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# Diverticular Disease of the Appendix Is Associated with Complicated Appendicitis

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**Keywords**
Diverticular disease of appendix · Appendicitis

**Abstract**
***Introduction:*** Diverticular disease of the vermiform appendix (DDA) has an incidence of 0.004 to 2.1% in appendicectomy specimens. DDA is variably associated with perforation and malignancy. We report a single-center experience of DDA. The primary aim is to validate the association of DDA with complicated appendicitis or malignancy, and the secondary aim is to validate systemic inflammatory response syndrome (SIRS) criteria and quick Sepsis-related Organ Failure Assessment (qSOFA) scores. ***Methods:*** The histopathology reports of 2,305 appendicectomy specimens from January 2011 to December 2015 were reviewed. Acute appendicitis was found in 2,164 (93.9%) specimens. Histology of the remaining 141 (6.1%) patients revealed: normal appendix ($n$ = 110), DDA ($n$ = 22), endometriosis of appendix ($n$ = 6), and an absent appendix ($n$ = 3). Patient demographics, clinical profile, operative data, and perioperative outcomes of DDA patients are studied. Modified Alvarado score, Andersson score, SIRS criteria, and qSOFA scores were retrospectively calculated. ***Results:*** The incidence of DDA was 0.95%. Ten patients (45.5%) had diverticulitis. The mean age of DDA patients was 39.5 years (range 23–87), with male preponderance ($n$ = 12, 54.5%). The median Modified Alvarado score was 8 (range 4–9), and the median Andersson score was 5 (range 2–8). Fourteen patients (63.6%) had SIRS, and none had a high qSOFA score. Eight patients (36.4%) had complicated appendicitis (perforation [$n$ = 2] or abscess [$n$ = 6]). Eleven (50%) patients underwent laparoscopic appendicectomy. There were three 30-day readmissions and no mortality. ***Conclusion:*** DDA is a distinct clinical pathology associated with complicated appendicitis.



**Doença diverticular do apêndice está associada com apendicite complicada**

**Palavras Chave**
Doença diverticular do apêndice · Apendicite

**Resumo**
***Introdução:*** A doença diverticular do apêndice vermiforme (DDA) tem uma incidência de 0,004 a 2,1% em peças de apendicectomia. DDA está de forma variável associada a perfuração e malignidade. Reportamos uma experiência unicêntrica de DDA. O objectivo primário é validar a associação de DDA com apendicite complicada ou malignidade, e o objectivo secundário é validar os crité-

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rios de Systemic Inflammatory Response Syndrome (SIRS) e o score de quick Sepsis-related Organ Failure Assessment (qSOFA). ***Métodos:*** Os relatórios histopatológicos de 2,305 peças de apendicectomia de Janeiro 2011 a Dezembro de 2015 foram revistos. Apendicite aguda foi verificada em 2,164 (93,9%) peças. A histologia das restantes 141 (6,1%) revelou: apêndice normal (*n* = 110), DDA (*n* = 22), endometriose do apêndice (*n* = 6) e apêndice ausente (*n* = 3). As características demográficas dos doentes, perfil clínico, dados cirúrgicos e perioperatórios dos doentes com DDA foram avaliados. Modified Alvarado score, Andersson score, SIRS criteria, e o qSOFA scores foram calculados retrospectivamente. ***Resultados:*** A incidência de DDA foi de 0,95%. Dez doentes (45,5%) tinham diverticulite. A idade média dos doentes com DDA foi de 39,5 anos (âmbito 23–87) com predominância masculina (*n* = 12, 54,5%). A mediana do Modified Alvarado score foi de 8 (âmbito 4–9), e a mediana do Andersson score foi de 5 (âmbito 2–8). Quatorze doentes (63,6%) tinham SIRS e nenhum tinha um qSOFA score alto. Oito doentes (36,4%) tinham apendicite complicada (perfuração *n* = 2; abcesso *n* = 6). Onze (50%) doentes foram submetidos a apendicectomia laparoscópica. Verificaram-se 3 readmissões aos 30 dias e nenhuma morte. ***Conclusão:*** DDA é uma entidade clínica e patológica distinta e está associada a apendicite complicada.


