A comparative cohort study of post-COVID-19 conditions based on physical examination records in China

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Summary

Background Coronavirus disease-2019 (COVID-19), caused by SARS-CoV-2 virus infection, is characterized as a multisystem disease, potentially yielding multifaceted consequences on various organs at multiple levels. At the end of 2022, over 90% of the Chinese population was infected by SARS-CoV-2 within 35 days because of adjustments to epidemic prevention and control policies. This short-term change provides an unprecedented opportunity for comparative studies on COVID-19 infection among large populations.

Methods In this study, the physical examination data of 136,713 people in the past three consecutive years was employed to study the impact of COVID-19. Standard physical examination data, comprising evaluations of nearly a hundred indicators, were investigated for a comprehensive assessment of COVID-19's effect on human health.

Findings The results suggested that most indicators remained stable or changed within a permissible range after the COVID-19 outbreak in December 2022, but several specific indicators presented abnormal patterns of varying durations. There was an observed increase in the fraction of T-wave abnormalities during the outbreak, especially in people with chronic diseases such as hypertension, liver steatosis, and hyperglycemia.

Interpretation These findings highlighted the impact of COVID-19 on cardiovascular health and its potential interaction with chronic diseases.

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Keywords: COVID-19; Physical examination; T-wave abnormality; Chronic disease; Big data

Introduction

The post-acute sequelae of COVID-19, also known as PASC, can affect various organ systems. PASC may elevate the vulnerability to cardiovascular disorders,[1,2] neurological system disorders,[3] endocrine/genitourinary disorders,[4,5] dermatological disorders,[6] and cardiological disorders.[7,8] A few studies have investigated the impact on different human organs during the post-acute phase of COVID-19.[9–11] However, most were limited to hospitalized or individuals without paired data before COVID-19 and had a short duration of follow-up. A comprehensive assessment of PASC across a broad array of organ systems for 3–6 months after infection is not yet available.[12] Additionally, large, long-term cohort studies investigating PASC are also lacking.

Since the first recognition of COVID-19 in December 2019, China's practices have been remarkably successful in controlling the transmission of SARS-CoV-2. In December 2022, following China's easing of its quarantine protocols, it was estimated that over 90% of the population experienced their first COVID-19 infection within a 35-day timeframe.[13,14] This unique scenario created an opportunity to utilize the annual physical examination data from that particular period compared

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Research in context

Evidence before this study

COVID-19 infection can negatively impact various organ systems, exacerbating existing cardiovascular, neurological, and endocrine diseases. Understanding the effects of COVID-19 on different health aspects can provide insights into COVID-19 pathogenesis and potentially shape future care strategies. However, existing studies mainly focus on hospitalized individuals with short follow-up time and lack baseline data before COVID-19 infection. There is a shortage of extensive, long-term cohort studies that compare the health parameters before and after COVID-19 infection.

Added value of this study

Following the restructuring of China's epidemic prevention and control policies, most of the Chinese population experienced their initial COVID-19 infections from December 2022 to January 2023. Leveraging this period, we compared physical examination indicators between 2023 and the preceding years. Our study analyzed data from 136,713 individuals over three consecutive years, covering ten major categories and 70 sub-items. The results revealed that after the COVID-19 outbreak in December 2022, most indicators either remained stable or changed within permissive ranges. However, some specific indicators displayed abnormal patterns for various durations. Notably, during the outbreak, there was an increase in the incidence of T-wave abnormalities, particularly among individuals with chronic conditions such as hypertension, hepatic steatosis, and hyperglycemia.

Implications of all the available evidence

This study reveals the effects of the COVID-19 infection on cardiovascular health and associated indicators. The findings underscore the significance of managing and caring for individuals with preexisting health conditions, especially in the 1–2 months post-infection. The results highlight the necessity for targeted interventions and continuous surveillance to mitigate potential risks and improve cardiovascular health outcomes.

to the same period in previous years, effectively addressing the knowledge gap and informing strategies for post-acute COVID-19 care.

In this study, we used the annual physical examination data from the health management center of the First Affiliated Hospital of Zhejiang University School of Medicine. By comparing the physical examination data before and after COVID-19 mass infection event on the same set of subjects, the study aims to analyze the impact of COVID-19 infection on the general population's health.

Methods

Data collection

Electronic Medical Records (EMR) (including physical examination, laboratory tests and questionnaires, cognitive function testing, cardiopulmonary evaluation, electrocardiogram data, complete blood counts, pulmonary imaging scans, ultrasound scans, and biochemical tests, etc.) were collected from the health management center of the First Affiliated Hospital of Zhejiang University School of Medicine, spanning from November 2020 to June 2023, to build a cohort of 136,713 individuals. This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang University School of Medicine. The IRB approval number of this study is 2023-0754.

Raw Electronic Medical Records were obtained from the hospital database, and data cleaning was performed. Next, health indicators were extracted. The 48 numerical health indicators, such as the whole blood cell counts and lipid levels, were directly used in further analysis, whereas the 22 binary/categorical health indicators were extracted through a meticulous text-mining process. The text mining was based on the textual descriptions from medical images, colored ultrasound, and ECG results. For example, this process involved tasks like detecting the presence of ground-glass opacity in textual descriptions of lung CT scans and identifying sinus rhythm acceleration or T-wave abnormalities in ECG textual reports. Finally, these collected records were arranged into a more extensive tabular format with 70 indicators as columns and individuals as rows. To facilitate the processing of these raw records, we applied xorbits [https://xorbits.io/], an open-source Python big-data engine, with dedicated scripts available in our GitHub repository (https://github.com/jhuanglab/healthman). In addition, a questionnaire was administered to study the presence of adverse reactions following COVID-19 infection within the study population. The questionnaire was distributed in Hangzhou, Zhejiang, China, 10 months after the onset of the COVID-19 outbreak in late 2022, using the WJX platform (powered by http://www.wjx.cn). The questionnaire included the number of SAS-CoV-2 infection between December 2022 and February 2023, the number of COVID-19 vaccines received, and adverse effects after COVID-19. The adverse effects of the infection included: myalgia, headache, chest stuffy, palpitation, insomnia, nausea, and emesis. A total of 1340 valid questionnaires were collected.

