

How D-dimer in Coagulation Correlates with COVID-19?

D-dimer in COVID-19

As COVID-19 continues to swipe around the world, rapid diagnosis as well as prognosis and treatment of the COVID-19 patients has become an equally important topic among clinicians. Recently scientists have discovered that COVID-19 has a host cell receptor, Angiotensin Converting Enzyme II^[1] or ACE2. With the help of ACE2, COVID-19 invades the human body rapidly by reproducing on its own at a massive rate, destroying normal cell, tissue and microvascular system, finally causing acute lung injury, multiple organ failure^[2-4], and intravascular coagulation which occurs in 71.4% of patients who died from COVID-19^[5]. It is widely known that D-dimer is a significant bio-marker which correlates with hypercoagulability. More clinical studies have also revealed the relationship between D-dimer and COVID-19.

As published on Jama by Zhi Yong's Group, in the patients' death(non-survivor) group of novel coronavirus pneumonia, the D-dimer level initially increased as the disease developed, until the 7th day when the D-dimer level broke through the normal range, and finally plateaued at a high level [Figure 1 A]^[6]. In comparison, the survivor group remained within the normal range consistently. Another article published in the Lancet also claims that there is a close correlation between the D-dimer level and the mortality rate of victims [Figure 1 B]^[7]. The same conclusion was also drawn in Shah's research, which utilized a systematic meta-analysis method (including results from 18 articles and a total of 3,682 patients) to draw the forest plots [Figure 1 C, D]^[8]. To sum up, whether in severe or dead COVID-19 patients, the D-dimer level was higher than that which was found in non-severe or surviving patients.

