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Since its emergence in December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) has caused a pandemic affecting 216 countries, areas, or territories with >13 million cases and at least 574,464 deaths as of July 15, 2020. In China, the number of laboratory-confirmed cases has exceeded 80,000, resulting in >4000 deaths. Populations immuno-naïve to SARS-CoV-2 are considered to have markedly contributed to the dramatic increase in cases worldwide. Transmission modelling studies of SARS-CoV-2 assume that infection produces immunity for the appropriate amount of time that should be recommended for quarantine, but in the time between PSO and sampling, we collected a total of 112 serum samples. We collected serum at multiple time points for most patients (n = 16, 64%), collecting having ≥6 serum samples with 56% (n = 14) (Table 1). We collected 21 serum samples from 12 patients ≤7 PSO, 30 from 16 patients ≤14 days PSO, 19 from 11 patients ≤21 days PSO, 22 from 16 patients 28 days PSO, and 20 from 20 patients 3–4 months PSO.

Detection of virus-specific IgG and IgM in patients. The two structural proteins of SARS-CoV-2, nucleocapsid (N) and spike (S) protein, have been used as target antigens for serological assays. Although it is unlikely that antibody responses to N protein can directly neutralise SARS-CoV-2, this is the antigen targeted by multiple commercial assays. Therefore, to study antibody responses to SARS-CoV-2, we first qualitatively measured IgG against N and IgM against the receptor-binding domain (RBD) of the SARS-CoV-2 S protein in serum from patients at a 1:10 dilution using two well-validated commercial diagnostic ELISA kits. Four (33.3%) of 12 patients with serum samples collected from 1 to 7 days PSO tested positive for anti-N IgG, and 4 (33.3%) patients tested positive for anti-RBD IgM (Fig. 1a–d). Of these, one patient was positive for both anti-N IgG and anti-RBD IgM antibodies. Of 16 patients with serum samples collected from 8–14 days PSO, 13 (81.3%) and 14 (87.5%) were positive for anti-N IgG and anti-RBD IgM antibodies, respectively. Thereafter, 100% of patients with serum samples collected >14 days PSO were positive for both anti-N IgG and anti-RBD IgM antibodies, and the antibody levels rapidly decayed (Fig. 1c, d). By contrast, there were no detectable anti-N IgG or anti-RBD IgM antibodies among healthy controls (Fig. 1a, c).

Given that the neutralising antibody (NAb) response for SARS-CoV-2 primarily targets the S protein, using SARS-CoV-2-derived recombinant trimeric S protein and monomeric RBD, we then carried out ELISAs to quantitatively detect IgG antibody binding in serum. Similar to our observation of anti-N IgG and anti-RBD IgM responses, we detected IgG antibodies binding S (Fig. 1e–f; geometric mean endpoint titer 5,358; 95% confidence interval [CI], 3062.0–9375.6) or RBD (Fig. 1g–h; mean, 2056; 95% CI, 654.6–6471.4) in all patients >14 days PSO. Although there was a slight decline in antibody titre 3–4 months PSO, anti-S (mean 4345.1; 95%CI, 3097.4–6095.4) or anti-RBD (mean 1513.6; 95%CI, 635.3–3614.1) IgG antibodies remained detectable in all patients but one patient (patient 12). As expected, in the serum of healthy controls we observed a minimal reactivity against anti-S or anti-RBD IgG antibodies (Fig. 1e, g). Collectively, these findings indicate that COVID-19 patients produced IgG and IgM antibody responses to SARS-CoV-2, and that the IgG antibodies can persist at least 3–4 months PSO.

