Original Article

# Predictors risk factors for acute complex appendicitis pain in patients: Are there gender differences?

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## Abstract

**Objective:** The purpose of this study is to determine the predictive risk factors for appendicitis and the cost-effectiveness of using abdominal helical computed tomography (CT) in comparison to abdominal ultrasonography (US) for the diagnosis of acute appendicitis in patients. **Subjects and Methods:** The typical case was a patient with abdominal pain in the right lower quadrant and suspicion of appendicitis. A total of 643 patients who were consequently treated with appendectomy upon diagnosis of acute appendicitis between January 2015 and December 2018 were included in the study. The four diagnostic alternatives chosen were US, CT, biochemistry parameters, and physical examination in the hospital. **Results:** There were statistically significant differences between male and female patients with regards to age, BMI, cigarette smoking, sheesha smoking, family history of diabetes, hypertension and family history of gastrointestinal discomfort (GI), anxiety ($P < 0.001$), red eye ($P = 0.006$), dizziness ($P = 0.021$), headache ($P < 0.001$), muscular symptoms, weakness and cramps ($P < 0.001$), bloating or swollen stomach ($P < 0.001$), UTI ($P < 0.001$), chest pain ($P < 0.001$), guarding ($P < 0.001$), loss of appetite ($P = 0.004$), nausea ($P < 0.001$) vomiting ($P = 0.042$), anorexia ($P = 0.009$), and constipation ($P = 0.002$). Moreover, there were statistically significant differences between male and female patients for pain ($P < 0.001$), pain right belly ($P = 0.027$), severe crumps ($P = 0.007$), high temperature and fever ($P < 0.001$), irritable bowel syndrome ($P < 0.001$), right iliac fossa (RIF) pain ($P = 0.008$), rebound tenderness ($P = 0.024$), positive bowel sounds ($P = 0.029$), and pointing tenderness ($P < 0.001$). Multivariate stepwise logistic regression showed nausea ($P < 0.001$), C-reactive protein (CRP) ($P < 0.001$), dizziness ($P = 0.016$), vomiting ($P < 0.001$), muscular symptoms ($P = 0.007$), irritable bowel syndrome ($P = 0.034$), guarding ($P = 0.040$), and loss appetite ($P = 0.046$) were considered at higher risk as predictors for appendicitis patients. **Conclusions:** CT is more cost-effective than the US and clinical examination for determining appendicitis. The current study suggested that nausea, C-reactive protein, dizziness, vomiting, muscular symptoms, irritable bowel syndrome, guarding, and loss appetite were considered as higher risk predictors for appendicitis patients.

**Keywords:** Appendicitis, computed tomography, diagnosis, gender, predictors, ultrasound

## Introduction

Acute appendicitis diagnosis is complicated in approximately 35% of patients with pain in the lower right quadrant[1] which is the most common cause of surgical abdominal pain.[2] Therefore, timely diagnosis of acute appendicitis has an impact on the overall health and economic status of most countries.[3] The previously proposed disadvantages of computed tomography (CT) such

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as it is expensive, not being available everywhere, and the use of contrast medium[4] have gradually decreased, and today CT is more commonly used in the diagnosis of appendicitis. Using ultrasonography (US) and CT for assessing acute appendicitis has improved diagnostic accuracy for what can be a difficult clinical diagnosis.[5-9] The imaging diagnosis of acute appendicitis can be made accurately by US or CT.[6-12] Overall, fortunately, the advances in technology with the development of US and CT have shown considerable advantages in the diagnosis of patients with suspected acute appendicitis.[13-18] Several studies reported that both White blood cell (WBC) and C-reactive protein (CRP) proved to be a fair and very poor predictor of complex appendicitis.[19,20]

This study aims to determine the predictive risk factors and cost-effectiveness for appendicitis using CT and ultrasound in the diagnosis of acute appendicitis in patients who have consequently been treated with appendectomy upon preliminary diagnosis.

## Subjects and Methods

This prospective cohort study included adult patients between the ages of 20 and 60 who visited the emergency department, gastroenterology, and surgery and outpatient clinics in the İstanbul Medipol University, Faculty of Medicine Teaching Hospitals. The study was conducted between January 2016 and July 2019 using a total of 643 consecutive patients who underwent both CT and appendix the US for suspected acute appendicitis. Institutional Review Board (IRB) ethical approval for the current study was obtained from the Medipol International School of Medicine, Istanbul Medipol University.

