

## COULD ISCHEMIA HAVE A PRE-DEFINED LACTATE?

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**Abstract:** Acute abdomen can be defined as sudden abdominal pain, of non-traumatic origin, accompanied or not by other symptoms, varying in intensity and lasting up to seven days. Within this diagnosis, there are cases of intestinal ischemia, which consists of the interruption of the arterial blood supply to the intestinal loops, usually of thromboembolic etiology, which can cause death and necrosis of large areas. Thus, the objective of this review was to evaluate the predictive value of the lactate biomarker in the diagnosis of intestinal ischemia. With the application of the inclusion and exclusion criteria, 15 articles were selected in PubMed, 04 in the VHL and none in the DOAJ, totaling 19 articles. The descriptors chosen for the search for articles on the platforms were “predictive value”, “lactate” and “intestinal ischemia”, connected by the Boolean operator “AND”. Of the 19 studies analyzed, 15 treat lactate as a marker with positive predictive value for the diagnosis of intestinal ischemia. On the other hand, 4 studies suggest that lactate has a Negative predictive value. Thus, lactate proved to be an important diagnostic tool for intestinal ischemia. However, its analysis must be associated with a quality physical examination and anamnesis. It is not possible to use this serological marker alone for the definitive diagnosis of any vascular involvement of the gastrointestinal tract. In terms of its high sensitivity, the predominant predictive value of lactate is Positive.

**Keywords:** Predictive value, lactate, intestinal ischemia.

## **INTRODUCTION**

Acute abdomen can be defined as sudden abdominal pain, of non-traumatic origin, accompanied or not by other symptoms, varying in intensity and lasting up to seven days. It often requires immediate diagnosis and therapeutic management, whether

surgical or not<sup>1</sup>. According to data from the SUS Hospital Information System (SIH/SUS), 40,494 patients were hospitalized in 2020 due to abdominal or pelvic pain<sup>2</sup>. Within this diagnosis, there are cases of intestinal ischemia, which consists of the interruption of the arterial blood supply to the intestinal loops, usually of thromboembolic etiology, which can cause death and necrosis of large areas<sup>1</sup>.

The clinical picture is generally characterized by periumbilical pain that progresses to an acute open abdomen, and the physical examination is usually inconsistent with the patient's complaints<sup>1</sup>. However, early diagnosis, preferable, is difficult, which contributes to mortality rates of 58-80% in intensive care centers. Angiography is a diagnostic method of high sensitivity and specificity, placing it in the position of the best diagnostic test<sup>3</sup>.

In an attempt to circumvent late diagnosis and, often, the lack of access to imaging tests, a range of laboratory markers has been studied to assist in this diagnosis<sup>4</sup>. Among these markers is lactate, which comes from the anaerobic metabolism of cells, which happens when the levels of arterial blood supply fall by less than 50%, triggering anaerobic glycolysis and consequently there is greater release of lactate into the circulation. Elevated lactate levels alone are a nonspecific sign<sup>5</sup>.

The sensitivity and specificity of lactate are, respectively, 86% and 44%<sup>6</sup>. This substance can be divided into two isomers: L-lactate and D-lactate. The first comes from the anaerobic cascade of energy generation, being common to all tissues. The second, in turn, is due to the anaerobic bacterial action from the intestinal flora, and its gain in circulation is limited by the healthy mucosa. D-lactate is not favorable for cases of intestinal ischemia; however, the opposite occurs with L-lactate<sup>7</sup>. To date, there is no pathognomonic laboratory marker

of intestinal ischemia, however, lactate falls within the group of promising non-invasive markers<sup>8</sup>. Thus, the objective of this review was to evaluate the predictive value of the lactate biomarker in the diagnosis of intestinal ischemia.

## METHOD

This is a study with a qualitative approach, through an integrative literature review, in which the databases used were: National Library of Medicine (PubMed), Virtual Health Library (VHL) and Directory of Open Access Journals (DOAJ). The descriptors chosen for the search for articles on the platforms were "predictive value", "lactate" and "intestinal ischemia", connected by the Boolean operator "AND" and being possible to find them in the Health Sciences Descriptors (DeCS). The literature review was carried out following the following steps: establishment of the theme; definition of eligibility parameters; definition of inclusion and exclusion criteria; verification of publications in databases; examination of the information found; analysis of the studies found and exposition of the results<sup>9</sup>. In this study, randomized or non-randomized clinical trials and cohort studies and case reports were included, without time cutout. Articles that touched on the topic, articles in which the descriptors were not related, articles of the literature review and meta-analyses type, and articles duplicated between platforms were excluded.

