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Association between anatomical position of the appendix and appendiceal perforation in patients with acute appendicitis: a protocol for a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review stage at the time of initial registration - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 November 2026 and was last updated on 23 November 2026.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis aims to determine whether a posterior or concealed anatomical position of the appendix—particularly the retrocecal position—is associated with an increased risk of appendiceal perforation and other severity outcomes (complicated appendicitis, gangrene, and intra-abdominal abscess) in patients undergoing appendectomy for acute appendicitis, compared with anterior or other positions. By restricting eligibility to studies that report both appendix position and at least one severity outcome, and by excluding cohorts that are uninformative or prone to selection bias (perforation-only cohorts, design-based samples, and conservatively managed abscess populations), this review seeks to generate an unbiased pooled estimate of the position–perforation association and to clarify whether concealed appendix positions contribute to adverse outcomes primarily through delayed diagnosis.

Rationale Acute appendicitis in an atypical position (retrocecal, pelvic, subhepatic, or retroileal/retroperitoneal) often presents with non-classical symptoms, which may reduce the sensitivity of clinical examination and ultrasonography and delay diagnosis. Diagnostic delay is a recognized driver of perforation and other complications. However, the evidence linking appendix position itself to perforation risk is scattered across individual observational studies with heterogeneous position classifications, outcome definitions, and ascertainment methods (CT-based versus intraoperative). No previous quantitative synthesis has specifically pooled the position–perforation association. This review aims to clarify whether position per se determines perforation risk, or whether concealed positions increase perforation mainly through delayed diagnosis — a distinction with direct implications for imaging strategies and surgical decision-making.

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Condition being studied Acute appendicitis is one of the most common surgical emergencies worldwide and a leading indication for emergency abdominal surgery. It typically presents with migratory right lower quadrant pain, but symptoms vary considerably with the anatomical position of the appendix, and atypical presentations frequently delay diagnosis. If untreated or diagnosed late, appendicitis may progress to gangrene, perforation, abscess formation, and peritonitis, with substantially increased morbidity. Perforation is therefore the key severity outcome of the disease. The appendix shows wide anatomical variation (e.g., anterior, retrocecal, pelvic, subhepatic, retroileal), which may influence both clinical presentation and disease severity.

METHODS

Search strategy Electronic databases: PubMed, Embase, Web of Science, Scopus, and CNKI, Wanfang Data, and VIP for Chinese-language literature, searched from database inception to 31 December 2026 (all searches executed between June 2026 and December 2026), restricted to English- and Chinese-language publications. The search combines three concept blocks: (1) appendicitis or appendectomy; (2) appendix position or location (position*, location*, anatom*, retrocecal, retrocaecal, pelvic, subhepatic, retroileal, pre-ileal, post-ileal, subcecal, paracecal, undescended cecum, malrotation); and (3) outcomes (perforat*, ruptur*, gangren*, complicated, complication*, outcome*, delay*).
PubMed search formula:
("Appendicitis"[Mesh] OR appendicitis[tiab] OR appendectomy[tiab] OR appendicectomy[tiab]) AND ("appendix"[tiab] OR "appendiceal"[tiab] OR "appendicular"[tiab]) AND (position[tiab] OR location[tiab] OR anatom*[tiab] OR retrocecal[tiab] OR retrocaecal[tiab] OR pelvic[tiab] OR subhepatic[tiab] OR retroileal[tiab] OR "pre-ileal"[tiab] OR "post-ileal"[tiab] OR subcecal[tiab] OR subcaecal[tiab] OR paracecal[tiab] OR "undescended cecum"[tiab] OR malrotation[tiab]) AND (perforat*[tiab] OR ruptur*[tiab] OR gangren*[tiab] OR complicated[tiab] OR complication*[tiab] OR outcome*[tiab] OR delay*[tiab])
A broader supplementary PubMed search without outcome restriction was also run to avoid missing studies that report position data without outcome terms in the title/abstract:
("Appendicitis"[Mesh] OR appendicitis[tiab] OR appendectomy[tiab] OR appendicectomy[tiab]) AND (position*[tiab] OR location*[tiab] OR anatom*[tiab] OR retrocecal[tiab] OR retrocaecal[tiab] OR pelvic[tiab] OR subhepatic[tiab] OR "sub-hepatic"[tiab] OR retroileal[tiab] OR "pre-ileal"[tiab] OR "post-ileal"[tiab] OR subcecal[tiab] OR subcaecal[tiab] OR paracecal[tiab] OR retroperitoneal[tiab] OR hidden[tiab] OR "undescended cecum"[tiab] OR "undescended caecum"[tiab] OR malrotation[tiab]).
Chinese databases (CNKI/Wanfang/VIP): 主题 =（阑尾炎 OR 阑尾切除）AND（异位 OR 位置 OR 盲肠后 OR 腹膜外 OR 腹膜后 OR 盆腔位 OR 高位 OR 肝下 OR 壁内 OR 左位）AND（穿孔 OR 坏疽 OR 脓肿 OR 并发症 OR 误诊）。

Participant or population Patients of any age with acute appendicitis undergoing appendectomy. Adults and children are pre-specified subgroups. Pregnant patients and conservatively managed peri-appendiceal abscess cohorts are excluded because of selection bias.

Intervention Posterior or concealed anatomical positions of the appendix, as defined in the original studies. The primary analysis uses the retrocecal position as the exposure. A pre-specified sensitivity analysis applies a broad concealed-position category encompassing retrocecal, pelvic, subhepatic, and retroileal/retroperitoneal positions.

