

suPARcharging triage

Empowering clinical

decisions



About us

ViroGates A/S is an international medical technology company. We develop and market blood test products under the suPARnostic[®] brand for better triaging in hospitals to improve patient care, reduce healthcare costs and empower clinical staff.

The products are primarily used in emergency departments in hospitals for risk stratification of acute medical patients to improve clinical decisions on discharge and hospitalization.

ViroGates' suPARnostic[®] product range measures the protein suPAR (soluble urokinase Plasminogen Activator Receptor). The protein is naturally occurring in human blood and reflects the immune system's activation level. A patient's suPAR level predicts negative outcomes such as short-term mortality across acute and chronic diseases.

The suPARnostic[®] tests are easily integrated into existing hospital workflows and instruments, and the results are available in minutes.

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The suPAR biomarker predicts critical illness across diseases by measuring the level of activation of the immune response.

suPARnostic[®] is a reliable prognostic tool that enables healthcare professionals to make quick and informed patient triaging decisions in emergency departments.

suPAR in acute care - Anonymous patient story

Miss Thompson, a retired bookkeeper, lives alone with her cat "Major Tom". Her husband died several years ago, but at age 73 she enjoys life and all her hobbies. One morning in February, she wakes up feeling all bad. Her stomach hurts, the head aches, and she has difficulty breathing. She feels like staying in bed, but the meowing of her cat gets her on her feet. The dizziness almost makes her faint, but she gets to the kitchen. While bending over to feed the cat, she loses control and stumbles onto the floor. She gets back up and calls an ambulance.

At the emergency department, she is triaged by a handsome doctor to orange, based on her vital signs. For the decision of whether miss Thompson should have further clinical investigations or can be sent home, blood is taken and sent to the lab. The circulating biomarkers which are easily measured in blood, give information about organs, presence of disease, and disease severity.

In emergency medicine, the use of biomarkers has changed the approach of diagnosis and treatment procedures. Biomarkers are pivotal in clinical decision making where they help in diagnosis as well as in prognosis and for improving physicians' admission or early discharge decisions. Traditionally, specific biomarkers for e.g. cardiac disease or organ disease have been measured. But in recent years, emergency medicine physicians are becoming accustomed to the use of biomarkers that may lack specificity for any one particular condition, but provide important prognostic information.

An example of this is lactate, and its interpretation has become an important skill for emergency physicians. And more recently, suPAR has been introduced as a stronger non-specific prognostic biomarker in the acute care setting.

Now, to get back to Miss Thompson, she had a high level of the biomarker CRP and her blood sugar was somewhat elevated, but her other organ markers were fine. Her su-PAR level was low for her age and condition. Miss Thompson was, therefore, discharged after having some fluids, a prescription for antibiotics and a note to talk to her general practitioner about her elevated blood sugar. Her cat would have been strung out if miss Thompson had had a high suPAR as this would have pointed towards a sepsis development which could require admission and intravenous antibiotics. We improve patient outcomes and reduce healthcare costs by suPARcharging triage

Seamlessly implemented by clinicians and laboratory technicians, suPARnostic[®] products fit existing workflows in hospitals, are approved for all the major clinical chemistry analyzers, and delivers results in minutes.

Introduction - suPAR in triage

suPAR (soluble uPAR) is a protein measurable in blood. The concentration of suPAR reflects the level of immune activation and chronic inflammation. All humans have a suPAR baseline level which increases slightly with age.

Typically, healthy individuals have a suPAR level of 2-3 ng/mL. An unhealthy lifestyle, in particular smoking, can add an extra nanogram. The suPAR blood level is highly stable with no diurnal variation and no changes following fasting. The suPAR level reflects the individual's level of chronic inflammation and the ability of the immune system to cope with the disease.

A high suPAR level > 6 ng/mL indicates disease presence and progression to severe disease and supports further clinical attention. In contrast, in patients with low su-PAR level < 4 ng/mL the immune system is well functioning in combatting disease and these patients have a good prognosis, e.g. low risk of readmission and progressing to severe illness. Therefore, a low suPAR level indicates a good prognosis and supports the decision to discharge the patient. *"It is essential to have the help of biomarkers, such as suPAR, which can support the discharge decision"*

Juan González del Castillo, Dr PhD, Hospital Clínico San Carlos, Spain

The suPAR level can be used for triage in the hospital's emergency department and measured using the suPARnostic[®] products, the only CE-IVD certified product range applied for clinical determination of suPAR.

