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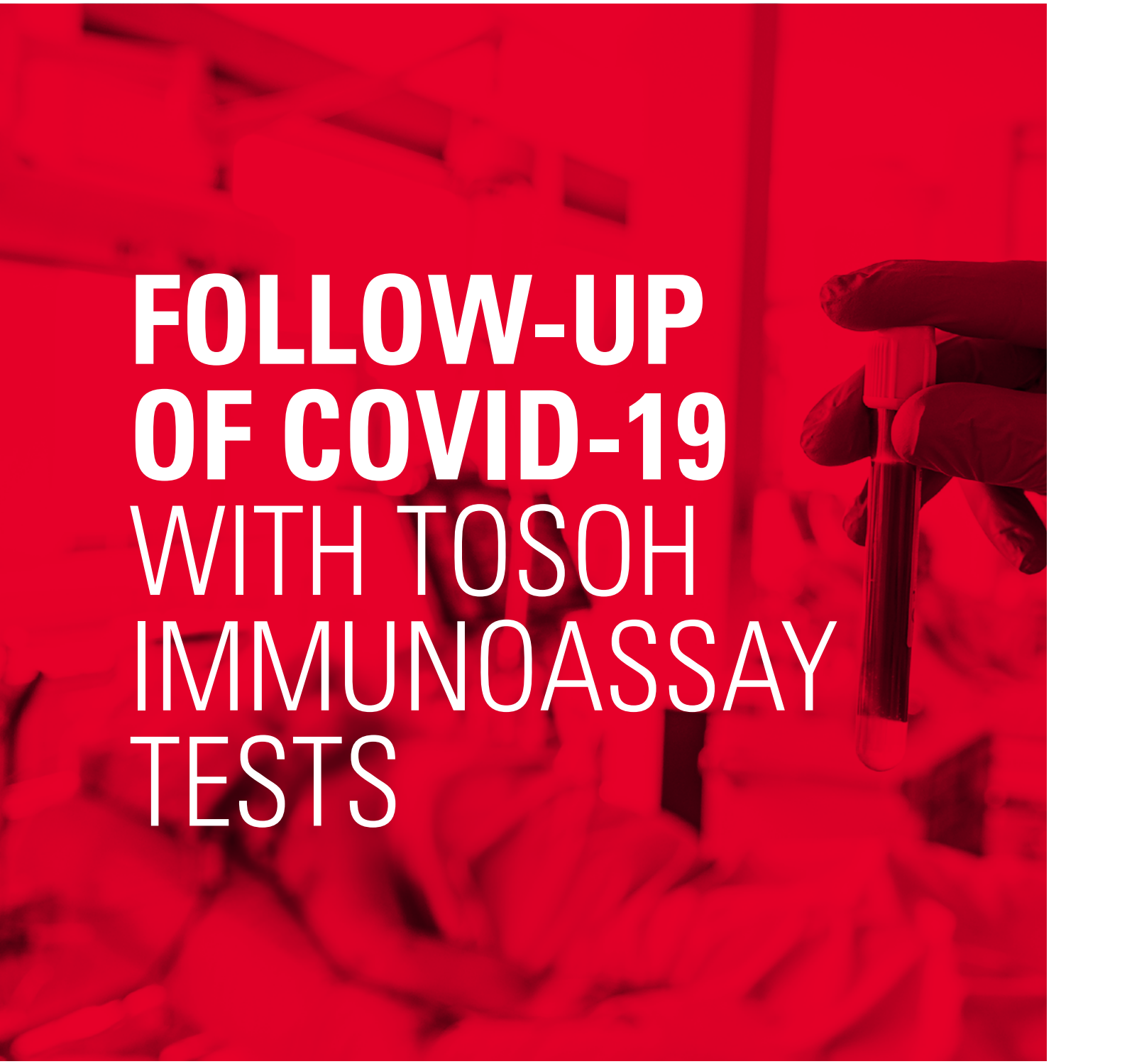

FOLLOW-UP OF COVID-19 WITH TOSOH IMMUNOASSAY TESTS

TOSOH BIOSCIENCE

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FOLLOW-UP OF COVID-19 WITH TOSOH IMMUNOASSAY TESTS

With a number of vaccination strategies now being rolled out over the world, the pandemic SARS-CoV-2 may appear to be under control. However, the prospect of persistent and seasonal COVID-19 is real[1]. This means that the follow-up of patients will still be needed for the considerable future.

Tosoh's immunoassay analysers offer a substantial number of test that allow a fast, sensitive and easy way to assess and monitor COVID-19 patients.

Scientists and clinicians are drowned in publications about the SARS-CoV-2 virus and COVID-19 disease; by February 2021 over 87,000 scientific papers have been published on the subject of COVID-19[2] and this number is increasing every day. This brochure intends to give a comprehensive overview of clinical laboratory tests that can be used in the follow-up of the disease and to assess the outcome for the patients.

TABLE OF CONTENTS

PITUITARY, ADRENAL, THYROID AND GONADAL BIOMARKERS

Reviewing several publications, Ponti et al.[3] highlight the following biomarkers playing a role during SARS-CoV-2 infection:

- Haematological (lymphocyte count, neutrophil count, neutrophil–lymphocyte ratio (NLR))
- Inflammatory (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin (PCT))
- Immunological (Interleukin 6 (IL-6))
- Biochemical (**D-dimer, Troponin**, creatine kinase (CK), aspartate aminotransferase (AST))
- Especially those related to coagulation cascades in disseminated intravascular coagulation (DIC) and acute respiratory distress syndrome (ARDS).