**Results**

**Characteristic of patients and samples.** We enroled 25 laboratory-confirmed SARS-CoV-2 patients, of which 3 were severe patients, 18 were moderate patients, and 4 were asymptomatic (Table 1). Their median age was 40 years (interquartile range [IQR], 33–53), and 13 (52%) were male. The most commonly reported symptoms were fever and cough. Seventy-two percent of patients experienced moderate illness. Fifty-two percent of these individuals had known underlying medical illnesses. In the time between PSO and sampling, we collected a total of 112 serum samples. We collected serum at multiple time points for most patients (n = 16, 64%), collecting having ≥6 serum samples with 56% (n = 14) (Table 1). We collected 21 serum samples from 12 patients ≤7 PSO, 30 from 16 patients ≤14 days PSO, 19 from 11 patients ≤21 days PSO, 22 from 16 patients 28 days PSO, and 20 from 20 patients 3–4 months PSO.
| Pt# | Age, y/sex | Symptoms | Underlying disease | Days to admission | Days in hospital | Days in ICU | CT findings of ground-glass opacities | Days of sample collection | Disease severity |
|-----|------------|----------|--------------------|------------------|-----------------|------------|--------------------------------------|---------------------------|-----------------|
| 1   | 25/M       | 1, 2, 9  | FL                 | 2                | 27              | 5          | Both lungs                           | 4, 7, 9, 13, 16, 27, 106 | Severe          |
| 2   | 64/M       | 1, 2, 6, 7, 10 | RC | 4                | 19              | 4          | Both lungs                           | 6, 9, 12, 15, 19, 23, 37, 71, 116 | Severe          |
| 3   | 27/M       | 1, 2, 7, 9 | DM, NEP            | 0                | 23              | 7          | Both lungs                           | 1, 4, 7, 11, 15, 18, 29 | Severe          |
| 4   | 51/M       | 1, 2     | No                 | 4                | 17              | 0          | Both lungs                           | 1, 4, 6, 10, 13, 24, 103 | Moderate         |
| 5   | 46/F       | 1, 2     | AST, HTN           | 0                | 15              | 0          | Both lungs                           | 1, 4, 6, 10, 13, 24, 103 | Moderate         |
| 6   | 23/F       | 1, 2     | No                 | 4                | 14              | 0          | Both lungs                           | 6, 9, 13, 16, 27, 106 | Moderate         |
| 7   | 51/M       | 1, 2     | HTN                | 8                | 17              | 0          | Both lungs                           | 13, 15, 19, 22, 33, 112 | Moderate         |
| 8   | 61/F       | 1, 2, 4, 6, 7, 8, 10 | No | 9                | 16              | 0          | Both lungs                           | 11, 14, 18, 20, 22, 24, 42, 121 | Moderate         |
| 9   | 36/M       | 1, 2, 5, 6 | CB, FLUL          | 0                | 13              | 0          | Both lungs                           | 2, 5, 8, 10, 12, 30, 109 | Moderate         |
| 10  | 38/F       | 1, 2     | HTA, PTC, HTM      | 1                | 17              | 0          | Both lungs                           | 3, 8, 11, 15, 18, 29, 108 | Moderate         |
| 11  | 41/M       | 1, 2, 6  | No                 | 7                | 20              | 0          | Both lungs                           | 9, 15, 17, 21, 24, 35, 114 | Moderate         |
| 12  | 34/M       | 1, 2, 5  | No                 | 8                | 15              | 0          | Both lungs                           | 11, 14, 16, 20, 23, 34 | Moderate         |
| 13  | 32/F       | 1, 2, 6, 7, 8, 11 | No | 1                | 17              | 0          | Both lungs                           | 5, 8, 27 | Moderate         |
| 14  | 46/F       | 1, 2     | LT, HTM            | 5                | 17              | 0          | Both lungs                           | 106 | Moderate         |
| 15  | 54/M       | 1, 2     | No                 | 0                | 15              | 0          | Both lungs                           | 97 | Moderate         |
| 16  | 72/M       | 1, 2, 5  | DM, HTN            | 13               | 13              | 0          | Both lungs                           | 109 | Moderate         |
| 17  | 40/M       | 1, 2, 5  | No                 | 7                | 11              | 0          | Both lungs                           | 101 | Moderate         |
| 18  | 40/F       | 1        | CS                 | 11               | 14              | 0          | Both lungs                           | 98 | Moderate         |
| 19  | 38/F       | 1, 2     | No                 | 7                | 13              | 0          | Left lung                            | 103 | Moderate         |
| 20  | 54/F       | 1, 2     | LEU                | 1                | 15              | 0          | Both lungs                           | 102 | Moderate         |
| 21  | 61/F       | 3        | CHD, HTN           | 1                | 12              | 0          | Right lung                           | 92 | Moderate         |
| 22  | 52/F       | No       | No                 | 0                | 21              | 0          | Both lungs                           | 2, 5, 8, 10, 12, 16, 30 | Asymptomatic     |
| 23  | 33/F       | No       | No                 | 1                | 10              | 0          | Both lungs                           | 1, 3, 7, 8, 10, 28, 107 | Asymptomatic     |
| 24  | 33/M       | No       | HH                 | 0                | 18              | 0          | Normal                               | 5, 8, 27 | Asymptomatic     |
| 25  | 3/M        | No       | No                 | 1                | 14              | 0          | Normal                               | 98 | Asymptomatic     |

