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Review article

Positron emission tomography with ^{18}F-FDG in the evaluation of patients with rheumatoid arthritis - a systematic review

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a disease characterized by inflammation of the synovial membrane. Several authors have investigated the role of positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose (^{18}F-FDG) in RA.

Objectives: To systematically review the current literature on the role of ^{18}F-FDG PET in the diagnosis, determination of disease activity and assessment of treatment response in patients with RA.

Methods: Searches were conducted in Medline, Cochrane Library, Lilacs, Pubmed and Scopus in Portuguese, English and Spanish languages, using the keywords «rheumatoid arthritis», «synovitis», «FDG», «PET», «glycolytic metabolism» and «disease activity».

Results: One hundred and forty-two articles were initially identified, of which only 40 were related directly to the subject. Twelve original articles and three case reports that met the inclusion criteria were selected.

Discussion: The presence of activated macrophages and fibroblasts in pannus are responsible for the intense periarticular uptake of ^{18}F-FDG. The uptake patterns do not allow the differential diagnosis with other arthritides. The uptake intensity and the number of joints involved are metabolic parameters of disease activity that correlate well with the composite indices. Longitudinal studies of PET have proven useful in assessing the response to treatment with anti-TNF. When performed early, PET can predict the therapeutic response.

Conclusion: Although the actual role of this new technique for the investigation of RA is not yet established, ^{18}F-FDG PET is a promising tool in determining the activity and prediction of response to treatment of patients with RA.

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Tomografia por emissão de pósitrons com FDG-^{18}F na avaliação de pacientes com artrite reumatoide – revisão sistemática

Palavras-chave:
Tomografia por emissão de pósitrons (PET)
Flúor-18 (FDG-^{18}F)
Artrite reumatoide

RESUMO

Introdução: a artrite reumatoide (AR) é uma doença caracterizada pela inflamação da membrana sinovial. Diversos autores têm investigado o papel da tomografia por emissão de pósitrons (PET) com flúor-18 (FDG-^{18}F) na AR.

Objetivos: REVISÃO sistemática da literatura atual sobre o papel do PET com FDG-^{18}F no diagnóstico, determinação da atividade da doença e avaliação da resposta ao tratamento em pacientes com AR.

Métodos: Foram realizadas buscas nas bases de dados Medline, Biblioteca Cochrane, Lilacs, Pubmed e Scopus nos idiomas português, inglês e espanhol, utilizando as palavras-chave «artrite reumatoide», «sinovite», «FDG», «PET», «metabolismo glicolítico» e «atividade da doença».

Resultados: Cento e quarenta e dois artigos foram inicialmente identificados, dos quais apenas 40 relacionavam-se diretamente ao tema. Foram selecionados 12 artigos originais e três relatos de caso que preenchiam os critérios de inclusão.

Discussão: A presença de fibroblastos e macrófagos ativados no *pannus* é responsável pela intensa captação periarticular de FDG-^{18}F. Os padrões de captação não permitem o diagnóstico diferencial com outras artrites. A intensidade de captação e o número de articulações envolvidas são parâmetros metabólicos de atividade da doença que apresentam boa correlação com os índices compostos. Estudos longitudinais de PET têm se mostrado úteis na avaliação da resposta ao tratamento com anti-TNF. Quando realizado precocemente, PET pode predizer a resposta terapêutica.

Conclusão: Embora o real papel dessa nova técnica na investigação da AR ainda não esteja estabelecido, PET com FDG-^{18}F é uma ferramenta promissora na determinação da atividade e na predição de resposta ao tratamento de pacientes com AR.

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic inflammation of the synovial membrane. Its prevalence in adults is up to 1%. When not properly treated, RA can lead to osteoarticular destruction and functional limitations, with marked socioeconomic impact.[1]

Rheumatoid synovitis shows intense inflammatory infiltrate associated with neovascularization and proliferation of the synovial membrane. The thickened and inflamed synovial membrane, also known as pannus, is directly linked to bone and joint destruction.[2]

The diagnosis of RA in its early stages (up to 12 months after the onset of the first symptoms) is of paramount importance for a successful treatment. The establishment of an adequate treatment in this period, also known as "window of therapeutic opportunity" may prevent or limit considerably the consequences of long-term RA.[3,4] However, this diagnosis in an early stage can present difficulties. Multiple conditions may clinically manifest themselves in a similar manner to RA, including infectious diseases, systemic rheumatic diseases, spondyloarthritis, arthritis by crystal deposition, endocrine and neoplastic diseases.[1,3,4]

Laboratory tests, such as those for inflammatory activity (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]) are not specific, and rheumatoid factor (RF) may be absent in more than 30% of patients in the early phase of the disease.[5] The preesence of anti-protein and anti-citrullinated peptides (ACPA) antibodies, including anti-citrullinated cyclic peptide (anti-CCP) antibody, is quite specific, but its sensitivity is limited (70-75%).[1.3]

Methods of diagnostic imaging such as conventional radiography have been used to aid in the diagnosis of early RA, but usually these techniques detect bony and cartilaginous structural changes that occur late in natural history of the disease. Ultrasonography (US) and magnetic resonance imaging (MRI) have also been employed, and MRI shows great potential for determining the thickness of the synovial membrane and in detecting bone marrow edema, being considered by many authors as the gold standard (in terms of imaging procedures) for the diagnosis of synovitis.[1,3,6]

Despite many advances in understanding the pathophysiology, diagnosis and treatment of RA, the current prognostic and diagnostic (clinical, laboratory and radiographic) indicators have limited value for early diagnosis and for establishing individual prognosis.[3,7]

The delay of several weeks to establish the diagnosis in patients with arthritis deprives those with RA from an adequate treatment in the therapeutic window of opportunity. In this context, other diagnostic strategies have been studied using new diagnostic imaging technologies now available.[8]

Positron emission tomography, also called PET, is a widely used tool in oncology. Neoplastic cells exhibit an exuberant