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HOW TO UNDERTAKE A CLINICALLY RELEVANT SYSTEMATIC REVIEW IN A RAPIDLY EVOLVING FIELD

Magnetic Resonance Angiography

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Abstract

Objectives: The aim was to determine which generations of the evolving technology of magnetic resonance angiography (MRA) are currently of clinical relevance in two clinical applications. Our purpose was to plan a systematic review that would be valuable both to purchasers driven by cost-effectiveness and to practicing clinicians.
Methods: Information was gathered from a search of major bibliographic databases, from a short questionnaire sent to 500 U.K. vascular radiologists and vascular surgeons, and from local clinical

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experts. We asked which of the MRA techniques were currently used and, assuming availability, what would be their technique of choice.
Results: There were 206 published articles that satisfied preliminary inclusion criteria: 69 discussed 2D time of flight (TOF); 47, 3D TOF; and 38, contrast-enhanced techniques. There were 162 questionnaires returned (60 radiologists, 102 surgeons). Of the total respondents, 77/162 (48%) used MRA in the assessment of carotid artery stenosis; 47/77 (61%) used 2D TOF; 32/77 (42%), 3D TOF; and 26/77 (34%), contrast-enhanced techniques. Thirty-five of 162 (22%) respondents used MRA in the assessment of peripheral vascular disease (PVD); 15/35 (43%) used 2D TOF, 4/35 (11%) used 3D TOF, and 22/35 (63%) used contrast-enhanced techniques. For those wishing to use MRA, contrast-enhanced techniques were the method of choice.
Conclusions: The TOF methods that represent earlier generations of the technology remain clinically relevant, and will therefore be included in our systematic review. To ensure complete and relevant coverage in reviews of other evolving technologies, it would be advisable to obtain data for guidance in a similar way.

Keywords: Technology, Health care, Assessment, Technology, Angiography, Magnetic resonance, Review literature, Online systems

The use of the systematic literature review as a tool to inform evidence-based therapeutics is common. Its use in diagnostic practice, although equally necessary to ensure quality of care and cost-effective use of resources, has yet to gain widespread acceptance. Although there is extensive literature in the field of diagnostic imaging, systematic reviewing in this area carries particular difficulties. The appropriate concepts and methods for rigorous evaluation of a diagnostic technology are well understood (6;8;11;16;17). In practice, however, the quality of the available literature is generally poor, with few large-scale studies and low standards of study design and reporting (1;9;14). The literature may not necessarily reflect practice in the country in which the review findings are to be applied. In addition, the diagnostic technology is evolving rapidly, and uptake of new generations often precedes the availability of evidence by some time (10;13). Uptake of new generations may also be guided by the needs of diagnostic practitioners rather than by the requirements of medical or surgical end-users. Under these circumstances, it is particularly important that any systematic review undertaken addresses a tightly predefined clinical question and that all generations of the technology that remain clinically relevant are considered.

Patients with atherosclerosis of the carotid or peripheral arteries may be investigated by conventional catheter angiography and/or magnetic resonance angiography (MRA) or ultrasound. Although conventional catheter x-ray angiography remains the definitive imaging technique, it involves the use of ionizing radiation and is an invasive procedure carrying a risk of stroke of up to 4%, when used in the carotid arteries of a symptomatic population (5). These drawbacks have helped drive the introduction of duplex ultrasound and of MRA, although MRA can lead to overestimation of the degree of stenosis caused by imaging artifacts and low spatial resolution. MRA may also be of particular use in individuals not normally suitable for conventional angiography, such as the frail and elderly (12) and patients with renal insufficiency.

MRA is a rapidly evolving diagnostic imaging technology. The generations of the technology include 2D time of flight (TOF), 3D TOF, and most recently, contrast-enhanced techniques. Phase contrast techniques have been widely investigated in technical studies but have not generally entered clinical practice. Use of the techniques has overlapped, and none has completely replaced the others. Where MRA is applied to the surgical assessment of carotid artery stenosis and peripheral vascular disease (PVD), it is important that both the indications for, and the clinical utility of, all generations in current use be established as rapidly as possible. The aim is to avoid expenditure on units that are not needed and to ensure the most appropriate use. The primary research question to be addressed by the full

systematic review (3) was set in the U.K. National Health Service (NHS) Health Technology Assessment (HTA) commissioning brief: What is the cost-effectiveness of MRA compared with conventional angiography in carotid artery stenosis and peripheral vascular disease? The results of the review are intended to be used within the U.K. NHS, so the work has a U.K. focus.