New laboratory biomarkers could such as **Homocysteine** and angiotensin II could play a significant role.

At the beginning of the pandemic, the endocrine involvement with COVID-19 remained largely unexplored. This started to change when Pal and Banerjee[4] stated *that as premature as it may sound, endocrinologists need to be aware of these possibilities in clinical practice, especially while dealing with COVID-19 survivors.*

In this context Bellastella et al[5] refer to the unknown impact of the SARS-CoV-2 infection on subclinical thyroid conditions **(free thyroid hormones and TSH)** that would allow early diagnosis, appropriate therapy and help avoid more severe complications. Timely screening for pituitary–adrenal axis function **(PTH, ACTH, Cortisol**) and identification of this condition could allow adequate replacement therapy avoiding severe shock.

Somasundaram et al[6] reviewed the literature looking for endocrine pathologies. The table below is a simplified summary.

PATHOLOGY	EFFECT ON HORMONAL AXIS	MANAGEMENT ISSUES AND SOLUTIONS
PITUITARY		
Central hypocortisolism and hypothyroidism	Impaired **ACTH/Cortisol** production	Measurement of **ACTH and Cortisol**
	Low thyroid hormones, sometimes low TSH	**TSH and Free T4** measurement If deficient, hormone replacement in physiological doses
Hyperprolactinemia	Transient hyperprolactinemia	**Prolactin** levels maybe high during acute illness
ADRENAL		
Hypoadrenalism	Hypocortisolism	Serum 9 AM **Cortisol** measurement
THYROID		
Hypothyroidism	Primary hypothyroidism	High **TSH** and low **free T4** Thyroxine replacement
	Sick euthyroidism	Difficulty in differentiating during acute illness, test **TSH and free T4** following recovery
	Central hypothyroidism	Low **TSH and free T4**
GONADAL		
Hypogonadism	Impaired spermatogenesis and androgen synthesis	Follow-up after recovery from acute infection

VITAMIN D

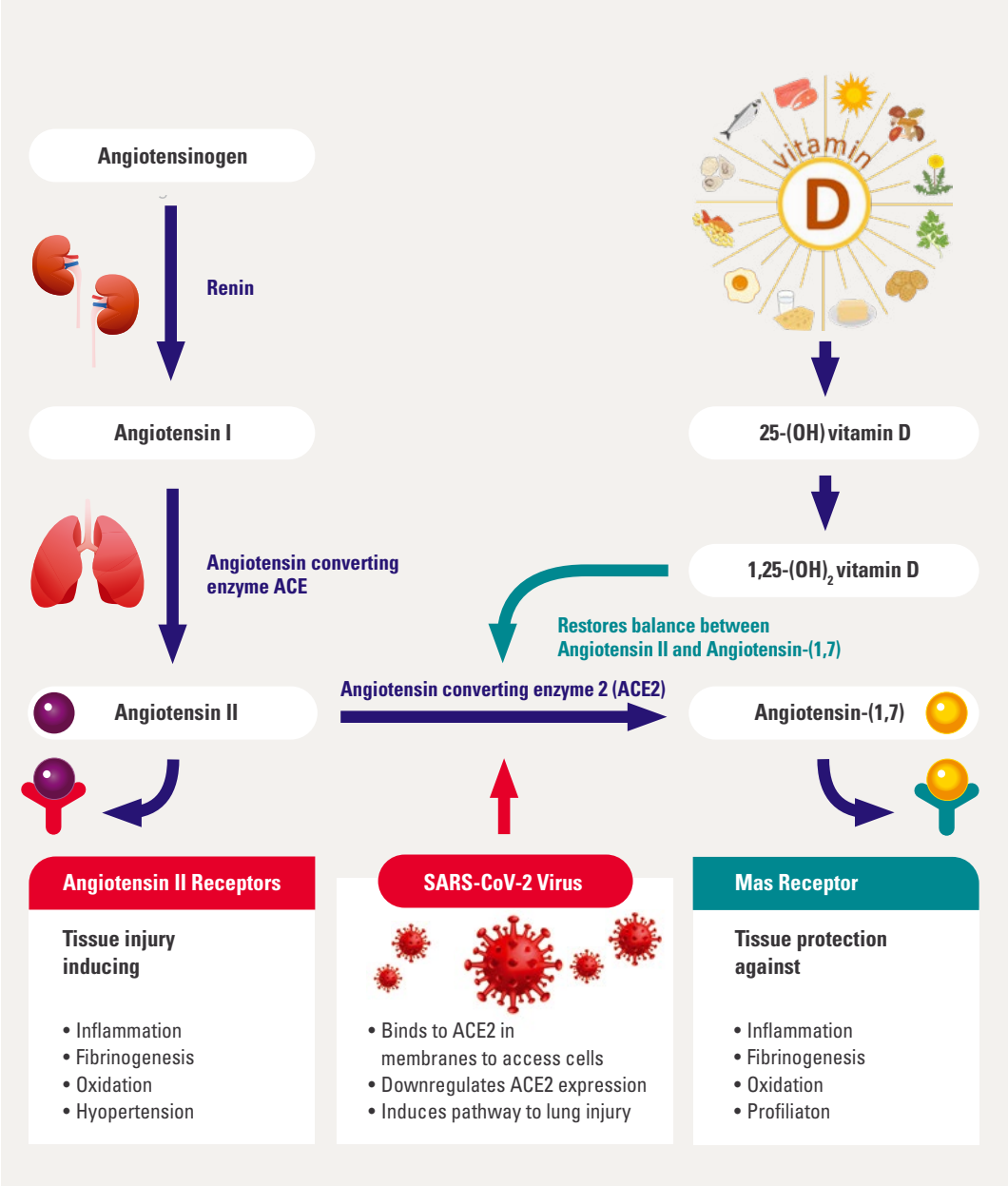
Weir et al[7] state that T regulatory lymphocyte levels have been reported to be low in many COVID-19 patients and can be increased by **vitamin D** supplementation. Low **vitamin D** levels have been associated with an increase in inflammatory cytokines and a significantly increased risk of pneumonia and viral upper respiratory tract infections. Vitamin D deficiency is associated with an increase in thrombotic episodes, which are frequently observed in COVID-19. Vitamin D deficiency has been found to occur more frequently in patients with obesity and diabetes. These conditions are reported to carry a higher mortality in COVID-19.