### Radiological measurements

#### *Ultrasound*

A general abdominal examination was performed using sonography. The results of the examination were recorded on a digital case record form; the following potential appendiceal abnormalities on imaging were used as diagnostics for appendicitis: inability visualizing the appendix completely (using General Electric Logic P6 Pro, (transducer) 4 MHz, 5 MHz, and 10 MHz), the presence of local transducer tenderness, the presence of a thickened appendix (diameter greater than 6 mm), and the presence of an incompressible appendix. Most recent study reported[12] that the diagnostic performance of ultrasound reevaluation were 96.3% sensitivity, 91.2%, specificity, 89.7% PPV, 96.9%, NPV, and 91.9% accuracy.

### Computed tomography

CT exams were performed using the General Electric Light speed VCT XT 64 detector helical CT, width 5 mm. The patients based on contrast (nonenhanced) and (enhanced) visualized. CT findings[12] provided excellent performance of 96.3% sensitivity, 91.2% specificity, 89.7% PPV, 96.9% NPV, and 91.9% accuracy for diagnosing appendicitis.

The final diagnosis was based altogether on clinical physician examination, laboratory, surgical, pathological histopathology reports, radiological diagnostics with US and CT, and measurements.

The Student´s *t*-test was performed for significant differences between the mean of two continuous values and the Chi-square test used for the differences variables between two or more categorical variables. Multivariate logistic regression analysis was used to establish a model to determine factors that are predictive of complicated appendicitis. The statistical significance was defined as $P < 0.05$.

## Results

Table 1 gives the comparison of sociodemographic and clinical characteristics of the appendicitis patients by gender. There were statistically significant differences between patients regarding age ($P < 0.001$), BMI ($P = 0.031$), cigarette smoking ($P = 0.038$), sheesha smoking ($P = 0.037$), family history of diabetes ($P = 0.025$), hypertension ($P = 0.019$), family history of gastrointestinal discomfort (GI) ($P = 0.011$), and family history of appendicitis ($P = 0.021$).

Table 2 shows the clinical characteristics symptoms' value among appendicitis by gender. Statistically significant differences were found between males and females for anxiety ($P < 0.001$), red eye ($P = 0.006$), dizziness ($P = 0.021$), headache ($P < 0.001$), muscular symptoms, weakness and cramps ($P < 0.001$), bloating or swollen stomach ($P < 0.001$), urinary tract infection (UTI) ($P < 0.001$), chest pain ($P < 0.001$), guarding ($P < 0.001$), loss appetite ($P = 0.004$), nausea ($P < 0.001$) vomiting ($P = 0.042$), anorexia ($P = 0.009$), and constipation ($P = 0.002$).

Table 3 presents the clinical sign and medical condition value among appendicitis by gender. There were statistically significant differences between males and females for pain ($P < 0.001$), pain right belly ($P = 0.027$), severe crumps ($P = 0.007$), high temperature and fever ($P < 0.001$), irritable bowel syndrome ($P < 0.001$), RIF pain ($P = 0.008$), rebound tenderness ($P = 0.024$), positive bowel sounds ($P = 0.029$), and pointing tenderness ($P < 0.001$). Besides, Table 4 gives radiological diagnostic tests comparisons and their costs for appendicitis patients

Table 5 indicates multivariate stepwise logistic regression analysis of independent predictors for the presence of appendicitis and risk factors. Multivariate stepwise logistic regression analysis result showed nausea [3.46 (2.18–5.50) $P < 0.001$)]; C-reactive protein [2.95 (1.86–5.34) $P < 0.001$]; dizziness [2.48 (1.18–5.20) $P = 0.016$]; vomiting [2.37 (1.53–3.68) $P < 0.001$]; muscular symptoms [1.98 (1.20–3.26) $P = 0.007$]; irritable bowel syndrome [1.84 (1.55–218) $P = 0.034$]; guarding [1.73 (1.44–3.36) $P = 0.040$]; loss appetite [1.62 (1.19–2.60) $P = 0.046$] were considered at higher risk as a predictors for appendicitis patients.

