

The Diagnosis of Complicated Appendicitis: An Update on the Definition and Diagnosis: Review Article

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Abstract: The definition of complicated appendicitis has been an area of concern due to the absence of any universal consensus. Complicated appendicitis often means perforation of the appendix with either peritonitis, abscess, or mass formation. The diagnosis of complicated appendicitis is another area where there is no consensus and there is no one investigation that can diagnose this condition. Diagnosis often involves the use of clinical examinations, blood investigations, and imaging modalities. In this chapter, we will look at the definition and diagnosis of complicated appendicitis.

Keywords: Complicated appendicitis, Definition, Diagnosis, Blood Investigations, perforated appendix, imaging.

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INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdominal pain that is seen in young patients. It occurs at a rate of 5.7 to 50 patients per 100,000 population per year with a peak incidence in the 10 to 30 years of age. Appendicular perforation, which is a complication of acute appendicitis, is associated with higher morbidity and mortality. The definition of complicated appendicitis is not uniform, and it varies according to the studies, with most surgeons agreeing that perforation of the appendix with either free pus in the peritoneal cavity causing acute peritonitis, an appendicular abscess formation and the formation of an inflammatory mass in the right iliac fossa (Di Saverio *et al.*, 2020).

The diagnosis of complicated appendicitis involves history taking, clinical examination, and blood investigation. Blood investigations involve using full blood count and inflammatory markers like C-reactive protein. Imaging modalities like ultrasound and computerized tomography may be used when the diagnosis is in doubt (Becker *et al.*, 2018). The incidence of complicated appendicitis is related to factors like increasing age, and the presence of co-morbidities like

diabetes mellitus, chronic anemia, and hypertension. Complicated appendicitis is also seen in more rural populations when compared to urban ones (Araim *et al.*, 2022). The diagnosis and classification of complicated appendicitis are important as the management will depend on what type of complicated appendicitis has occurred (Gorter *et al.*, 2016).

As there is no current consensus on the definition and diagnosis of complicated appendicitis, we have conducted this review article looking into the definition, and diagnosis of complicated appendicitis. The role of various investigation modalities like full blood count, C-reactive protein (CRP), and imaging modalities like ultrasound and computerized tomography are evaluated. We conducted a literature review using PUBMED, the Cochrane database of systemic reviews, Google Scholar, and semantic scholar looking for randomized control trials, non-randomized trials, observational and cohort studies, clinical reviews, systemic reviews, and meta-analyses from 1980 to 2024. The following keywords were used, "complicated appendicitis", "definition", "diagnosis", "blood investigations", "perforated appendix" and "imaging". All articles were in English, and all articles were assessed by manual cross-referencing of the literature.

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Commentaries, case reports, and editorials were excluded from this review. Adult and pediatric patients were included in this study and pregnant patients with complicated appendicitis were excluded.

DISCUSSION

Definition of Complicated Appendicitis

There is currently no universal definition for complicated appendicitis, leading to difficulty managing this condition. Complicated appendicitis is usually meant to imply inflammation of the appendix that proceeds to perforation, necrosis, or abscess formation (Mekakas *et al.*, 2022; Moris *et al.*, 2021). The definition of complicated appendicitis can be made preoperatively or during surgery, where it is defined as perforated appendicitis, perpendicular abscess, or peritonitis due to inflammation of the peritoneum secondary to infection of the appendix (Mariage *et al.*, 2019). Appendicular mass is also included in the definition of complicated appendicitis and this includes an inflammatory mass in the right iliac fossa which is formed by the perforated

appendix, cecum, terminal ileum, and omentum or surrounding adnexal structures (Collard *et al.*, 2021). Some have used the term complex appendicitis to mean complicated appendicitis which means perforation and abscess formation of the appendix (Bhangu *et al.*, 2015).

In pediatric patients, the definition of perforated appendicitis is stated as the presence of a hole in the appendix or fecalith in the abdomen which is then used to predict the risk of developing complications like appendicular abscess or acute peritonitis (Rogers *et al.*, 2017; St. Peter *et al.*, 2008). This definition helps to differentiate perforated from non-perforated appendicitis in pediatric patients as well as risk stratification of patients who may develop complications (Holcomb & St Peter, 2012). Most surgeons agree that the definition of complicated appendicitis as acute appendicitis with perforation, gangrenous appendicitis, the presence of fecalith, appendicular abscess, and purulent peritonitis. This definition is then used to classify the management of complicated appendicitis (de Wijkerslooth *et al.*, 2019).