Predictive modeling of T-wave abnormality

Physical examination records from January to February were collected, and T-wave abnormalities in 2023 served as labels (Y). The features (matrix X) were derived from the raw data by applying feature engineering techniques. Specifically, we excluded features with excessive missing data and calculated correlations among the remaining features. Based on the feature-wise correlation matrix, we clustered the features and selected those relatively independent and representative features. Additionally, we extracted electrocardiographic parameters from textual descriptions, as depicted in Supplementary Fig. S2C. The difference in physiological parameters between 2023 and 2022, as well as between 2022 and 2021, were calculated. These derived features were then used as input features for predictive modeling.

A supervised machine learning model XGBoost [https://arxiv.org/abs/1603.02754] was applied. The parameters used in xgb.XGBClassifier were max_depth = 2, min_child_weight = 40, gamma = 10. The dataset was divided into training (80%) and testing set (20%). To prevent overfitting, model fitting was performed on the training set, and predictive performance evaluation was based on the testing set. The performance of the model on both the training and the testing set was reported. Features with high importance scores were considered as strongly correlated with abnormal T-wave occurrences.

Controlling of confounding factors

To reduce the influence of unmeasured confounders, we focused the analysis on the 23,838 subjects with three consecutive annual physical exams and the last physical exam between November 2022 and June 2023. We compared the physiological parameters from their last physical exam ("2023-test") to those from their previous physical exams ("2022-control"). Since the comparisons were made on the same set of subjects, we effectively controlled many subject-level confounding variables. To control for seasonal variation, we stratified the comparisons by month. The month-wise comparisons also enabled us to study the trajectory of the differences, and we were particularly interested in studying the pattern around the mass infection period (December 2022 – February-2023). As the comparison between "2023-test" and "2022-control" did not control for yearly variation or aging effect, we also compared "2022-control" to "2021-control" (the first physical exam). Those parameters with much larger differences in "2023-test"-versus-"2022-control" comparison than "2022-control"-verus-"2021-control" comparison in the mass infection months provide strong evidence of the COVID-19's impact.

Statistical analysis

We extracted the relevant demographic variables and health indicators from electronic health records. The Tableone R package (Version 0.13.2) was applied to generate a basic statistical summary table. Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as percentages of the categories. As these longitudinal comparisons are paired, we used the non-parametric Wilcoxon signed-rank test for continuous parameters and McNemar's test for categorical parameters. To address multiple testing, false discovery rate (FDR) control (Benjamini-Hochberg procedure) was applied, and FDR-adjusted p-values or q-values were reported. Wilcoxon rank-sum test was used to assess the association between T-wave abnormality and physiological parameters indicative of chronic conditions. Chi-squared tests were used to study the correlations between symptoms.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang University School of Medicine with number: 2023-0754. The research conformed to the principles of the Helsinki Declaration.

Role of funders

The funders had no role in the study design, data collection, data analyses, interpretation, or writing of the report.

Results

Baseline characteristics in the overall cohort

The cohort included 235,681 physical examination records from 136,713 individuals between November 2020 and June 2023. Specifically, there were 16,836 records from November to December 2020, 85,752 in 2021, 92,020 in 2022, and 41,073 from January to June 2023 (Fig. 1A). A total of 23,838 individuals had physical examination records for three consecutive years (Fig. 1B and C, Supplementary Fig. S1A and B and Table S1). Additionally, 1340 people participated in a questionnaire on adverse reactions after COVID-19 infection, which included myalgia, headache, chest tightness, palpitations, insomnia, nausea, and vomiting (Fig. 1D). The questionnaire revealed that 86.3% reported at least one COVID-19 infection by December 2022, with 72.3% experiencing their first infection in December 2022 and 14% having been infected previously (Fig. 1D).

Among the 23,838 individuals, 6786 had physical examinations during the COVID-19 outbreak from December 2022 to February 2023, pre-break on November 2021 and after-break from March 2023 to June 2023 (Fig. 1E). Among these subjects, 46.6% were males and 53.4% were females. The age is 44.3 ± 14.5 years.-Over 90% of individuals who participated in three consecutive years of physical examinations did so within two months around the scheduled dates (Supplementary Fig. S2A). The physical examination data comprised ten major categories and 70 sub-items. Categories such as cardiovascular, ECG, chest X-ray/CT, color ultrasound, blood lipids, biochemical-metabolism, and glycemic indicators had relatively low missing data percentages,