The purpose of this preliminary study was to determine which of the various generations of the technology are currently of clinical relevance, in order to establish the scope of the full systematic review into the cost-effectiveness of MRA.

METHODS

Two approaches, determined in advance by review team discussion, were taken. First, to determine which MRA techniques have been evaluated in the literature, a preliminary literature search was performed. Second, to define the appropriate clinical questions and to determine which generations of MRA technology remain clinically relevant, advice was sought from practitioners other than those on the review team by national survey.

Preliminary information on the available published evidence was gathered using the major electronic bibliographic databases: MEDLINE, EMBASE, HealthSTAR, Science Citation Index (SCI), and Index of Scientific and Technical Proceedings (ISTP). A broad search strategy for MRA and related terms was used to maximize sensitivity (2). Before the number of articles published describing the various generations of the technology was determined, the first of several sets of exclusion criteria to be applied in the full systematic review (3) was used. Duplicated references were excluded, then criteria designed to exclude articles that did not present relevant original research were applied. The criteria were first applied within the databases, where possible, using the database indexing to electronically exclude review articles, editorials, letters, case reports, conference abstracts, and articles using nonhuman subjects. In the second application, a reviewer manually repeated these criteria for the remaining references, and excluded articles that did not involve the target technology in the correct clinical application, articles on technical developments, those involving pediatric subjects, and those with 10 or fewer subjects. A breakdown of the number of exclusions for each bibliographic database was made to help inform the execution of future systematic reviews.

To define the appropriate clinical questions and to determine which generations of MRA technology remain clinically relevant, advice was sought using a structured approach predetermined by the review team, which included experts in radiology, vascular surgery, and Neurology. A questionnaire was sent to 100 radiologists and 400 vascular surgeons in the United Kingdom, and the survey results were processed by nonclinical members of the review team. In order to determine the continuing clinical relevance of each generation of the technology, the questionnaire sought information on MRA techniques currently available to each group. Recipients were also asked to state their technique of choice, if all methods were equally available, for each clinical application (carotid artery stenosis and PVD). This was to provide an indication of both the level and source of demand; is the rapid evolution of MRA primarily led by the needs of clinical end-users or by diagnostic practitioners? To encourage responses, the questionnaire comprised only six questions and was in the form of a single-page letter suitable for return by fax.

RESULTS

The initial literature search of the bibliographic databases identified 16,185 articles. However, there was a high rate of duplication between databases (Table 1), leaving a total of

7,183 unique articles. Many articles were not original research relevant to MRA and to carotid artery stenosis or PVD (Table 2), and a total of 206 potentially useful articles was left, just 1% of the original retrieval. Many of the articles were concerned with more than one MRA technique. It could be seen from the abstracts that 69 were concerned with the use of 2D TOF, 47 with 3D TOF, and 38 with contrast-enhanced techniques. Twenty discussed phase-contrast MRA, and the focus of a further 73 was not clear from the abstract. Only nine of the 206 articles were from the United Kingdom, while there were 93 from the United States, and 75 from countries in western Europe other than the United Kingdom.

The review team experts in radiology, vascular surgery, and neurology favored contrast-enhanced techniques, although in one hospital only contrast-enhanced techniques are employed. TOF techniques are commonly used in the other hospitals to which they are affiliated.

There were 162 (32%) questionnaires returned from 60 radiologists out of a total of 100 surveyed and 102 vascular surgeons out of a total of 400 surveyed. Of 142 respondents, 162 (88%) respondents had MRA available on site (Figure 1), with 108 of 162 (67%) having access to 2D TOF, 96 of 162 (60%) to 3D TOF, and 85 of 162 (52%) to contrast-enhanced techniques. Seventy-seven of 162 (48%) respondents gave details of the MRA methods they currently used in the assessment of carotid artery stenosis (Figure 2A), with 47 of 77 (61%) using 2D TOF, 32 of 77 (42%) using 3D TOF, and 26 of 77 (34%) using contrast-enhanced techniques. Thirty-five of 162 (22%) respondents gave details of the MRA methods they currently used in the assessment of PVD (Figure 2B), with 15 of 35 (43%) using 2D TOF, 4 of 35 (11%) using 3D TOF, and 22 of 35 (63%) using contrast-enhanced techniques. Fifty-one of 60 (85%) responding radiologists expressed a preference, and 49 of 51 (96%) would use MRA for the evaluation of carotid artery stenosis (Figure 3A); 32 of 49 (65%) would choose contrast-enhanced techniques. For the evaluation of PVD, 45 of 60 (75%) responding

