Pediatric Surgery International (2020) 36:735–742
https://doi.org/10.1007/s00383-020-04655-7

ORIGINAL ARTICLE

A novel and simple machine learning algorithm for preoperative diagnosis of acute appendicitis in children

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Accepted: 7 April 2020 / Published online: 20 April 2020

Abstract

Introduction There is a tendency toward nonoperative management of appendicitis resulting in an increasing need for preoperative diagnosis and classification. For medical purposes, simple conceptual decision-making models that can learn are widely used. Decision trees are reliable and effective techniques which provide high classification accuracy. We tested if we could detect appendicitis and differentiate uncomplicated from complicated cases using machine learning algorithms.
Materials and methods We analyzed all cases admitted between 2010 and 2016 that fell into the following categories: healthy controls (Group 1); sham controls (Group 2); sham disease (Group 3), and acute abdomen (Group 4). The latter group was further divided into four groups: false laparotomy; uncomplicated appendicitis; complicated appendicitis without abscess, and complicated appendicitis with abscess. Patients with comorbidities and whose complete blood count and/or pathology results were lacking were excluded. Data were collected for demographics, preoperative blood analysis, and postoperative diagnosis. Various machine learning algorithms were applied to detect appendicitis patients.
Results There were 7244 patients with a mean age of 6.84 ± 5.31 years, of whom 82.3% (5960/7244) were male. Most algorithms tested, especially linear methods, provided similar performance measures. We preferred the decision tree model due to its easier interpretability. With this algorithm, we detected appendicitis patients with 93.97% area under the curve (AUC), 94.69% accuracy, 93.55% sensitivity, and 96.55% specificity, and uncomplicated appendicitis with 79.47% AUC, 70.83% accuracy, 66.81% sensitivity, and 81.88% specificity.
Conclusions Machine learning is a novel approach to prevent unnecessary operations and decrease the burden of appendicitis both for patients and health systems.
Levels of evidence III.

Keywords Appendicitis · Machine learning · Artificial intelligence · Nonoperative management · Children

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Abbreviations

ANOVA	Analysis of variance
AUC	Area under curve
CBC	Complete blood count
KNN	Kth nearest neighbor
MPV	Mean platelet volume
PDW	Platelet distribution width
RDW	Red cell distribution width
SVM	Support vector machine
USA	United States of America
WBC	White blood cell count

Introduction

Acute appendicitis is the most common indication for emergency abdominal surgery both in adults and children [1–3]. Since the first description of appendectomy by McBurney, surgical intervention has remained the gold standard of treatment. Despite advances in diagnosis and treatment, it still has 10% morbidity and 1–5% mortality, with relatively high negative appendectomy rates (5–42%) [2–4]. In the USA, it was reported that 0.6% of all hospital admissions were related to appendicitis and its complications which resulted in almost one million hospital days and $3 billion in hospital charges in 1997 [5]. Due to this debate, there is a tendency toward nonoperative management of appendicitis which results in an increased need for preoperative diagnosis and classification [6]. Many biomarkers, either through blood or urine analysis, have been proposed to predict appendicitis and the degree of inflammation, but none have been sufficiently accurate [7, 8].

Complete blood count (CBC) is analyzed routinely in all acute abdomen patients. CBC parameters such as neutrophil–lymphocyte ratio, mean platelet volume (MPV), and red cell distribution width (RDW) have been proposed as biomarkers in the differential diagnosis of acute appendicitis [9–13]. There is still an enigma, however, regarding their significance in this context. Some studies state that they are significantly higher in acute appendicitis, while others state that they are significantly lower, and some could not determine a statistically significant difference [9, 10, 14]. Moreover, the specificity and sensitivity of these markers are too low to be generalized.

There are several machine learning algorithms and approaches which can be used for developing multivariate decision criteria in medical studies. For diagnosis and classification purposes, simple conceptual decision-making models that can learn are widely used [15–18]. The decision tree is a reliable and effective decision-making technique which in general provides high classification accuracy; moreover, interpretation and implementation of these models are quite easy compared to most classification algorithms.

