

# Assessing Disease Severity in COVID-19



## Calmark POC - Covid

POC instrument measuring LDH  
- enabling easy and rapid triage of COVID-19 patients

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# 1. Executive Summary

The platform Calmark POC - Covid is an innovative medical diagnostic device based on a unique blood filtering technology allowing efficient, rapid and straightforward measurement of lactate dehydrogenase (LDH).

A large number of consistent scientific research studies have since the spring of 2020 shown that LDH (lactate dehydrogenase) is one of the most important biomarkers for disease assessment. Elevated LDH levels are associated with a 6-fold increase in the risk of serious illness and a 16-fold increase in the risk of mortality<sup>1</sup>. Measurement of LDH has been included in the IFCC guidelines for monitoring COVID-19 patients since October 2020.<sup>2</sup>

Being able to quickly detect elevated LDH values provides the opportunity to identify patients at risk, predict the degree of severity, start treatment and thereby improve the prognosis. Thus, LDH is an important biomarker for an effective triage system of COVID-19 patients. If the biomarker LDH is being measured in an easy and rapid way already at the frontline health unit or at admission, before hospitalization, it will contribute to an improved emergency management supporting correct and fast prioritization, resource efficiency and saving lives.

## 2. Background

The outbreak of Coronavirus disease 2019 (COVID-19), first reported in Wuhan, China, on December 2019, was declared a pandemic by the World Health Organization on the 11th of March 2020.<sup>3</sup> Since then, the COVID-19 has spread all over the world and up to the 15th of April 2021, more than 137 million world citizens have been confirmed infected and three million human beings have been confirmed dead as a result of the infection.<sup>4</sup>

## 3. COVID-19

### 3.1 Symptoms of COVID-19

The most common symptoms of COVID-19 are fever, tiredness and dry cough. The infection can lead to development of pneumonia and in worst case progress to Acute Respiratory Distress Syndrome (ARDS). ARDS is a serious complication and the most common reason of death in these patients.<sup>5-7</sup> It is crucial to promptly identify patients at high risk for developing ARDS and respiratory failure<sup>5,7</sup> which is a challenge for clinicians.<sup>5</sup>

### 3.2 CT as diagnostic tool

Computed tomography (CT) has been used as a marker to detect pneumonia and estimate the pulmonary damage in patients with COVID-19. However, the CT scan has limited availability since healthcare resources have been forced to be prioritized due to limitations.<sup>5,6</sup> In addition, CT scan is not always available worldwide, especially not in small emergency departments.<sup>5</sup> Therefore a more sensitive and a specific disease progression marker of COVID-19 is required.<sup>6</sup>

### 3.3 Health care resources

Due to the rapid increase of COVID-19, healthcare services worldwide is under great pressure and there is a shortage of intensive care resources.<sup>7</sup> Since the healthcare resources is limited it is urgent to find a routine laboratory biomarker that is sensitive and specific, and to fast and early be able to predict and assess the severity of the disease and potentially reduce the mortality rate in COVID-19 patients.<sup>5-7</sup> This is especially important in departments worldwide where CT scan is not available.<sup>5</sup> It would also enable the healthcare to allocate resources and make earlier clinical interventions and monitoring which would lead to improved outcomes.<sup>1</sup>

## 4. LDH - the Biomarker

### 4.1 Lactate dehydrogenase (LDH)

LDH is an intracellular enzyme involved in energy production and is found in almost every cell in the body. When body tissue is damaged, due to for example disease or injury, LDH is released from the cells into the blood. Thus, elevated LDH levels can be used as an indicator of tissue damage in pulmonary disorders such as pneumonia.<sup>1, 5-7</sup> Since LDH is a non-specific biomarker it is not possible to identify the underlying cause of disease just by measuring LDH alone. But in combination with other blood tests, it is a great biomarker to be used for evaluation.<sup>5,6</sup>

### 4.2 LDH as a predictive factor

Several published studies show that if elevated LDH levels can be detected at an early stage of COVID-19 infection, there is a greater chance to identify patients at risk, predict the severity and begin clinical intervention and monitoring. In this way, the prognosis improves and the possibility of recovery increases among the patients.<sup>1,5-7</sup> It has been shown that patients with elevated LDH are at >6 fold increased risk to develop severe disease and a >16 fold increased odds of mortality.<sup>1</sup> LDH in combination with CRP, has at an early stage been proven useful in identifying patients at high risk of developing acute respiratory failure.<sup>5</sup> It has also been validated that increasing and decreasing LDH is in line with results from radiographic deterioration or improvement of the disease.<sup>6</sup> Thus, LDH is an important biomarker for rapid triage of patients with COVID-19.<sup>1,5-8</sup> In patients with severe pulmonary disease, the increase of LDH is significant and therefore one of the most important biomarkers to prove the prognostic of injury.<sup>7</sup>

In addition, it is already known that LDH rises and is associated with poorer outcomes in patients with other respiratory infections. Among other things, it was shown in the previous coronavirus outbreak SARS (Severe Acute Respiratory Syndrome) and also in MERS (Middle East Respiratory Syndrome) that LDH levels are elevated in patients with confirmed infection.<sup>1</sup>

LDH has proven to be a good predictor for disease development, even in patients without obvious respiratory problems. These patients can therefore benefit from early hospitalization and closer observation so that they can be treated correctly.<sup>5</sup>

Poggiali et al. (2020) and Henry et al. (2020) state in their articles, that were published in *Clinica Chimica Acta* and *American Journal of Emergency Medicine*, that larger studies are needed to confirm the findings, and, in the meantime, it is suggested that LDH levels should be used as an important biomarker in determining prognosis in patients with COVID-19.

In October 2020, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) published their Interim Guidelines on biochemical/hematological monitoring of COVID-19 patients.<sup>2</sup> Lactate dehydrogenase (LDH) emerges as one of the most consistently elevated markers in patients infected with COVID-19 at higher risk of developing adverse outcome.

## 5. References

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