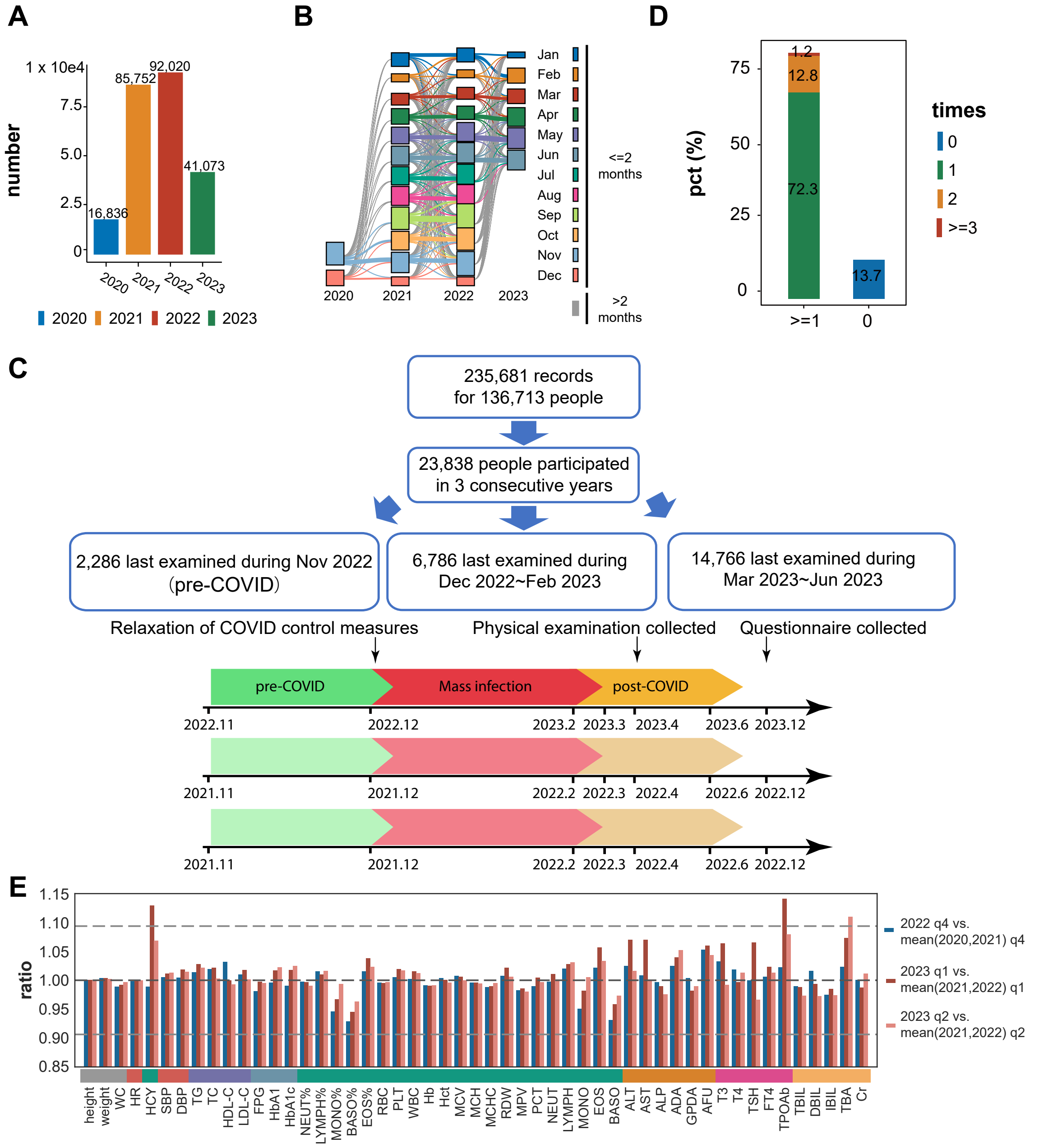

Fig. 1: **An overview of the key features for the entire physical examination cohort. (A)** 235,681 physical examination records from November 2020 to June 2023. **(B)** Sankey plot for examination time across different years. Individuals with >2 months intervals between their physical examinations across two different years were colored gray. **(C)** Data filtering process and group definitions in this cohort study. **(D)** Number of infection in December, 2022. **(E)** Alteration ratios for the indicators at specific periods.

averaging less than 12% (Supplementary Fig. S2B). Other indicators, including liver biochemical and thyroid-related indicators, had more missing data, all below 32% (Supplementary Fig. S2B). Closely related indicators tended to cluster together (Supplementary Figs. S1C and S2C).

Most of the 70 sub-items of physical examination indicators fluctuated within a range of 10% in 2023 compared to the average of 2021 and 2022 (Fig. 1E). However, notable differences were observed in certain common indicators. For instance, the average systolic blood pressure (SBP) in November 2022 was similar to previous years but increased after the COVID-19 outbreak.

Changes in blood test parameters and thyroid function-related factors

Examination of the complete blood count (CBC) index revealed fluctuations in red blood cell-related parameters. Among these indicators, RDW exhibited the most persistent and significant increase (2%) in January 2023 ($p < 0.00001$) compared with their measurements in 2022, while it had no significant increase in 2022 compared with 2021 (Supplementary Fig. S3A). This increase gradually declined after three months (Fig. 2). The PLT count showed a 2% increase in January compared to the previous two years ($p = 0.00037$), while Hb exhibited the opposite trend (2% decrease, $p < 0.00001$). The MPV indicator in 2023 was 2% lower compared to the previous two years ($p < 0.00001$), with a more pronounced decline during the COVID-19 outbreak period. However, by March, most of these indicators had returned to levels before the COVID break. This was also observed in all gender and age groups (Supplementary Fig. S4A–D). This suggested that the impact of COVID-19 infection on red blood cells and platelets may persist for several months, confirming the findings in other studies.[15–19]

Additionally, a subtle uptick was observed in thyroid-related indicators (Fig. 2). Triiodothyronine (T3) levels exhibited a noteworthy 11% increase in January 2023, significantly surpassing the levels observed in the previous two years ($p < 0.00001$), followed by a subsequent decrease to average levels in the April to May 2023 timeframe. Similarly, free thyroxine (FT4) levels also increased by 4% in December 2022 ($p < 0.00001$) and gradually reverted to the average levels in April 2023.