The main questions we investigated in this study were: "Can we detect patients with an acute abdomen who were operated on, using only age, gender, and CBC parameters?; and if we assume that only patients proven to have complicated appendicitis by surgical and/or histopathological examination need surgical intervention, can we detect these patients using only age, gender, and CBC parameters?" These questions are classification problems. Herein, we aimed not only to derive an accurate classification model but also one that could be automated and was easy to interpret, so that in the future a decision-making workflow could be built upon it.

Materials and methods

Study design

After Institutional Review Board approval was obtained (2018.322.IRB2.048), data of all cases under 18 years of age admitted between 2010 and 2016 with a diagnosis of the diseases listed in Table 1 were retrieved from hospital electronic medical records. The diagnosis of the patients was confirmed by two researchers through analysis of all records of the patients. Patients who had comorbidities reported in the electronic records that would affect CBC parameters and those whose CBC and/or pathology results were lacking were excluded from the study. The remaining patients were divided into four groups. All patients were free of tumor, infection, and hematological disorders.

Table 1 Groups and diagnoses of the study population

	n (%)
Group 1	
Circumcision	3055 (42.2)
Hernia	353 (4.9)
Undescended testis	110 (1.5)
Group 2	
Abdominal pain	323 (4.5)
Constipation	149 (2.1)
Group 3	
Intussusception	254 (3.5)
Group 4	
Acute abdomen	3000 (41.4)
Group 4a: False	169 (5.6)
Group 4b: Uncomplicated	1272 (42.4)
Group 4c: Complicated without abscess	1205 (40.2)
Group 4d: Complicated with abscess	354 (11.8)

Participants

Group 1 comprised healthy controls; that is, patients who had elective surgeries unrelated to the gastrointestinal system; since any infection or abnormality in their routine preoperative blood workup would have precluded these patients from being eligible for surgery, their CBC parameters were included in the study to serve as the reference value. Group 2 was the healthy sham group of patients admitted to hospital with gastrointestinal symptoms but without any organic cause or documented inflammation, who did not require any surgical operation in the follow-up per the electronic health records. Group 3 was the sham disease group of patients who were admitted to hospital for ileocolic intussusception confirmed by clinical examination and radiology; that is, they had an inflammatory process other than appendicitis in the ileocolic segment of the intestine requiring intervention. All patients in this group were treated by pneumatic reduction. Lastly, Group 4 was the acute abdomen group of patients who had emergency abdominal surgery with a preoperative diagnosis of acute appendicitis (approximately 90% of patients in this group were subsequently found to have appendicitis). All patients had abdominal ultrasonography by a radiologist. The final surgical decision was given by a surgeon and all had appendectomy regardless of the underlying pathology. None of the patients with acute abdomen had medical treatment due to appendicitis per the preference of the surgeons in the clinics. This group was further divided according to the results of pathological examination of the appendix; the first subgroup included patients whose histopathological examination did not confirm appendicitis; the second subgroup consisted of patients with early appendicitis whose histopathological examination revealed only hyperemia and edema without any necrosis or perforation; the third subgroup included patients who had necrosis and/or perforation on the appendix without any abscess formation, and the fourth and last sub-group included patients who had appendicitis complicated with abscess.

Data

Data included demographics, preoperative blood analysis, and post-operative diagnosis based on clinical and pathological opinions. Clinical and radiological data were not included to generate operator-independent data. C reactive protein, which is another common parameter preferred in some centers was not included per majority of the patients did not have this data. Parental consent was obtained both for surgical approach and publication of the data. Diagnosis and management of appendicitis were determined through clinical, laboratory, radiological, and surgical findings (by different surgeons) [19].