Table 1. Number of Unique Articles Retrieved from Each Database

	MEDLINE	EMBASE	HealthSTAR	SCI	ISTP	Total
Initial number of articles retrieved	4,649	4,040	3,523	3,732	241	16,185
Number remaining after exclusion of duplicates	4,649	1,208	147	1,055	124	7,183
(Percentage shown in parenthesis)	(100%)	(30%)	(4%)	(28%)	(51%)	(44%)

The last column shows the sum from all five databases. The databases were assessed for duplication in a hierarchical manner, moving from left to right of the table.

Table 2. Number of Articles Excluded from Each Database Using the Exclusion Criteria

Exclusion criterion	MEDLINE	EMBASE	HealthSTAR	SCI	ISTP	Total
Review	951	240	45	66	2	1,304
Editorial	42	35	0	46	0	123
Letter	46	37	1	27	0	114
Case report	1,130	383	23	16	0	1,552
Conference abstract	1	1	1	473	11	487
Nonhuman subjects	260	102	2	2	6	407
Not applicable (see text)	1,823	389	66	336	80	2,694
Technical development	78	16	5	37	23	159
Pediatric subjects	12	1	0	1	0	14
Ten or fewer subjects	105	9	1	8	0	123
Number of articles excluded	4,474	1,190	144	1,047	122	6,977
Number remaining after exclusions	175	18	3	8	2	206

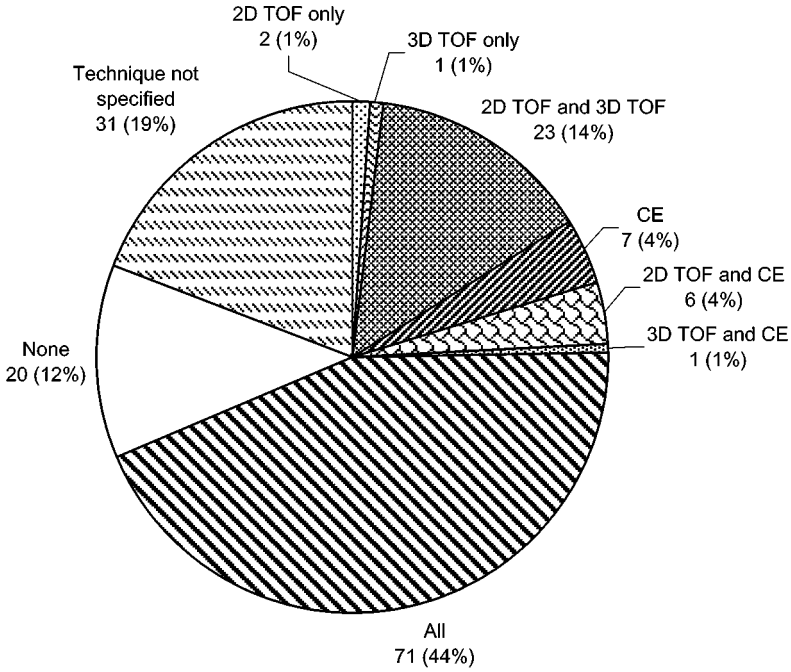

Figure 1. Response to questionnaire: Availability of MRA techniques on site (n = 162).

radiologists expressed a preference, and 39 of 45 (87%) would use MRA (Figure 3B); 36 of 39 (92%) of these would choose contrast-enhanced techniques. For the evaluation of carotid artery stenosis, 77 of 102 (75%) responding surgeons expressed a preference, and 37 of 77 (49%) would use MRA (Figure 4A); 28 of 37 (76%) would choose contrast-enhanced techniques. For the evaluation of PVD, 75 of 102 (74%) responding surgeons expressed a preference, and 41 of 75 (55%) would use MRA (Figure 4B); 40 of 41 (98%) of these would choose contrast-enhanced techniques.