Lanham-New et al[9] strongly endorse avoidance of **vitamin D** deficiency in the population and complete adherence to government's advice worldwide on the prevention of the spread of COVID-19, while Aygun[10] states that COVID-19 infection-induced multiple organ damage might be prevented by **vitamin D**.

In the same way Carpagnano et al[11] write that severe **vitamin D deficiency** may be a marker of poor prognosis in these patients, suggesting that adjunctive treatment might improve disease outcomes.

ACCURATE MEASUREMENT OF VITAMIN D CAN PREDICT THE SUSCEPTIBILITY TO AND THE PROGRESS OF THE COVID-19 DISEASE

Somasundaram et al[6] and Zwart et al[8] describe a postulated mechanism of Vitamin D in the prevention of COVID-19.



FERRITIN

Elevated **Ferritin** levels have been reported in some cases of COVID-19 (Da et al[12]). According to Feld et al[13] many patients with COVID-19 present with hyperferritinaemia, but elevated ferritin levels are not accurate predictors of outcomes and do not appear to be indicative of disease outcome. This is however countered by Colafrancesco et al[14].

In a more recent review, Kappert et al[15] conclude that serum **Ferritin** may be considered both a prognostic and stratifying biomarker that can also contribute to therapeutic decision-making concerning patients with COVID-19.

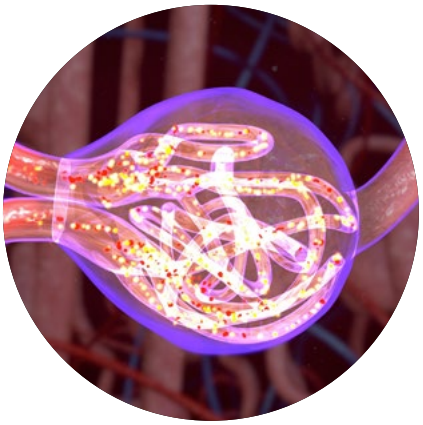
While trying to biologically profile COVID-19 patients Khourssaji et al[16] concluded that **Ferritin** is increased in 92% of male and female COVID-19 patients.

EVIDENCE IS INCREASING IN THE LITERATURE FOR FERRITIN AS BEING AN EARLY MARKER OF SEVERITY IN COVID-19 PATIENTS

CYSTATIN C

Cystatin C was found to be significantly elevated in some COVID-19 patients (Wei et al.[17]).
Serum Cystatin C was significantly higher in imaging progression patients compared to those in imaging progression-free ones (Yang et al[18]).

Among other biomarkers, **Cystatin C** was significantly increased in 82 survivors and 25 non-survivors with COVID-19 (Ouyang[19]).

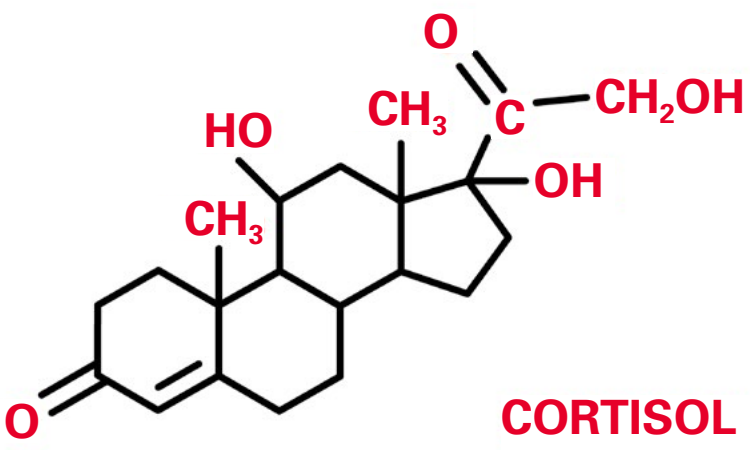


AMONG OTHER MARKERS, CYSTATIN C CAN BE MEASURED TO ASSESS THE SEVERITY OF COVID-19 DISEASE

CORTISOL

The impact of SARS-CoV-2 infection on the pituitary–adrenal axis function has already been demonstrated by Bellastella et al[5] and Somasundaram et al[6].