1. fever; 2. cough; 3. dry throat; 4. rhinorrhea; 5. chest tightness; 6. fatigue; 7. nausea; 8. vomiting; 9. diarhoea; 10. abdominal discomfort; 11. bloody stools. 2. After symptom onset or initial positive RT-PCR results (for asymptomatic patients). AST asthma, CB chronic bronchitis, CHD coronary heart disease, CS caesarean section, DM diabetes mellitus, FL fatty liver, FLUL fracture of left upper limb, HI hepatic hemangioma, HTA hystereomyoma, HTM hypothyroidism, HTN hypertension, LT lumbar tuberculosis, LEU leukopenia, NEP nephritis, PTC papillary thyroid carcinoma, RC renal calculus, HH hepatic insufficiency.
85% (17/20) of patients still had high NAb titre of ≥1:640 3–4 months PSO, whereas we observed relatively low NAb titre (≤1:80) for two moderate illness patients (patients 18 and 19) and one asymptomatic individual (patient 25, a 3-year-old boy). We detected no NAb in the serum from healthy controls. We observed a significant correlation between NAb titre and anti-N IgG (Spearman $r = 0.672$, $p < 0.0001$), anti-S IgG (Spearman $r = 0.668$, $p < 0.0001$), and anti-RBD IgG (Spearman $r = 0.707$, $p < 0.0001$) (Fig. 2c). Anti-RBD IgM antibodies were also correlated with NAb titre (Spearman $r = 0.714$, $p < 0.0001$). We additionally observed a strong correlation between anti-S IgG and anti-RBD IgG antibodies (Fig. 2c; Spearman $r = 0.908$, $p < 0.0001$). These findings suggest that patients produced robust NAb responses after SARS-CoV-2 infection, and that the majority of patients’ NAb titre persisted 3–4 months PSO.

**Fig. 1** IgG and IgM antibody response kinetics in the serum of patients with SARS-CoV-2 infection, by days after symptom onset. a–d The percentages (blue line) of patients (P) with serum samples that were positive for IgG to the nucleocapsid (N) protein (a), IgM to the receptor-binding domain (RBD) of SARS-CoV-2 spike (S) (b), IgG to the S (c) and RBD (d), and the corresponding mean optical density (OD) for anti-N IgG and anti-RBD IgM and log10-transformed geometric mean endpoint titer (GMT) for anti-S and -RBD IgG (red dashed line). Error bars represent the 95% confidence interval. Each circle represents the titer for a serum sample. e–h Individual level for anti-N IgG (e), anti-RBD IgM (f), anti-S IgG (g), and anti-RBD IgG (h) in serum samples collected from patients, and the samples from the same patients are connected by the lines. Black dashed line indicates the threshold for positivity (anti-N IgG = 0.19, anti-S IgG = 439.5, anti-RBD IgG = 33.2, and anti-RBD IgM = 0.105). Source data included as a Source Data File.
CD4+ and CD8+ T cell responses to SARS-CoV-2 in recovered patients. To assess SARS-CoV-2-specific T cell responses, we used a recombinant replication-deficient adenovirus type 5 vector encoding the SARS-CoV-2 S (rAd5-S) protein or N (rAd5-N) protein with flow cytometry in a serial intracellular cytokine (IFN-γ, TNF-α, and GzmB) staining (ICS) assay with peripheral blood mononuclear cells (PBMCs) from 20 patients 3–4 months PSO (Fig. 3a). Because Ad5 can efficiently transduce many types of cells, including antigen presentation cells, we used rAd5-S and rAd5-N instead of peptides or proteins for these assays to better mimic the in vivo stimulation and avoid possible negligence of specific epitopes. As shown in Fig. 3b, we respectively detected CD4+ T cells producing IFN-γ in response to rAd5-S and rAd5-N in 10 (50%) and 13 (~65%) of 20 recovered patients; in 10 of them we detected CD4+ T cells producing IFN-γ in response to both rAd5-S and rAd5-N. For CD8+ T cell responses, we detected CD8+ T cells producing IFN-γ in response to rAd5-S in only 3 (15%) of 20 patients, while detecting rAd5-N in 10 (50%) patients. We detected CD4+ and CD8+ T cells producing IFN-γ in response to both rAd5-S and rAd5-N in only two patients. These results indicate that most of the recovered patients had detectable SARS-CoV-2-specific CD4+ or CD8+ T cell responses 3–4 months PSO. Additionally, rAd5-S typically elicited CD4+ T cell responses, whereas rAd5-N elicited both CD4+ and CD8+ T cell responses.