DISCUSSION

Although there was considerable overlap between the bibliographic databases searched, all the databases returned some articles unique to that database, and there were articles remaining from all the databases after the exclusion criteria had been applied. Our purpose here was to determine the approximate proportion of published articles for each generation of the technology. The results suggest that a search restricted to MEDLINE, EMBASE, and the Science Citation Index would have been adequate. A description of the full systematic review, including the final inclusion criteria and consideration of quality issues, is given elsewhere (3). In spite of the large pool of candidate articles, only 35 articles concerning assessment of the carotid arteries and 20 articles on assessment of the peripheral circulation were included in the systematic review and quantitative meta-analysis.

The existing literature on the diagnostic performance of MRA broadly reflected current usage patterns, although there remains a dearth of evidence to support the expanding use of contrast-enhanced techniques. It would be unwise to rely solely upon preliminary literature searches to determine the scope of a systematic review in a rapidly evolving field because of the time lag between uptake of the latest generation and publication of studies evaluating it. There are also potential differences in usage and publication patterns between different countries.

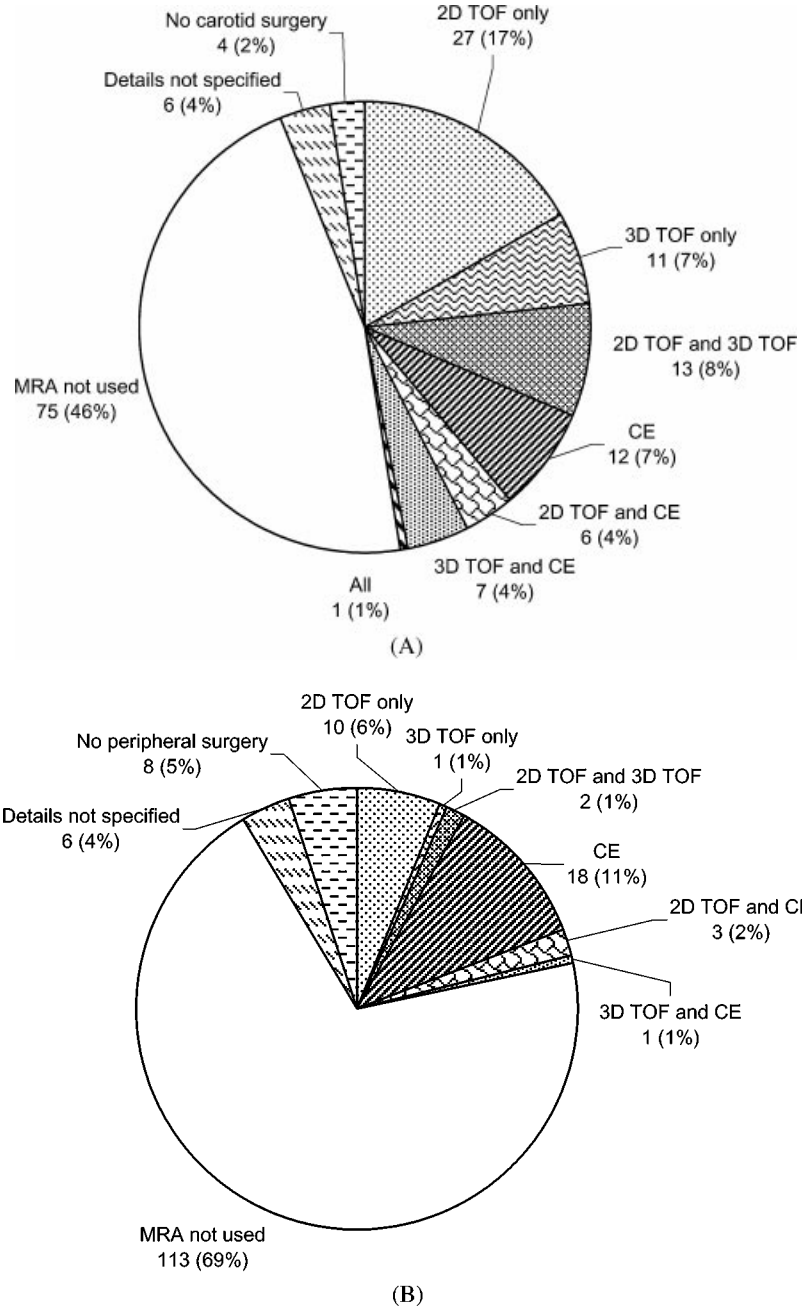

Figure 2. Current use of MRA techniques in the assessment of (A) carotid artery stenosis and (B) peripheral vascular disease (n = 162).

In general, TOF techniques remain in widespread use, and there is a significant body of published work evaluating their diagnostic performance. Where users—in particular, radiologists—expressed a preference, they tended to favor the most recent technology, even though the published evidence evaluating its diagnostic performance may be limited. Clinical end-users, in this case vascular surgeons, were more cautious in their use of MRA,

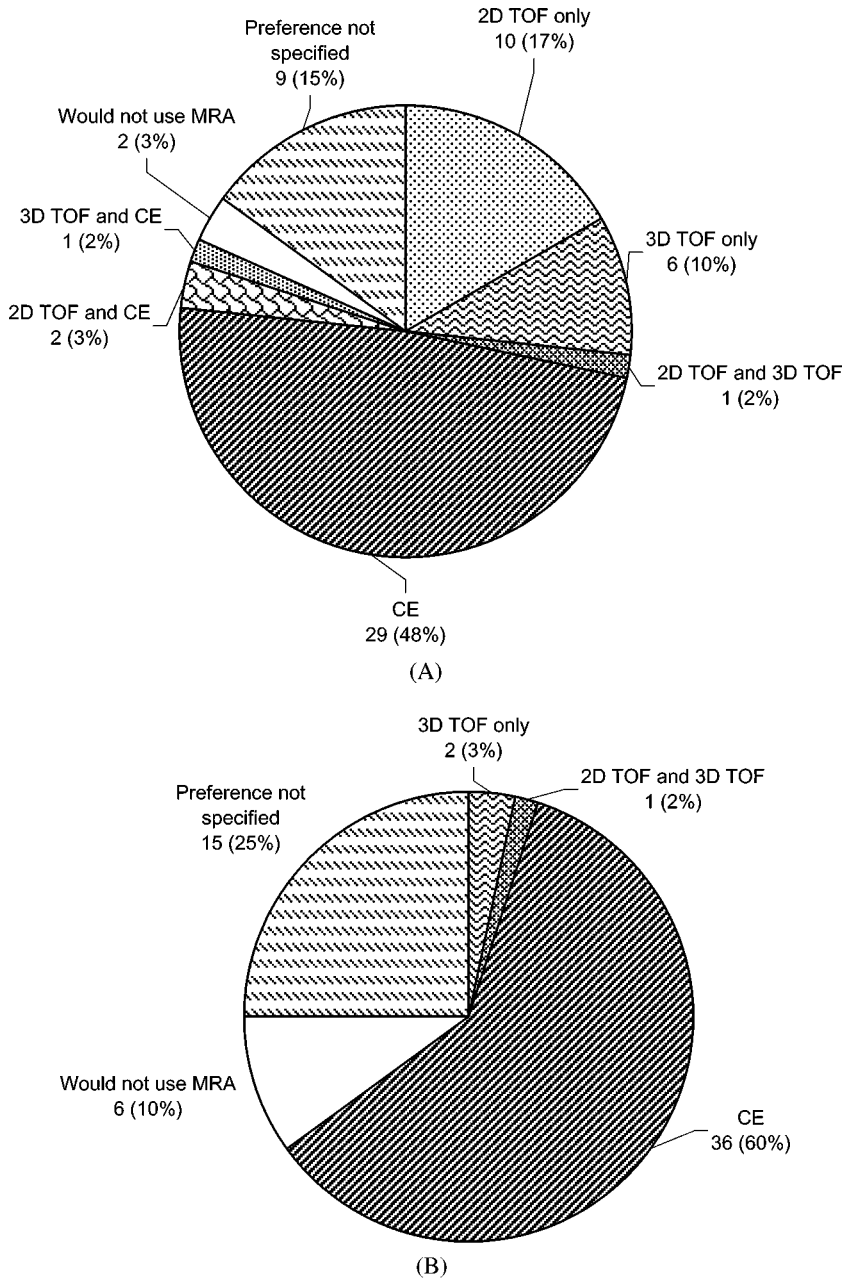

Figure 3. Techniques preferred by radiologists for the assessment of (A) carotid artery stenosis and (B) peripheral vascular disease (n = 60).