Table I

European Association of Emergency Surgeons (EAES) consensus-2015	Gangrenous, inflamed appendix with or without perforation, intra-abdominal abscess, peri-appendicular phlegmon, or purulent free fluid.
World Society of Emergency Surgeons (WSES) consensus-2020	Acute appendicitis with perforation, intra-abdominal abscess, or purulent peritonitis.

Table showing the definition of complicated appendicitis

The Incidence of complicated appendicitis

The global incidence of acute appendicitis is about 100 to 150 per 100,000 population in most Western countries and it has stabilized, whereas the incidence has been increasing in Central and East Asia, South America and Africa. The peak incidence is seen in the second and third decade of life and mortality has been steadily decreasing over the past decade 21 (Ferris *et al.*, 2017; Wickramasinghe *et al.*, 2021, Yang *et al.*, 2022).

The incidence of complicated appendicitis varies between 10% to 30% and it is seen in pediatric and elderly patients. The following risk factors are male gender, presence of co-morbidities like diabetes mellitus, chronic anemia, and malnutrition. Complicated appendicitis is associated with a higher incidence in rural hospitals rather than in urban hospitals (Araim *et al.*, 2022).

Diagnosis of complicated appendicitis

Biomarkers

The diagnosis of complicated appendicitis involves a combination of biomarkers like C-reactive protein (CRP) and total white cell counts which are elevated in this condition. Clinical scoring systems like the Alvarado and Appendix Inflammatory scores have been used to stratify which patients risk developing complicated appendicitis. Imaging in the form of ultrasound of the abdomen and computerized

tomography are often used to confirm the diagnosis of complicated appendicitis (Bom, Scheijmans, *et al.*, 2021).

Among the biomarkers, the total white cell count is the most common agent that is used to diagnose complicated appendicitis. Leukocytosis with a count of more than 13,000 and above is associated with a higher risk of complicated appendicitis (Dinç *et al.*, 2022). The diagnostic accuracy of leukocytosis on its own is moderate in its ability to diagnose complicated appendicitis but when combined with other inflammatory markers its diagnostic ability improves (Beecher *et al.*, 2016; Kanlioz *et al.*, 2016). Other inflammatory markers like C-reactive protein (CRP) is useful in diagnosing complicated appendicitis in younger patients especially when the clinical signs are equivocal. This parameter is associated with good sensitivity and specificity in the diagnosis of complicated appendicitis especially in the pediatric patients (Ha *et al.*, 2024).

The neutrophil-to-lymphocyte ratio can also be used to diagnose complicated appendicitis and a cut-off of 7.2 to 8.39 were taken to diagnose complicated appendicitis (Bălănescu *et al.*, 2023; Bekdas *et al.*, 2017). A systemic review and meta-analysis were conducted by Hajibandeh *et al.*, to look at its ability to diagnose acute appendicitis and compare complicated from uncomplicated appendicitis. 17 studies with 8914 patients were included in this study, and a neutrophil-to-lymphocyte ratio of 8.8 was used to diagnose

complicated appendicitis. The sensitivity was 76.92% and the specificity was 100% hence the neutrophil-to-lymphocyte ratio can distinguish complicated appendicitis (Hajibandeh *et al.*, 2020).

Hyponatremia is another parameter that has been used to diagnose complicated appendicitis. A systemic review was conducted by Giannis *et al.*, to look at the role of hyponatremia as a marker of complicated appendicitis. 7 studies with 2682 patients were included in this study and a value of 135mEq and below was associated with a risk of complicated appendicitis if it is associated with other parameters although its diagnostic accuracy will need to be prospectively assessed (Giannis *et al.*, 2020). Hyperbilirubinemia is another marker that when elevated is associated with a higher risk of complicated appendicitis, with a serum cut-off value of more than 23.3mmol/l. Hyperbilirubinemia when used with hyponatremia is associated with a higher predictor rate for complicated appendicitis (Shuaib *et al.*, 2022).