Influence on pulmonary rehabilitation and lung X-ray/CT manifestations

The lung X-ray/CT manifestations of COVID-19 include ground-glass opacities (GGOs), consolidation, crazy paving patterns, and linear shadows, as mentioned in previous studies.[5,20] The proportion of pulmonary GGOs in 2023 was higher than in the previous two years (Fig. 3A, 14.6% versus 13.1% in 2022 and 10.1% in 2021). However, the increase ratio did not exhibit statistical significance when compared to the previous years. To further explore the relationship between this increase and COVID-19 infection, the dataset was further divided by gender and month. The analysis revealed a consistent elevation in the proportion of GdGOs both before and after the COVID-19 infection period in 2023 compared to the previous year 2022 (Fig. 3B and C, Supplementary Fig. S5A and B). Further comparisons were conducted between the years 2021 and 2022. The results showed no substantial differences in the fold change from the comparison between years 2022 and 2023 within various age and gender groups (Fig. 3D). Considering the increase in age for the same participant, age-related factors may contribute to this observation. Similar trends were also observed when evaluating the fraction of lung calcification compared to the previous year (Supplementary Fig. S5C and D).

Evaluation of electrocardiographic variables

COVID-19 can particularly affect the cardiovascular system, leading to abnormal electrocardiographic (ECG). In this study, we undertook a further analysis of potential associations between abnormal ECG findings in the physical examination records. The ECG findings were examined by month, revealing a noteworthy surge in the proportion of T-wave changes in January 2023 (12.7%, n = 1722) when compared to the same cohort from the previous years (7.0% in 2021 and 9.2% in 2022) (Fig. 4A).

The physical examination records were then grouped by gender and age. Subsequent analysis revealed an increase in the proportion of abnormal T-wave patterns from 2022 to 2023, especially for individuals aged 45 and above (Fig. 4B, Supplementary Fig. S6A and B). In

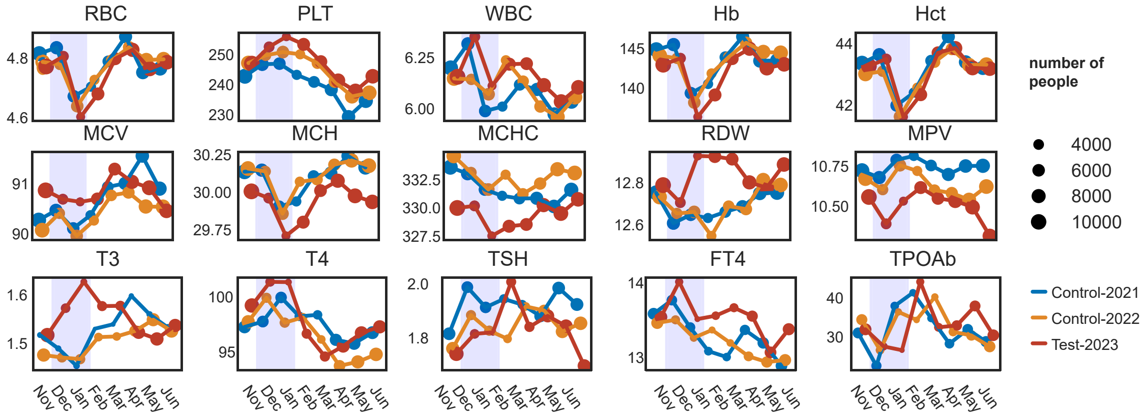

Fig. 2: **Analysis of alterations observed in various CBC/Thyroid indicators over time.** Line chart for CBC indicators and thyroid-related indicators of all individuals by months grouped by different periods.

