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Protocol

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Predictors of rupture and mortality in uncommon true visceral artery aneurysms: A protocol for a systematic review and pooled analysis.

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Abstract

Background: Visceral artery aneurysms (VAAs) are rare vascular lesions associated with a substantial risk of rupture and high mortality. Splenic artery aneurysms (SAAs) are the most common and best studied, with relatively well-established risk factors and management strategies. In contrast, uncommon VAAs arising from the hepatic, celiac, superior mesenteric, gastroduodenal, pancreaticoduodenal, gastroepiploic, gastric, jejunal, ileal, colic, and inferior mesenteric arteries are exceedingly rare, and their natural history and rupture predictors remain poorly defined. Rupture has been reported at small diameters, challenging size-based thresholds derived largely from SAA data.

Objectives: This systematic review and pooled analysis aims to determine rupture rates, predictors of rupture, and rupture-related mortality of uncommon true VAAs, and to compare these outcomes with those reported for SAAs, which will serve as reference lesions.

Methods: The review will be conducted in accordance with PRISMA 2020 guidelines and is registered in PROSPERO (CRD420251155062). A comprehensive search of PubMed/MEDLINE, Embase, Web of Science, Scopus, and Google Scholar will be performed. For uncommon VAAs, eligible studies will include meta-analyses, systematic reviews, cohort studies, case series, and case reports. For SAAs, only meta-analyses, systematic reviews, and large cohort studies will be included. Pooled patient-level data will be extracted where available. Primary outcomes are rupture rate and rupture-related mortality; secondary outcomes include predictors of rupture according to aneurysm location, size, patient characteristics, and clinical presentation. Risk of bias will be assessed using JBI, ROBINS-I, and AMSTAR 2 tools.

Expected Impact: This review aims to clarify rupture behaviour of uncommon VAAs, identify clinically relevant predictors, and provide a stronger evidence base to support risk stratification and harmonisation of clinical decision-making.

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Introduction

Visceral artery aneurysms (VAAs) constitute rare vascular lesions with an estimated incidence of 0.1-2% in the general population [1,2]. However, their true prevalence may be underestimated, as in postmortem studies, splenic artery aneurysms (SAAs) may reach up to 10% [3]. Despite their rarity, VAAs carry a rupture risk of 10-20%, and a mortality rate ranging from 25% to 75%, making them a potentially life-threatening condition [2,4,5]. The pathogenesis of VAAs is heterogeneous and not fully understood. While many cases are related to atherosclerosis, infection, blunt trauma, or inflammatory diseases such as polyarteritis nodosa [6,7,8], a smaller proportion of cases are associated with connective tissue disorders such as Ehlers-Danlos syndrome, Marfan syndrome, or Kawasaki disease, conditions that are associated with a higher risk of rupture. In addition, in other cases, the cause remains uncertain [2,6].

SAAs account for 60% of all VAAs, followed by uncommon VAAs: the hepatic artery aneurysms (20%), superior mesenteric artery (SMA) aneurysms (5%), and celiac trunk aneurysms (4%). Arterial aneurysms of the jejunal, ileal, gastroduodenal, pancreaticoduodenal, gastric, gastroepiploic, colic branches, and inferior mesenteric artery (IMA) are extremely rare, representing only 3.5% of all VAAs. Renal artery aneurysms are excluded from this category due to their distinct embryological and pathophysiological origin [2,6,8-12]. In recent decades, the widespread use of cross-sectional imaging has led to an increase in the number of incidental VAA diagnoses [6, 12].

Rupture risk factors for SAAs are relatively well established, with pregnancy and high-flow states (portal hypertension) being the most recognized. They are the most prevalent VAAs and, in consequence, have been analyzed in large series and systematic reviews [10,12,13]. In contrast, rupture predictors for uncommon VAAs remain poorly defined, often limited only to case reports, small case series, or institutional single-centre registers [6,12,13], with a high variability of management in clinical practice. Consequently, much of the current understanding of the rupture risk of uncommon VAAs is extrapolated from SAA data. Interestingly, rupture of uncommon VAAs has been reported at diameters smaller (<10mm) than those traditionally considered for SAAs [6,14-18], suggesting potential differences in clinical behaviour and challenging the traditional 2cm intervention threshold. This suggests that variables beyond size, such as anatomical location, underlying pathology, or patient-specific risk factors, may play a more decisive role [14,15]. Moreover, some authors recommend even to treat specific VAAs based solely on the location, regardless of the size, such as gastroduodenal or pancreaticoduodenal artery aneurysms [6,19-21].

Recent international clinical practice recommendations also reflect this uncertainty. The Society for Vascular Surgery (2020 SVS guidelines) recommends to treat all gastric, gastroepiploic, SMA, gastroduodenal, pancreaticoduodenal and colic artery aneurysms regardless of size; while establishes a diameter threshold of 3 cm for all asymptomatic SAAs, 2 cm for jejunal and ileal artery aneurysms, celiac trunk artery aneurysms and hepatic artery aneurysms, or lower when connective tissue disorders or symptoms are present [9]. In contrast, the 2025 European Society for Vascular Surgery (ESVS) clinical practice guidelines adopts a more conservative approach, suggesting that the natural history of VAAs may be benign with a low risk of rupture and recommends intervention for asymptomatic SAA ≥3 cm, hepatic artery aneurysms ≥3cm, SMA aneurysms ≥3 cm, celiac trunk artery aneurysms ≥3cm and pancreaticoduodenal artery aneurysms ≥15 mm [2].