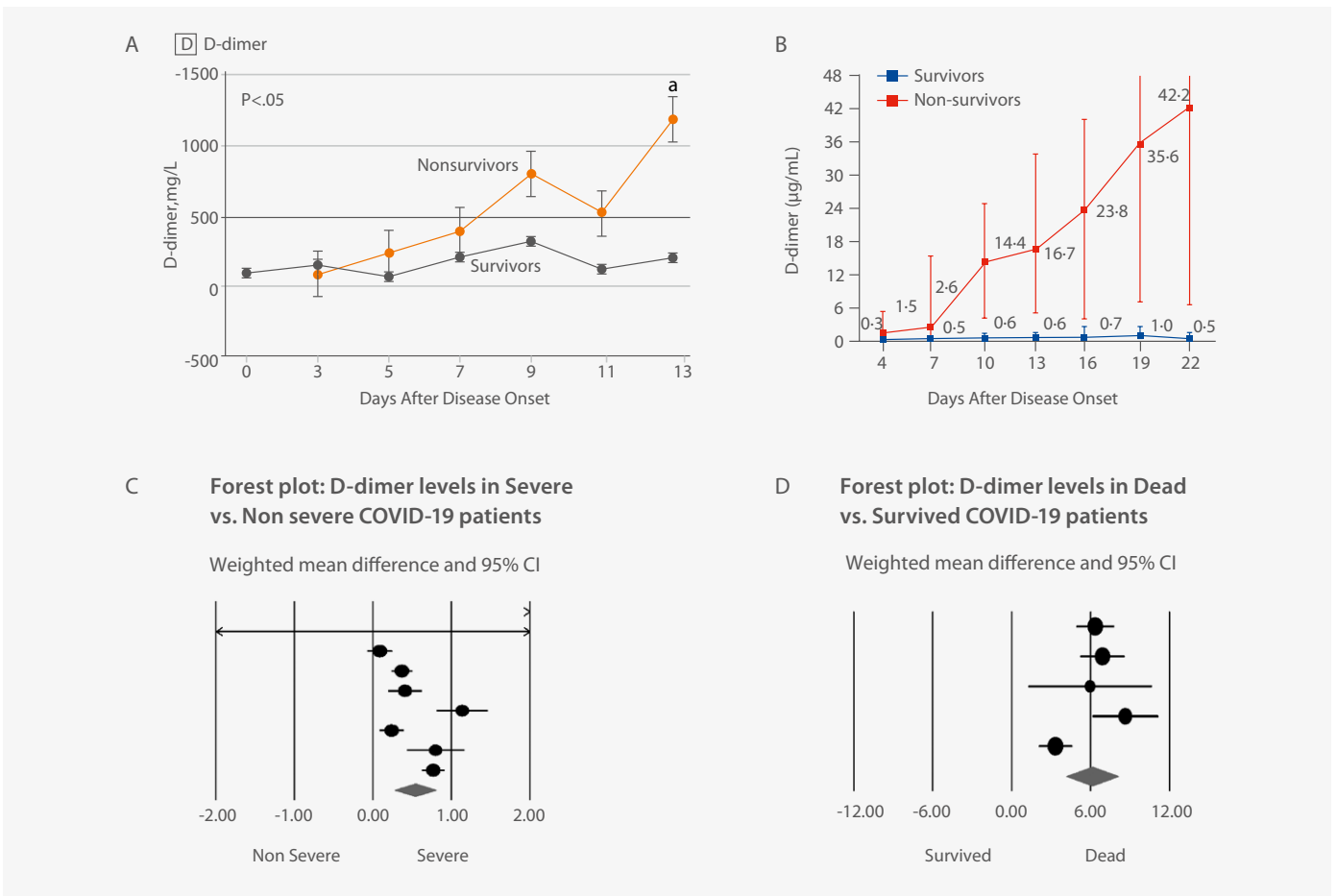


Figure 1: Correlation between D-dimer and COVID-19

Application of D-dimer in COVID-19 Prognosis

According to the study by Zhang’s group, D-dimer among all parameters tested in patients with COVID-19 had the highest C-index, which indicates that it has the highest prediction coincidence rate in routine lab testing methods [Figure 3A]. In addition, they also found the 2 µg/ml of D-dimer could be the cut-off value of mortality risk of COVID-19, as DD > 2 µg/ml the survival probability will decrease dramatically [Figure 2B]. Consequently, they based the evaluation of this value and manifested that when 2 µg/ml was set as the cut-off value, 92.3% of sensitivity and 83.3% of specificity is the optimum in all groups [Figure 2C]^[9].

There has been evidence regarding an increased incidence of venous thromboembolic events (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE), in patients with severe COVID-19 infection^[9], and D-dimer can also be used as a monitoring indicator of VTE and PE with a cut-off value of 0.55 µg/ml. Furthermore, Yao not only found that patients with over 2 µg/ml D-dimer needed intensive care and early intervention, but suggested a cut-off value of 1 µg/ml could help doctors identify patients with a poor prognosis^[10].