## Introduction

The vermiform appendix is described as "un organe inutile et nuisible" (French, a useless and a harmful organ). Acute appendicitis (AA) is a common disease, but infrequent appendix pathologies can also present with right iliac fossa (RIF) symptoms. Diverticular disease of the appendix (DDA) is one such pathology for which often the diagnosis is made after appendicectomy. DDA is rare, with an incidence of 0.004 to 2.1% in appendicectomy specimens [1]. DDA may be associated with or without AA, and the diverticula itself may be inflamed or non-inflamed. Clinical presentation of appendix diverticulitis is indistinguishable from AA [2]. Imaging features can distinguish appendix diverticulitis from AA, but histological examination remains a gold standard for diagnosis [3]. Owing to its rarity and lack of awareness related to its association with complicated AA, DDA remains underreported and poorly understood. Further, there is a minimal clinical incentive to invest efforts in studying DDA as eventual treatment is appendicectomy.

However, diagnosis of DDA may be relevant due to association with perforation or appendiceal neoplasms. Some reports suggest that patients with AA on a background of appendix diverticulitis are more likely to perforate, and DDA is associated with appendiceal neoplasms [4, 5]. In a retrospective Danish study including 4,413 appendix specimens from 2001–2010, Kallenbach et al. [6] reported that 39 patients had DDA and 4 (10.3%) patients had colorectal neoplasm. In a Spanish study reporting on 7,044 appendicectomies, Marcacuzco et al. [7] have shown a 46% association with perforation and 7.1% concomitant neoplasm incidence. They discuss the role of prophylactic appendicectomy in asymptomatic patients with an incidental diagnosis of DDA. In a retrospective report from the USA, Stockl et al. [8] observed association of DDA with Schwann cell proliferation (42%) and postulated that Schwann cell proliferation is a histologic harbinger of underlying DDA. In a Kuwaiti study over 8 years, Al-Brahim et al. [9] reported that none of the 25 patients with AD had associated neoplasm. Hence more data is needed to understand DDA with regards to its association with perforation and appendix neoplasms. We report our experience of DDA and validate association with complicated appendicitis or neoplasms. The secondary aim was to validate sepsis-3 criteria and quick Sepsis-related Organ Failure Assessment (qSOFA) scores in context of DDA.

## Materials and Methods

A retrospective audit of appendicectomy histopathology reports from January 2011 to December 2015 was done. The list of patients who had appendicectomy was generated by accessing the International Classification of Diseases 9 and 10 codes of the hospital discharge database. All patients who had right hemicolectomy for primary colorectal malignancy or small bowel pathology were excluded. All listed histopathological reports were screened, and all patients with DDA reports were included.

Electronic medical records, operative records, and discharge summaries were reviewed for all DDA patients. Demographic and clinical data, including investigations, perioperative outcomes, 30-day mortality, and 30-day readmissions, were analyzed. Complicated appendicitis was defined as peritoneal abscess, free intraperitoneal air, perforation, or gangrenous appendicitis. Histology reports were reviewed for any form of malignancy. Modified Alvarado score, Andersson score, Systemic Inflammatory Response Syndrome (SIRS) criteria, and qSOFA scores were retrospectively calculated. All histology reports were reviewed to confirm a diagnosis of appendix neoplasm if any.