Considering these uncertainties, a systematic review focusing specifically on these uncommon VAAs is warranted. This review aims to identify rupture rate, risk factors for rupture, and mortality of uncommon VAAs and to compare the outcomes with the data available for SAAs, considered as reference lesions. Finally, this work aims to provide a stronger evidence base for risk-stratification and to support more tailored clinical decision-making in the management of these rare, but potentially fatal aneurysms, and, finally, to harmonize clinical practice.

Methods

Aims and objectives

This systematic review and pooled analysis aims to

estimate the rupture rate of uncommon true visceral artery aneurysms (VAAs) in predefined visceral vascular territories, to identify patient- and aneurysm-related predictors of rupture, and to quantify rupture-related mortality. In addition, outcomes for uncommon VAAs will be compared with those reported for splenic artery aneurysms (SAAs), which will serve as reference lesions.

The primary objective is to determine rupture rates of uncommon VAAs at presentation and during follow-up and to identify predictors of rupture, including aneurysm location and size, patient demographics, medical history, and clinical presentation, as well as mortality associated with rupture. Secondary objectives are to compare rupture rates, predictors of rupture, and mortality between uncommon VAAs and SAAs using data derived from large cohort studies, systematic reviews, and meta-analyses.

Study design and registration

A systematic review and pooled patient-level analysis will be conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The protocol has been registered prospectively in the PROSPERO database (International Prospective Register of Systematic Reviews) under registration number CRD420251155062.

Eligibility Criteria

Eligible studies will include reports of true aneurysms of the hepatic artery, celiac trunk, superior mesenteric artery and its jejunal, ileal, and colic branches, gastroduodenal and pancreaticoduodenal arteries, gastroepiploic and gastric arteries, and the inferior mesenteric artery and its branches. Studies will be included provided that aneurysm size, anatomical location, and rupture status are reported together with at least one of the following variables: patient demographics, medical history, clinical presentation, mortality, or treatment strategy. Only English-language studies will be considered, with no restriction on publication date. Renal artery aneurysms will be excluded because of their distinct embryological and pathophysiological characteristics. Splenic artery aneurysms will be included exclusively as a comparator group to contextualise outcomes for uncommon VAAs. For uncommon VAAs, eligible study designs will include meta-analyses, systematic reviews, retrospective and prospective single-centre or multicentre studies, registry studies, case series, and case reports. Given the rarity of these aneurysms, inclusion of case reports and small case series is necessary to ensure comprehensive data capture. For SAAs, only meta-analyses, systematic reviews, and large cohort studies will be included to provide robust reference data for comparative analyses. Randomised controlled trials are not anticipated but will be included if identified.

Information sources and search strategy

A comprehensive literature search will be conducted in PubMed/MEDLINE, Embase, Web of Science, Scopus, and Google Scholar. Reference lists of included studies will be screened manually to identify additional relevant publications. Search terms will include anatomical descriptors of uncommon VAAs and SAAs, together with terms related to rupture, risk factors, mortality, and study design. Full search strategies and keyword combinations are provided in the supplementary material. No publication date restrictions will be applied.

Study selection and data extraction

Two independent reviewers will screen titles and abstracts for eligibility, followed by a full-text review of potentially relevant studies. Discrepancies will be resolved by consensus or, if required, by consultation with the supervising co-author. The study selection process will be documented using a PRISMA 2020 flow diagram.

Data will be extracted independently by two reviewers using a predefined data extraction template and recorded in a Microsoft Excel database. Extracted variables will include aneurysm location, aneurysm size, rupture status, patient demographics, relevant medical history, clinical presentation, mortality, and treatment strategy. A complete list of variables is provided in Supplementary Table S2. When individual patient-level data are reported, each case will be entered as a separate observation and included in the pooled.

patient-level analysis. When studies report only aggregated data, these studies will be entered as a single summary row and clearly labelled as aggregated data, with individual-level analysis not possible.

Outcomes

The primary outcomes are rupture rate of uncommon VAAs at presentation or during follow-up, predictors of rupture, including demographic characteristics, medical history, aneurysm location and size, clinical presentation, and rupture-related mortality. Secondary outcomes will compare rupture rates, predictors of rupture, and mortality between uncommon VAAs and SAAs, using SAAs as reference lesions.

Risk of bias and publication bias

Risk of bias will be assessed independently by two reviewers. Case reports and case series will be evaluated using the Joanna Briggs Institute critical appraisal checklists. Observational studies will be assessed using the ROBINS-I tool. Systematic reviews and meta-analyses will be evaluated using the AMSTAR 2 tool. Disagreements will be resolved by discussion or consultation with the supervising co-author.

