

Meta-analysis: Accuracy of Contrast-Enhanced Magnetic Resonance Angiography for Assessing Steno-Occlusions in Peripheral Arterial Disease

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**Clinical Bottom Line:** Contrast-enhanced magnetic resonance angiography (MRA) has a high accuracy for both identifying and excluding clinically relevant arterial steno-occlusions in adults with peripheral arterial disease (PAD) symptoms.

**Introduction:** Four methods are currently used to image steno-occlusions in PAD: Duplex ultrasonography, Intra-arterial digital subtraction angiography (DSA), Contrast-enhanced computed tomographic angiography (CTA), and Gadolinium-enhanced MRA. While the diagnostic accuracy of contrast-enhanced MRA in PAD has been regarded as great for some time now, the Intra-arterial DSA is still considered the gold standard in the imaging of PAD. DSA combines the highest available image resolution with high image contrast, but it is invasive and is a relatively expensive test. Therefore, most of the advances in MRA modification were associated with improving its cost-effectiveness which left previous meta-analyses of its diagnostic accuracy with fewer studies to evaluate.

**Objectives:** To summarize evidence of prospective studies about how well MRA identifies or excludes arterial steno-occlusions in adults with PAD symptoms.

**Source of Funding:** None

**Study design:** Authors followed the PRISMA statement guidelines for their review which included a 27-item checklist and a four-phase flow diagram. They instituted a search of PubMed, Scopus, BIOSIS Previews, and Web of Science for *peripheral arterial disease*, *magnetic resonance angiography*, and related terms from January 1998 to December 2009, without language restriction; additionally they searched the references of retrieved articles. Two observers independently selected eligible publications, with disagreements resolved by consensus, and then evaluated the full text which resulted in 32 prospective studies being included in the meta-analysis.

**Participants:** The authors meta-analysis included summarized findings from 1,022 patients. However, since all of the primary studies evaluated the diagnostic accuracy of MRA on a per-segment basis, the meta-analysis also was performed on a per-segment basis.

**Inclusion criteria:** Prospective study design. Inclusion of at least 10 patients, all of whom were adults with known or suspected PAD of the lower extremities. Use of contrast enhanced MRA with intravenous injection of gadolinium chelates, except from blood-pool contrast agents, as the index test. Use of intra-arterial DSA as the reference standard. Application of homogenous imaging techniques. 50% or greater stenosis or occlusion of the aortoiliac, femoropopliteal, or tibiofibular arterial segments. Reporting of sufficient data to reconstruct 2x2 or 3x3 contingency tables for the studied arterial segments.

**Exclusion criteria:** The authors excluded studies that did not meet the above inclusion criteria.

**Primary Outcome Measure:** Confirm or exclude steno-occlusion compared to Digital Subtraction Angiography on per segment basis

**Analysis:** Data was extracted from the included studies and 2x2 or 3x3 contingency tables were constructed. For the construction of 2x2 tables, arterial segments with less than 50% stenosis were considered non-diseased and 50-99% stenosis were considered diseased. For the 3x3 contingency tables, the data was divided into 0-49%, 50-99%, or total occlusion.

From the 2x2 contingency tables, sensitivities and specificities were calculated. The Cochran Q test and  $I^2$  statistic were used to assess the between-study heterogeneity of the sensitivity and specificity. Pooled summary estimates for sensitivity and specificity were obtained from a bivariate random-effects meta-analysis by using PROC GLIMMIX procedures in SAS. The summary estimates were also converted to estimates of positive and negative likelihood ratios.

To analyze potential sources of heterogeneity, individual subgroup analyses were performed with each study characteristic as a covariate in a bivariate random-effects meta-regression of sensitivity and specificity. Summary of estimates of sensitivity and specificity were converted to estimates of positive and negative likelihood ratios. The study also generated graphs of conditional probabilities and a scattergram of likelihood ratios.

In addition, PROC GLIMMIX procedure was used on the 3x3 data in a multivariate fixed-effects meta-analysis to distinguish 50-99% stenoses from occlusions and to assess the degree which MRA overgrades or undergrades steno-occlusions compared with DSA.

**Results:** 32 prospective studies were included in the meta-analysis. For the MRA of the entire arterial tree, the meta-analysis gave a pooled sensitivity of 94.7% (CI, 92.1% to 96.4%) and specificity of 95.6% (CI, 94% to 96.8%) on a per-segment basis for diagnosing 50% or greater stenosis or occlusion in PAD. Pooled positive likelihood ratio was 21.56 (CI, 15.70 to 29.69). Pooled negative likelihood ratio was 0.056 (CI, 0.037 to 0.083). The scattergram of likelihood ratios and the bivariate plot of sensitivity and specificity indicated that MRA is suitable method for both confirming excluding relevant steno-occlusions in patients suspected of having PAD. The plot of conditional probabilities shows that MRA is accurate in detecting and excluding PAD over a wide range of pretest probabilities. The pooled sensitivity and specificity for MRA of the tibiofibular arteries was lower than for the aortoiliac or femoropopliteal regions, but this difference was small.

Subgroup analyses showed no significant influence on the sensitivity and specificity by study quality, number of patients per study, sex ratio, mean age, prevalence of critical limb ischemia, and percentage of DSA-proven steno-occlusion. Acquisition methods also did not affect the final results significantly. The analysis did show that studies that subdivided the arterial tree into 20 or fewer segments had a higher sensitivity ( $P = 0.023$ ) but did not significantly affect the specificity ( $P = 0.22$ ).

Multivariate meta-analysis of the 3x3 tables showed that MRA correctly classified 95.3% of segments, overstaged 3.1% of segments, and understaged 1.6% of segments.

### **Limitations:**

- The number of arterial tree segments per anatomical region varied among the studies and it is possible that subdividing the arterial tree further into more segments might artificially lead to an increase in specificity.
- The authors literature search may not have found all eligible studies
- The MRA should be interpreted with the same information as is available in clinical practice; however only two studies actually stated that MRA was interpreted with clinical information present.
- Possible spectrum bias due to varied prevalence of critical limb ischemia among the 32 studies.
- If any of the 32 selected studies were of bad design, then it will yield bad statistics.
- In comparing MRA to the other methods of imaging steno-occlusions in PAD, it is unknown whether its superior diagnostic accuracy will hold true once better studies of these other methods become available.