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics 26.0.0 (Chicago, IL). The characteristics of the study sample were summarized by descriptive statistics, with dichotomous or ordinal data presented as percentages, and continuous data as means with standard deviations. The Kolmogorov–Smirnov test was used to demonstrate normal distribution. One-way ANOVA was used for homogeneity of variables, while the Student's T test and Pearson correlation were used for parametric data. Mann–Whitney *U*, Wilcoxon, and Kruskal–Wallis tests and Spearman correlation were used for non-parametric data. Statistical associations were considered significant if the p value was < 0.05.

To detect patients with a diagnosis of acute appendicitis, CBC parameters and age were used as adjustment factors. To define decision criteria for CBC parameters and age, various machine learning techniques were performed and compared. A decision tree model was used for defining variables important in detecting appendicitis. All data mining and modeling techniques were performed in R version 3.4.0.

The learning approach

To detect patients who were operated on due to suspected or complicated appendicitis, data were divided 80:20 into training and test sets and a tenfold cross-validation for each model was applied to each training set. Six different learning models were trained over the same training set: naïve Bayes algorithm; k^{th} nearest neighbor algorithm; support vector machine; generalized linear model; random forest algorithm, and decision tree algorithm.

Results

There were 7244 patients included in the study with a mean age of 6.84 ± 5.31 years, of whom 82.3% (5960/7244) were male. Age and gender distributions, and CBC results in the all-study population are summarized in Table 2.

The comparison of algorithms gathered from different learning models to detect appendicitis patients is summarized in Table 3. All models were good at predicting the disease; however, the decision tree model was preferred for its superiority in interpreting the results. Each model performed at greater than 90% value in all four performance measures. The random forest algorithm was the best in all four measures. Our objective, however, was not to construct the best performing classification model in one of these or other measures but to provide an easily interpretable model to understand the relationship between blood variables and the disease so that in the future an automated decision support system can be created. In this regard, the decision tree

Table 2 Demographic data and CBC results of study groups

	Group 1 Control/healthy $n=3518$	Group 2 Sham/healthy $n=472$	Group 3 Sham/inflammation $n=254$	Group 4 Acute abdomen $n=3000$
Gender (male)	3472 (98.7%)	247 (52.3%)	156 (61.4%)	2085 (69.5%)
Age	3.16 ± 3.11	8.08 ± 4.39	2.97 ± 2.7	11.29 ± 3.99
WBC	9768 ± 3470	9869 ± 3941	9346 ± 3002	17,071 ± 4765
LYMP	4.33 ± 5.39	3.24 ± 1.91	4.2 ± 1.99	2.31 ± 1.92
NEUT	4.3 ± 3.07	5.7 ± 3.88	3.92 ± 2.52	10.18 ± 5.9
HGB	12.28 ± 1.42	13.03 ± 1.21	12.16 ± 1.59	12.71 ± 1.33
HTC	37.23 ± 8.59	38.64 ± 3.34	36.79 ± 4.42	37.76 ± 3.89
RDW	13.01 ± 1.75	10.99 ± 0.4	12.74 ± 1.52	13.64 ± 2.23
MCV	77.53 ± 14.31	93.46 ± 1.85	78.6 ± 8.09	81.09 ± 5.2
MCHC	33.16 ± 1.59	32.93 ± 1.13	33.06 ± 1.53	33.54 ± 5.49
PLT	322,167 ± 92,786	312,422 ± 88,184	322,512 ± 89,600	312,740 ± 97,863
MPV	7.07 ± 1.46	6.9 ± 1.3	7.1 ± 1.49	7.7 ± 1.38
PDW	17.95 ± 3.71	19.23 ± 1.46	18.02 ± 3.17	31.84 ± 16.01

Values expressed as means ± standard deviations or counts (percentage of the group)

WBC white blood cell, *HGB* hemoglobin, *HTC* hematocrit, *RDW* red cell distribution width, *MCV* mean corpuscular volume, *MCHC* mean corpuscular hemoglobin concentration, *MPV* mean platelet volume, *PLT* platelet, *PDW* platelet distribution width, *LYMP* lymphocyte, *NEUT* neutrophil