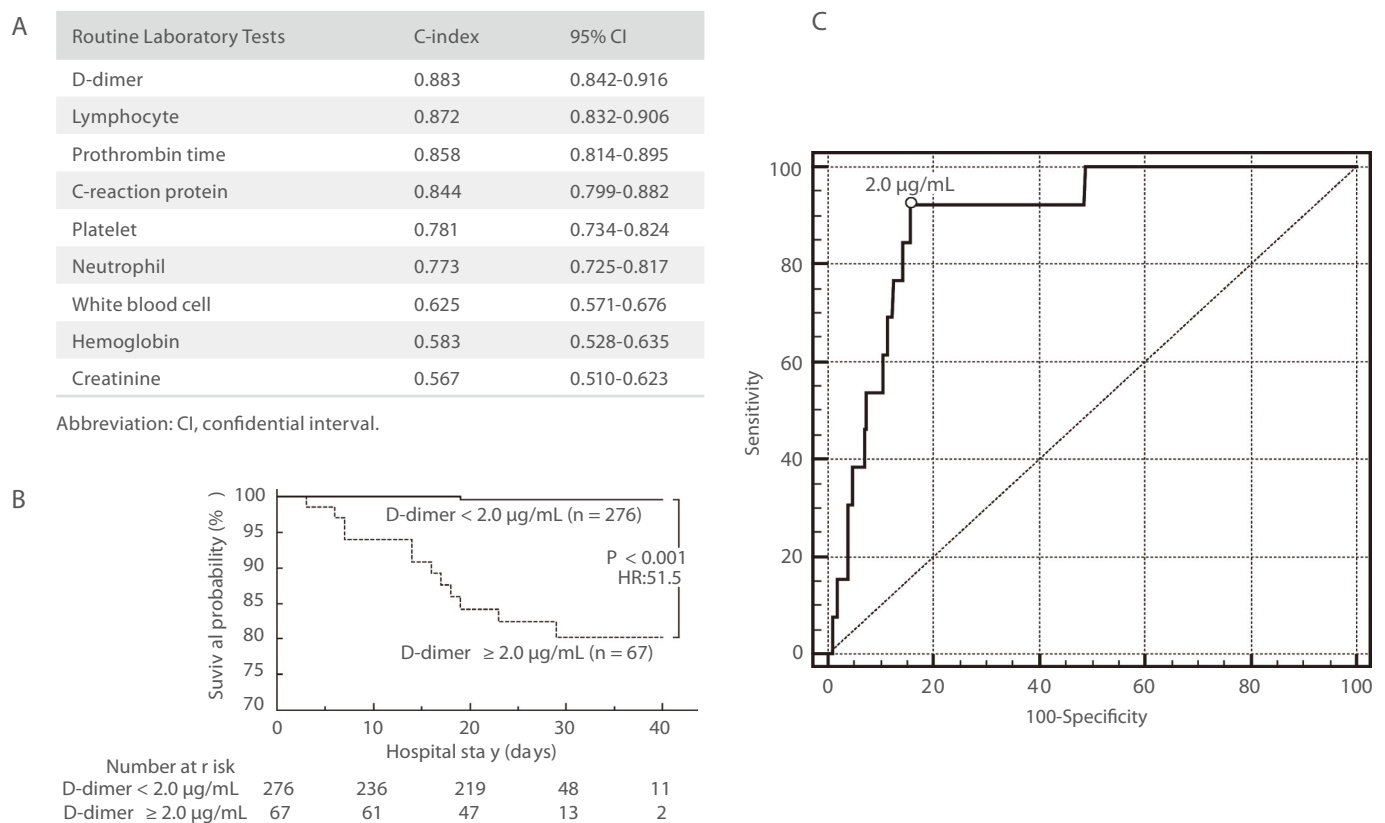


Figure 2: Numeric Results of D-Dimer by Zhang’s Group

In conclusion, D-dimer has enormous clinical values in the treatment and prognosis of COVID-19 as a sensitive monitoring index. In consideration of disordered coagulation micro-environment in patients infected with COVID-19 or at high risk of VTE induced by reduced activity, increased bed time, or in people being quarantined for hospitalization, testing of D-dimer on a regular basis is necessary for rapid monitoring of disease treatment. While a cut-off value of over 2 ug/ml has been proved by many researchers monitoring patients’ treatment, laboratories are still advised to set their own standard so the variation in demographics can be taken into account.

Mindray's Coagulation D-dimer Solution

Mindray's auto-coagulation analyzers C3100 & C3510 are equipped with both classic mechanical and optical detection mechanisms. The mechanical methodology is insensitive to interference from icteric, lipemic, chylus and hemolytic samples. Moreover, the patented VRIM(VLin-Rate Integrative Method) algorithm has also been developed to combine "Two Point End Method" at a low D-dimer concentration together with "Rate Method" at a higher level [Figure 3]. This has enabled a much wider linearity range of D-dimer results compared with other models on the market [Figure 4].