**Table 1: Comparison of sociodemographic and clinical characteristics of the patients by gender (*n*=643)**

| Variables | Gender | | *P* |
|---|---|---|---|
| | Males *n*=401 | Females *n*=242 | |
| Age groups (in years): | | | |
| 20-29 | 152 (37.9) | 47 (19.4) | 0.001 |
| 30-39 | 108 (26.9) | 58 (24.0) | |
| 40-49 | 63 (15.7) | 33 (13.6) | |
| 50-59 | 43 (10.7) | 54 (22.3) | |
| 60 and above | 35 (8.7) | 50 (20.7) | |
| BMI (kg/m$^2$) | | | |
| Normal (<25 kg/m$^2$) | 94 (23.4) | 82 (33.9) | 0.013 |
| Overweight (29-30 kg/m$^2$) | 171 (42.6) | 94 (38.8) | |
| Obese (>30 kg/m$^2$) | 136 (33.9) | 66 (27.3) | |
| Physical activity | | | |
| Yes | 111 (27.7) | 53 (23.6) | 0.248 |
| No | 290 (72.3) | 185 (76.4) | |
| Smoking status | | | |
| Never | 317 (79.1) | 209 (86.4) | 0.038 |
| Current smoker | 60 (15.0) | 20 (8.3) | |
| Past smoker | 24 (6.0) | 13 (5.4) | |
| Sheesha smoking status | | | |
| Yes | 69 (77.2) | 27 (11.2) | 0.037 |
| No | 332 (60.7) | 215 (88.8) | |
| Family history of DM | | | |
| Yes | 75 (18.7) | 29 (12.0) | 0.025 |
| No | 326 (81.3) | 215 (88.0) | |
| Family history of hypertension | | | |
| Yes | 94 (23.4) | 38 (15.7) | 0.019 |
| No | 307 (76.6) | 204 (84.3) | |
| Family history of gastrointestinal discomfort (GI) | | | |
| Yes | 71 (17.7) | 25 (10.3) | 0.011 |
| No | 330 (82.3) | 217 (89.7) | |
| Family history of appendicitis | | | |
| Yes | 72 (18.0) | 27 (11.2) | 0.021 |
| No | 329 (84.0) | 215 (88.8) | |

**Table 2: Clinical biochemistry baseline value and symptoms among appendicitis patients by gender (*n*=643)**

| Variables | Males=401 *n* (%) | Females=242 *n* (%) | *P* |
|---|---|---|---|
| Anxiety | 66 (16.5) | 17 (7.0) | 0.001 |
| Red Eye | 63 (15.7) | 20 (8.3) | 0.006 |
| Dizziness | 76 (19.0) | 29 (12.0) | 0.021 |
| Headache | 105 (26.2) | 25 (10.3) | 0.001 |
| Muscular symptoms, weakness | 87 (21.7) | 27 (11.2) | 0.001 |
| Bloating/swollen stomach | 75 (18.7) | 18 (7.4) | 0.001 |
| Urinary tract infections -UTI | 68 (17.0) | 16 (6.6) | 0.001 |
| Chest pain | 53 (13.2) | 12 (5.0) | 0.001 |
| Guarding | 77 (19.2) | 18 (7.4) | 0.001 |
| Loss appetite | 96 (23.9) | 35 (14.5) | 0.004 |
| Nausea | 96 (23.9) | 31 (12.8) | 0.001 |
| Vomiting | 108 (26.9) | 48 (19.8) | 0.042 |
| Anorexia | 80 (20.0) | 29 (12.0) | 0.009 |
| Constipation | 90 (22.4) | 30 (12.4) | 0.002 |
| **Biochemistry** | | | |
| **Parameters** | **Mean±SD** | **Mean±SD** | ***P*** |
| C-reactive protein - CRP (mg/L) | 37.4±13.9 | 34.3±16.4 | 0.002 |
| White Blood Count (/mL) | 13840.1±5,346.5 | 12,528.5±4,864.2 | 0.005 |
| Systolic blood pressure (mmHg) | 128.5±15.1 | 125.1±12.4 | 0.001 |
| Diastolic blood pressure (mmHg) | 80.4±9.3 | 78.2±9.1 | 0.002 |

**Table 3: Clinical biochemistry baseline value among appendicitis patients by gender (*n*=643)**

| Variables | Males *n*=401 *n* (%) | Females *n*=242 *n* (%) | *P* |
|---|---|---|---|
| Pain | 134 (33.4) | 45 (18.6) | 0.001 |
| Pain right belly | 46 (11.5) | 15 (6.2) | <0.027 |
| Pain left belly | 45 (11.2) | 17 (7.0) | <0.081 |
| Severe crumps | 116 (28.9) | 47 (19.4) | 0.007 |
| High temperature-fever | 67 (16.7) | 19 (7.9) | 0.001 |
| Painful peeing | 50 (12.5) | 28 (11.6) | 0.735 |
| Irritable bowel syndrome | 69 (17.2) | 20 (8.3) | 0.001 |
| RIF Pain | 64 (16.0) | 21 (8.7) | <0.008 |
| Rigidity | 72 (18.0) | 36 (14.9) | 0.312 |
| Rebound tenderness | 53 (13.2) | 18 (7.4) | 0.024 |
| Positive bowel sound | 82 (20.4) | 33 (13.6) | 0.029 |
| Obturator Sign | 55 (13.7) | 28 (11.6) | 0.432 |
| Psoas Sign | 46 (11.5) | 26 (10.7) | 0.777 |
| Rovsing's Sign | 88 (17.0) | 32 (13.2) | 0.206 |
| Percussion Tenderness | 42 (10.5) | 15 (6.2) | <0.065 |
| Pointing Tenderness | 58 (14.5) | 14 (5.8) | 0.001 |