Table 3 Comparison of algorithms from different learning models to detect appendicitis

	AUC (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
RF	99.67	97.45	97.79	97.21
KNN	98.68	95.58	95.08	95.93
NB	98.71	94.76	94.06	95.25
DT	93.97%	94.69	93.55	96.55
SVM	96.76	91.24	90.32	91.86
GLM	96.83	90.96	90.66	91.16

NB naïve Bayes algorithm, *GLM* generalized linear model, *SVM* support vector machine, *RF* random forest algorithm, *DT* decision tree algorithm, *KNN* kth nearest neighbor algorithm, *AUC* area under the curve

algorithm was our preferred option; this model performed worse than the random forest algorithm but better than the generalized linear model and support vector machine, and very close to the naïve Bayes and kth nearest neighbor algorithm in terms of misclassification rate (1-Accuracy). Compared to other models, decision trees are simpler, easier to interpret, and a widely used concept in medical decision making. In our study, the decision tree model also provided satisfactory performance in terms of all four measures in predicting appendicitis patients.

The optimal decision tree we developed, and the variable importance table, are shown in Fig. 1. Age of the patient was a normalization factor while the rest were independent variables. Platelet distribution width (PDW), white blood cell count (WBC), and its subunits neutrophils and lymphocytes were the most important factors to detect appendicitis patients in the all-study population. The decision tree starts with WBC count. If the patient's WBC value is more than 13,265, we would look for age over 3.5 years. This would be followed by RDW value over 11.02. Results indicate that 32.85% of patients fall into this branch and among these, 96.85% have appendicitis.

The second objective of this study was to differentiate patients with complicated appendicitis regardless of the presence or absence of abscess since these groups would definitely not be treatable with antibiotics (albeit not all patients with uncomplicated appendicitis would be suitable for antibiotic treatment either). One more subanalysis was performed, therefore, to detect these patients among all patients operated on for suspected appendicitis. The resulting performance measures were all worse than those achieved when trying to detect patients with acute abdomen among the whole data set, with the decision tree again being the easiest to interpret. The accuracy to detect complicated appendicitis was 70.83%, sensitivity 66.81% and specificity 81.88% with AUC being 79.47%. The decision tree we constructed is presented in Fig. 2.

Discussion

Despite being one of the most common surgical emergency causes in children, no algorithms have been established to objectively diagnose appendicitis [5–9]. Clinical evaluation has been the gold standard for diagnosis