The Modified Alvarado score [10] is the most common clinical scoring system used in the diagnosis of AA and has a possible total of 10 points from eight variables, which consist of three symptoms (abdominal pain that migrates to the RIF, anorexia, and nausea or

**Table 1.** Demographic and clinical profile of patients with DDA ($n$ = 22)

| | |
|---|---|
| Mean age, years (range) | 39.5 (23–87) |
| Gender | |
| Male | 12 (54.5) |
| Female | 10 (45.5) |
| Presenting symptoms | |
| Abdominal pain | 22 (100) |
| Nausea/vomiting | 18 (81.8) |
| Fever | 16 (72.7) |
| Diarrhoea | 6 (27.3) |
| Clinical signs | |
| Abdominal tenderness | 19 (86.4) |
| Abdominal rigidity | 6 (27.3) |
| Abdominal mass/lump | 1 (4.5) |
| Serum biochemistry | |
| Elevated white blood cell count >12,000/mm$^3$ | 18 (81.8) |
| Neutrophilia with shift to left | 13 (59.1) |
| Clinical scores | |
| Median modified Alvarado score (range) | 8 (4–9) |
| Median Andersson score (range) | 5 (2–8) |
| Patients who presented with SIRS | 14 (63.6) |
| Median qSOFA score (range) | 0 (0–1) |
| Appendicectomy done based on clinical decision | 5 (22.7) |
| Pre-operative CT scan | 17 (77.3) |
| Reported as acute appendicitis | 16 (94.1) |

Data are $n$ (%) except where indicated otherwise. DDA, diverticular disease of appendix; SIRS criteria, systemic inflammatory response syndrome criteria; qSOFA score, quick Sepsis-related Organ Failure Assessment score; CT, computerized tomography.

vomiting), three signs (tenderness in RIF, rebound tenderness, and pyrexia), and two laboratory tests (leucocytosis and left shift). Its diagnostic value is validated. The Andersson score [11, 12] was proposed as a diagnostic tool that outperforms the Modified Alvarado score, and it is computed from two symptoms (RIF pain and vomiting), two signs (rebound tenderness and fever), and three laboratory tests (leucocytosis, left shift, and C-reactive protein). The Andersson score can safely reduce the use of diagnostic imaging and hospital admissions in patients with suspicion of AA [11]. The SIRS refers to the clinical response to a non-specific insult of either infectious or non-infectious origin. SIRS criteria were established in 1992 as part of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference [13]. It is defined by the presence of two or more variables out of four (temperature, heart rate, respiratory rate/$PaCO_2$, and leucocytes). SIRS is highly sensitive for determining the severity of sepsis. The Sepsis-related (sequential) Organ Failure Assessment (SOFA) score is a mortality prediction tool that is based on six organ system dysfunctions: respiratory, cardiovascular, renal, coagulation, central nervous system, and liver function [14]. It is widely used in the intensive care setting. qSOFA score consists of three components, with one point each: respiratory rate >22/min (1 point), change in mental status (1 point), and systolic blood pressure <100 mm Hg (1 point), and a score of two or more indicates organ dysfunction.

Summary statistics were constructed for the baseline values, using frequencies and proportions for categorical data, and means for continuous variables. Length of stay is defined as the duration in days between the time of admission and time of discharge. Mortality is defined as death occurring within 30 days of surgery.

## Results

During the study period, 2,305 appendicectomies were done. Histology established AA in 2,164 (93.9%) specimens, while 141 (6.1%) specimens had other pathology. A histologically normal appendix was noted in 110 (4.8%) specimens. Twenty-two patients (0.95%) had DDA, 6 (0.3%) patients had appendix endometriosis, and the appendix itself was absent in 3 (0.1%) specimens.

The mean age of patients with DDA was 39.5 years (range: 23–87 years). Appendix diverticulitis was noted in 10 (45.5%) patients. Table 1 demonstrates the demographic data and clinical profile of patients with DDA. Appendicectomy was performed based on admission clinical judgment in 5 (22.7%) patients, while computerized tomography (CT) scan was obtained in 17 (77.3%) patients. CT scan established diagnosis of AA in 16 patients, while one patient had a normal CT scan. In this patient, the decision for appendicectomy was based on clinical deterioration. Three patients (13.6%) underwent an interval appendicectomy – two (9.1%) patients for appendix phlegmon managed with antibiotics and one (4.5%) patient for peritoneal abscess drained percutaneously.

