despite AA being a cause of involuntary weight loss,

studies on this aspect were considered to be beyond the remit of the present review, although we have not dismissed the possibility of undertaking a future review on this problem.

#### 2.3. Selection and quality assessment

One of the authors was in charge of selecting the papers according to our inclusion criteria. We read the abstract of all potentially eligible papers and where it was not clear from the abstract whether the inclusion or exclusion criteria had been met, we read the full text. Doubts the authors had were resolved by joint critical assessment of the papers.

The quality of the included papers was evaluated subjectively according to the DRAFT criteria [9].

#### 2.4. Data abstraction

We extracted from every paper the design of the study, where it was carried out, the demographic characteristics of included subjects and their division into groups, the body mass index (BMI) of the subjects, and the study's exclusion criteria and main results. The main characteristics of the studies are summarized in Table 1.

#### 3. Results

#### 3.1. Study characteristics and quality assessment

We included 27 studies, with a total population of 6208 patients. Fig. 2 presents a flow chart showing the paper selection process.

None of the protocols of the studies included in this revision was registered in any international registers.

We considered 11 studies to be good, 12 fair and 4 wanting. The main area which caused papers to be evaluated as 'wanting' was their statistical analysis, whether because an incorrect test was chosen or because the test that would best represent the data was not used, thereby causing confusion and complicating the assessment and interpretation of results. A low number of subjects, the fact that part of the sample populations had been used in earlier studies, often not specified, and an incomplete presentation of results are other reasons for studies to be judged as being of lower quality.

None of the studies specified how the sample size was chosen.

#### 3.2. Outcomes measured

We employed a fourfold classification of the results of the 27 studies: (1) physiopathology; (2) prevalence and comorbidity; (3) mortality; and (4) treatment.

## 3.3. Physiopathology

#### 3.3.1. Hormones related to appetite regulation

Cholecystokinin (CCK) is secreted by cells in the duodenum and jejunum in response to certain foods. It inhibits appetite at a central level and at a peripheral level it delays gastric emptying and the production of ghrelin [10].

Statistically higher levels of CCK in fasting conditions were observed in elderly people compared with younger people in a number of studies [11–14], while a further study reported a difference that was not statistically significant [15]. One study found

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