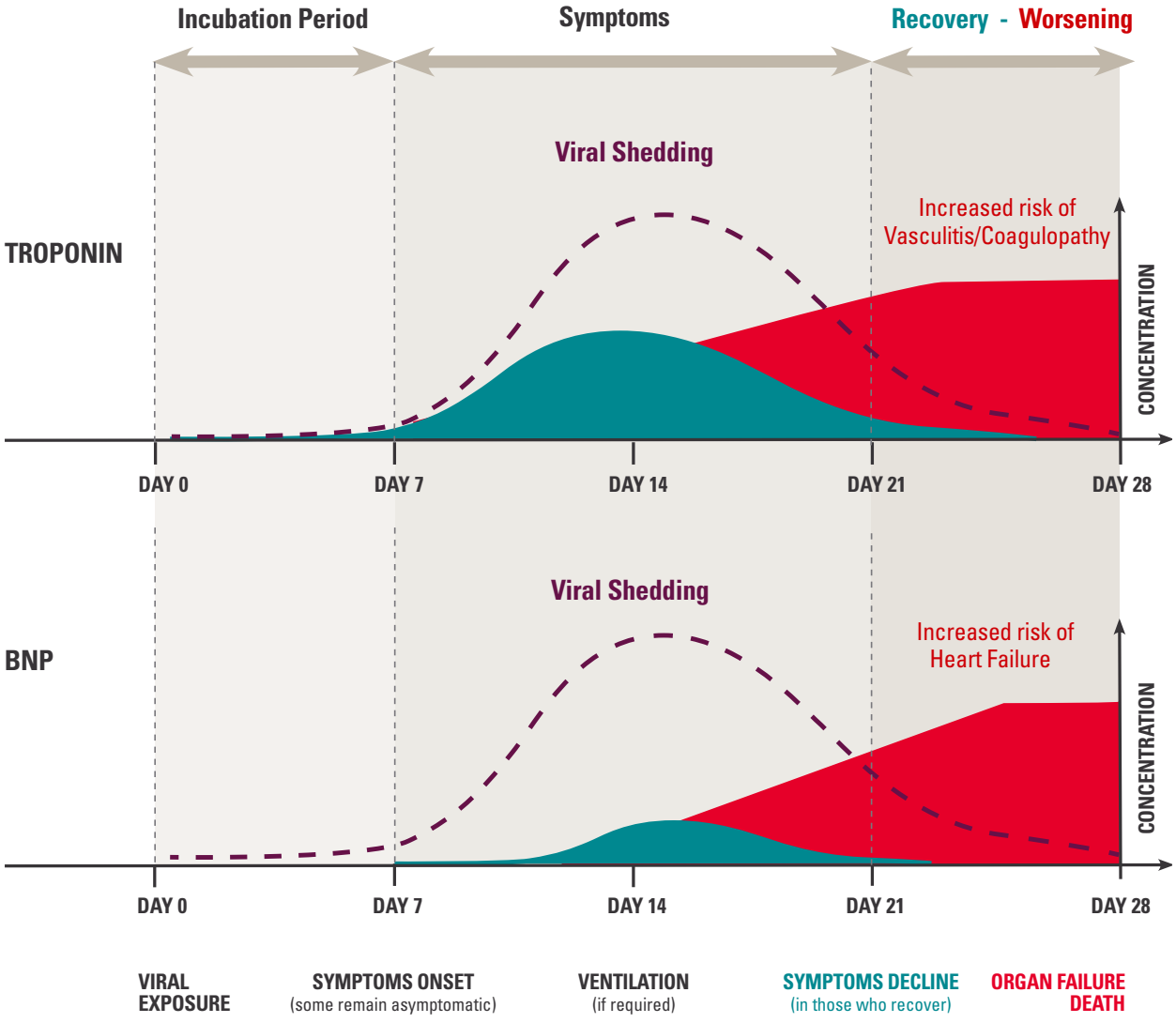
Tan et al[20] found that high **Cortisol** concentrations were associated with increased mortality and a reduced median survival, probably because this is a marker of the severity of illness, although highly debated by Choy[21].



ALTHOUGH RESULTS SHOULD BE INTERPRETED WITH CARE, CORTISOL CAN BE A PREDICTOR OF COVID-19 MORTALITY

CARDIOVASCULAR MARKERS

Lippi et al[22] conclude from a literature review that Troponin I **(cTnI)** values are significantly increased in patients with severe SARS-CoV-2 infection compared to those with milder forms of disease. They hypothesize that initial measurement of cardiac damage biomarkers immediately after hospitalization for SARS-CoV-2 infection, as well as longitudinal monitoring during hospital stay, may help identify a subset of patients with possible cardiac injury and thereby predict the progression of COVID-19 towards a worse clinical picture.