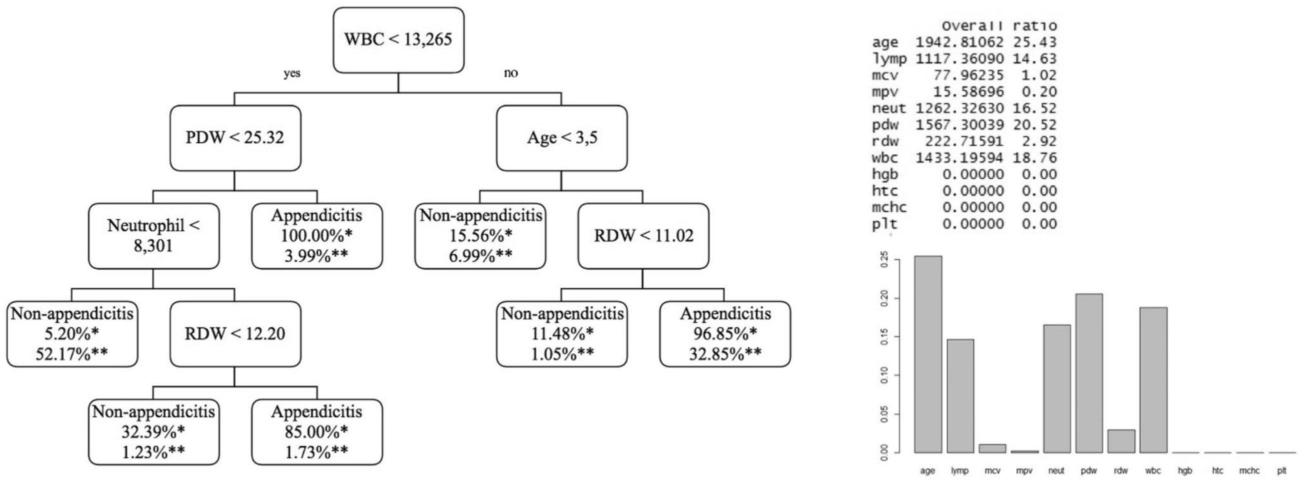

Fig. 1 Decision tree to detect patients operated on due to appendicitis. If the condition in the box is satisfied, then the next level on the left (yes) should be followed while if the condition is not satisfied the next level on the right (no) should be followed. *Indicates the percentage of patients who have the disease, and **indicates the percentage of patients who fall into that branch

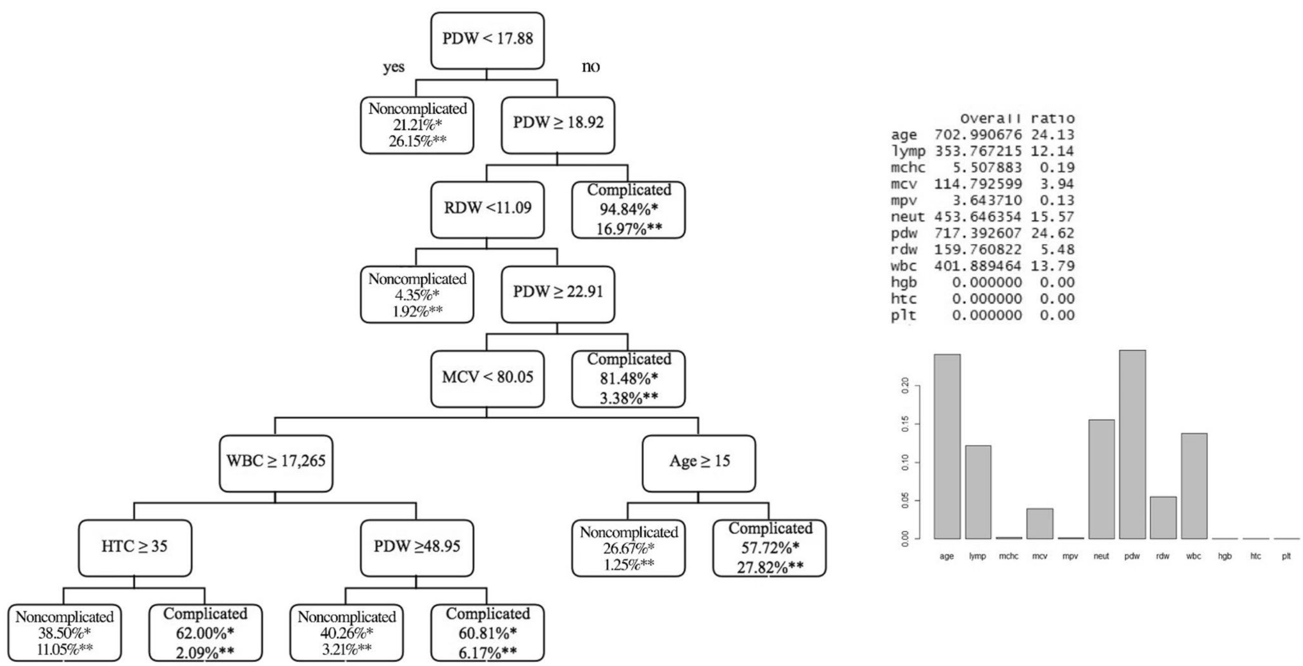

Fig. 2 Decision tree to detect patients diagnosed with complicated appendicitis. If the condition in the box is satisfied then the next level on the left (yes) should be followed while if the condition is not satisfied the next level on the right (no) should be followed. *Indicates the percentage of patients who have the disease, and **indicates the percentage of patients that fall into that branch