## RESULTS

The search result totaled 74 articles. 48 were found in PubMed, 25 in the VHL and 1 in the DOAJ. With the application of the inclusion and exclusion criteria, 15 remained in PubMed, 04 in the VHL and none in the DOAJ. The selection is schematized in figure 1.

All studies were performed with symptomatic patients, which were suggestive

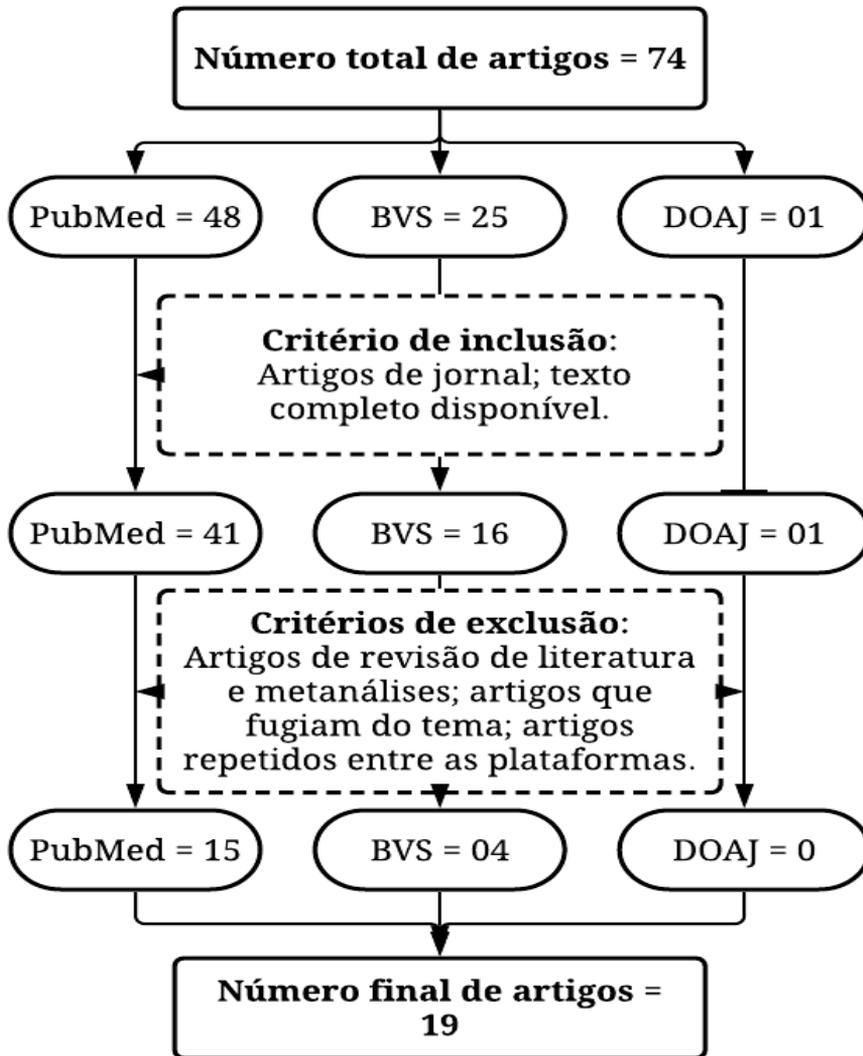


Figure 1. Flowchart of identification and selection of articles selected in PubMed, VHL and DOAJ databases.

Source: Authors (2021).

of intestinal ischemia. Of the 19 studies analyzed, 15 treat lactate as a marker with positive predictive value for the diagnosis of intestinal ischemia. On the other hand, 4 studies suggest that lactate has a Negative predictive value, as outlined in Table 1.

## DISCUSSION

Of the 19 articles studied, 15 showed a positive predictive value for lactate in the diagnosis of intestinal ischemia. It is worth mentioning that the use of biomarkers, whether in the contribution or replacement of diagnostic methods, depends on statistical values, such as pre-test probabilities, and on their interpretation along with the patients' clinical information. According to Treskes N, Persoon AM, van Zanten ARH (2017), the sensitivity and specificity of d-lactate are relatively low, not containing ideal values for diagnosis<sup>29</sup>.

