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Scientific letters

Diagnostic performance studies: interpretation of ROC analysis and cut-offs

Estudios de rendimiento diagnóstico: interpretación del análisis ROC y de los puntos de corte

Diagnosis is a fundamental part of the medical practice. Much scientific literature has been published about the implementation of new diagnostic tools, so it is essential for every clinician to know the methods used to evaluate the validity of these tools and determine their usefulness.

1 Diagnostic performance studies: Diagnostic performance studies evaluate the ability of a clinical tool (for example, a radiological test or biomarker) to diagnose a certain pathology. These studies include:
- A group of patients affected by a pathology
- A group of control patients who generally have the same symptoms as the patient group. For example, in the case of studies evaluating the performance of a specific test for the diagnosis of acute appendicitis, the control group usually consists of patients with acute abdominal pain in whom the diagnosis of acute appendicitis has been ruled out.
- A diagnostic tool for evaluation: for example, a new serum biomarker
- A ''gold standard'' or reference test, which is the best existing diagnostic test for that pathology. For example, in acute appendicitis, this would be the histopathological study of the surgical specimen of the appendix. The objective of this test in this type of studies is to be used as a reference against which to compare the new tool being evaluated.

2 Description of diagnostic performance: In the evaluation of a diagnostic test, important indicators should be described:
- Sensitivity (Se): the probability that the test will correctly classify (as positive) an individual affected by the pathology (ill or sick)
- Specificity (Sp): the probability that the test will correctly classify (as negative) a control subject (healthy)
- Positive predictive value (PPV): the probability that a subject has the pathology in question (ill or sick) if the test result was positive
- Negative predictive value (NPV): the probability that a subject does not have the pathology in question (healthy) if the test result was negative.
- Receiver Operating Characteristic (ROC) analysis: This analysis establishes the capacity of diagnosis of a binary classification system as its discrimination treshold is varied.[1,2] The result of a ROC analysis is expressed as an area under the curve (AUC), which reflects the discriminatory capacity of the diagnostic tool, meaning its ability to classify the healthy subject as healthy and the ill or sick as ill or sick. The AUC is usually expressed as a number and a confidence Interval and is usually accompanied by a graph (Figure 1).

o AUC = 1: perfect discrimination
o AUC $\geq$ 0.9: excellent discrimination
o 0.7 $\leq$ AUC $<$ 0.9: moderate discrimination
o 0.5 $<$ AUC $<$ 0.7: poor discrimination

An AUC of 0.5 is considered a non-useful test for diagnosis, since the probability of it correctly classifying patients is the same as a coin toss. An AUC value of less than 0.5 indicates that the diagnostic criterion should be inverted.

3 The importance of disease prevalence: Se and Sp are intrinsic characteristics of a diagnostic test, but the predictive values depend on the prevalence of the disease in the population in which this test is applied. The same diagnostic tool will have a greater PPV if it is applied to a population where the prevalence of the disease is high than if it is applied in a population where the prevalence is low. Contrarily, the NPV decreases if the prevalence of the disease increases. In diagnostic performance studies, we can find different PPV and NPV for the same diagnostic tool when applied to different populations, depending on the prevalence of the disease in each population.[3]

4 The cut-off point: when a diagnostic tool is presented as a continuous variable, the cut-off point refers to the value

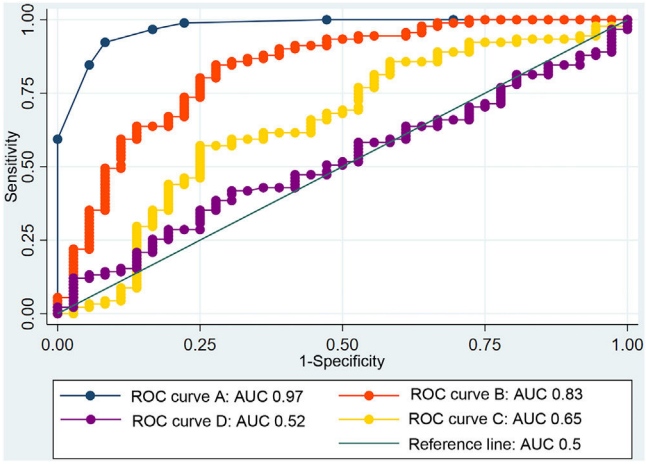

Fig. 1 – Example of real ROC curves with different diagnostic performances. The x-axis represents 1-Specificity and the y-axis represents Sensitivity. The straight line that divides the graph into 2 equal halves represents the AUC value of 0.5. (A) 0.97, excellent discrimination. (B) 0.83, moderate discrimination. C: 0.65, poor discrimination. (D) 0.52, practically no discrimination (like a coin toss).