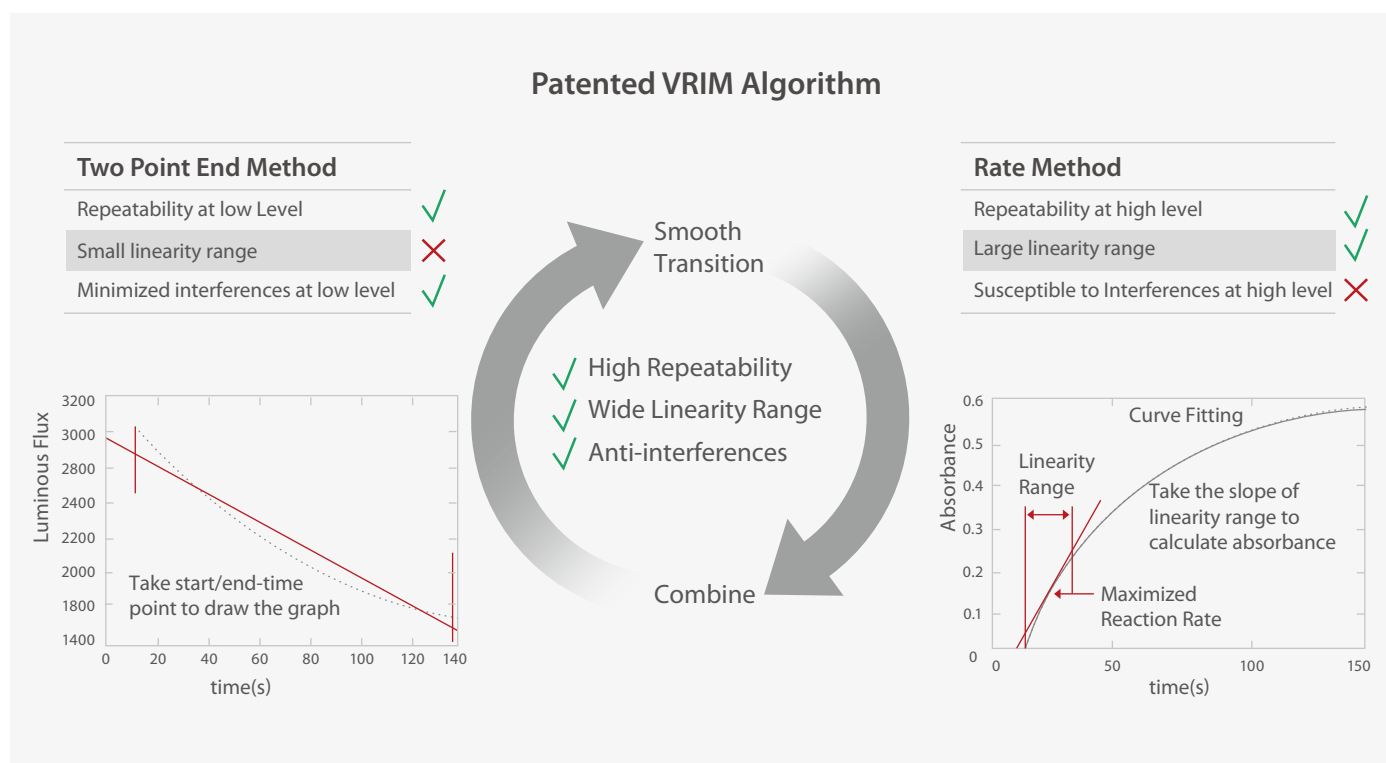


Figure 3: Mindray's patented VRIM Algorithm for D-dimer testing

Manufacturer	Algorithm	Linearity Range (µg/ml)
Mindray	VRIM	0.20~8.0
Brand A	Rate	0.17~4.4
Brand B	Two Point End	0.15~3.7
Brand C	Two Point End	0.22~3.0

Figure 4: Comparison of Linearity Range (without dilution) between Mindray and other brands

In addition, Mindray's coagulation solution to D-dimer testing is less susceptible to common interferences. As is shown in [Figure 5], when the serum samples are added with bilirubin, hemoglobin, triglycerides and rheumatoid factors at respective concentration, D-dimer results remain at constant levels as before. The Comparison study with Sysmex CS5100 has also shown a good correlation with R2> 97% with interferences added.

Interferent (Concentration)	Before Adding	After Adding
Bilirubin (40 mg/dL)	2.43	2.38
Hemoglobin (200 mg/dL)	2.31	2.36
Triglycerides (1800 mg/dL)	2.39	2.25
Rheumatoid Factor (1300 IU/mL)	1.54	1.55

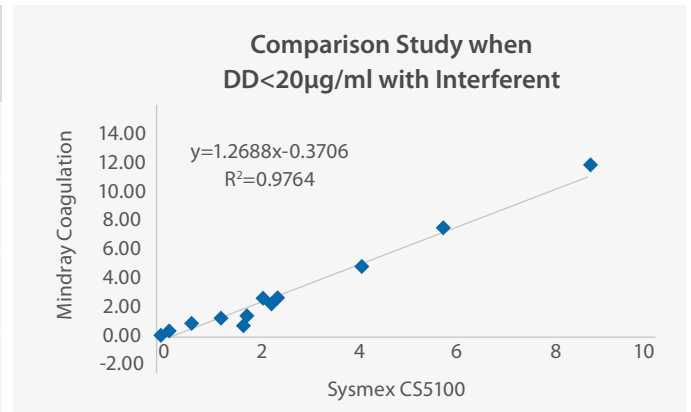



Figure 5: Comparison study with interferents




Figure 6: Mindray's D-dimer coagulation reagents

Mindray's D-dimer coagulation reagents are all manufactured in a bottled liquid state which are ready to use [Figure 6], while the majority of coagulation testing kits are made into powder. Simply by opening the cap and loading D-dimer reagents onto the analyzer, preparation can be set up rapidly with ease on Mindray's coagulation analyzers.



C3100

- Throughput: up to **200** test/h (PT), up to **44** test/h (D-dimer)
- D-dimer tested with special optical channel
- **61** sample position, 11 reagent position
- **12** incubation channel, 4 mechanical testing channel
- Separate sample/reagent probe ensure low carry over



C3510

- Throughput: up to **300** test/h(PT), up to **91** test/h(D-dimer)
- D-dimer tested with special optical channel
- **80** sample position, 24 (cooling) + 4 reagent position
- **16** incubation channel, 4 mechanical+6 optical testing channel
- Separate sample/reagent probe ensure low carry over

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