For Block T et al. (2008), the efficacy of lactate and isoenzymes has already been confirmed in different studies, however their high sensitivity and low specificity transforms this common marker for several vascular disorders. Therefore, in emergency situations, lactate, depending on the context of its use, may have low utility. Thus, this information corroborates the result found, where lactate is associated with PPV, even though its sensitivity increases false-positive cases<sup>30</sup>.

Furthermore, according to Assadian A et al (2006), d-lactate is not only useful in cases of intestinal ischemia of evolutionary origin from pre-existing non-surgical pathologies, but also in the postoperative period of patients undergoing vascular surgeries. In their study, twelve surgical patients with aortic pathology had their postoperative follow-up with a serial dose of serum lactate and an enteric endotoxin. In turn, lactate has already been able to assist in the diagnosis of

histologically proven ischemic colitis as early as two hours postoperatively. Demonstrating 100% sensitivity in this sample of patients with a specific type of intestinal ischemia, lactate plays an important role in the PPV of this condition<sup>31</sup>.

Murray MJ, et al, on the other hand, points to lactate as a serological marker with a more significantly negative predictive value, that is, capable of showing true negative cases among all others in the same group. The study conducted by this author included 31 patients and generated a NPV of 96% from its analysis. In this study, only one patient had intestinal ischemia with low lactate levels<sup>28</sup>. This analysis is in line with the results demonstrated by Kilcoyne I, Nieto JE, Dechant JE studied in this article<sup>12</sup>.

In agreement, Shi H et al., in the analysis of their study with two hundred and seventy-two patients diagnosed with acute abdomen, reported the high specificity of lactate for the diagnosis of intestinal ischemia<sup>31</sup>. Therefore, serum lactate levels within the normal range are able to rule out the diagnosis of this vascular involvement, increasing its negative predictive value, information which, finally, supports the data of Heo S, et al.<sup>16</sup> and others<sup>31, 22, 28</sup> articles included in the results of this study.

## CONCLUSION

Lactate is an important diagnostic tool for intestinal ischemia. However, its analysis must be associated with a quality physical examination and anamnesis. It is not possible to use this serological marker alone for the definitive diagnosis of any vascular involvement of the gastrointestinal tract. Once amended, its interpretation must be placed in the individual context of each case. In terms of its high sensitivity, the predominant predictive value of lactate is positive; however, false positive frames can be common.

Author	Year	Sample	Symptoms for Intestinal Ischemia?	Predictive value
Rieser CJ, et al <sup>10</sup> .	2021	305	Sim	Positive
Destek S, et al <sup>11</sup> .	2020	44		Positive
Kilcoyne I, Nieto JE, Dechant JE <sup>12</sup> .	2020	75		Negative
Canfora A, et al <sup>13</sup> .	2019	55		Positive
Canfora A, et al <sup>14</sup> .	2019	55		Positive
Grotelüschen R, et al <sup>15</sup> .	2019	302		Positive
Heo S, et al <sup>16</sup> .	2019	51		Negative
Wang X, et al <sup>17</sup> .	2019	158		Positive
Ferrada P, et al <sup>18</sup> .	2017	127		Positive
Liu D, et al <sup>19</sup> .	2017	63		Positive
Reichert M, et al <sup>20</sup> .	2015	30		Positive
DuBose JJ, et al <sup>21</sup> .	2013	500		Positive
Kintu-Luwaga R, Galukande M, Owori FN <sup>22</sup> .	2013	70		Negative
Sobhian B, et al <sup>23</sup> .	2012	24		Positive
Sommer T, Larsen JF <sup>24</sup> .	2009	10		Positive
Danse EM, et al <sup>25</sup> .	2000	24		Positive
Czerny M, et al <sup>26</sup> .	1997	145		Positive
Jonas J, Schwarz S, Alebrahim-Dehkordy A <sup>27</sup> .	1996	21		Positive
Murray MJ, et al <sup>28</sup> .	1994	31	Negative	

Table 1. Characterization of articles according to year of publication, sample, symptoms of intestinal ischemia and predictive value.

Source: Authors (2021).

It is essential that this and other biomarkers be studied at the molecular level in order to improve their use even more. The democratization of access to imaging exams,

such as computed tomography, can complete the effectiveness of this marker and this, in turn, may be able to be a formal indication for performing such exams.

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