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REVIEW

Animal Models Used to Explore Abdominal Aortic Aneurysms: A Systematic Review

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WHAT THIS PAPER ADDS

No systematic review has previously been published on animal models of abdominal aortic aneurysms. This review presents different induction models of abdominal aortic aneurysms. Advantages and limitations of the most commonly used experimental models are highlighted and discussed.

Objective: Experimental animal models have been used to investigate the formation, development, and progression of abdominal aortic aneurysms (AAAs) for decades. New models are constantly being developed to imitate the mechanisms of human AAAs and to identify treatments that are less risky than those used today. However, to the authors' knowledge, there is no model identical to the human AAA. The objective of this systematic review was to assess the different types of animal models used to investigate the development, progression, and treatment of AAA and to highlight their advantages and limitations.

Methods: A search protocol was used to perform a systematic literature search of PubMed and Embase. A total of 2,830 records were identified. After selection of the relevant articles, 564 papers on animal AAA models were included.

Results: The most common models in rodents, including elastase, calcium chloride, angiotensin II, xenograft, and transgenic models, and the most common models in non-rodents, including chemically induced, graft models, and patch models, all have limitations with regard to the pathological interpretation of human AAA.

Conclusion: Although findings from animal models of AAAs cannot be directly translated to human AAAs, the identification and awareness of animal models of AAA will provide knowledge for further investigation and insight into human AAA disease.

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INTRODUCTION

Abdominal aortic aneurysm (AAA) is a disease associated with sudden death caused by rupture of the aneurysm. Thus far, no medical treatment is available, with options including only surveillance and open or endovascular repair. Both active interventions are costly and dangerous to the patient.[1,2] If a medical treatment was available, the costs and risks of surgical repairs could be reduced.

To identify potential medical treatments, understanding of the formation and development of AAA must be improved. Animal models can be useful strategic tools to investigate the mechanisms underlying the formation and development of AAAs. Several animal models reproduce inflammation, destruction of the fibrillar extracellular matrix (ECM), and aortic dilatation,[3–5] all of which are predicted to be determinants in aortic aneurysm development in humans.

In addition to the advantages of experimental AAA models, there are also limitations, including that they do not copy the exact pathologic conditions in human AAAs. Therefore, it can be difficult to translate the results of experimental studies to clinical use for the human AAA. The variety of injuries used to obtain experimental aortic dilatation reflects the multiplicity of pathways that may be triggered or compromised in aneurysms.

The objective of this systematic review was to identify the different types of animal models used to investigate the

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development, progression, and treatment of AAAs, and to highlight their advantages and limitations. This review does not give mechanistic insight into the process of aneurysm initiation or progression. Proteolytic activity by MMPs is mentioned in the different models, as this is considered, by the authors, to be a key process during aneurysm development.

MATERIALS AND METHODS

Embase and PubMed were searched from their earliest dates up to November 20, 2014. The search was performed by J.L.P. with assistance from a research librarian. The keywords used in the search are shown in Fig. 1. All syntaxes were searched by keyword, and if listed as such, by exploded subject headings and MeSH terms, respectively, in PubMed and Embase. No filters for time or language were requested.

All relevant animals were included in the search protocol (Fig. 1). The terms "monkey, monkeys," "monkey model," and "monkey models" were not included in the search because of the unmanageable number of papers added by them, and also because monkey models in general are not accepted for ethical reasons.

A total of 2,830 papers were found using this search strategy. The papers were imported to Endnote and duplicates were removed. Only original papers were accepted, and the model used in the study should have attempted to induce an AAA. Review articles were excluded. The papers were screened for relevance, first by title and then by abstract. If the abstract left uncertainty about the relevance of the study or about the model used, the full article was read to determine the relevance and model. Two researchers

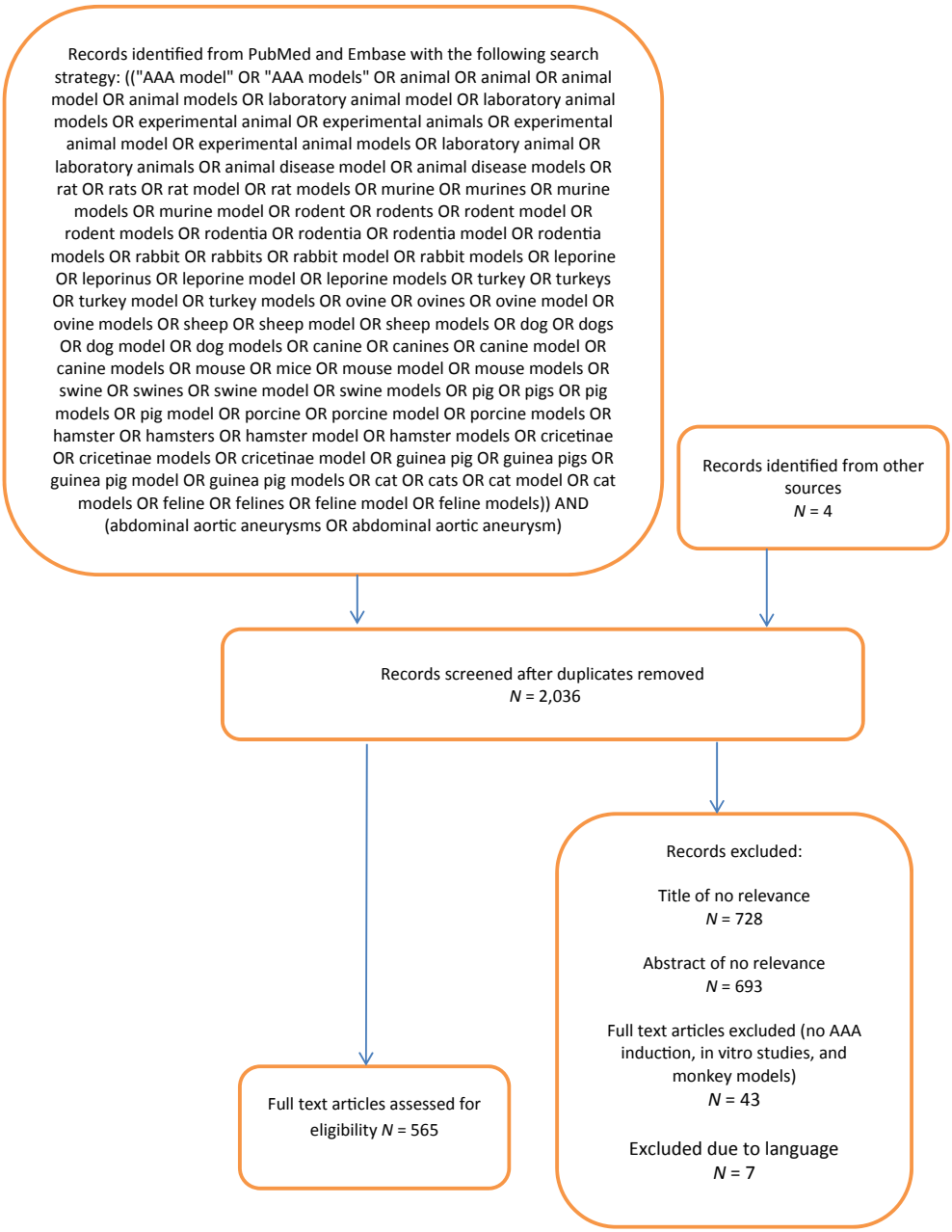

Figure 1. PRISMA flow chart for the selection of articles.

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