By using suPARnostic[®] in the triage process, emergency department crowding is reduced. suPARnostic[®] can identify 22% more patients that can be sent home without hospitalization and help to avoid unnecessary treatments and readmissions.

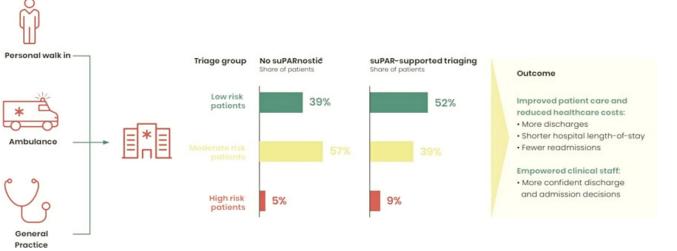
<u>Availability of suPAR in emergency departments may improve risk stratification: a secondary analysis of the TRIAGE III trial.</u> <u>Schultz et al. Scand J Trauma Resusc Emerg Med 27, 43 (2019).</u>

Evaluation of Plasma Soluble Urokinase Plasminogen Activator Receptor Levels in Patients With COVID-19 and Non-COVID-19 Pneumonia: An Observational Cohort Study. Dimitrios Velissaris et al. Clin Med Res. 2021.



Empowering clinical decisions

Compared to standard of care emergency department triage practices, suPAR-guided triage can help identify 13% more low-risk patients, reduce the moderate risk category by 18% and identify 4% more high-risk patients. Identifying these groups of patients more accurately and ensuring the right clinical decision early on in the emergency department, saves critical resources and allocates more clinical care to those who need it.



In studies of the prognostic value of suPAR in acute medical patients, suPAR has been shown to add significant independent value to currently used markers (clinical scoring systems, demographics, other biomarkers) in the prediction of patient outcomes. This means that suPAR-supported triage empowers healthcare professionals to make better informed clinical decisions.



Implementing suPAR in the emergency department improves efficiency and reduces healthcare costs by discharging more lowrisk patients and bringing attention to highrisk patients.



suPAR levels < 4 ng/mL indicate low risk

These patients' immune defence system copes well with their disease and they can therefore be categorized as low-risk patients. A suPAR level < 4 ng/mL, therefore, supports a discharge decision. Identifying more lowrisk patients who can be discharged early on reduces emergency department crowding. Also, it benefits the patients as unnecessary admission can lead to muscle loss, hospital acquired infections and may cause domestic household challenges.

suPAR levels between 4 and 6 ng/mL

A suPAR result between 4-6 ng/mL is of value because the hospital staff will now know that this is not a low-risk or a high-risk patient.

suPAR levels > 6 ng/mL indicate high risk

suPAR levels > 6 ng/mL indicate high risk and support an admission decision. These patients are not coping well with their disease and are severely ill or likely to develop severe illness. The risk of mortality is typically 20-30 fold higher than patients with suPAR < 4 ng/mL. Identifying more high-risk patients allows timely allocation of clinical care to those in high need.

Combining National Early Warning Score With Soluble Urokinase Plasminogen Activator Receptor (suPAR) Improves Risk Prediction in Acute Medical Patients: A Registry-Based Cohort Study. Rasmussen et al. Critical Care Medicine.

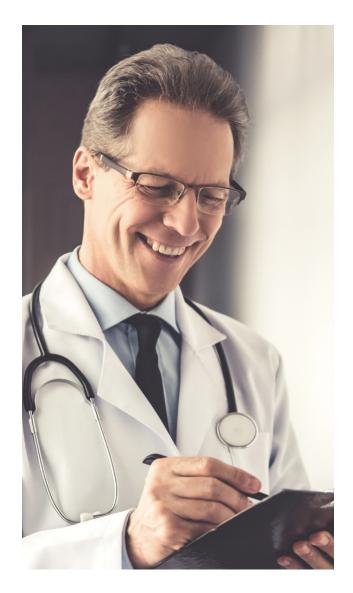
suPAR cut-offs for risk stratification in patients with symptoms of COVID-19

During the COVID-19 pandemic, there has been a high need for research into biomarkers that early can identify patients who will or will not progress to severe disease such as respiratory failure.

suPAR has emerged as a very strong marker of COVID-19 disease progression.

The same cut-offs as used in triage of acute medical patients were also tested for COV-ID-19 patients. The result found was that patients with symptoms of COVID-19 and suPAR < 4 or > 6 ng/mL have low or high risk, respectively, concerning the need for mechanical ventilation or mortality. Therefore, suPAR cut-offs of < 4 or > 6 ng/mL are suggested to identify risk groups in patients presenting to the emergency department with symptoms of or confirmed COVID-19.