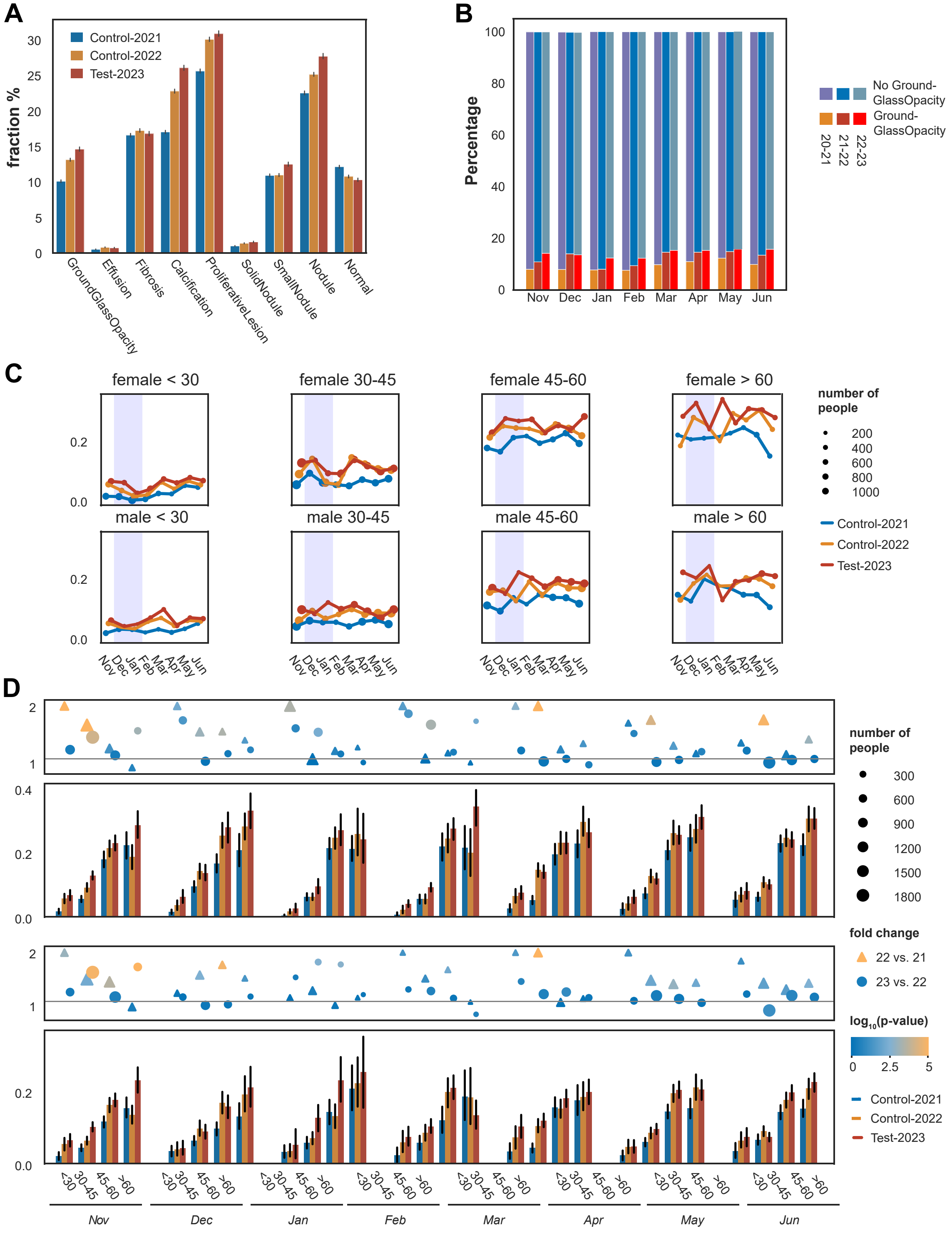

Fig. 3: **Interpreting the effects on the lungs based on chest X-ray/CT findings. (A)** Bar plot for fractions of lung-related description in physical examination records for all people. **(B)** Fractions for Ground Glass Opacity (GGO) by months grouped by 3 time periods for all people. **(C)** Fractions for Ground Glass Opacity by months grouped by gender (up: female, down: male), 4 age groups (left to right: <30, 30–45, 45–60, >60), and 3 time periods for all people. **(D)** Bar plot with fold-change and p-value for GGO for female (up) and male (down). For each bar plot, x indicates different months, and colors indicate the 3 time periods. The fold change(y) and p-values (color gradient) between periods were shown above the bar plot.