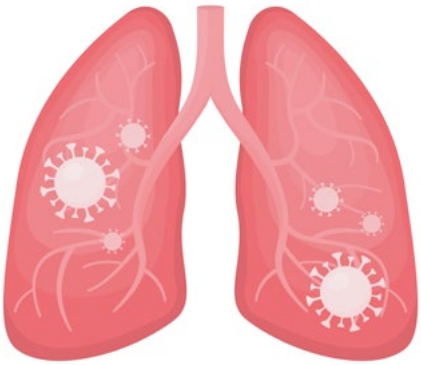
Guzik et al[23] discuss the impact on COVID-19 on cardiovascular complications. Among other recommendations, they state that *"evaluation of cardiac damage (particularly **cTnI** levels) immediately after hospitalization for COVID-19, as well as monitoring during the hospital stay, may help in identifying a subset of patients with possible cardiac injury and thereby predict the progression of COVID-19 complications."*

In their literature review Azevedo et al[24] conclude that myocardial injury is a factor of poorer prognosis and is directly associated with a higher mortality in COVID-19. Thus, making it imperative to implement a thorough screening through measurement of troponin.

Liu et al[25] reviewed the complications of COVID-19 for the cardiovascular system. **Troponin and BNP** may play a role in the assessment of the patient.

CARDIOVASCULAR MARKERS SUCH AS TROPONIN I AND BNP ARE IMPORTANT TO MONITOR THE FURTHER DEVELOPMENT OF SEVERELY ILL COVID-19 PATIENTS

PRESEPSIN AND SEPSIS



In a manner similar to sepsis, a dysregulated immune response is responsible for a cascade of events occurring in severe COVID-19 cases.
This results in a dynamic process that leads to the activation of the adaptive immune system including T lymphocytes and B lymphocytes, which can ultimately lead to cell and tissue necrosis and multiorgan organ dysfunction (Wiersinga et al[26], Zafer[27]).

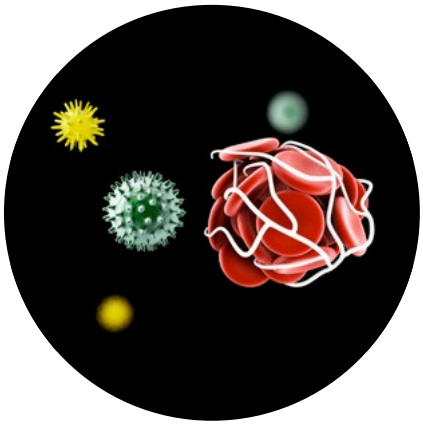
Zaninotto et al[28] provide data that seem to demonstrate the role of Presepsin in providing prognostic information in COVID-19 patients, allowing to identify during the early phase of the monitoring, the patients suffering from a more severe disease which will be hospitalized for a prolonged time.

Similarly the findings of Fukada et al[29] show that Presepsin has potential as a biomarker for severe COVID-19 pneumonia.

Fukuda et al[43] describe a few cases showing where Presepsin increased immediately following elevation of CRP in the moderate-to-severely ill COVID-19 patients, resulting in invasive mechanical ventilation with exacerbation of COVID-19 pneumonia.

PRESEPSIN IS AN IMPORTANT TEST TO DETECT THE EARLY ONSET OF SEPSIS IN SARS-COV-2 INFECTIONS

D-DIMER AND COAGULATION



Since the onset of the SARS-CoV-2 pandemic an elevated D-dimer at admission (≥1.0 µg/mL) is associated with an increased mortality with remarkably high odds ratio of 18.42 (95% CI 2.64-128.55), and D-Dimer continues to rise throughout the course of hospitalization in non-surviving patients (Zhou et al[30]).

Based on a meta-analysis of 35 publications, Bao et al[31] conclude that D-Dimer among other laboratory parameters provide valuable signals for preventing the deterioration of the disease.

Zhang et al[32] describe that D-dimer on admission greater than 2.0 µg/mL (fourfold increase) could effectively predict in-hospital mortality in patients with Covid-19. This indicates D-dimer could be an early and helpful marker to improve management of Covid-19 patients.

There is a strong association between high D-dimer values, thrombosis and the presence of Lupus Anticoagulant early in the COVID-19 course (Helms et al[33]).

Although based on a small number of observations, Ranucci et al[34] observed that D-dimer values were higher than the upper limit of the normal range in all their COVID-19 patients.

Oudkerk et al[35] conclude that for all intensive care patients with proven COVID-19, D-dimer could be the dichotomous test for those at increased risk of thrombotic complications versus those that have a good prognosis.

MEASUREMENT OF D-DIMER HAS BECOME OF EXTREME IMPORTANCE TO ASSESS THE SEVERITY OF COVID-19 AND MANAGEMENT OF THE AFFECTED PATIENTS

KL-6

Xue et al[36] state that KL-6 could be an indicator to evaluate the progression of COVID-19, which is parallel to the level of lung injury and inflammation in patients. Moreover, it can also reflect the pulmonary ventilation function.

Nakamura et al[37] describe two cases which indicate that serum KL-6 levels are a useful non-invasive tool to discern COVID-19-related acute respiratory distress syndrome phenotypes and predict their prognosis.

Also Awano et al[38] observed that serum KL-6 levels were significantly elevated in severe COVID-19 and is useful for evaluating its severity. A similar observation was done by d'Alessandro et al[39].

