

Singapore study finds link between Covid-19 and risk of blood clot formation even after recovery



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Researchers from the Nanyang Technological University embarked on a study in April 2020 after medical reports of Covid-19 patients experiencing blood clots emerged.

- **A study led by NTU has found that recovered Covid-19 patients may be at risk of developing blood clots**
- **This is especially for those with pre-existing cardiovascular conditions**
- **Their bodies continue to mount an immune response to the coronavirus even when the virus is not there**
- **This produces inflammatory proteins that damage blood vessels, increasing the risk of blood clots forming**

SINGAPORE — A new study on a small sample of patients has found that those who have recovered from Covid-19, especially those with pre-existing cardiovascular conditions, may be at risk of developing blood clots.

Blood clots may block major arteries to vital organs, inviting the risk of heart attack, stroke or organ failure.

The study of 30 recovered Covid-19 patients was led by scientists from the Nanyang Technological University (NTU) and published in peer-reviewed scientific journal eLife on March 23 this year.

The study also involved other agencies such as the Agency for Science, Technology and Research (A*Star) and the National Centre for Infectious Diseases (NCID).

Acknowledging the small sample size, Assistant Professor Christine Cheung of NTU who led the study said that an ongoing, larger-scale study with NCID will build on the current findings.

The larger study will analyse at least 100 patients who have recovered from the infection for at least six months or longer. The published study examines patients who have already recovered from the infection for at least a month.

Speaking at a media briefing on Tuesday (April 13), Asst Prof Cheung, who is from NTU's Lee Kong Chian School of Medicine, said that the study started last April after medical reports of Covid-19 patients experiencing blood clots emerged.

For instance, a [41-year-old man died](#) from a blood clot in his lung artery last June, more than two weeks after recovering from Covid-19.

"This is very serious and points to the impact of the virus infection itself and what it means for survivors later on. That in itself warranted the motivation (for the study)," she said.

HOW THE STUDY WAS DONE

As part of the study, the blood samples of 30 Covid-19 patients were collected a month after they had recovered from the infection. The sample was split among those who had mild, moderate and severe infections.

They were then analysed for the patient's immune responses to the coronavirus.

The researchers found that the recovered patients continued to produce a high level of cytokines, which are proteins produced by immune cells that activate the immune response against pathogens. This occurred even though the virus was absent in the body.

An unusually high number of immune cells, known as T-cells, which attack and destroy the virus were also present in the blood of recovered patients.