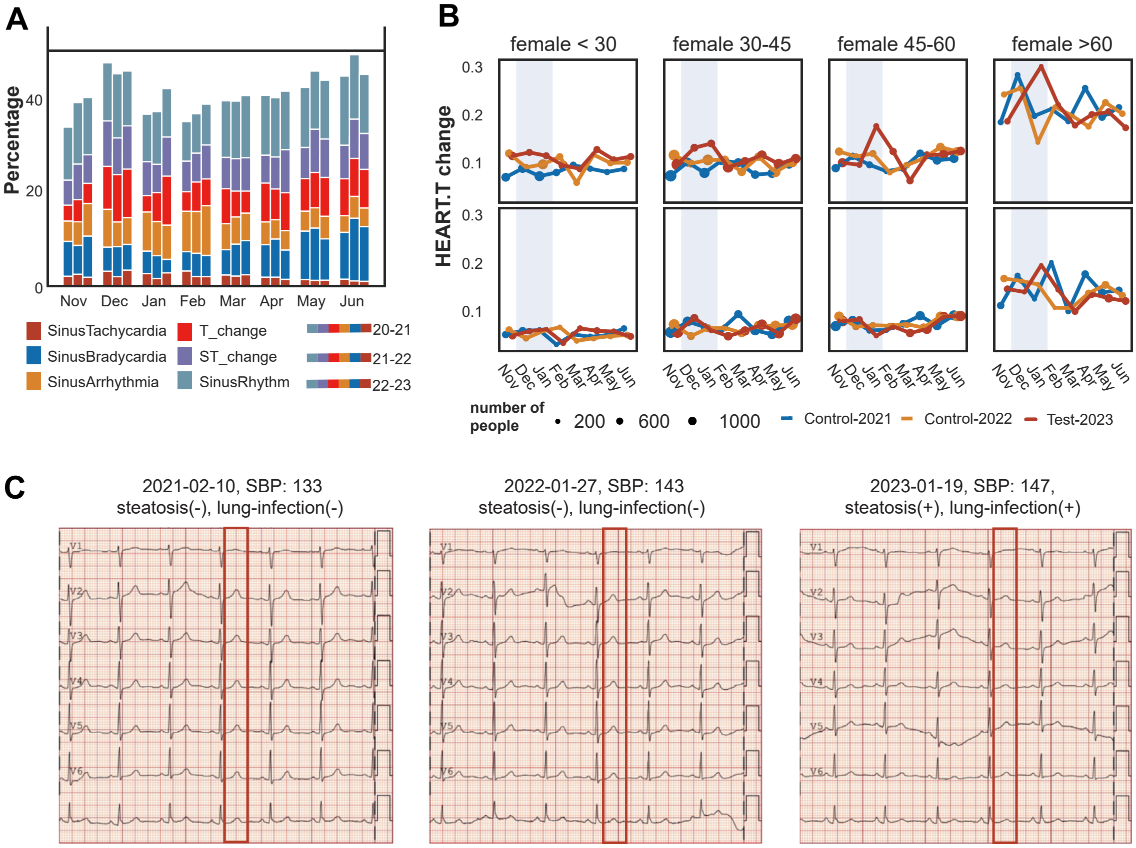

***Fig. 4:* Assessments of various electrocardiographic (ECG) variables. (A)** Bar plot for fractions of ECG descriptions in physical examination records for all people. **(B)** Scatter plot for T-wave abnormality for all individuals by months grouped by gender (up: female, down: male) age-groups (left to right: <30, 30–45, 45–60, >60), and 3 time periods. **(C)** An example ECG for individuals diagnosed with abnormal T-wave during Jan–Feb 2023.

the temporal context, an increment of 42% (n = 1088) was observed in January to February 2023 compared with the same period in 2022 while not observed in November to December (13%, n = 1231) and had attenuated by the time March to April (14%, n = 2616), suggesting a distinct correlation with the COVID-19 infection (Supplementary Table S2).

T-wave alterations may correlate with chronic conditions

Due to the significant impact of COVID-19 on individuals with pre-existing conditions, we focused on hyperglycemia, hyperlipidemia, and hypertension indicators. SBP/DBP, TG, and FPG/HbA1c were associated with these conditions. Individuals with T-wave alterations during COVID-19 (December 2022–February 2023) had elevated levels of these indicators in 2023, 2022, and 2021 (Supplementary Fig. S7A and B). No significant relationship was found between hypertension (SBP > 140) and T-wave changes in both males and females. However, for individuals aged 45 and above, the significance was higher in females ($p = 0.0002$) compared to males ($p = 0.0058$) (Supplementary Table S3). For liver steatosis, the relationship was not significant for females under 45 ($p = 0.08$) but was significant for males ($p = 0.017$). For those aged 45 and above, the significance was higher in females ($p = 0.0004$) but not in males ($p = 0.78$) (Supplementary Fig. S7C and Table S4).

Regarding hyperglycemia and T-wave changes, no significant relationship was found for females under 45 ($p = 0.99$), but moderate evidence was found for males ($p = 0.046$). For those aged 45 and above, the significance was higher in females ($p = 0.00018$) compared to males ($p = 0.036$) (Supplementary Fig. S7A and B and Table S5). The fraction of GGO for individuals with T-wave alteration during COVID-19 showed no difference from control groups (Supplementary Fig. S7D). A case study illustrated T-wave abnormalities: In February 2021 (aged 52), an individual had a normal ECG and blood pressure of 133, with no steatosis. By January 2023 (aged 54), the ECG showed T-wave changes, with

SBP = 147, pneumonia lesions in a chest CT, and steatosis. The T-wave in 2023 was lower compared to 2022 (Fig. 4C), exemplifying the progression of chronic conditions during COVID-19.

We developed an XGBoost model to classify and predict T-wave anomalies, achieving AUC values of 0.78 and 0.74 in the training and testing sets, respectively (Supplementary Fig. S8A and Table S6). Blood glucose, blood lipids, and blood pressure were key predictors of T-wave abnormalities (Supplementary Fig. S8B and C).

Adverse reactions after the COVID-19 infection

Following the COVID-19 outbreak, we investigated adverse outcomes related to PASC, focusing on significant electrocardiographic abnormalities. We collected and analyzed questionnaire data from 995 individuals reporting non-respiratory adverse reactions. The most common reactions were myalgia (59.3%) and headache (55.4%) (Fig. 5A). Additionally, 20.2% experienced chest tightness, palpitations, and insomnia, while 10% reported nausea and vomiting. Specifically, 437 individuals reported one non-respiratory adverse reaction, 408 reported two, 209 reported three, and 101 reported four or more (Fig. 5B).

Significant correlations were found: insomnia was associated with chest tightness and palpitations, and myalgia correlated with headaches (Fig. 5C). Further analysis indicated that insomnia often co-occurred with