	Severe cases (n=14)	**Non-severe cases** (n=40)	**p value**
KL-6 (U/mL)	1,125 (495-2,034)	316 (210-398)	< 0.0001

Patient body temperature and KL-6 were associated with the presence of Computer Tomography (CT) infiltrates. Infiltrate volume, percent lung involvement and consolidation were associated with subsequent development of COVID-19 symptoms (Varble et al[40]).

Findings from Deng et al[41] support KL-6 as a biomarker of COVID-19 severity and also a predictor of the prognosis of lung injury of discharged patients. The dynamic profile of KL-6 was closely correlated to coagulation disorder and immune dysfunction, especially among severe/critical patients, highlighting the possibility that coagulation disorder and immune dysfunction may be a contributor to lung injury of COVID-19.

Even when based on a relatively small number of patients, the data of Scotto et al[42] suggest the evidence of a major role played by KL-6 in predicting survival of patients with SARS-CoV2 interstitial lung disease.

Peng et al[44] conclude that, given a potential role of antifibrotic therapy in preventing fibrosis after SARS-CoV-2 infection, maybe antifibrotic therapies could be performed to further evaluate the treatment effectiveness according to the value of serum KL-6 in the early stage of COVID-19 disease.

KL-6 IS MORE AND MORE SHOWING TO BECOME AN EVER MORE IMPORTANT VARIABLE IN THE ASSESSMENT OF COVID-19 AS IT REFLECTS THE STATUS OF THE PATIENTS' LUNG FUNCTIONALITY IN AN EARLY STAGE

REFERENCES

1 Murray CJL, Piot P. The Potential Future of the COVID-19 Pandemic: Will SARS-CoV-2 Become a Recurrent Seasonal Infection? JAMA. Published online March 03, 2021. doi:10.1001/jama.2021.2828

2 Grabmeier J, 2021, More than 87,000 scientific papers on coronavirus since pandemic (2021, February 23) https://medicalxpress.com/news/2021-02-scientific-papers-coronavirus-pandemic.html

3 Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Crit Rev Clin Lab Sci. 2020;57(6):389-399. doi:10.1080/10408363.2020.1770685

4 Pal R, Banerjee M. COVID-19 and the endocrine system: exploring the unexplored. J Endocrinol Invest. 2020;43(7):1027-1031. doi:10.1007/s40618-020-01276-8

5 Bellastella G, Maiorino MI, Esposito K. Endocrine complications of COVID-19: what happens to the thyroid and adrenal glands?. J Endocrinol Invest. 2020;43(8):1169-1170. doi:10.1007/s40618-020-01311-8

6 Somasundaram NP, Ranathunga I, Ratnasamy V, et al. The Impact of SARS-Cov-2 Virus Infection on the Endocrine System. J Endocr Soc. 2020;4(8):bvaa082. Published 2020 Jul 2. doi:10.1210/jendso/bvaa082

7 Weir EK, Thenappan T, Bhargava M, Chen Y. Does vitamin D deficiency increase the severity of COVID-19?. Clin Med (Lond). 2020;20(4):e107-e108. doi:10.7861/clinmed.2020-0301

8 Zwart SR, Smith SM. Vitamin D and COVID-19: Lessons from Spaceflight Analogs. J Nutr. 2020 Jul 25:nxaa233. doi: 10.1093/jn/nxaa233. Epub ahead of print. PMID: 32710111; PMCID: PMC7454737.

9 Lanham-New SA, Webb AR, Cashman KD, et alVitamin D and SARS-CoV-2 virus/COVID-19 diseaseBMJ Nutrition, Prevention & Health 2020;3:doi: 10.1136/bmjnph-2020-000089

10 Aygun H. Vitamin D can prevent COVID-19 infection-induced multiple organ damage. Naunyn Schmiedebergs Arch Pharmacol. 2020;393(7):1157-1160. doi:10.1007/s00210-020-01911-4

11 Carpagnano GE, Di Lecce V, Quaranta VN, et al. Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory failure due to COVID-19 [published online ahead of print, 2020 Aug 9]. J Endocrinol Invest. 2020; 1-7. doi:10.1007/s40618-020-01370-x

12 Da BL, Mitchell RA, Lee BT, et al. Kinetic patterns of liver enzyme elevation with COVID-19 in the USA [published online ahead of print, 2020 Jun 2]. Eur J Gastroenterol Hepatol. 2020;10.1097/MEG.0000000000001792. doi:10.1097/MEG.0000000000001792

13 Feld J, Tremblay D, Thibaud S, Kessler A, Naymagon L. Ferritin levels in patients with COVID-19: A poor predictor of mortality and hemophagocytic lymphohistiocytosis [published online ahead of print, 2020 Aug 13]. Int J Lab Hematol. 2020;10.1111/ijlh.13309. doi:10.1111/ijlh.13309

14 Colafrancesco S, Alessandri C, Conti F, Priori R. COVID-19 gone bad: A new character in the spectrum of the hyperferritinemic syndrome?. Autoimmun Rev. 2020;19(7):102573. doi:10.1016/j.autrev.2020.102573

15 Kappert K, Jahi A, Tauber R, Assessment of serum ferritin as a biomarker in COVID-19: bystander or participant? Insights by comparison with other infectious and non-infectious diseases, Biomarkers, 2020; 25:8, 616-625, DOI: 10.1080/1354750X.2020.1797880

16 Khourssaji M, Chapelle V, Evenepoel A, Belkhir L, Yombi J, van Dievoet M et al, A biological profile for diagnosis and outcome of COVID-19 patients. Clinical Chemistry and Laboratory Medicine (CCLM), vol. 58, no. 12, 2020, pp. 2141-2150. https://doi.org/10.1515/cclm-2020-0626

17 Wei XY, Jing D, Jia B, Li Q, Zhou XQ, Gong MF, Zou JB, Zhang Q, Huang WX, Tian WG. Characteristics of in peripheral blood of 70 hospitalized patients and 8 diarrhea patients with COVID-19. Int J Med Sci. 2020 May 17;17(9): 1142-1146. doi: 10.7150/ijms.45743. PMID: 32547309; PMCID: PMC7294916.