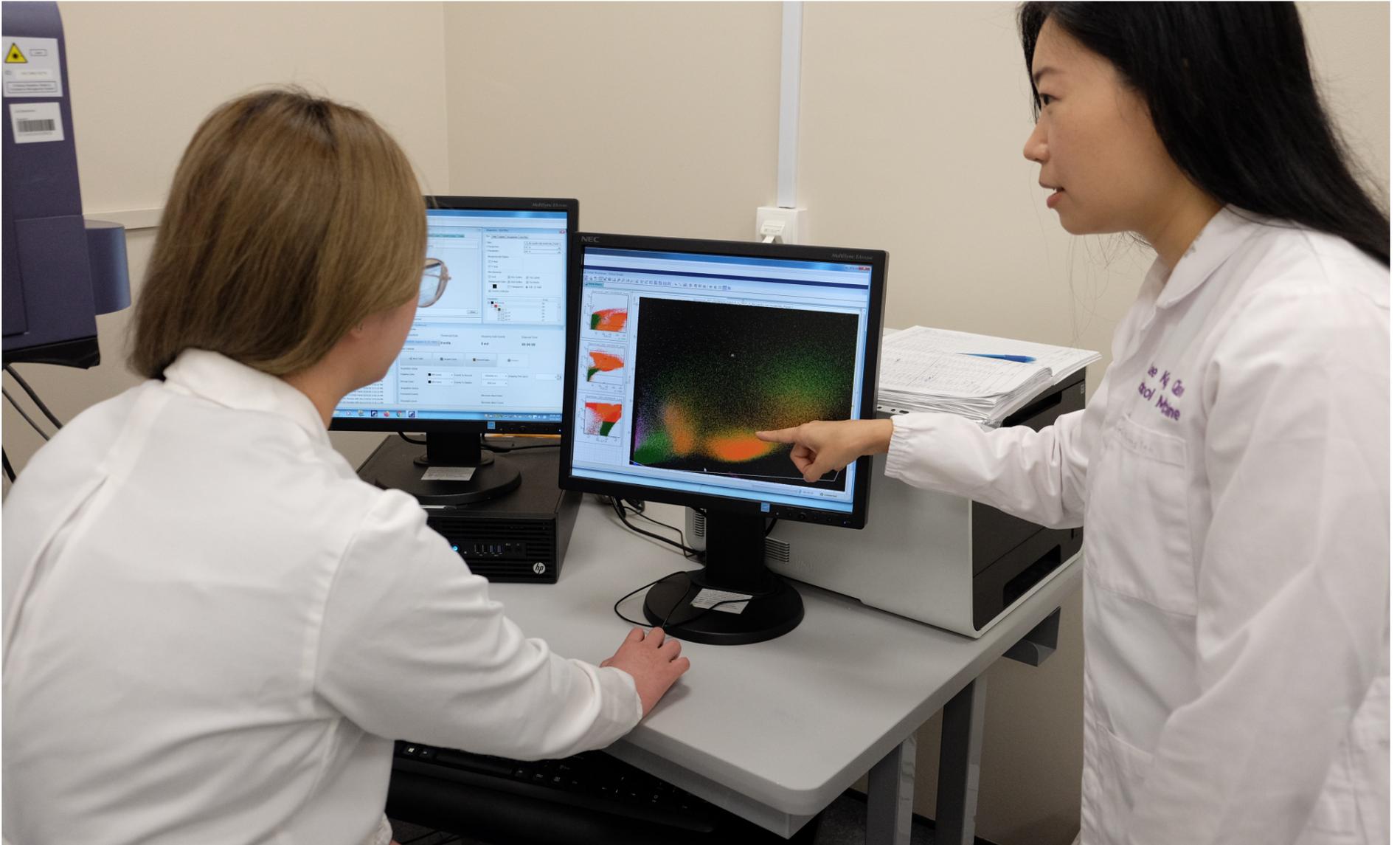
The presence of both cytokines and higher numbers of T-cells suggested that the immune systems of recovered patients remain activated, even after the coronavirus is no longer present, Asst Prof Cheung said.

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Research assistant Florence Chioh (left) and Assistant Professor Christine Cheung (right) analysing data from 30 blood samples of recovered Covid-19 patients. The team also includes Dr Wu Kanxing, a research fellow at the NTU Lee Kong Chian School of Medicine. Photo: Nanyang Technological University

At the same time, the blood samples of patients were analysed to assess the level of endothelial cells, which are blood vessel cells shed from the damaged inner lining of vessels.

What they found was that the recovered patients had twice the number of endothelial cells in their bloodstream compared with healthy individuals. The elevated levels of such cells indicate that the patients have injured blood vessels even after recovering from Covid-19.

Taken together, the researchers hypothesised that the persistently activated immune responses in recovered patients may damage their blood vessels.

“The heightened immune response leads to higher levels of inflammatory proteins, which damages the blood vessels, causing them to leak.

“Consequently, leaky blood vessels may trigger the activation of platelets, a blood component involved in blood clotting,” Asst Prof Cheung explained.

She also noted that the degree of blood vessel damage for Covid-19 patients with pre-existing cardiovascular conditions was at least 20 per cent more than in patients with no such conditions.

However, further research is needed to establish if this means that Covid-19 patients with pre-existing cardiovascular conditions were at greater risk of blood clots compared with those without.

CLOSE MONITORING OF RECOVERED PATIENTS

Asst Prof Cheung said that the study provided “a new angle” to previous medical studies by identifying how such persistently activated immune responses damage blood vessels.

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She noted that the World Health Organization had recommended that hospitalised patients use low-dose anticoagulants, or blood thinners, to prevent blood clots from forming.

However, more research has to be done to ascertain if this recommendation should be extended to discharged patients.

“If Covid-19 survivors experience symptoms such as fatigue, breathlessness and especially chest pain, they should consult their doctors immediately. The doctor will be able to evaluate their risk of blood clotting, and carry out preventive therapy if necessary,” she added.

TODAY reported last June when studies into Covid-19 were still quite new that NCID saw some critically ill patients in Singapore who had [blood clot complications](#) when infected.

Its clinical director said then that blood clots were found in patients with other viral infections but the mechanism causing clots in Covid-19 patients appeared more pronounced.

People who are obese, have diabetes and have been diagnosed with venous thromboembolism (blood clot in the deep veins of the legs or groin) are more likely to require intensive care treatment and tend to have worse outcomes when they get Covid-19, another medical expert said.

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