Table 2 shows the operative data and postoperative outcomes of patients with DDA. Eleven (50%) patients had laparoscopic appendicectomy, including one (4.5%) with single-incision laparoscopic appendicectomy. There were no conversions to open. Eight patients (36.4%) had complicated appendicitis. The mean operative time was 94 min (50–170 min), and the mean length of stay was 2 days (range: 1–9 days). Three (13.6%) patients had 30-day readmissions. Two (9.1%) patients had a postoperative abdominal collection. Of note, one of these patients developed the collection in the gallbladder fossa following synchronous appendicectomy and cholecystectomy (for symptomatic cholelithiasis). Both patients were discharged well after non-operative management with antibiotics and percutaneous drainage. The third patient was admitted for health-care-associated pneumonia. She was discharged well after treatment with antibiotics. There was no 30-day mortality.

**Table 2.** Operative data and postoperative outcomes of patients with DDA ($n$ = 22)

| | |
|---|---|
| Timing of appendicectomy | |
| Interval elective appendicectomy | 3 (13.6) |
| Emergency appendicectomy | 19 (86.4) |
| Access for appendicectomy | |
| Laparoscopic appendicectomy | 11 (50) |
| Conventional (3-port) laparoscopy | 10 (45.5) |
| Single-incision laparoscopy | 1 (4.5) |
| Conversion to open | nil |
| Open appendicectomy | 11 (50) |
| Intra-operative findings | |
| Uncomplicated appendicitis | 14 (63.6) |
| Complicated appendicitis (perforation or abscess) | 8 (36.4) |
| Lipton classification | |
| Type 1, appendix – normal and appendix diverticulitis | 8 (36.4) |
| Type 2, AA and appendix diverticulitis | 2 (9.1) |
| Type 3, AA and appendix diverticulosis | 9 (40.9) |
| Type 4, appendix – normal and appendix diverticulosis | 3 (13.6) |
| Mean operative time, min (range) | 94 (50–170) |
| 30-day readmission | 3 (13.6) |
| Postoperative collection | 2 (9.1) |
| Posterior abdominal wall abscess | 1 (4.5) |
| Gallbladder fossa abscess (simultaneous cholecystectomy for cholelithiasis) | 1 (4.5) |
| Septic shock due to health-care-associated pneumonia | 1 (4.5) |
| Median length of stay in hospital, days (range) | 2 (1–9) |
| 30-day mortality | nil |

Data are $n$ (%) except where indicated otherwise. AA, acute appendicitis; DDA, diverticular disease of appendix.

## Discussion

DDA is associated with older age and high incidence of complicated AA but not with neoplasms. Kelynack [15] first described appendix diverticulitis in 1893 in his thesis: "A contribution to the pathology of the vermiform appendix." More than 125 years later, it remains uncommonly reported and poorly understood. The incidence of DDA in our experience (0.95%) is within the reported range of 0.004% to 2.1% [1]. Appendix diverticula may be either congenital (true) or acquired (pseudodiverticula), with the latter being more common. Congenital diverticula result from abnormal bowel recanalization during the intestine's solid phase, compromises of all four layers of the bowel wall, found on the anti-mesenteric wall, and maybe single or multiple [16, 17]. They are associated with "D" trisomy or cystic fibrosis [18, 19]. None of our patients had "D" trisomy or cystic fibrosis. Acquired diverticula include only the mucosa or submucosa, are found in the mesenteric border, and may be single or multiple. Lipton et al. [20] classified DDA into four morphological types (Table 2) and also added subtypes according to the presence or absence of appendix perforation. AA with appendix diverticulosis (type 3) was most common in our experience.

Known risk factors for DDA are male gender, age over 30 years, Hirschsprung's disease, and cystic fibrosis [18]. In a prospective observational study on AA, including 4,282 patients, Sartelli et al. [19] reported a median age of 29 years and 55% male gender. In our series, 54.5% were male, and the mean age of DDA was 39.5 years. In a retrospective study including 44 patients with appendix diverticulitis, Ito et al. [3] reported a median age of 59 years, which was higher than the median age of AA patients in their cohort. Thus, DDA is acquired and associated with old age, similar to diverticulosis disease of the colon.

