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Review

Towards developing criteria for scleroderma renal crisis: A scoping review☆

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ABSTRACT

Objective: The absence of a gold standard for scleroderma renal crisis (SRC) has hindered our understanding of this problem. The objective of this scoping review was to identify the criteria used to define SRC in order to guide the development of a consensus definition for SRC.
Methods: We conducted a search in three databases: Medline, Embase and non-Ovid Pubmed. Papers were eligible for inclusion if they were full-length articles in English whose main topic was SRC or scleroderma renal disease. Two reviewers independently screened eligible papers for final study selection. Data was extracted using a customized form. A web-based survey of members of the Scleroderma Clinical Trials Consortium was used to identify unpublished definitions of SRC.
Results: We identified 415 papers that met inclusion criteria. Forty original definitions of SRC were identified from 36 studies, 9 reviews and 2 editorials. There was significant heterogeneity in definitions. As a rule, though, in addition to new-onset hypertension and acute kidney injury, other common items used to define SRC included hypertensive encephalopathy and seizures, microangiopathic hemolytic anemia and characteristic changes on kidney biopsy. The web-based survey identified unpublished definitions of SRC that were largely consistent with the results of the published literature.
Conclusion: SRC was defined in a minority of studies and criteria were heterogeneous. A consensus definition of SRC is urgently needed to standardize data collection on SRC and further our understanding of this serious problem.

Abbreviations: ANCA, anti-neutrophil cytoplasmic antibody; HUS, hemolytic uremic syndrome; MAHA, microangiopathic hemolytic anemia; SRC, scleroderma renal crisis; SSc, systemic sclerosis; TTP, thrombotic thrombocytopenic purpura.

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Contents

1. Introduction

Systemic sclerosis (SSc) is an autoimmune disease of unknown etiology characterized by vascular injury and fibrosis, leading to varying degrees of skin hardening and organ involvement as well as reduced quality of life [1–3]. Scleroderma renal crisis (SRC) is a rare complication of SSc, affecting approximately 11% of diffuse and 4% of limited cutaneous SSc subjects [4]. Its clinical spectrum is broad, ranging from full-blown disease presenting as new onset of accelerated arterial hypertension and rapidly progressive oliguric renal insufficiency, to more modest elevations in blood pressure and renal dysfunction, and at times normotensive presentations. On the other hand, non-malignant hypertension without uremia, urine abnormalities and/or mild uremia attributable to other factors in the absence of SRC are common in SSc and should not be confused with it [5,6].

The absence of a gold standard for SRC has hindered our understanding of this problem. Outcomes of SRC have been reported to vary widely, but different studies have used different criteria to define SRC. Although a hallmark of SSc, SRC was not retained in the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2013 classification criteria for SSc because, although considered in the development and analysis of the criteria, it did not add to sensitivity and specificity of the final set of items retained [7]. This speaks not only to the rarity of SRC, but possibly also to the difficulty in ascertaining SRC. To date, two sets of criteria for SRC have been proposed and partially validated [8,9]. We wish to build on these preliminary efforts to develop a consensus definition for SRC and improve systematic research in this condition.

The purpose of this paper was to undertake a scoping review to identify definitions and items that have been used to define SRC. A search of the published literature was conducted to identify papers whose main topic was SRC or scleroderma renal disease. This search was supplemented by a web-based survey of members of the Scleroderma Clinical Trials Consortium to identify unpublished definitions of SRC. The primary objective was to map out the range of formal definitions used to define SRC. The secondary objectives were to 1) examine clinical features or predictors that have been shown to characterize SRC, and 2) identify items that have been proposed to distinguish SRC from diseases that are part of its differential diagnoses. Results from this review will be used to guide the development of a consensus definition for SRC.

2. Methods

This scoping review was conducted using the Arksey and O'Malley framework [10] and further guided by the methodology from recent scoping review publications [11]. The review included the following six key phases: 1) identifying the research question, 2) identifying relevant studies, 3) study selection, 4) charting the data, 5) collating, summarizing, and reporting the results, and 6) consultation exercise.

2.1. Research question

This scoping review was guided by the question, "What are the items that have been used to define, characterize or predict scleroderma renal crisis in the literature?"

2.2. Data sources and search strategy

The comprehensive search was implemented on June 17, 2016, in three electronic databases including MEDLINE (Ovid) (1946–present), EMBASE (Ovid) (1947–present) and Pubmed (1966–present) by one author (SH), with the assistance of a professional librarian. No limits on date, language, subject or type were placed on the database search. The search query was constructed to capture articles that addressed the topics of renal insufficiency or malignant hypertension in SSc. The search query was tailored to the specific requirements of each database (Supplementary Table 1).

The reference lists of 15 pre-selected relevant review articles were manually searched to identify any further studies not yet captured. A "snowball" technique was also adopted in which citations within articles were searched if they appeared relevant to the review [11].

2.3. Citation management

Duplicate citations were initially removed in Ovid for citations from Medline and EMBASE. Citations from Ovid and Pubmed were then imported into the bibliographic manager EndNote X7.4 (Thomson Reuters) and duplicate citations were further removed manually following a 12-step method of de-duplication [12]. Citations were finally