The ability of suPAR of being able to early identify high-risk COVID-19 patients, led to the use of suPAR as an inclusion biomarker in a randomized controlled trial (SAVE MORE) where the intervention was blocking of the IL-1 receptor with anakinra to prevent the hyper inflammation patients often develop when having high suPAR. It makes good sense to only intervene in a central innate immune pathway when patients have a high level of immune activation. The trial showed strong results of COVID-19 disease progression.



suPAR Cut-Offs for Risk Stratification in Patients With Symptoms of COVID-19. Izzet Altintas et al. SAGE journal.

Early treatment of COVID-19 guided by soluble urokinase plasminogen receptor plasma levels: a double-blind,

randomized controlled phase 3 trial. Kyriazopoulou E et al. Nat Med. 2021.

Results

The study showed a significant reduction in the number of patients who developed severe disease or died and a significantly faster recovery in patients who received the IL-1 inhibitor compared to placebo.

The suPAR-guided anakinra treatment in COVID-19 patients was approved by the European Medical Agency (EMA) in December 2021. By implementing suPAR, the hospitals will be better prepared in the likely event that a new wave of COVID-19 hits the world.



"It is not true that variants will get less virulent over time – their evolution is unpredictable. This is not the time to let up and cut resources. It's vital to anticipate the worst-case scenario instead of just hoping it won't occur. We'd all be relieved if everything calmed down following the wave of different BA. Variants that are cropping up around the world now. Let's not pretend this is over or we're at some illusory "endemic" steady state. Beyond preempting the human toll, any further investment in preparedness would be worthwhile when one considers: The pandemic has also been responsible for a 6.5% drop in gross domestic product globally in 2020 and is projected to cause a total economic loss worldwide of US\$ 28 trillion by 2025." We have the tools and ingenuity to get ahead of this virus rather than consistently trail behind it."

Eric Topol, Ground Truths 2022

suPAR cut-offs for stratification of low, medium, and high-risk acute medical patients in the emergency department

Conclusion

suPAR cut-offs of 6 ng/mL can identify acute medical patients with low, medium, or high risk of 30- and 90-day mortality. The suPARnostic[®] products provides fast suPAR results that may aid in the decision of discharge or admission of acute medical patients.

suPAR is a biomarker of risk in unselected acute medical patients as it is an unspecific marker elevated by diseases in general. The severity of the disease informs the clinicans of the progression of disease (prognostic). suPAR has prognostic value in patients both without comorbidities as well as in patients with comorbidities.

Results

A total of 1747 acute medical patients in the Emergency Department were included, with a median age of 70.

Statistical analysis showed that suPAR, independently of age, sex, and CRP levels, predicted 30- and 90-day mortality. suPAR was measured using the suPARnostic Turbilatex assay.



At 90-day follow-up:

Patients with suPAR < 4 ng/mL

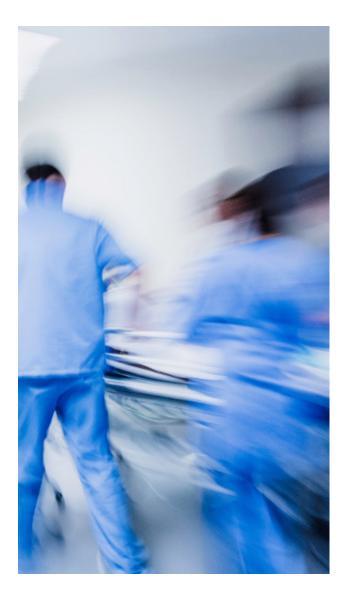
- NPV of 99.0%
- Sensitivity of 94.2%

Patients with suPAR > 6 ng/mL

- PPV of 20.1%
- Specificity of 78.7%

suPAR cut-offs for stratification of low, medium, and high-risk acute medical patients in the emergency department. Seppälä Santeri et al. BMC Emergency Medicine.

Reasons to implement suPAR in the emergency department



Implementing suPAR in clinical care improves patient management:

- More efficient triage
- Better patient outcomes
- Faster and safer patient discharges
- Reduced healthcare costs
- Avoids unnecessary admissions
- Lowers hospital length of stay

suPAR is a prognostic biomarker that provides independent and additional information on patient prognosis.

This enables healthcare professionals to make faster and better-informed acute patient triaging decisions in hospital emergency departments.

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