regardless of innovations in technology [6]. On the other hand, more and more doctors are looking for alternative approaches in the management of appendicitis in children to prevent unnecessary surgeries and stress, to decrease health care costs, and to improve the child's quality of life. Studies in the literature have reported conflicting results both in parameters used for predicting the diagnosis of appendicitis and in its categorization for determining treatment [9–12, 20, 21].

The increasing availability of large healthcare datasets enables the development of analytic tools in the management of many diseases. Decision-making models of data analysis have been very popular recently among the medical community, specifically, in cancer management [19, 22–24]. To predict disease outcome or recurrence, blood counts, age, and sex are the most commonly used parameters for computational analyses [21, 22]. Accurate patient selection was important to minimize the risk of misdiagnosis. With the help of machine learning–specifically, using decision trees and cross-validation techniques–data-driven prediction models could be produced and evaluated [25]. Some of the models included (SVM, random forest, KNN, Naïve Bayes, generalized linear model) may not clearly identify which variables are more likely to be associated with appendicitis. As a result, clinicians may not be able to discern the specific findings that are indicative of appendicitis based on these algorithms. Since the decision tree had been applied in medical practice and had some familiarity among clinicians, then despite being among the worst for predicting cases, it enables the physician to understand how the algorithm reached its decision by printing every branch of the tree. This knowledge, indeed, could be validated by the known functions of the stated biomarker in each branch. The decision tree model has the advantage of allowing the clinician to see the specific variables used in the model and their weights toward a specific classification.

MPV and RDW are indicators of platelet activation. Platelet size is correlated with activity and function – the larger, the more active. MPV is a marker determined from megakaryocytes during platelet production, which is associated with platelet function and activation [20, 21]. There are many hypotheses regarding how MPV is affected in appendicitis. It is found to decrease in acute inflammatory conditions of the gastrointestinal tract due to consumption and sequestration of platelets in vascular segments of an inflamed bowel [26]. Although the exact pathophysiology has not been fully understood, it has also been proposed that in acute inflammatory conditions, activated leukocytes secrete interleukin-6 which causes a decrease in MPV value by reducing platelet production. As a result, a decrease in MPV occurs in acute cases while in chronic events, it increases [27]. PDW, on the other hand, is an indicator of variation in platelet size which might dictate active platelet release. RDW is a quantitative measurement of variability and size of erythrocytes. Higher RDW values have been reported with worse prognosis in other diseases [28, 29]. It has been thought that increased cytokines may inhibit maturation of erythrocytes in the bone marrow and may cause increased RDW values. Cytokine levels are higher in patients with appendicitis compared to normal counterparts as well as in complicated compared to uncomplicated appendicitis [30].

Studies reported in the literature were structured classical hypothesis tests with two groups. Our study is the first to use a multivariate learning approach to evaluate the relationship between the degree of inflammation in the appendix and all parameters of CBC and compare this with healthy control and sham groups. The novelty of this study is the algorithm proposed is dynamic, which means it continues to learn and improves its outcome as more data imported. Hence, we propose an algorithm which has high potential to help physicians in the diagnosis of appendicitis. Although physical examination and history-taking remain pivotal in the management of patients with abdominal pain, computational measurements of CBC parameters, utilizing artificial intelligence, represent promising decision support systems for further evaluation of these patients.