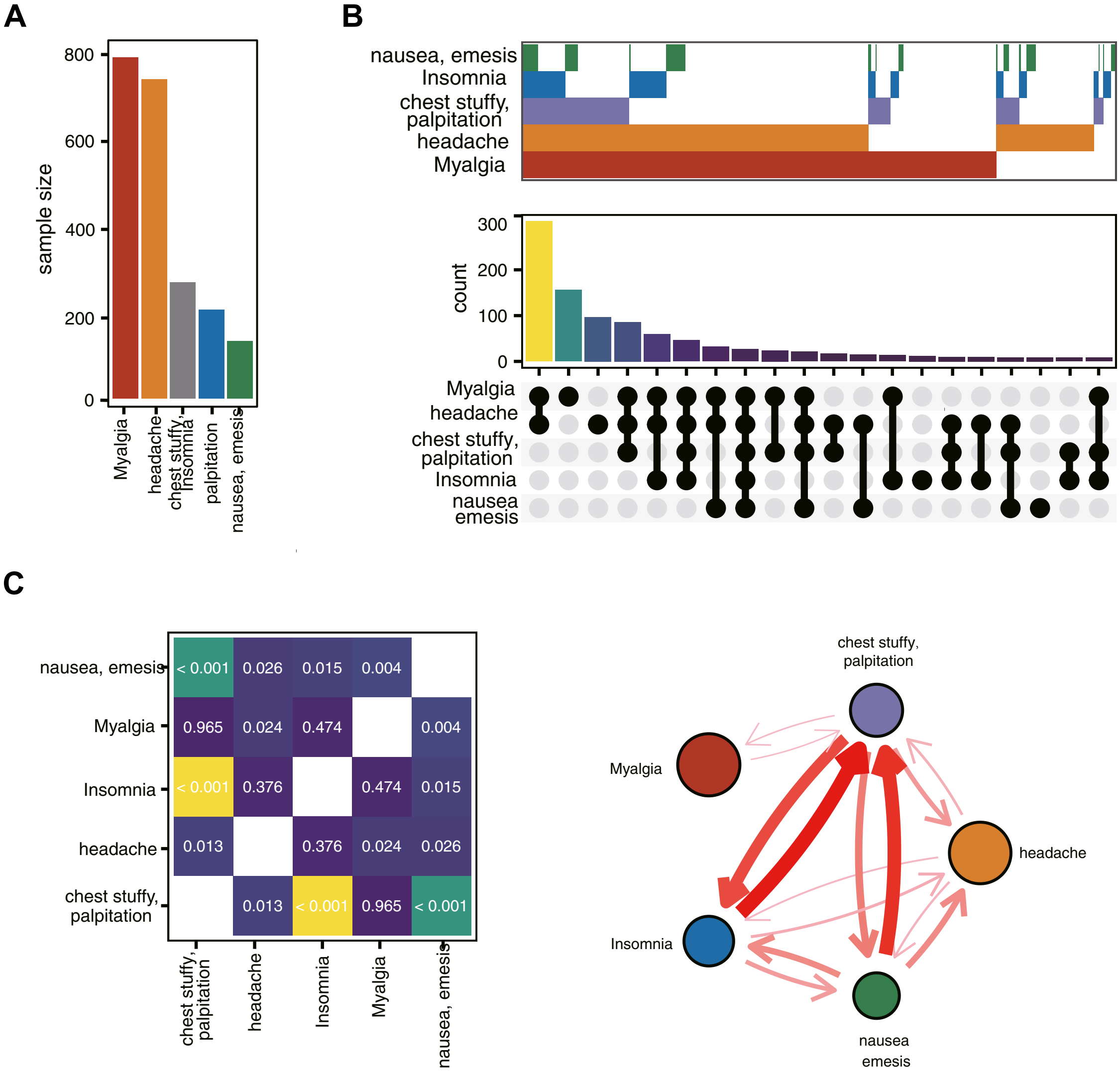

Fig. 5: **Adverse reactions after a COVID-19 infection. (A)** Non-respiratory adverse reactions occur in people infected Omicron. **(B)** Distribution of non-respiratory adverse reactions in people infected with Omicron. The proportion of different symptoms in people infected with the new coronavirus (up). Number of people who exhibit one or more adverse effects at the same time (down). **(C)** Dependence of adverse effects of different non-respiratory symptoms. Chi-square test significance heat map (left). Dependency network diagram of adverse reactions (right).

chest tightness and palpitations. Nausea and vomiting were also linked to chest tightness and palpitations (Fig. 5C).

In summary, COVID-19 primarily caused flu-like symptoms such as myalgia and headache, with some individuals experiencing chest tightness, palpitations, nausea, vomiting, and insomnia. Other respiratory infections like influenza and RSV were present but less common. These complex symptoms may be due to population heterogeneity and suggest potential cardiac issues post-COVID-19 infection, consistent with ECG analysis. Further research is needed to confirm these findings.

Discussion

As most of the Chinese population experienced their first COVID-19 infections during the period from December 2022 to January 2023, we conducted a comparison of physical examination indicators between 2023 and previous years in our large-scale population cohort to assess the potential impact of PASC. Meanwhile, we investigated the adverse effects of the COVID-19 infection by a questionnaire. Although most indicators exhibited stability or fluctuations within acceptable thresholds, some notable differences were still observed. Particularly, we found a significant increase in the proportion of T-wave abnormalities, especially for individuals aged 45 and above. Moreover, the individuals with T-wave alteration had a high level of chronic condition-related indicators after and before the COVID-19 outbreak.

Cardiovascular comorbidities are frequent in patients presenting with COVID-19.[21,22] Early studies suggested that severe clinical manifestations or adverse events in patients could be attributed in part to cardiac injury brought on by COVID-19 infection.[23,24] It is, therefore, important to focus on the cardiac consequences of COVID-19 infection after the global epidemic has ended. Although cardiac manifestations of COVID-19 infection, such as elevated troponin, arrhythmias, myocarditis, and T-wave abnormalities, have been previously reported, these studies mainly relied on hospital-based patients with small sample sizes, and explorations regarding large samples of ambulatory populations are relatively scarce. In this study, we took advantage of China's prevention and control policies and used a large-sample cohort to examine medical examination data before and after the end of the epidemic. Our results revealed a noteworthy surge in the proportion of T-wave changes in January 2023 when compared to the same cohort from the previous years (Fig. 4A), which is consistent with the findings of some other studies.[25–27] For instance, a New York COVID-19 cohort study revealed that 70% of cases had cardiac damage and that the proportion of aberrant ECGs (including T-wave abnormalities) was higher. The group with cardiac injury was also older.[28] Age itself contributes significantly to adverse events in COVID-19 infections. A striking feature of the COVID-19 pandemic is the high incidence of fatalities in elderly patients.[29] In our study, the proportion of T-wave abnormalities was more pronounced in individuals aged 45 and above. There is also a strong correlation between age and various chronic diseases. It is well known that chronic disease groups such as hypertension, hyperlipidemia, and hyperglycemia are less resistant to COVID-19 infections and are more likely to result in a worse prognosis.[30] Our results showed that individuals with T-wave alteration during the COVID-19 outbreak had a high level of chronic condition-related indicators, not only in 2023 but also in 2022 and 2021. The findings indicated that these conditions had a significant relationship with T-wave changes in old age groups.