With regards to symptoms, existing literature has a publication and reporting bias as only patients who had appendicectomy are included. Further, patients with right hemicolectomy for colon cancer are excluded. DDA can be asymptomatic and incidentally detected on radiological studies (e.g., barium enema). Clinical presentation of DDA and appendix diverticulitis mimics that of AA and varies from mild gastrointestinal disturbances to de-

layed presentation with an increased risk of perforation [20]. Ito et al. [3] reported that AD usually occurs in acquired diverticula containing only mucosa and submucosa and hence can easily perforate with peri-appendix abscess formation. Gomes et al. [21] proposed a grading system of AA based on complications. They included necrosis, phlegmon, abscess, and peritonitis as complicated AA. In our experience, DDA is associated with complicated appendicitis. A multicenter study, including 4,282 patients, reported 25.5% of patients with complicated AA as compared to this DDA study report of 36.4% [19]. Complicated AA is associated with delayed presentation or diagnosis and treatment. Delayed presentation is associated with inferior outcomes in acute care surgery [22–25]. However, the outcomes of DDA patients in our experience are not inferior. This is possible due to prompt resuscitation, adoption of sepsis guidelines, and timely multidisciplinary care [26–28]. It is not possible to derive conclusions about the clinical profile of DDA patients based on available literature. The reports on DDA either focus on imaging features or histopathology and lack clinical data [6, 29]. In a study including 1,329 patients with appendicectomy, Yardimci et al. [29] included 28 patients with appendix diverticulitis and reported on imaging features but not on clinical presentation or perioperative outcomes. In a study including 4,413 appendicectomy specimens, Kallenbach et al. [6] included 39 patients with DDA and reported on histopathology details but not on clinical presentation or perioperative outcomes. Thus, our study bridges the gap in the existing literature by reporting clinical profile, imaging, and histology of all the patients.

The pre-operative diagnosis of AD remains challenging due to various reasons. In some patients, the diagnosis of AA is made based on clinical judgment, and imaging is not done. In patients with imaging, the diverticula may not be seen due to a small size or involved by inflammatory mass [30]. Ultrasonographic findings include a hypoechoic lesion adjacent to the appendix suggestive of an inflamed diverticulum [31]. We do not do an ultrasound scan of the abdomen in patients with RIF pain due to the non-availability of ultrasound after office hours. Ito et al. [3] and Osada et al. [32] reported CT scan features compatible with appendix diverticulitis, such as rounded cystic appendix outpouchings with wall enhancement and solid enhancing masses emanating from the appendix. In our experience, pre-operative imaging did not contribute to the diagnosis of DDA.

The common complications of DDA include diverticulitis and perforation, which may lead to a localized abscess or generalized peritonitis. Lipton et al. [20] reported that appendix diverticulitis was four times as likely to perforate as AA, with a resultant increase in mortality [19]. More than a third of patients in our series had perforation, although there was no 30-day mortality. This could be attributed to early diagnosis, prompt resuscitation, and timely surgical intervention [33, 34]. All patients with AA are enrolled in the emergency waiting list, and they receive priority based on a physiologic insult. Our 30-day readmission rate of 13.6% is higher than reported by a recent multicenter study from the USA (6%) [35]. The association of DDA with complicated appendicitis is essential for the determination of the non-operative management of AA. Some studies have included such patients for non-operative management [36, 37], while some authors have excluded complicated appendicitis patients for non-operative management [38, 39]. It is our policy to reserve non-operative management to patients who refuse surgery, and our data exclude such patients. In our experience, SIRS criteria are more sensitive than qSOFA scores in patients with DDA. qSOFA score is reported to lack sensitivity in acute care surgery [24].