Comparator Anterior and other appendix positions, as grouped in the original studies. A position-group mapping table is prepared in advance documenting, for each study, how position categories were mapped to exposure and comparator groups. Comparator groups contaminated with concealed positions are handled in sensitivity analyses.

Study designs to be included Peer-reviewed observational studies: prospective or retrospective cohort studies, case-control studies, and cross-sectional studies. Reviews, case reports and minimal-sample case series (e.g., ≤6 cases), and duplicate publications are excluded.

Eligibility criteria Inclusion: (1) patients with acute appendicitis undergoing appendectomy; (2) reporting of appendix anatomical position AND at least one severity outcome (perforation, complicated appendicitis, gangrene, abscess), ideally as a position × outcome cross-tabulation or derivable data; or reporting position distribution data (for descriptive synthesis only). Exclusion: (1) studies in which perforation was an inclusion criterion (100% perforated), which are uninformative for the primary outcome; (2) studies without position data; (3) reviews, minimal-sample case series, and duplicate cohorts; (4) pregnancy or conservatively managed peri-appendiceal

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abscess cohorts. Studies with internally inconsistent data or design-based samples (e.g., 1:1 sampling by perforation status) are excluded from proportion pooling and addressed in sensitivity analyses.

Information sources PubMed, Embase, Web of Science, CNKI, Wanfang Data, and VIP from June 2026 through December 2026 and manual scanning of reference lists of included original studies and review articles.

Main outcome(s) The primary outcome is appendiceal perforation, expressed as the odds ratio (OR) with 95% confidence interval comparing retrocecal versus non-retrocecal appendix positions, with perforation definitions recorded and annotated as reported in the original studies.

Additional outcome(s) Complicated appendicitis (definitions of individual studies reported side-by-side; not forcibly pooled); gangrenous appendicitis; intra-abdominal abscess (pooled only after harmonizing intraoperative versus postoperative time windows); diagnostic delay as a narrative outcome, including imaging false-negative rates, preoperative diagnostic rates, and time to diagnosis.

Data management Records retrieved from all databases are exported to EndNote for deduplication. Two reviewers independently screen titles/abstracts and full texts; disagreements are resolved by discussion or a third reviewer. A screening log records the inclusion/exclusion decision and one-line reason for every full-text article, providing the basis for the PRISMA 2020 flow diagram. Data extraction uses a standardized, piloted form; data calculated from reported percentages are flagged ("calculated from reported percentages"); SE(logOR) values are not pre-filled manually but computed by the software at synthesis.

Quality assessment / Risk of bias analysis Included cohort and case-control studies are assessed with the Newcastle-Ottawa Scale (NOS): selection (4 items), comparability (2 points), and outcome/exposure ascertainment (3 items), total 9 stars. Two reviewers score independently; disagreements are resolved by discussion, and inter-rater agreement (Cohen's κ) is recorded. Studies scoring ≥7 are rated high quality, 5–6 moderate, and ≤4 low. Studies scoring ≤6 are not excluded but are addressed in a "high-quality studies only" sensitivity analysis.

Strategy of data synthesis The primary analysis will compare retrocaecal versus non-retrocaecal appendix positions with respect to perforation, using a random-effects model (DerSimonian–Laird method) with odds ratios (ORs) and 95% confidence intervals as the effect measure. Heterogeneity will be assessed with Cochran's Q, I^2 and τ^2. If I^2 exceeds 50%, we will not emphasize a single pooled estimate and will instead report the pattern of subgroup and sensitivity analyses. If fewer than 10 studies are available, Egger's test will not be performed and funnel plots will be inspected visually only, with this limitation acknowledged. Secondary outcomes (complicated appendicitis, gangrene, intra-abdominal abscess) will be pooled only when definitions are sufficiently homogeneous: complicated appendicitis will be reported with each study's definition listed side by side rather than forcibly pooled, and intra-abdominal abscess will be pooled only after harmonising intra-operative versus post-operative time windows. Diagnostic delay will be reported as a narrative outcome.

Subgroup analysis Two subgroup analyses are pre-specified on the basis of clinical and biological plausibility: (1) adults versus children — children have a thinner appendiceal wall and an underdeveloped omentum (faster progression to perforation), undergo ultrasound rather than CT as first-line imaging, and are less able to articulate localised symptoms, all of which may amplify the effect of occult positions on diagnostic delay and perforation; (2) CT-based versus intra-operative determination of appendix position, as the ascertainment method affects classification accuracy. Subgroup differences will be evaluated using a formal test for interaction rather than by comparing statistical significance across subgroups. Given the limited number of included studies, these analyses are considered exploratory and hypothesis-generating.

Sensitivity analysis NA

Language restriction Only articles published in English or Chinese will be included.

Country(ies) involved China (中国).

Other relevant information This is a retrospective registration: preliminary literature collection and data extraction began before protocol registration, while the formal systematic search, citation tracking, quality assessment, and quantitative synthesis are conducted according to this protocol. The registration timing will be disclosed in the Methods and Limitations of the final

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publication. The review team consists of clinical medical students who have completed formal training in medical statistics and are proficient in reference-management software (EndNote/Zotero) and quantitative synthesis tools (RevMan 5.4 / R meta package), working under the supervision of the principal investigator.
Current review status: Ongoing.

Keywords Appendicitis; appendix position; retrocecal; perforation; complicated appendicitis; diagnostic delay; meta-analysis.

Dissemination plans Publication in a peer-reviewed journal (targeting general surgery or emergency/pediatric specialty journals), reported according to PRISMA 2020 with the checklist submitted as a supplement. Retrospective registration is disclosed in the Methods, and the timing of registration relative to data extraction is declared in the Limitations.

Contributions of each author

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