Given the rarity of uncommon VAAs, publication bias is anticipated, with more severe or dramatic cases more likely to be reported. Publication bias will be explored using Egger's test, where sufficient data are available, and will be considered in the interpretation of results.

Handling of missing data and data synthesis

Studies or cases that do not report the minimum required data, defined as aneurysm location, size, and rupture status, together with at least one additional clinical variable, will be excluded from quantitative analyses. Analyses will be performed on a complete-case basis. The proportion of missing data for each variable will be reported, and the potential impact on findings will be discussed.

Categorical variables, including rupture, medical history, mortality, and clinical presentation, will be summarised as frequencies and percentages. Continuous variables, such as aneurysm size and patient age, will be reported as means with standard deviation or medians with interquartile ranges, depending on data distribution.

For uncommon VAAs, a pooled patient-level descriptive synthesis will be performed. Rupture rates and mortality will be calculated overall and stratified by aneurysm location, aneurysm size (<10 mm, 10–20 mm, and >20 mm), and patient-related variables. Comparative analyses between SAAs and uncommon VAAs will be conducted using risk ratios or odds ratios with 95% confidence intervals where appropriate. Statistical heterogeneity will be assessed using the I^2 statistic.

When quantitative pooling is not appropriate due to heterogeneity or limited data, results will be reported descriptively in tables and narrative form in accordance with the Synthesis Without Meta-analysis framework.

Ethics and dissemination

Ethical approval is not required for this study, as it involves secondary analysis of published data. The completed systematic review will be submitted to a peer-reviewed medical or surgical journal and presented at national and international scientific meetings.

Discussion

Uncommon VAA is a vascular lesion with an unpredictable behaviour that can result in fatal rupture with mortality rates from 25 to 75% [8,12]. Among VAAs, SAAs are the most frequently investigated with well-established rupture risk factors, such as pregnancy or portal hypertension. Consequently, management strategies for SAA are supported by relatively robust evidence. In fact, both the 2020 SVS and 2025 ESVS guidelines recommend intervention for asymptomatic SAAs ≥ 3cm [2,9,17]. However, the natural behavior of uncommon VAAs remains unpredictable. Rupture has been reported at diameters <10 mm, with catastrophic outcomes in some cases [2,5,12, 14,15,18], suggesting that factors beyond size may play a more decisive role in rupture [6, 12,14-18, 21]. Reported factors include anatomical location, connective tissue disease, infection, pregnancy, or blunt trauma; however, in many other cases, the etiology of rupture remains unclear [2,6,8,9]. Some studies have suggested that the rate of growth may be slower

than previously assumed and may be influenced by factors such as smoking, younger age, absence of calcification, and presence of mural thrombus [20,22]. However, the data are limited, and conclusions cannot be generalized.

The two main international guidelines from The Society for Vascular Surgery (SVS) and The European Society for Vascular Surgery (ESVS), differ on the management for some specific and uncommon VAAs, reflecting the uncertainty that remains in the understanding and management of uncommon VAAs [2,9]. The recent 2025 ESVS guidelines adopt a more conservative strategy on certain uncommon VAAs, with a higher diameter threshold for intervention, and suggest that some VAAs may follow a benign course [2]. In contrast, the SVS (2020) is more aggressive and recommends intervention for some uncommon VAAs regardless of the size, such as gastric, gastroepiploic, superior mesenteric, gastroduodenal, pancreaticoduodenal, and colic artery aneurysms[9]. This discrepancy underscores the lack of high-quality evidence and the ongoing debate regarding appropriate management strategies.

Furthermore, in the literature, there are many examples of this lack of consensus with different authors recommending different managements, often based on single- institutional experience [6,12,17,18,21]. This knowledge gap generates significant heterogeneity in clinical practice. Most of the recommendations of uncommon VAA management are based on single-institution experience and are subject to selection and publication bias. Comparing uncommon VAAs with SAAs is crucial to clarify whether extrapolation is adequate or whether uncommon VAAs require location-specific recommendations, according to the different vascular territories and risk factors. Our primary aim is to investigate rupture rate, predictor variables of rupture and mortality rate of uncommon VAAs and secondarily, to compare the findings with the available data for SAAs. SAAs will be considered as “reference lesions” as they are well-characterized and explored in the existing literature with a clear and well-defined consensus of management, and therefore provide a valuable benchmark [2,9,23]. By systematically analyzing all available patient-level data on uncommon VAAs and comparing them with SAAs, this study seeks to identify similarities, differences, and unresolved knowledge gaps in rupture behaviour and clinical outcomes across different vascular territories.

We anticipate limitations related to the rarity of this entity, the heterogeneity of the cases, the probability of publication bias with more dramatic cases being more frequently reported, potentially overestimating rupture risk, and selection bias, as single-center series often reflect institutional expertise and may not be generalizable. However, pooled patient-level analysis will allow the most robust evidence synthesis possible.

Conflicts of interest: All authors declare no conflict of interest.

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