DDA has also been associated with pseudomyxoma peritonei [40] and appendiceal neoplasms like carcinoid tumors, mucinous adenomas, tubular adenomas, and primary appendiceal adenocarcinomas. Lamps et al. [41] found a 42% association between DDA and appendiceal mucinous neoplasms, while Dupre et al. [4] cited a 48% association between DDA and underlying appendiceal carcinoids and mucinous adenomas. None of our patients had any of the above associations, and it remains to be validated if such associations reflect diverse demography. Malignant lesions of the appendix are treated by right hemicolectomy, and it is possible that since we excluded right hemicolectomy specimens, our study is not able to detect such associations [34]. Rare complications of DDA include intestinal obstruction, hemorrhage, and fistula formation [42, 43]. Some authors advocate prophylactic appendicectomy when DDA is incidentally diagnosed during an unrelated surgical procedure in order to reduce complications or subsequent development of appendiceal neoplasms [7]. We did not study the colonoscopy database for lower gastrointestinal bleeding patients and hence were unable to comment association of DDA with bleeding. Our study has several limitations. This is a retrospective audit of patients treated with appendicectomy for clinically diagnosed AA. Due to the exclusion of patients managed with right hemicolectomy, the real association of DDA with malignancy remains unproven. Bleeding and inflammation of diverticular dis-

ease of the colon are distinct pathologies and mostly do not coexist. We did not study colonoscopy records or analyzed records of patients with a lower gastrointestinal bleed and hence were unable to detect a real association with bleeding. A large sample or prospective study, including all right hemicolectomy specimens, would provide more information about such associations. Due to lack of awareness of DDA and of little therapeutic importance, it is possible that pathology doctors may not actively look for and report DDA in appendix or right hemicolectomy histology specimens. Cadaveric dissection of subjects without AA and a histology review for the type of diverticulum is necessary to establish this entity. Lastly, due to small sample size we did not compare the results of uncomplicated with complicated AA for inflammatory scores.

In conclusion, DDA is a distinct clinical entity as it is associated with complicated appendicitis. Its association with appendiceal neoplasms is not observed due to the exclusion of right hemicolectomy specimens in our series. Existing reports selectively exclude the clinical profile of patients. qSOFA score lacks sensitivity in patients with DDA. More data is needed, and future reports must include right hemicolectomy specimens and report clinical profile and perioperative outcomes to enhance current evidence.

## Statement of Ethics

This study is exempted since it is a retrospective analysis of clinical data and does not involve live patients.

## Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

## Author Contributions

All authors contributed to the conception of the work and interpretation of data and substantively revised the manuscript. All authors have approved the submitted version.