There are limitations to our study. It is a retrospective review which includes inherent bias. We also could not confirm antibiotic usage prior to CBC analyses in all patients, or the time between the onset of abdominal pain and CBC analysis, which are possible confounding factors. The lack of patient symptoms, physical examination findings, and diagnostic imaging findings as variables is another limitation in the study, not only due to inability to collect it from the medical records, but also these parameters are operator dependent and may have had a confounding effect on the result. On the other hand, there are certain strengths of the study. The algorithm developed has high accuracy in the diagnosis of appendicitis, although the subanalysis to differentiate complicated from uncomplicated appendicitis cases was not as accurate and necessitates further prospective studies with larger datasets. We are currently conducting a prospective validation study including more cases with preliminary results expected in 2020.

Conclusion

Artificial intelligence is an emerging and fast-improving field with a specific emphasis on health issues. The successful coordination of both will have the potential to improve health statistics. Appendicitis, which is one of the oldest and commonest diseases throughout all ages, would certainly benefit from these new models. Our model can be automated, is easy to interpret, and its accuracy will certainly increase once more data have been included.

What is known

- There are few scoring systems that advocates the preoperative diagnosis of appendicitis.
- The machine learning algorithms are widely used in classification problems health.

What is new

- The algorithm proposed which predicts the preoperative diagnosis of appendicitis in a clinically readable manner is not static but dynamic meaning has the capacity to improve itself.

- The new patient data could be imported into the dataset to validate the results as well as the algorithm could be inserted into the health systems software to help the physicians.

Author contributions All authors have made substantial contributions to the conception and design of the study, acquisition, analysis, and interpretation of data, drafting the article and revising it for important intellectual content and final approval of the version to be submitted.