The exact mechanism by which COVID-19 causes cardiac injury is not known. The main mechanism of SARS-CoV-2 infection is the binding of the viral surface spike protein to the human angiotensin-converting enzyme 2 (ACE2) receptor. ACE2 is broadly distributed in the heart and the lungs,[31] which results in the heart and lungs being more vulnerable to attack by SARS-CoV-2. Moreover, multiple studies have found that microvascular thrombosis, vascular endothelial injury, and imbalances in the renin-angiotensin-aldosterone and kinin-releasing enzyme system may be important mechanisms leading to myocardial tissue injury.[32–34] Hypoxemia has also been proposed as a potential contributing factor for COVID-19 infection-related cardiac injury. Due to inflammation and lung injury, COVID-19 infected patients can develop hypoxemia, or low circulating oxygen level, which can lead to heart muscle defects.[35,36] In our data, we also found abnormalities in oxygen-related Hb, as well as other cardiac injury-related markers, including PLT and thyroid markers. However, further study is required to determine whether these abnormal indicators are associated with cardiac T-wave abnormalities. Of interest, the T-wave abnormalities observed in our study returned to normal levels in March–April after COVID-19 infection. Nevertheless, the potential cardiac burden of future recurrent COVID-19 infections still needs vigilant monitoring. A Japanese study suggested that there may be an increased risk of suffering "cardiac decompensation" in the future due to persistent SARS-CoV-2 infection.[37]

Furthermore, to investigate potential causes of cardiac T-wave abnormalities, we thoroughly examined the liver function indicators. The results did not show abnormalities in the myocardium-related indicator AST, but we observed some abnormalities in other liver function-related indicators. The levels of alanine transaminase (ALT) exhibited a pronounced upsurge surpassing those of the preceding two years, corroborating the observations detailed in other studies (Supplementary Fig. S9A and B) ($p = 0.00003$).[38,39] Adenosine deaminase (ADA, increasing, $p < 0.00001$), homocysteine (HCY, increasing, $p < 0.00001$), Creatinine (Cr, decreasing, $p = 0.0022$), and Glycyl-proline-dipeptidyl aminopeptidase (GPDA, decreasing, $p < 0.00001$) also had significant abnormalities (Supplementary Fig. S9A). Many studies have reported liver damage from the COVID-19 infection.[40,41] These abnormal liver function indicators could be directly related to liver damage from SARS-CoV-2, but they could also be brought on by medication use following COVID-19 infection. More precise studies are needed to determine whether SARS-CoV-2 affects the liver.

Overall, leveraging China's epidemic prevention and control policies, we conducted a detailed analysis of annual physical examination data from health management centers before and after the COVID-19 outbreak. The results revealed an increase in the proportion of abnormal T-wave patterns after the COVID-19 outbreak, especially for individuals aged 45 and above. This study contributes to our understanding of the long-term effects of COVID-19 and informs post-acute care strategies.

However, it is important to note that our annual physical examination data may have limitations. Firstly, factors such as testing availability and demographic variations could influence the results. Secondly, the study may not account for all potential confounding factors that could affect the observed associations. For instance, comorbidities, medication use, and lifestyle factors could impact the relationship between COVID-19 and the health parameters examined. Notably, the lack of vaccine status information and other respiratory infection could potentially confound the results.

Although we used matched data to ensure consistent population characteristics, this led to a slight increase in the age distribution by one year, which may influence the development of certain indicators. Additionally, our records were collected from a population of healthy individuals and lacked information on COVID-19 diagnosis timing, severity, vaccine administration, and other related factors. Therefore, further analysis and research are needed to understand the underlying mechanisms and clinical implications of these observations.

Contributors

J.H. and Z.L. conceptualized and supervised the study. B.H. and Z.T. conducted the bioinformatic and statistical analyses. J.D., N.L., C.L., P.J., X.F., and Z.L. were part of the clinical team and were involved in the investigation. J.C. and J.H. validated the bioinformatic and statistical analyses. J.D., N.L., C.L., P.J., and X.F. were responsible for collecting detailed clinical data. The initial draft of the manuscript was written by B.H., Z.T., C.Y., J.C., J.H., and Z.L. And J.H. and Z.L. accessed and verified the underlying data. All authors participated in result interpretation, contributed to the manuscript writing, engaged in discussions, provided critical feedback, and approved the final version of the manuscript for submission.

Data sharing statement

Upon reasonable request, deidentified participant data and code used in the analyses can be shared with other researchers. For further information, please contact the corresponding author (liuzhongzheyi@zju.edu.cn and huangjinyan@zju.edu.cn).

Declaration of interests

None of the authors have received funding or any other form of financial support related to this project. Additionally, the authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ebiom.2024.105549.

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