We further measured TNF-α co-expression in all the 14 patients with IFN-γ+ CD4+ or CD8+ T cells and co-expression of GzmB in 8 of them (Fig. 3c). In response to rAd5-S, we detected TNF-α co-expression with IFN-γ in 7 of the 10 patients with S-specific CD4+ T cells and 2 of the 3 patients with S-specific CD8+ T cells, while finding GzmB co-expression with IFN-γ in 4 of the 6 patients examined with S-specific CD4+ T cells and one patient examined with S-specific CD8+ T cells (Fig. 3d, e). In response to rAd5-N, we detected TNF-α co-expression with IFN-γ in 11 of the 13 patients with N-specific CD4+ T cells and 6 of the 7 patients with N-specific CD8+ T cells, while finding GzmB co-expression with IFN-γ in 5 of the 7 patients examined with N-specific CD4+ T cells and 5 of the 6 patients examined with N-specific CD8+ T cells (Fig. 3d, e). The variation in the co-expression was dramatic; in most patients, we detected less than 50% of IFN-γ+ CD4+ and CD8+ T cells co-expressing TNF-α or GzmB (Fig. 3d, e). A similar varied and overall low proportion of co-expression was observed in convalescent patients with COVID-19 in the United Kingdom23 and in Sweden24.

Virus-specific memory CD4+ and CD8+ T cells in recovered patients. We then characterised the phenotypic memory of SARS-CoV-2-specific CD4+ and CD8+ T cells by CD45RA and CCR7 staining to determine the frequency of the naive (CD45RA+CCR7+), central memory (CD45RA−CCR7+), effector memory (CD45RA−CCR7−), and late effector (CD45RA+CCR7−) subsets (Fig. 4a). In response to both rAd5-S and rAd5-N, the IFN-γ+ CD4+ T cells were phenotypically effector memory (CD45RA−CCR7−) and effector (CD45RA+CCR7−) cells (Fig. 4b). We observed similar constitutions for IFN-γ+ CD8+ T cells in response to rAd5-S and rAd5-N (Fig. 4b). However, in contrast, the virus-specific CD4+ and CD8+ memory T cells were highly heterogeneous (Fig. 4c). Additionally, only three patients had detectable memory CD8+ T cells in response to rAd5-S. Of note, varied the frequencies of virus-specific CD4+ and CD8+ T cells we
detected in patients in this study exhibited similar phenotypes, suggesting that infection produced poor T cell memory. Further assessment of the correlation between SARS-CoV-2-specific CD4+ and CD8+ T cell responses and antibody titre showed a moderate correlation between CD4+ T cell responses and anti-N IgG antibody (Spearman \( r = 0.53, p = 0.02 \) for rAd5-N, and Spearman \( r = 0.49, p = 0.039 \) for rAd5-S) (Supplementary Fig. 1), anti-S IgG (Spearman \( r = 0.53, p = 0.02 \) for rAd5-N, and Spearman \( r = 0.49, p = 0.039 \) for rAd5-S) (Supplementary Fig. 2), and anti-RBD IgG (Spearman \( r = 0.495, p = 0.031 \) for rAd5-N, and Spearman \( r = 0.486, p = 0.041 \) for rAd5-S) (Supplementary Fig. 3), whereas we found no correlation between CD8+ T cell responses and antibody titre or CD4+ T cell response and NAb titre (Supplementary Figs. 1–4).

