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Review

Imaging modalities for the diagnosis and disease activity assessment of Takayasu's arteritis: A systematic review and meta-analysis

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ABSTRACT

Background: Early diagnosis of Takayasu's Arteritis (TAK) and detection of disease activity may reduce the risk of vascular complications. The objective of this study was to determine the effectiveness of imaging modalities for the management of TAK.
Methods: MEDLINE and EMBASE were searched for studies of patients undergoing various imaging modalities for TAK diagnosis or to assess disease activity. We excluded case reports, reviews and case series with <10 patients. The methodologic quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2). Random effects meta-analyses with inverse-variance weighting were performed.
Results: From the 1126 citations screened, 57 studies met our inclusion criteria. Many of the studies were of small sample size (average N = 27), cross-sectional design and low methodological quality. Ultrasound (US) had a lower pooled sensitivity (SN) of 81% (95% CI: 69–89%) than Magnetic Resonance Angiography (MRA) with SN = 92% (95% CI: 88–95%) for TAK diagnosis (by clinical criteria and/or X-Ray angiography). Both had high specificities (SP) of >90% for TAK diagnosis. Fewer studies investigated computed tomography angiography (CTA), but SN and SP for TAK diagnosis was high (>90%). The utility of vessel wall thickening and enhancement by MRA and CTA to predict disease activity varied across studies. The pooled SN and SP of ^{18}F-fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) for disease activity was 81% (95% CI: 69–89%) and 74% (95% CI: 55–86%), respectively.
Conclusion: US, CTA and/or MRA are effective for the diagnosis of TAK. The utility of these imaging modalities for assessing disease activity remains unclear.

Contents

Abbreviations: ACR, American College of Rheumatology; APR, acute phase reactant; AUC, area under the curve; ASRCJ, Aortitis Syndrome Research Committee of Japan; CA/DSA, Conventional Angiography/Digital Subtraction Angiography; CIMT, carotid intima-media thickness; CRP, C-Reactive Protein; EBCECTA, Electron-Beam Contrast-Enhanced Computed Tomography Angiography; ESR, Erythrocyte Sedimentation Rate; FDG-PET, ^{18}F-fluorodeoxyglucose-Positron Emission Tomography; FMD, Flow-Mediated Dimension; HC, healthy control; IMT, intima-media thickness; ITAS, Indian Takayasu's Activity Score; MRI, Magnetic Resonance Imaging; MRA, Magnetic Resonance Angiogram; NIH, National Institutes of Health criteria for TAK disease activity; NA, Not applicable; NR, Not reported; QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies-2; SN, Sensitivity; SP, Specificity; $SUV_{ratio}BP$, Standardized Uptake Value ratio of maximum aortic wall uptake to mean aortic blood pool uptake; TAK, Takayasu's Arteritis.

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1. Introduction

Takayasu Arteritis (TAK) is a primary granulomatous large vessel vasculitis, affecting predominantly young women with substantial morbidity and mortality [1]. Early in the disease course, symptoms can be non-specific making diagnosis difficult. X-Ray angiography, the "gold standard" for TAK diagnosis, can image luminal defects but does not detect changes of the vessel wall [2]. The diagnosis of TAK can be confirmed with histopathological examination; however, tissue from blood vessels is obtained only in the minority of patients requiring a surgical intervention. There are currently no specific biomarkers for diagnosing TAK.

Identifying disease activity in TAK is also challenging. The commonly utilized National Institute of Health (NIH) disease activity score is not validated and despite NIH-defined clinical remission, 61% and 44% of patients show serial angiographic and/or histologic signs of activity or disease progression, respectively [3]. There are currently no fully-validated outcome measures for use in TAK management. Composite disease activity scores that include history, physical exam and acute phase reactants (APR), such as the Indian Takayasu Activity Score (ITAS) and Disease Extent Index-Takayasu Arteritis (DEI·Tak) are available [4,5]. It is unclear whether these tools accurately predict patients that would go on to have progression of vascular lesions and end-organ damage.