## References


1 Place RJ, Simmang CL, Huber PJ Jr. Appendiceal diverticulitis. South Med J. 2000 Jan;93(1):76–9.
2 Majeski J. Diverticulum of the vermiform appendix is associated with chronic abdominal pain. Am J Surg. 2003 Aug;186(2):129–31.
3 Ito D, Miki K, Seiichiro S, Hata S, Kobayashi K, Teruya M, et al. Clinical and computed tomography findings of appendiceal diverticulitis vs acute appendicitis. World J Gastroenterol. 2015 Apr;21(13):3921–7.
4 Dupre MP, Jadavji I, Matshes E, Urbanski SJ. Diverticular disease of the vermiform appendix: a diagnostic clue to underlying appendiceal neoplasm. Hum Pathol. 2008 Dec;39(12):1823–6.
5 Deschênes L, Couture J, Garneau R. Diverticulitis of the appendix. Report of sixty-one cases. Am J Surg. 1971 Jun;121(6):706–9.
6 Kallenbach K, Hjorth SV, Engel U, Schlesinger NH, Holck S. Significance of acquired diverticular disease of the vermiform appendix: a marker of regional neoplasms? J Clin Pathol. 2012 Jul;65(7):638–42.
7 Marcacuzco AA, Manrique A, Calvo J, Loinaz C, Justo I, Caso O, et al. Clinical implications of diverticular disease of the appendix. Experience over the past 10 years. Cir Esp. 2016 Jan;94(1):44–7.
8 Stockl T, Ross JS, Walter O, Dresser K, Lee H. Appendiceal mucosal Schwann cell proliferation: a putative histologic marker of appendiceal diverticular disease. Int J Surg Pathol. 2013 Dec;21(6):603–9.
9 Al-Brahim N, Al-Kandari I, Munahai M, Sharma P. Clinicopathological study of 25 cases of diverticular disease of the appendix: experience from Farwaniya hospital. Patholog Res Int. 2013;2013:404308.
10 Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med. 1986 May;15(5):557–64.
11 Andersson M, Andersson RE. The appendicitis inflammatory response score: a tool for the diagnosis of acute appendicitis that outperforms the Alvarado score. World J Surg. 2008 Aug;32(8):1843–9.
12 Andersson M, Kolodziej B, Andersson RE; STRAPPSCORE Study Group. Randomized clinical trial of Appendicitis Inflammatory Response score-based management of patients with suspected appendicitis. Br J Surg. 2017 Oct;104(11):1451–61.
13 Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al.; The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest. 1992 Jun;101(6):1644–55.
14 Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, et al.; Sepsis Definitions Task Force. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016 Feb;315(8):775–87.
15 Kelynack TN. A contribution to the pathology of the vermiform appendix. London: H.K. Lewis; 1893. p. x. 223.
16 Everts-Suarez EA, Noteboom G. Congenital diverticula of the appendix. A review of the world's literature and report of a case. Pa Med J. 1961 Nov;64:1454–8.
17 Stout AP. A study of diverticular formation in the appendix. Arch Surg. 1923 May;6(3):793–829.
18 Abdullgaffar B. Diverticulosis and diverticulitis of the appendix. Int J Surg Pathol. 2009 Jun;17(3):231–7.
19 Sartelli M, Baiocchi GL, Di Saverio S, Ferrara F, Labricciosa FM, Ansaloni L, et al. Prospective Observational Study on acute Appendicitis Worldwide (POSAW). World J Emerg Surg. 2018 Apr;13(1):19.
20 Lipton S, Estrin J, Glasser I. Diverticular disease of the appendix. Surg Gynecol Obstet. 1989 Jan;168(1):13–6.
21 Gomes CA, Sartelli M, Di Saverio S, Ansaloni L, Catena F, Coccolini F, et al. Acute appendicitis: proposal of a new comprehensive grading system based on clinical, imaging and laparoscopic findings. World J Emerg Surg. 2015 Dec;10(1):60.