Clinical scoring systems

Clinical scoring systems employ clinical items and laboratory markers to diagnose acute appendicitis and decide which patients will require surgery and assessment with imaging modalities. The common scoring systems that are used include the Alvarado score, the modified Alvarado score, the RIPASA score, the Appendicitis Inflammatory Score (AIR), and others. These clinical scoring systems are useful for assessing and interpreting the clinical situation and those with a higher score are associated with a higher likelihood of acute appendicitis but none of them can differentiate between acute appendicitis and complicated appendicitis (Balakrishnan *et al.*, 2024; Haak *et al.*, 2022). Most reviews that have been performed have found that these scores have various abilities to diagnose acute appendicitis, but they are not sensitive to differentiate between uncomplicated and complicated appendicitis (Mundada *et al.*, 2020).

Imaging modalities

The common imaging modalities that are used to diagnose acute appendicitis include ultrasound, computerized tomography, and magnetic resonance imaging. Ultrasound is economical, easy to use, and readily available, while computerized tomography and magnetic resonance imaging are done in cases where the diagnosis is equivocal on ultrasound. Imaging is also required when differentiating uncomplicated from complicated appendicitis. A systemic review was done by Bom *et al* discriminating complicated from uncomplicated appendicitis by ultrasound, computerized tomography, and magnetic resonance imaging. 13

studies with 1892 patients of which 620 had complicated appendicitis. The sensitivity and specificity of computerized tomography could only be calculated, and they were 78% and 91%, the positive and negative predictive values were 74% and 93%. This study concluded that ultrasound, computerized tomography, and magnetic resonance tomography had limited ability to diagnose complicated appendicitis (Bom, Bolmers, *et al.*, 2021).

Ultrasound was found to be useful to differentiate uncomplicated from complicated appendicitis in the pediatric population. Among the features that were observed include appendicular wall thickening and edema, peri appendiceal fat thickening, the presence of appendicolith, and free fluid in the right iliac fossa were observed in patients with complicated appendicitis but the experience of the sonographer is important when detecting these signs to differentiate uncomplicated from complicated appendicitis (Rawolle *et al.*, 2019; Tong *et al.*, 2023).

Computerized tomography is the most common imaging modality that is used to differentiate uncomplicated from complicated appendicitis. The features that are observed include contrast-enhanced defects of the appendiceal wall, extra and intraluminal air, intraluminal appendicolith, abscess formation, moderate to severe peri appendiceal fat streaking, and peri appendiceal fluid. The presence of these features is sensitive for the diagnosis of complicated appendicitis (Kim *et al.*, 2019; Leite *et al.*, 2005; Skjold-Ødegaard & Søreide, 2022). A systemic review and meta-analysis on the analysis of computerized tomography features to differentiate uncomplicated from complicated appendicitis. 23 studies with 4427 patients were included of which 1173 were complicated appendicitis. Extraluminal appendicolith, abscess, appendiceal wall enhancement defect, extraluminal air, ileus, peri appendiceal fluid collection, ascites, intraluminal air, and intraluminal appendicolith were associated with a specificity of 70% and a sensitivity of 50%. This study showed that computerized tomography has a low sensitivity but high specificity in diagnosing complicated appendicitis (Kim *et al.*, 2018).

Magnetic resonance Imaging (MRI) is a new imaging modality that does not use ionizing contrast and may be used in pregnant patients with suspected appendicitis, but it is rarely done to differentiate uncomplicated from complicated appendicitis and may be used in patients where the use of ionizing contrast agent usage is contraindicated (Mervak *et al.*, 2019; Rybkin & Thoeni, 2007).

Table II

Study	Study Type	Year	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
W. J. Bom <i>et al.</i> ,	Systemic review and meta-analysis	2021	78	91	74	93
Bolmers <i>et al.</i> ,	Retrospective study	2022	45	88	81	58

Table showing the sensitivity, specificity, positive predictive value, and negative predictive value of computerized tomography in the diagnosis of complicated appendicitis

CONCLUSION

There is no universal definition of complicated appendicitis, so diagnosing this condition is difficult. The diagnosis of complicated appendicitis involves a clinical examination of the patient, blood investigations like full blood count which may show leukocytosis, C-reactive protein (CRP), and imaging modalities like ultrasound and computerized tomography. The early diagnosis of complicated appendicitis is important as early management can lead to decreased morbidity and mortality. Patients with complicated appendicitis should undergo imaging modalities like computerized tomography as this can aid in planning the management.

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