chosen to classify the subjects as healthy or ill or sick. The cut-off point with the best discriminatory capacity is closest to the upper left corner of the ROC. There are different methods for its calculation[4,5]:

- Cut-off point with the greatest Youden Index (Sensitivity + Specificity − 1)
- Cut-off point with the lowest value for the formula: $(1-\text{sensitivity})^2 + (1-\text{specificity})^2$

With the cut-off point, we can calculate the Se, Sp, and predictive values of the diagnostic tool in a table that compares the results of our test with those of the standard reference. The cut-off point with the best discrimination capacity is usually chosen, but it may also be interesting to evaluate other cut-off points, such as the most sensitive (in severe pathologies) or the most specific (in pathologies whose treatment entails important adverse effects).

Strengths and limitations: ROC analysis is able to evaluate the discriminatory capacity of a diagnostic tool and compare it with others in a simple and graphic manner. Its limitations include the need for a gold standard against which the new tool can be compared and and the difficulty to generalize the results (cut-off points, sensitivity and specificity) to other populations (Fig. 1).

Contributions of the authors

All the authors have made substantial contributions, both directly and intellectually, to the manuscript and have approved the final version for publication.

Original paper

All of the authors of this manuscript declare that this is an original contribution that has not been previously published.

Conflict of interest

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REFERENCES

1. Aggarwal R, Ranganathan P. Understanding diagnostic tests - Part 3: receiver operating characteristic curves. Perspect Clin Res. 2018;9(3):145–8. http://dx.doi.org/10.4103/picr.PICR_87_18.
2. Zou KH, O'Malley AJ, Mauri L. Receiver-operating characteristic analysis for evaluating diagnostic tests and predictive models. Circulation. 2007;115(5):654–7. http://dx.doi.org/10.1161/CIRCULATIONAHA.105.594929.
3. Arredondo Montero J, Bardají Pascual C, Antona G, Bronte Anaut M, López-Andrés N, Martín-Calvo N. Diagnostic performance of calprotectin and APPY-1 test in pediatric acute appendicitis: a systematic review and a meta-analysis. Eur J Trauma Emerg Surg. 2022. http://dx.doi.org/10.1007/s00068-022-02000-2.
4. Youden WJ. Index for rating diagnostic tests. Cancer. 1950;3(1):32–5. doi: 10.1002/1097-0142(1950)3:1<32::aid-cncr2820030106>3.0.co;2-3.
5. Arredondo Montero J, Antona G, Rivero Marcotegui A, Bardají Pascual C, Bronte Anaut M, Ros Briones R, et al. Discriminatory capacity of serum interleukin-6 between complicated and uncomplicated acute appendicitis in children: a prospective validation study. World J Pediatr. 2022;18(12):810–7. http://dx.doi.org/10.1007/s12519-022-00598-2. Epub 2022 Sep 16. PMID: 36114365; PMCID: PMC9617836.

Javier Arredondo Montero[a*], Nerea Martín-Calvo[abc]

[a]*Preventive Medicine and Public Health Department, School of Medicine, University of Navarra, Pamplona, Spain*
[b]*IdiSNA, Instituto de Investigación Sanitaria de Navarra, Pamplona, Spain*

[c]CIBER de Fisiopatología de la Obesidad y la Nutrición, Instituto de Salud Carlos III, Madrid, Spain

*Corresponding author. Javier.montero.arredondo@gmail.com jarredondom@alumni.unav.es (J. Arredondo Montero).

