Review

Risk Factors for Multiple Myeloma: A Systematic Review of Meta-Analyses

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Abstract

The epidemiology of multiple myeloma (MM) is an increasingly investigated field, with many controversies. This systematic review aims to synthesize meta-analyses examining risk factors for MM so as to provide a comprehensive, parsimonious summary of the current evidence. Eligible meta-analyses were sought in PubMed adopting a predefined algorithm, without any restriction of publication language; end-of-search date was October 10, 2014. The selection of eligible studies and data extraction were performed by working in pairs, independently and blindly to each other; in case of disagreement, consensus with the whole team was reached. Among the 22 ultimately included meta-analyses, 9 examined occupational factors, 4 assessed aspects of lifestyle (smoking, alcohol, body mass index), 5 evaluated the presence of other diseases, and 4 addressed genetic factors as potential risk factors of MM. A vast compendium of significant associations arose, including farming, occupation as a firefighter, occupation as a hairdresser, exposures to chemicals or pesticides, overweight and obesity, patterns of alcohol intake, pernicious anemia, ankylosing spondylitis, gene promoter methylation, and polymorphisms. In conclusion, MM is a multifactorial disease, encompassing a wide variety of risk factors that span numerous life aspects. Further accumulation of evidence through meta-analyses is anticipated in this rapidly growing field.

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Introduction

Multiple myeloma (MM) is a mature B-cell neoplastic proliferative disease and is also known as plasma cell myeloma, myelomatosis, or Kahler disease.[1] Bone marrow plasmacytosis and production of monoclonal immunoglobulin are key features, while symptomatic disease is associated with anemia, hypercalcemia, renal insufficiency, and osteolytic bone disease.[2] MM is the second most common hematologic malignancy and represents 10% to 20% of all hematologic malignancies. Interestingly, its prevalence is expected to rise in Western countries in light of the aging population, given that nearly 30% of patients are aged 75 years or older.[3] The 5-year relative survival has been estimated at approximately 41%.[4]

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The epidemiology of MM is an increasingly investigated field, with many controversies. Older age, positive family history, male sex, black race, and genetic factors[5] have been described as risk factors for the disease.[5] Monoclonal gammopathy of undetermined significance is a condition that precedes MM[6] and is the most important factor associated with the development of MM. Regarding environmental factors, exposure to benzene, petroleum products, and ionizing radiation, as well as agricultural or industrial occupation have been acknowledged, whereas tobacco smoking, obesity, and dietary characteristics are probably less implicated but have been addressed in the literature.[7,8]

Systematic reviews and meta-analyses represent the corollary in the hierarchy of study types; indeed, high quality meta-analyses play a pivotal role in the determination of level A grades of recommendations.[9] Given the significance of meta-analysis in the field of epidemiology, this systematic review focuses especially on the published meta-analyses summarizing risk factors in the epidemiology of MM, aiming to present a systematic review. This approach may represent a useful contribution to the summary of current evidence given that, to our knowledge, only narrative reviews have been published on the field of MM epidemiology.[5,7,8] To this end, we aimed to

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synthesize meta-analyses examining risk factors in the epidemiology of MM in a systematic manner so as to provide a comprehensive, parsimonious summary of the current evidence on the field.

Methods

Search Strategy and Study Eligibility

This systematic review of meta-analyses was conducted in accordance with the PRISMA guidelines[10] and in line with the a priori protocol agreed on and signed by all authors. Eligible studies were sought in PubMed without any restriction of publication language; end-of-search date was October 10, 2014. The following search algorithm was used: (myeloma OR "plasma cell" OR "plasma cells" OR plasmacell OR plasmacytoma OR myelomatosis OR "Kahler's disease" OR "Kahler disease") AND (meta-analysis OR meta-analyses OR "systematic review").

Eligible articles included meta-analyses examining potential risk factors for MM. We excluded systematic reviews without quantitative synthesis and nonsystematic pooled analyses (namely, synthesis of data from studies retrieved in a nonsystematic manner—for example, in consortia). Furthermore, we excluded meta-analyses that referred to MM therapy or examined prognostic factors for MM. In case of overlapping meta-analyses, only the most recent study of was included, taking into consideration the study design of eligible individual studies (eg, meta-analyses confined solely to cohort or case−control studies).

Authors working independently and blindly to each other in pairs (G.T., A.T., M.T.) performed the selection of eligible studies; in case of disagreement, consensus with the whole team was reached.

Data Extraction and Effect Estimates

The extraction of data comprised general information (author, year) and meta-analyses characteristics (time frame of eligible studies, eligibility criteria for the inclusion of studies in the analyses, risk factors that the analyses examined, number of studies included,

Figure 1 Flow Chart Presenting Successive Steps During Selection of Studies