Imaging modalities, such as Doppler ultrasound (US), Magnetic Resonance Angiography (MRA), Computed Tomography Angiography (CTA) and ^{18}F-fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) have the potential to recognize early vessel wall inflammation and replace X-ray angiography [6]. The objective of this systematic review and meta-analysis was to assess the sensitivity (SN) and specificity (SP) of US, MRA and FDG-PET imaging modalities for the diagnosis and assessment of disease activity in TAK.

2. Methods

2.1. Literature search and study selection

This systematic review included studies examining the effectiveness of US, FDG-PET, CT/CTA, Magnetic Resonance Imaging (MRI)/MRA or hybrid imaging (FDG-PET/CT or FDG-ET/CTA) for the diagnosis or assessment of disease activity in patients with TAK. For diagnostic studies, subjects with suspected TAK were also included. We excluded case reports, case series with <10 TAK patients, and reviews. Any method for TAK diagnosis was accepted, including the American College of Rheumatology (ACR) 1990 Classification Criteria [7], other published diagnostic or classification criteria, physician opinion and/or X-Ray angiography. Similarly, studies using any method for assessing disease TAK disease activity were included, such as the NIH criteria, ITAS or DEI.Tak [3–5], physician opinion, acute phase reactants (APR) and/or another imaging. The reported outcomes were SN, SP and concordances. We also included studies that compared imaging parameters in TAK vs. control subjects and active vs. inactive disease.

In the primary search, citations were compiled from the following electronic databases: MEDLINE (1966-July 2017) and EMBASE (1980-July 2017) using search strategies detailed in Table A.1 with terms for TAK and the various imaging modalities. To further identify relevant studies, a secondary search was performed, making use of reference lists of studies identified in the primary search. Two authors (TK and JM) completed the first phase of screening using titles and abstracts. The second phase of screening, using full-text manuscripts, was subsequently completed (TK and LB). All disagreements for both phases were resolved by consensus.

2.2. Data abstraction and quality assessment

Two authors (TK and LB) independently extracted data for each included study using standardized forms. Age of study subjects was at time of study enrollment and disease duration was defined as time from diagnosis to study enrollment. For consistent reporting of study characteristics, Hozo's method to estimate mean and standard deviation based on median, range and sample size was used [8].

Quality assessment of the studies was also completed in duplicate (TK and LB) using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) [9]. Abstracts had insufficient data to complete all domains of the QUADAS-2; therefore, their methodological quality was scored as unclear. Disagreements from both data abstraction and quality assessment were resolved through consensus. The non-English language studies were written in Chinese, German, Spanish, French and Italian; data from Spanish, French and Italian studies was extracted by one author (TK or LB) with the assistance of a translator for the Chinese and German studies.

2.3. Data synthesis and meta-analysis

Random-effects meta-analyses with inverse-variance weighting were completed using Comprehensive Meta-Analysis (Biostat, Englewood, NJ) for poolable outcomes reported in ≥3 studies. *I*-squared (I^2) was calculated to quantify the heterogeneity between studies. True positives, true negatives, false positives and false negatives were extracted from studies and inputted into two by two tables to calculate pooled SN, SP and concordances in the meta-analyses. Publication bias was assessed visually using Funnel plots.

3. Results

3.1. Search results and characteristics of included studies

Primary electronic database searches identified 932 citations after the removal of duplicates (Fig. 1). Full-text review was performed on 86 articles: 29 were included in the meta-analyses (Table 1) [10–39], 28 had insufficient outcome data for pooling but were included in the systematic review (Table 2) [40–67] and 29 failed to meet inclusion/exclusion criteria (Fig. 1).

The studies were from 15 different countries and most were single-centre with relatively small sample sizes (average N of 27; range 10–85 TAK patients). Consistent with the known demographics of TAK, the proportion of female subjects was high (47–100%) with mean ages ranging from 23 to 47 years. Two studies were of early TAK (disease duration <1 year) and 2 were of patients with suspected TAK; all others were of long-standing TAK. Four studies included controls other than healthy subjects (systemic lupus erythematosus, hypertension and non-inflammatory vasculopathy). Most of the studies used accepted criteria for the diagnosis or classification of TAK and X-ray angiography (conventional angiography (CA) or digital subtraction angiography (DSA)) was performed to confirm the diagnosis. For disease activity assessment, the NIH criteria were commonly used; a minority of studies