often preferring not to use it at all. They were more likely to be satisfied with the technique that is currently available to them. However, these observations were not obtained using a rigorous methodology such as conjoint analysis, which is increasingly being applied to study both patient (4;15) and clinician (7) preferences.

Although decisions on new purchases should be driven by data on the generation of technology that is to be acquired, information about other generations in current use is of

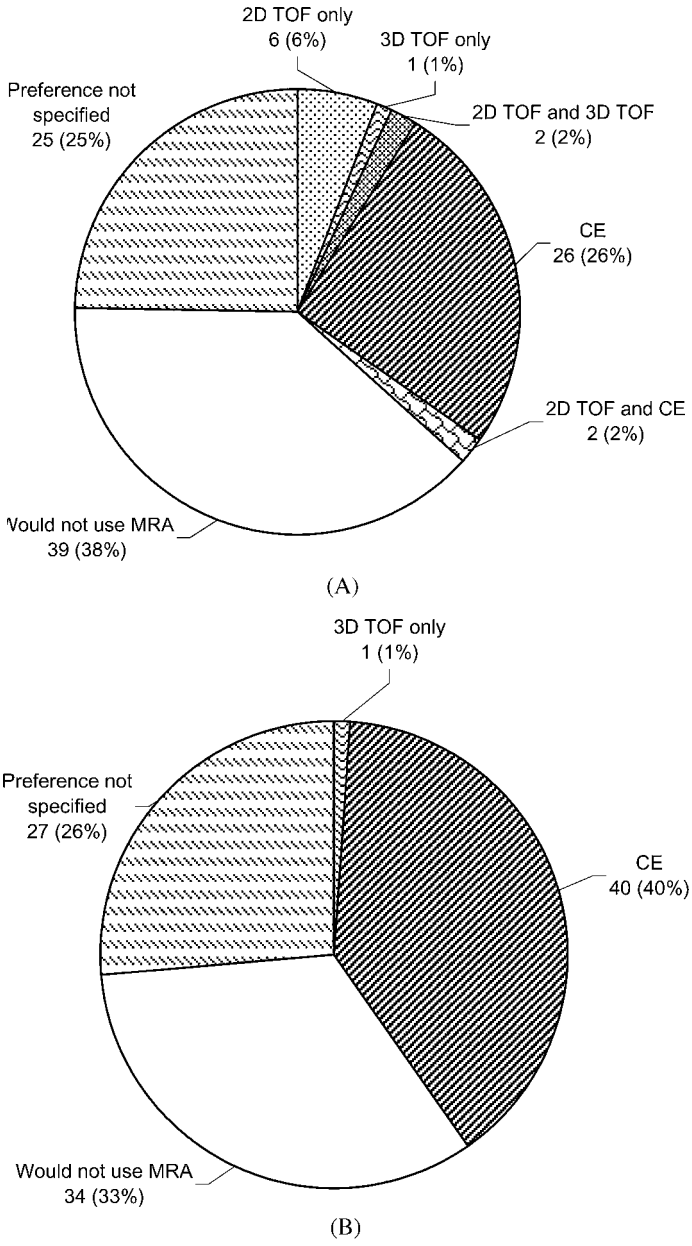

Figure 4. Techniques preferred by vascular surgeons for the assessment of (A) carotid artery stenosis and (B) peripheral vascular disease (n = 102).

value in measuring incremental cost-effectiveness and informing clinical practice. In the case of MRA, we found from this survey that time-of-flight techniques remain clinically relevant to the assessment of both carotid artery stenosis and PVD, so they were included in our systematic review.

To ensure complete and relevant coverage in reviews of other evolving technologies, it would advisable to gather data from the target population of users in a similar way to that illustrated here.

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