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Urachal adenocarcinoma

Adenocarcinoma de uraco

Urachal cancer is one of the rarest and most aggressive neoplasms affecting the bladder. First described in 1863 by Hue and Jacquin, it represents less than 1% of bladder cancers and 0.01% of adult neoplasms, with an estimated annual incidence of one case per 5 million individuals[1]. The urachus is a tubular structure located in the midline that connects the umbilicus with the dome of the bladder[2]. It is an embryonic remnant of the cloaca and allantois that usually involutes from the third trimester of gestation to a fibrous structure that has no function, known as the median ligament. However, several autopsy studies describe the presence of urachal remnants in 32% of the adult population[3,4]. Its histological composition (internal-transitional epithelium, intermediate-connective tissue and external-muscular layer), metaplastic changes of the urothelium and the persistence of intestinal endodermal tissue help explain how an adenocarcinoma can present in an organ that has no glandular tissue[2]. Some 90% of cancers of the urachus are adenocarcinomas, which predominantly affect males (5:1) and usually present between the 5th and 6th decades of life[3]. In the Spanish literature, fewer than 40 cases have been published historically. Thus, we describe the diagnostic-therapeutic sequence followed in a patient with primary adenocarcinoma of the urachus, while also reviewing the existing scientific literature on this subject.

The patient is a 19-year-old woman with a history of right adnexectomy at the age of 15 due to a mucinous cystadenoma measuring 35 cm in diameter. She consulted for pain and a stone-like, immobile, hypogastric tumor located under the Pfannenstiel scar that had been progressing over the past 2 months. Abdominal-pelvic CT scan identified a solid infraumbilical lesion (8 × 8 × 4 cm) occupying both rectus muscles and showing signs of local invasion, suggestive of a desmoid tumor; likewise, a urachal remnant was observed connecting the umbilicus to the bladder (Fig. 1). The PET/CT scan ruled out distant involvement. An ultrasound-guided biopsy was performed, which provided a diagnosis of mucus-secreting adenocarcinoma with signet-ring cells, suggestive of urachal adenocarcinoma. The Multidisciplinary Team decided on the surgical resection, which included *en bloc* resection of the abdominal wall (anterior rectus muscles, umbilicus, median ligament, soft tissues, and parietal peritoneum) with a margin greater than 1.5 cm, but no excision of the dome of the bladder due to the absence of macroscopic invasion, followed by abdominal wall repair with partially absorbable macroporous bilayer mesh (Fig. 2). The anatomopathological study confirmed the diagnosis of adenocarcinoma of the urachus with a tubular pattern, undifferentiated areas and large necrotic areas (8.5 cm in diameter); free margins and 4/5 involved lymph nodes. Immunohistochemical profile (IHC): CK20q–, nuclear B-Catenin–, cytoplasmic B-Catenin+, CK34BetaE12+, GATA3–, CDX2+ (weak and very focal). All of this was compatible with Sheldon stage IIIB. Adjuvant chemotherapy was initiated with the FOLFOX regimen. Follow-up PET/CT scan 2 months later identified metastatic bone lesions in L5 as well as the right ischium and pubis. Currently, the patient continues with adjuvant therapy, and the distant lesions remain radiologically stable.

The most common form of presentation is hematuria, followed by a palpable suprapubic mass and mucus in urine. Other less frequent symptoms include bloody urethral discharge, recurrent urinary tract infections, and obstructive urinary symptoms[5]. However, these tumors usually remain asymptomatic for long periods of time, which allows them to locally invade other neighboring structures and metastasize to distant structures prior to their diagnosis[2].

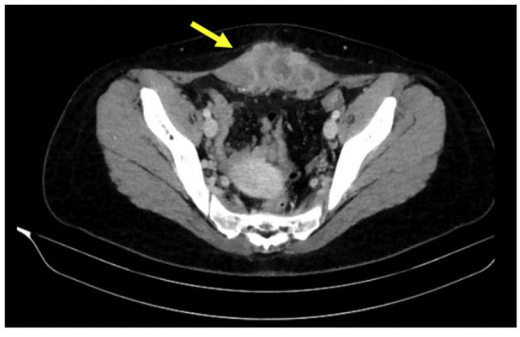

Fig. 1 – Axial abdominal-pelvic CT scan with intravenous contrast revealing a solid infraumbilical lesion (8 × 8 × 4 cm) occupying both rectus muscles with signs of local invasion, suggestive of a desmoid tumor (yellow arrow); likewise, urachal remnant connecting the umbilicus to the bladder is observed.