Discussion
The need to understand the kinetics of antibody and T cell responses to SARS-CoV-2 is critical. This study prospectively evaluated the durability of the SARS-CoV-2-specific antibody and the T cell responses in patients 3–4 months after infection. We were able to detect anti-S, anti-RBD or anti-N IgG and NAb >14 days after infection in all patients during hospitalisation and observed no drastic decline in IgG and NAb levels 3–4 months after infection. In contrast, similar to other findings,25,26 we observed a rapid decline in anti-RBD IgM responses in the serum. We also detected SARS-CoV-2-specific CD4+ and CD8+ T cell responses in approximately 65% of patients 3–4 months after infection. In summary, our data show durable IgG and NAb responses in all patients with COVID-19 and virus-specific T cell responses in most patients 3–4 months after infection.

Previous studies have shown that antibody responses against SARS-CoV and MERS-CoV infections can persist for at least 2 years.27–30 Investigating antibody responses to SARS-CoV-2, recent studies have shown a robust increment of IgG and NAb levels in patients after 2–3 weeks PSO or in early convalescent patients.4–7,21 However, the kinetics and durability of these antibody responses have rarely been reported. We report longitudinal antibody profiles in SARS-CoV-2 patients using serial blood samples (from day 1 to day 121 PSO). We observed that SARS-CoV-2-specific IgG, IgM, or NAb could be detected in some patients within the first week of illness onset. In particular, over 50% of patients became seropositive for NAb. Moreover, >80% of patients within two weeks PSO had detectable IgG (81.3%), IgM (87.5%), and NAb (93.8%) antibodies against SARS-CoV-2. We also observed a rapid decline in anti-RBD IgM responses in the serum.
pseudovirus. These data and ours contrast with those of Long et al. and Ibarrondo et al. showing a rapid decay of antibody levels. However, the factors contributing to the discrepant results are not entirely clear. In this study, in addition to employing ELISA used in other studies for IgG antibody detection, we also used a live-virus neutralising assay—a "gold standard assay"—to detect and measure NAb levels. Collectively, our results indicate that IgG and NAb persist at stable and high levels in the majority of patients 3–4 months after infection, which has important implications for vaccine development.

While it is essential to characterise the SARS-CoV-2-specific antibody response, it is also important to determine the SARS-CoV-2-specific T cell responses in recovered patients as memory T cells are known to protect against various viral infections. Recent studies carried out in Australia, Germany, Sweden, the United Kingdom, and the United States have reported a particularly high frequency of S-specific CD4+ T cell responses among COVID-19 early convalescent patients approximately 1 month after infection.
A*02:01 phenotype in Australian Caucasian COVID-19 convalescent patients; other studies have detected robust S-specific CD8+ T cell responses. In our study, we observed S-specific CD4+ and CD8+ T cell responses in 50% and 15% of the recovered Chinese COVID-19 patients, respectively. However, it is impossible to rule out, as potential confounding factors causing for such differences, the technical limitation of the assays used in our and other studies. Moreover, HLA genotypes may have played an important role. Another possibility is that S-specific T cells, especially for CD8+ T cell responses, degraded over the 3–4 months period.

On the other hand, the reported findings of SARS-CoV-2 N-specific T cell responses are highly controversial. Grifoni et al. reported that N protein contributes only about 10% to the total CD4+ and CD8+ T cell responses among convalescent patients in the United States. Peng et al. found a higher proportion of multifunctional M/N-specific T cells compared with S-specific T cells among patients who had recently just recovered from mild illness in the United Kingdom. However, Habel et al. similarly reported robust CD4+ T cell responses but weak CD8+ T cell responses directed against N and S proteins among Caucasian COVID-19 convalescent patients in Australia. Le Bert et al. detected CD4+ and CD8+ T cells that recognised multiple regions of the N protein among all convalescing patients tested in Singapore. Furthermore, among COVID-19 convalescent patients in Hong Kong, Zhou et al. reported higher N-specific CD4+ and CD8+ T cell responses than RBD-specific responses. Sekine et al. similarly reported robust CD4+ and CD8+ T cell responses directed against N and S proteins among convalescing individuals with asymptomatic and mild COVID-19 in Sweden. In our study, we observed N-specific CD4+ and CD8+ T cell responses in 65% and 50%, respectively, of recovered Chinese COVID-19 patients, respectively. Thus, N-specific T cell responses, especially for CD8+ T cells, are more robust than S-specific responses. Several factors may contribute to differences across studies. First, Grifoni et al. used predicted epitopes that capture about 50% of the total CD4+ T cell responses and target the 12 most prominent HLA class I A and B alleles. In this way, they may have narrowed their peptide patterns, and missed some epitopes. In contrast, we and others employed the entire N protein or overlapping peptides that covered the whole N protein. Second, the HLA genotypes have affected the responses. Hebel et al. chose the HLA-A*02:01 phenotype and detected suboptimal CD8+ T cell responses. Peng et al. identified SARS-CoV-2 CD8 optimum epitopes restricted by B*2705, B*0702, B*4001, A*0301, A*1101, and A*0101. Third, the experimental conditions, such as geographical and temporal variations, may also have contributed to the differences. Together, these results suggest the potential importance of including non-spikes proteins within future COVID-19 vaccine design.