Funding There is no funding source.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Omari AH, Khammash MR, Qasaimeh GR et al (2014) Acute appendicitis in the elderly: risk factors for perforation. World J Emerg Surg. https://doi.org/10.1186/1749-7922-9-6
2. Ashdown HF, D'Souza N, Karim D et al (2012) Pain over speed bumps in diagnosis of acute appendicitis: diagnostic accuracy study. BMJ. https://doi.org/10.1136/bmj.e8012
3. Andersson RE (2015) The magic of an appendicitis score. World J Surg 39:110–111
4. Atema JJ, Van Rossem CC, Leeuwenburgh MM et al (2015) Scoring system to distinguish uncomplicated from complicated acute appendicitis. Br J Surg 102:979–990. https://doi.org/10.1002/bjs.9835
5. Davies GM, Dasbach EJ, Teutsch S (2004) The Burden of Appendicitis-Related Hospitalizations in the United States in 1997. Surg Infect (Larchmt). https://doi.org/10.1089/1096296041839480
6. Simillis C, Symeonides P, Shorthouse AJ, Tekkis PP (2010) A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). Surgery 147:818–829. https://doi.org/10.1016/j.surg.2009.11.013
7. Yu CW, Juan LI, Wu MH et al (2013) Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. Br J Surg 100:322–329. https://doi.org/10.1002/bjs.9008
8. Acharya A, Markar SR, Ni M, Hanna GB (2017) Biomarkers of acute appendicitis: systematic review and cost–benefit trade-off analysis. Surg Endosc 31:1022–1031. https://doi.org/10.1007/s00464-016-5109-1
9. Kucuk E, Kucuk I (2015) Mean platelet volume is reduced in acute appendicitis. Turk J Emerg Med 15:23–27. https://doi.org/10.5505/1304.7361.2015.32657
10. Aktimur R, Cetinkunar S (2015) Mean platelet volume is a significant biomarker in the differential diagnosis of acute appendicitis. Inflamm Cell. https://doi.org/10.14800/ics.930
11. Bozkurt S, Köse A, Erdogan S et al (2015) MPV and other inflammatory markers in diagnosing acute appendicitis. J Pak Med Assoc 65:637–641
12. Fan Z, Pan J, Zhang Y et al (2015) Mean platelet volume and platelet distribution width as markers in the diagnosis of acute gangrenous appendicitis. Dis Markers. https://doi.org/10.1155/2015/542013
13. Yardımcı S (2015) Neutrophil-lymphocyte ratio and mean platelet volume can be a predictor for the severity of acute appendicitis. Turk J Trauma Emerg Surg 22:163–168. https://doi.org/10.5505/tjtes.2015.89346
14. Vijay Shankar SVMAK (2015) Mean platelet volume as a diagnostic marker of acute appendicitis in children and adolescents how useful it is? Indian J Pathol Oncol 2:236–239. https://doi.org/10.5958/2394-6792.2015.00023.X
15. Svanera M, Savardi M, Benini S et al (2019) Transfer learning of deep neural network representations for fMRI decoding. bioXriv. https://doi.org/10.1101/535377
16. Leaning MS, Ng KEH, Cramp DG (1992) Decision support for patient management in oncology. Inform Heal Soc Care. https://doi.org/10.3109/14639239209012134
17. Kourou K, Exarchos TP, Exarchos KP et al (2015) Machine learning applications in cancer prognosis and prediction. Comput Struct Biotechnol J 13:8–17. https://doi.org/10.1016/j.csbj.2014.11.005
18. Mani S, Ozdas A, Aliferis C et al (2014) Medical decision support using machine learning for early detection of late-onset neonatal sepsis. J Am Med Inform Assoc. https://doi.org/10.1136/amiajnl-2013-001854
19. Guzman-Valdivia Gomez G (2003) An useful classification for acute appendicitis. Rev Gastroenterol México 68:261–265
20. Uyanik B, Kavalci C, Arslan ED et al (2012) Role of mean platelet volume in diagnosis of childhood acute appendicitis. Emerg Med Int 2012:823095. https://doi.org/10.1155/2012/823095
21. Bilici S, Sekmenli T, Göksu M et al (2010) Mean platelet volume in diagnosis of acute appendicitis in children. Afr Health Sci 11(3):427–432
22. Hornbrook MC, Goshen R, Choman E et al (2017) Early colorectal cancer detected by machine learning model using gender, age, and complete blood count data. Dig Dis Sci 62:2719–2727. https://doi.org/10.1007/s10620-017-4722-8
23. Shalev V, Kinar Y, Kalkstein N et al (2016) Development and validation of a predictive model for detection of colorectal cancer in primary care by analysis of complete blood counts: a binational retrospective study. J Am Med Inform Assoc 23:879–890. https://doi.org/10.1093/jamia/ocv195
24. Kinar Y, Akiva P, Choman E et al (2017) Performance analysis of a machine learning flagging system used to identify a group of individuals at a high risk for colorectal cancer. PLoS ONE 12:1–8. https://doi.org/10.1371/journal.pone.0171759
25. Bae J-M (2014) Clinical decision analysis using decision tree. Epidemiol Health. https://doi.org/10.4178/epih/e2014025
26. Danese S, De La Motte C, Fiocchi C (2004) Platelets in inflammatory bowel disease: clinical, pathogenic, and therapeutic implications. Am J Gastroenterol 99(5):938–945. https://doi.org/10.1111/j.1572-0241.2004.04129.x
27. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD (2011) Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 17(1):47–58. https://doi.org/10.2174/138161211795049804
28. Zorlu A, Bektasoglu G, Kukul Guven FM et al (2012) Usefulness of admission red cell distribution width as a predictor of

early mortality in patients with acute pulmonary embolism. Am J Cardiol. https://doi.org/10.1016/j.amjcard.2011.08.015
29. Kaya A, Ayhan E, Kurt M et al (2012) Is red cell distribution width a marker for the presence and poor prognosis of cardiovascular disease? Eurasian J Med. https://doi.org/10.5152/eajm.2012.39
30. Yoon DY, Chu J, Chandler C et al (2002) Human cytokine levels in nonperforated versus perforated appendicitis: molecular serum markers for extent of disease? Am Surg 68(12):1033–1037