**Table 4: Radiological diagnostic test and their costs for appendicitis patients**

| Patient Group | Appendicitis | |
|---|---|---|
| | Number | % |
| Compliant population | | |
| Ultrasound | 185 | 28.8 |
| Computed tomography | 298 | 46.3 |
| Ultrasound and computed tomography | 160 | 26.9 |
| Radiological Test cost | Price TL | Price $-US Dollar |
| National Health Insurance | 5,500 TL | $1,000 |
| Private Insurance | 8000-12000 TL | $1,500-$2,000 |
| Non-Insurance | 8,000 TL | $1,500 |
| Physician exam cost | 800 TL | $150 |

TL='Turkish Lira and $1=0.5500 TL

**Table 5: Multivariate stepwise logistic regression analysis of independent predictors for the appendicitis**

| Variables | Odds ratio (95%CI) | *P* |
|---|---|---|
| Nausea | 3.46 (2.18-5.50) | <0.001 |
| C-reactive protein - CRP (mg/L) | 2.95 (1.86-5.34) | <0.001 |
| Vomiting | 2.37 (1.53-3.68) | <0.001 |
| Muscular symptoms | 1.98 (1.20-3.26) | 0.007 |
| Dizziness | 2.48 (1.18-5.20) | 0.016 |
| Irritable bowel syndrome | 1.84 (1.55-218) | 0.034 |
| Guarding | 1.73 (1.44-3.36) | 0.040 |
| Loss Appetite | 1.62 (1.19-2.60) | 0.046 |

## Discussion

The clinical diagnosis of acute appendicitis in the early phases of the disease is difficult as it may mimic other conditions. The newer techniques of US and CT have shown great promise in evaluation of patients with suspected acute appendicitis.

On patients suspected to have acute appendicitis admitted to the primary care institution, the US and CT should be used for diagnosis. Diagnosed and suspected patients should be directed to a surgical center.

However, advantages and limitations exist in both US and CT for evaluating patients with suspected acute appendicitis. In the current study, the US was performed on 185 (28.8%) patients, CT conducted on 298 (46.3%) patients, and 160 (26.9%) performed on both US and CT for diagnosing appendicitis. The outcome results are comparable and consistent with the previously reported studies.[12-16] Generally, CT is widely accepted and the preferred modality for evaluation of suspected appendicitis because of its great diagnostic performance,[19,20] speed and good interobserver agreement for interpretation regardless of experience. We were able to identify essential risk factors and predictors based on these images that can be used to assign a high probability of appendicitis in the US and CT.

Acute appendicitis is the most common abdominal surgical emergency that can affect individuals from all age groups. The prevalence of appendicitis in the current study occurred higher among young age groups 20–39 years old 48.0% among males and 43.4% among females and this confirmative with previous report study in United States age groups 18–39 years old by 55.4%.[21] The present study revealed that the prevalence of appendicitis is higher among males (62.6%) compared to the females (37.6%), this is consistent with the previously reported appendicitis prevalence by gender in France[22] (males 57.8% vs females 42.2%). Moreover, the increased risk of male versus female and age <50 versus age > is in line with the recent literature[23] and confirming our study.

An accurate diagnosis of acute appendicitis can be established with great confidence in the majority of patients, based on history, and physical examination. The present study revealed that pain, anorexia, vomiting, nausea, temperature >37.3°C, rebound tenderness, percussion tenderness, white cell count >10 × 109/L, loss appetite, constipation, and severe crumps were common significant risk factors among patients.[3,8,12-16,24]

A family history of acute appendicitis is an important factor determining the likelihood of appendicitis and must be considered during the medical visit. Clinicians attempting to confirm their diagnostic accuracy when patients present with acute abdominal pain should inquire about family history of appendicitis. Gauderer *et al.*[17] suggested that children who have appendicitis are twice more likely to have a positive family history than are those with right lower quadrant pain. The complex segregation analysis supported a polygenic or multifactorial model with a total heritability of 56%[25] among appendicitis patients.

### Limitations and strength of the study

Our study has several limitations. Firstly, the sample might be partially biased due to the consecutive series of patients with the prospective cohort study. Secondly, we did not have data

on family history in our study population. Hence, our results relied solely on the patients' knowledge of their family history response. Thirdly, the gender proportion of males and females were not balanced. Finally, no pathological results were available for some patients.

## Conclusion

In conclusion, CT offers the best cost-effectiveness in the prepaid system and public health system. The current study suggested that nausea, C-reactive protein, dizziness, vomiting, muscular symptoms, irritable bowel syndrome, guarding, and loss appetite were considered at higher risk as a predictor for appendicitis patients.


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Nil.


### Conflicts of interest

There are no conflicts of interest.

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