18 Yang Z, Shi J, He Z, Lü Y, Xu Q, Ye C, Chen S, Tang B, Yin K, Lu Y, Chen X. Predictors for imaging progression on chest CT from coronavirus disease 2019 (COVID-19) patients. Aging (Albany NY). 2020 Apr 10;12(7):6037-6048. doi: 10.18632/aging.102999. Epub 2020 Apr 10. PMID: 32275643; PMCID: PMC7185104.

19 Ouyang SM, Zhu HQ, Xie YN, Zou ZS, Zuo HM, Rao YW, Liu XY, Zhong B, Chen X. Temporal changes in laboratory markers of survivors and non-survivors of adult inpatients with COVID-19. BMC Infect Dis. 2020 Dec 11;20(1):952. doi: 10.1186/s12879-020-05678-0. PMID: 33308159; PMCID: PMC7729703.

20 Tan T, Khoo B, Mills EG, et al. Association between high serum total cortisol concentrations and mortality from COVID-19. Lancet Diabetes Endocrinol. 2020;8(8):659-660. doi:10.1016/S2213-8587(20)30216-3

21 Choy KW. Cortisol concentrations and mortality from COVID-19. Lancet Diabetes Endocrinol. 2020 Oct;8(10):808. doi: 10.1016/S2213-8587(20)30305-3. PMID: 32946816; PMCID: PMC7492026.

22 Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis. 2020;63(3):390-391. doi:10.1016/j.pcad.2020.03.001

23 Guzik TJ, Mohiddin SA, Dimarco A, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res. 2020;116(10):1666-1687. doi:10.1093/cvr/cvaa106

24 Azevedo RB, Botelho BG, Hollanda JVG, Ferreira LVL, Junqueira de Andrade LZ, Oei SSML, Mello TS, Muxfeldt ES. Covid-19 and the cardiovascular system: a comprehensive review. J Hum Hypertens. 2021 Jan;35(1):4-11. doi: 10.1038/s41371-020-0387-4. Epub 2020 Jul 27. PMID: 32719447; PMCID: PMC7384729.

25 Liu PP, Blet A, Smyth D, Li H. The Science Underlying COVID-19: Implications for the Cardiovascular System. Circulation. 2020;142(1):68-78. doi:10.1161/CIRCULATIONAHA.120.047549

26 Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review [published online ahead of print, 2020 Jul 10]. JAMA. 2020;10.1001/jama.2020.12839. doi:10.1001/jama.2020.12839

27 Zafer, M.M.; El-Mahallawy, H.A.; Ashour, H.M. Severe COVID-19 and Sepsis: Immune Pathogenesis and Laboratory Markers. Microorganisms 2021, 9, 159. https://doi.org/10.3390/microorganisms9010159

28 Zaninotto M, Mion MM, Cosma C, Rinaldi D, Plebani M. Presepsin in risk stratification of SARS-CoV-2 patients. Clin Chim Acta. 2020;507:161-163. doi:10.1016/j.cca.2020.04.020

29 Fukada A, Kitagawa Y, Matsuoka M, et al. Presepsin as a predictive biomarker of severity in COVID-19: A case series [published online ahead of print, 2020 Jun 12]. J Med Virol. 2020;10.1002/jmv.26164. doi:10.1002/jmv.26164

30 Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 28;395(10229):1054-1062. doi: 10.1016/S0140-6736(20)30566-3. Epub 2020 Mar 11. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. PMID: 32171076; PMCID: PMC7270627.

31 Bao J, Li C, Zhang K, Kang H, Chen W, Gu B. Comparative analysis of laboratory indexes of severe and non-severe patients infected with COVID-19. Clin Chim Acta. 2020;509:180-194. doi:10.1016/j.cca.2020.06.009

32 Zhang L, Yan X, Fan Q, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020;18(6):1324-1329. doi:10.1111/jth.14859

33 Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020;46(6):1089-1098. doi:10.1007/s00134-020-06062-x

34 Ranucci M, Ballotta A, Di Dedda U, et al. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. J Thromb Haemost. 2020;18(7):1747-1751. doi:10.1111/jth.14854

35 Oudkerk M, Kuijpers D, Oudkerk SF, van Beek EJ. The vascular nature of COVID-19. Br J Radiol. 2020;93(1113):20200718. doi:10.1259/bjr.20200718

36 Xue M, Zheng P, Bian X, et al. Exploration and correlation analysis of changes in Krebs von den Lungen-6 levels in COVID-19 patients with different types in China [published online ahead of print, 2020 Jun 21]. Biosci Trends. 2020;10.5582/bst.2020.03197. doi:10.5582/bst.2020.03197