22 Chan KS, Wang YL, Chan XW, Shelat VG. Outcomes of omental patch repair in large or giant perforated peptic ulcer are comparable to gastrectomy. Eur J Trauma Emerg Surg. 2019 Oct. https://doi.org/10.1007/s00068-019-01237-8.
23 Mak MHW, Low JK, Junnarkar SP, Huey TCW, Shelat VG. A prospective validation of Sepsis-3 guidelines in acute hepatobiliary sepsis: qSOFA lacks sensitivity and SIRS criteria lacks specificity (Cohort Study). Int J Surg. 2019 Dec;72:71–7.
24 Tarasconi A, Coccolini F, Biffl WL, Tomasoni M, Ansaloni L, Picetti E, et al. Perforated and bleeding peptic ulcer: WSES guidelines. World J Emerg Surg. 2020 Jan;15(1):3.
25 Kwan KE, Shelat VG, Tan CH. Recurrent pyogenic cholangitis: a review of imaging findings and clinical management. Abdom Radiol (NY). 2017 Jan;42(1):46–56.
26 Tay WM, Toh YJ, Shelat VG, Huey CW, Junnarkar SP, Woon W, et al. Subtotal cholecystectomy: early and long-term outcomes. Surg Endosc. 2020 Oct;34(10):4536–42.
27 Kwan JR, Lim M, Ng F, Shelat V. Fungal Isolates in Peritoneal Fluid Culture Do Not Impact Peri-Operative Outcomes of Peptic Ulcer Perforation. Surg Infect (Larchmt). 2019 Dec;20(8):619–24.
28 Shelat VG, Wang Q, Chia CL, Wang Z, Low JK, Woon WW. Patients with culture negative pyogenic liver abscess have the same outcomes compared to those with Klebsiella pneumoniae pyogenic liver abscess. Hepatobiliary Pancreat Dis Int. 2016 Oct;15(5):504–11.
29 Yardimci AH, Bektas CT, Pasaoglu E, Kinaci E, Ozer C, Sevinc MM, et al. Retrospective study of 24 cases of acute appendiceal diverticulitis: CT findings and pathological correlations. Jpn J Radiol. 2017 May;35(5):225–32.
30 Shelat VG, Kelvin Li K, Rao A, Sze Guan T. Meckel's diverticulitis causing small bowel obstruction by a novel mechanism. Clin Pract. 2011 Jul;1(3):e51–51.
31 Macheiner P, Hollerweger A, Gritzmann N. Sonographic features of diverticulitis and diverticulosis of the vermiform appendix. J Clin Ultrasound. 2002 Sep;30(7):456–7.
32 Osada H, Ohno H, Saiga K, Watanabe W, Okada T, Honda N. Appendiceal diverticulitis: multidetector CT features. Jpn J Radiol. 2012 Apr;30(3):242–8.
33 Sartelli M, Abu-Zidan FM, Labricciosa FM, Kluger Y, Coccolini F, Ansaloni L, et al. Physiological parameters for Prognosis in Abdominal Sepsis (PIPAS) Study: a WSES observational study. World J Emerg Surg. 2019 Jul;14(1):34.
34 Ng CY, Nandini CL, Chuah KL, Shelat VG. Right hemicolectomy for acute appendicitis secondary to breast cancer metastases. Singapore Med J. 2018 May;59(5):284–5.
35 Yeh DD, Eid AI, Young KA, Wild J, Kaafarani HM, Ray-Zack M, et al.; EAST Appendicitis Study Group. Multicenter Study of the Treatment of Appendicitis in America: Acute, Perforated, and Gangrenous (MUSTANG), an EAST Multicenter Study. Ann Surg. 2019 Oct28.DOI:10.1097/SLA.0000000000003661. Epub ahead of print.
36 Mentula P, Sammalkorpi H, Leppäniemi A. Laparoscopic Surgery or Conservative Treatment for Appendiceal Abscess in Adults? A Randomized Controlled Trial. Ann Surg. 2015 Aug;262(2):237–42.
37 Tingstedt B, Bexe-Lindskog E, Ekelund M, Andersson R. Management of appendiceal masses. Eur J Surg. 2002;168(11):579–82.
38 Vons C, Barry C, Maitre S, Pautrat K, Leconte M, Costaglioli B, et al. Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. Lancet. 2011 May;377(9777):1573–9.
39 Salminen P, Paajanen H, Rautio T, Nordström P, Aarnio M, Rantanen T, et al. Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. JAMA. 2015 Jun;313(23):2340–8.
40 Riss S, Moran B. Pseudomyxoma peritonei. In: Taylor I, Johnson CD (eds). Recent advances in surgery. Vol 26, 2014. pp 109–20.
41 Lamps LW, Gray GF Jr, Dilday BR, Washington MK. The coexistence of low-grade mucinous neoplasms of the appendix and appendiceal diverticula: a possible role in the pathogenesis of pseudomyxoma peritonei. Mod Pathol. 2000 May;13(5):495–501.
42 Delikaris P, Stubbe Teglbjaerg P, Fisker-Sørensen P, Balslev I. Diverticula of the vermiform appendix. Alternatives of clinical presentation and significance. Dis Colon Rectum. 1983 Jun;26(6):374–6.
43 Collins DC. A study of 50,000 specimens of the human vermiform appendix. Surg Gynecol Obstet. 1955 Oct;101(4):437–45.