Previous studies have also reported the two main phenotypic memory T cells as effector memory (CD45RA−CCR7−) and central memory (CD45RA−CCR7+) CD4+ T cells in recovered SARS and MERS patients, and the persistence in circulation of the late effector (CD45RA−CCR7−) CD8+ T cells. Each subset of these T cells plays a role in the protective immunity to reinfection by rapidly migrating effector subsets into tissues to provide protection and proliferating central memory T cells in the draining lymph node, so providing a pool of new effector cells. Peng et al. reported SARS-CoV-2-specific CD8+ T cells among convalescent patients in the United Kingdom were mainly effector memory (CD45RA−CCR7−, 50.3% ± 13.3%) and central memory (CD45RA−CCR7+, 20.7% ± 8.4%) phenotypes. Zhou et al. found similar trends for both CD4+ and CD8+ T cells responsive to SARS-CoV-2 N protein and RBD among COVID-19 convalescent patients in Hong Kong. In our study, although we detected varied frequencies of SARS-CoV-2-specific CD4+ and CD8+ T cells in patients, the majority of S- and N-specific CD4+ and CD8+ T cells were phenotypically effector memory (CD45RA−CCR7−) and late effector (CD45RA+CCR7−) T cells. This phenomenon was also observed in COVID-19 patients about 1 month after infection. It is possible that S- and N-specific T cells expressing the central memory (CD45RA−CCR7+) phenotype fall off rapidly after the infection has resolved.

Our study had several limitations. The small sample size, especially for severe patients and asymptomatic individuals, was dictated limited by expediency, which limited the analysis of the antibody responses stratified by patient age, sex, underlying condition, or disease severity. In addition, our follow-up of patients is currently at 3–4 months post-infection. Thus, assessment of the duration and resiliency of the SARS-CoV-2 antibody and T cell responses in a large cohort study would be desirable for validation of our results. Last, taking into consideration the biosecurity issue, because of the unavailability of patient blood from the BSL-3 facility as SARS-CoV-2 RNA has been detected in patient’s blood samples, we did not isolate serial PMBCs from patients during their hospitalisation which also limited to full characterisation of the dynamics of the T cell responses during infection.

In summary, we measured the dynamics of SARS-CoV-2-specific antibodies and CD4+ and CD8+ T cell responses in COVID-19 patients. All patients not lost to follow-up had high levels of antibodies 3–4 months after infection. We detected SARS-CoV-2-specific CD4+ and CD8+ T cells in approximately 65% of recovered patients. Our findings can inform the design of future serological studies and the development of SARS-CoV-2-targeted vaccines.

Methods

Ethics statement. All patients provided written informed consent. The study was conducted following the Declaration of Helsinki, and the Institutional Review Board of the Academy of Military Medical Sciences approved the study protocol (IRB number: AF/SC-08/02.60).