37 Nakamura H, Miyagi K, Otsuki M, et al. Serum KL-6 can distinguish between different phenotypes of severe COVID-19 [published online ahead of print, 2020 Jul 7]. J Med Virol. 2020;10.1002/jmv.26268. doi:10.1002/jmv.26268

38 Awano N, Inomata M, Kuse N, et al. Serum KL-6 level is a useful biomarker for evaluating the severity of coronavirus disease 2019 [published online ahead of print, 2020 Aug 21]. Respir Investig. 2020;S2212-5345(20)30115-5. doi:10.1016/j.resinv.2020.07.004

39 d'Alessandro M, Bergantini L, Cameli P, Curatola G, Remediani L, Sestini P, Bargagli E; Siena COVID Unit. Peripheral biomarkers' panel for severe COVID-19 patients. J Med Virol. 2020 Oct 2:10.1002/jmv.26577. doi: 10.1002/jmv.26577. Epub ahead of print. PMID: 33006404; PMCID: PMC7536919.

40 Varble, N., Blain, M., Kassin, M. et al. CT and clinical assessment in asymptomatic and pre-symptomatic patients with early SARS-CoV-2 in outbreak settings. Eur Radiol (2020). https://doi.org/10.1007/s00330-020-07401-8

41 Deng K, Fan Q, Yang Y, Deng X, He R, Tan Y, et al. Prognostic roles of KL-6 in disease severity and lung injury in COVID-19 patients: A longitudinal retrospective analysis. J Med Virol. 2021 Apr;93(4):2505-2512. doi: 10.1002/jmv.26793. Epub 2021 Jan 22. PMID: 33433006.

42 Scotto R, Pinchera B, Perna F, Atripaldi L, Giaccone A, Sequino D, et al. Serum KL-6 Could Represent a Reliable Indicator of Unfavourable Outcome in Patients with COVID-19 Pneumonia. Int J Environ Res Public Health. 2021 Feb 20;18(4):2078. doi: 10.3390/ijerph18042078. PMID: 33672761; PMCID: PMC7924557.

43 Fukada A, Kitagawa Y, Matsuoka M, Sakai J, Imai K, Tarumoto N, et al. Presepsin as a predictive biomarker of severity in COVID-19: A case series. J Med Virol. 2021 Jan;93(1):99-101. doi: 10.1002/jmv.26164. Epub 2020 Jun 24. PMID: 32530491; PMCID: PMC7307131.

44 Peng DH, Luo Y, Huang LJ, Liao FL, Liu YY, Tang P, Hu HN, Chen W. Correlation of Krebs von den Lungen-6 and fibronectin with pulmonary fibrosis in coronavirus disease 2019. Clin Chim Acta. 2021 Feb 22;517:48-53. doi: 10.1016/j.cca.2021.02.012. Epub ahead of print. PMID: 33631198; PMCID: PMC7898973.

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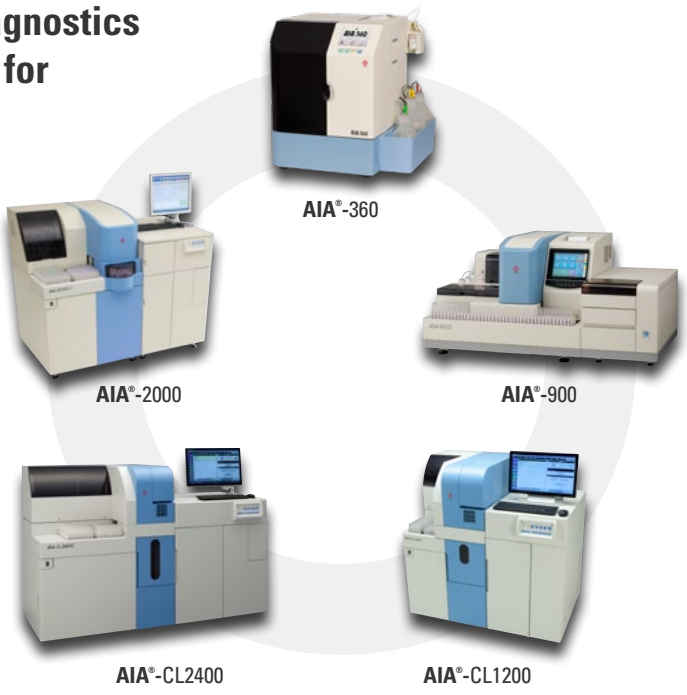
Better diagnostics **for better living**

TRUST THE EXPERTISE OF TOSOH

The laboratory tests described in this brochure can play an important role in the follow-up of COVID-19 patients. **Tosoh is offering these tests on its automated immunoassay analysers range.**

These robust and easy to use instruments provide a high quality and cost-effective solution to the ever growing needs in the clinical laboratory.

We at Tosoh believe that better diagnostics can and will lead to a better living for patients. This is especially true for SARS-CoV-2 infections. Often starting asymptomatically they can quickly evolve to a life-threatening disease.



Automated Immunoassay Analysers

INQUIRE TODAY ABOUT WHICH SOLUTIONS WE CAN OFFER YOU TO BETTER CONTAIN COVID-19

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