Study design and participants. From January 12, 2020, through February 14, 2020, we invited patients hospitalised with SARS-CoV-2 infection in the local hospitals in Linyi City of Shandong Province, China, to give informed consent to participate in this study. All potential patients had a diagnosis of SARS-CoV-2 confirmed by positive real-time reverse transcription-polymerase chain reaction (RT-PCR) results. We enrolled a total of 16 newly diagnosed patients, and prospectively collected their blood samples up to 3–4 months after illness onset. Of these 16 patients, 5 were lost to follow up at 3–4 months after infection. At the 3–4 month follow up visit, we additionally enrolled 9 recovered patients 3–4 months after infection. We collected blood from each participant using serum separator tubes with gel during hospitalisation and at hospital discharge. At the 3-4 month follow up visit, we collected blood was collected in an EDTA tube and serum separator tube for PMBCs and serum isolation, respectively. To compare the proportion of patients with detectable antibody responses at different time points post-symptom onset (PSO), we assessed serum samples collected ≤7 days (median 5, interquartile range [IQR] 3–6), ≤14 days (median 10, IQR 9–12), and ≤21 days (median 17, IQR 15–19) PSO; during 22–42 days (median 28, IQR 24–30) after onset; and then at 3–4 months (median 106, IQR 103–109). We recorded the demographic and clinical characteristics of patients, including baseline demographic data, date of symptoms onset, presenting symptom including fever, cough, sputum production, and sore throat, past medical and smoking history, hospitalisation, and radiological evidence of complication by pneumonia, were collected at enrolment. We additionally used 10 age- and sex-matched healthy control subjects whose serum samples had been collected before the pandemic as controls.

Case and disease severity definition. We defined a laboratory-confirmed patient of COVID-19 as an individual positive for SARS-CoV-2 by RT-PCR of nasopharyngeal swabs. We defined a symptomatic patient as an individual with laboratory-confirmed COVID-19 with symptoms such as fever, cough, sore throat, sputum, and so on. We defined a patient with an asymptomatic infection as an individual who was positive for SARS-CoV-2 by RT-PCR without any relevant symptoms post-symptom onset (PSO).
Flow cytometry

**Virus-specific T cells stimulation.** PBMCs were stimulated with recombinant SARS-CoV-2 nucleocapsid antigen (rAd5N) at an MOI of 100 (GenBank: MN908947.3, Vigenebio, Jinan, China) in plain RPMI-1640 for 1 h at 37 °C. Then 10% FBS and 20 U/ml human interleukin-2 (IL-2, R & D Systems, Abingdon, United Kingdom) were added to the cultures. After 66 h incubation, 1 μl brefeldin A (BFA, Cat No. 90-4306-51, eBioscience, San Diego, CA, USA) was added to block cytokine secretion for 6 h, thereafter, the cells were subjected to flow cytometry analysis.

**Surface staining of surface markers and cytokines.** For surface staining, single-cell suspensions were washed once with fluorescence-activated cell sorting (FACS) washing buffer (2% FBS, 0.1% NaN3 in PBS) and blocked with Fc receptor blocking solution. Cells were then incubated with fluorescence-conjugated antibodies against cell surface molecules for 30 min at 4 °C. After washing with FACS buffer, the cells were fixed and permeabilized using a fixation/permeabilisation kit (eBioscience) and stained with fluorescence-conjugated specific antibodies against cytokines following the manufacturer’s instructions. Flow cytometry was performed using a Becton Dickinson FACS Canto (BD Biosciences, San Jose, CA, USA). Samples were analysed using FlowJo software (FlowJo, Ashland, OR, USA). The following anti-human monoclonal antibodies were used in the staining assay: BV510-labelled anti-CD3 (300448), APC-labelled anti-CD4 (357408), PE-labelled anti-CD8α (300908), PE-Cy7-labelled anti-CD45RA (304126), BV421-labelled anti-CCR7 (353208), PerCP-Cy5.5-labelled anti-TNF-a (502926), BV421-labelled anti-GzmB (396414), and FITC-labelled anti-IFN-γ (11-7319-82); all antibodies were from eBioscience or BioLegend.

**Statistical analysis.** We analysed the anti-S and anti-RBD IgG and NAb titre with log-transformed geometric means and 95% confidence intervals (95%CIs) and determined the mean and 95%CIs of the OD value for anti-N IgG and anti-RBD IgM. The log-transformed mean and 95%CIs were then back-transformed to the original scale. We calculated the proportion of antibody titre equal to or greater than the threshold and associated 95%CIs. We used the two-tailed paired t-test or two-tailed Mann–Whitney U-test for testing the differences in virus-specific T cell responses. We used nonparametric Spearman correlation analyses to determine associations between analysed parameters. All statistical tests were 2-sided with a significance level of 0.05. We performed all statistical analyses in Prism (GraphPad Software).

**Data availability.** The data that support the findings of this study are available within the paper and its supplementary information files. Source data are provided with this paper.

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