

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you '**Physician connect**' which contains latest and interesting news in the field of Medicine

This issue contains

- Factors Associated with Postdischarge Thrombosis in COVID-19 Patients
- A study on high blood pressure progression in type 2 diabetes mellitus indicated by metabolomic analysis of human serum.
- Hampton's Hump – Case Report

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

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Best Regards,
Medical Team, Micro Labs Limited

Factors Associated with Postdischarge Thrombosis in COVID-19 Patients

COVID-19 causes coagulopathy, which is characterised by an increase in dimerized plasmin fragment D (D-dimer) levels. As a result, patients with COVID-19 are more likely to develop both arterial and venous thromboembolism (VTE). Although COVID-19 is linked to a high rate of thrombotic events, the requirement for continued thromboprophylaxis following hospitalisation is unknown.

This study aimed to determine the rate of postdischarge arterial and venous thromboembolism in COVID-19 patients, identify risk factors for postdischarge venous thromboembolism, and assess the relationship between postdischarge anticoagulation use and the incidence of venous thromboembolism.

This is a cohort study of adult COVID-19 patients who had a positive SARS-CoV-2 test. Between March 1 and November 30, 2020, eligible patients were enrolled at five Henry Ford Health System hospitals. From April through June 2021, data was analysed. Following discharge, the individuals were given anticoagulant treatment. The key outcome was the start of symptomatic arterial and venous thromboembolic events within 90 days of release from the index admission for COVID-19 infection, which was detected using ICD-10 codes.

The mean (SD) age of the 2832 adult COVID-19 patients in this cohort research was 63.4 (16.7) years (IQR, 53-75 years), and 1347 patients (47.6%) were men. Thirty-six patients (1.3%) suffered venous thromboembolic episodes after discharge (16 pulmonary embolism, 18 deep vein thrombosis, and 2 portal vein thrombosis). A total of fifteen (0.5%) arterial thromboembolic episodes occurred after discharge (1 transient ischemic attack and 14 acute coronary syndrome). With a median (IQR) time to incident of 16 (7-43) days, the risk of venous thromboembolism reduced over time (Mann-Kendall trend test, $P=0.001$). With a median (IQR) time to incident of 37 (10-63) days, there was no change in the risk of arterial thromboembolism with time (Mann-Kendall trend test, $P=0.37$).

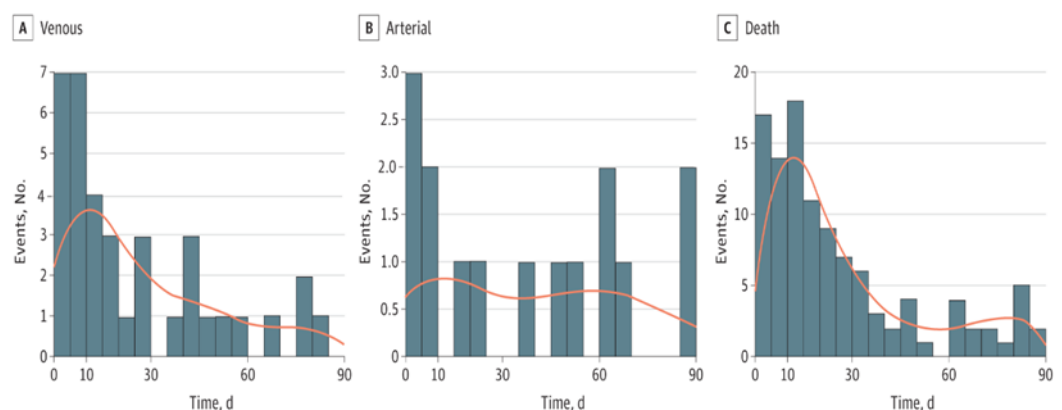


Figure 1: Event Counts of Postdischarge Venous Thromboembolism, Arterial Thromboembolism, and Death Without Events

Patients with a history of venous thromboembolism (odds ratio [OR], 3.24; 95 percent confidence interval [CI], 1.34-7.86), peak dimerized plasmin fragment

D (D-dimer) level greater than 3 g/mL (OR, 3.76; 95 percent confidence interval [CI], 1.86-7.57), and predischARGE C-reactive protein level greater than 10 mg/dL (OR, 3.02; 95 percent CI, 1.45-6.29) Therapeutic anticoagulation prescriptions at discharge were linked to a lower risk of venous thromboembolism (OR, 0.18; 95 percent CI, 0.04-0.75; P =.02).

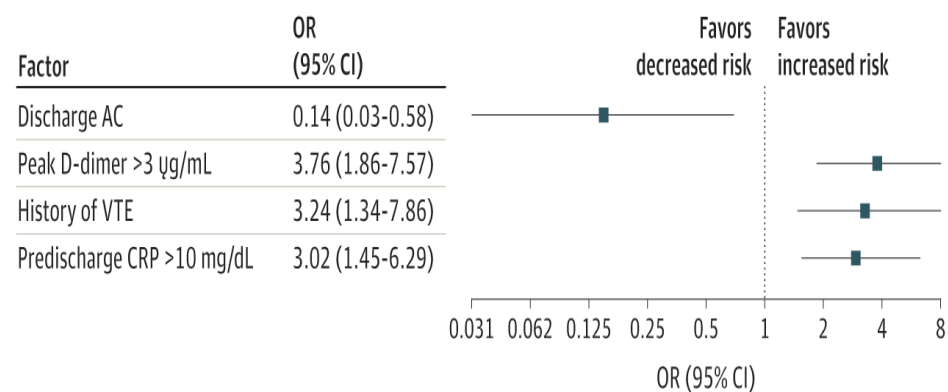


Figure 2: Multivariable Analysis of the Factors Associated With Risk of Postdischarge Venous Thromboembolism (VTE) in Patients With COVID-19

Type of AC	OR (95% CI)	P value
Prophylactic AC	0.17 (0.00-2.09)	.26
Therapeutic AC	0.18 (0.04-0.75)	.02

Table 1: Average Treatment Effect of Post discharge AC to Prevent VTE in Patients With COVID-19

Patients having a history of VTE, a peak D-dimer greater than 3 g/mL, and a predischARGE CRP greater than 10 mg/dL were shown to be at a high risk of developing new onset of VTE after discharge from hospital in this cohort analysis of adult patients hospitalised with COVID-19. If the patient's bleeding risk is modest, we recommend that patients with these risk factors be evaluated for postdischarge therapeutic AC.

Reference:

Li P, Zhao W, Kaatz S, Latack K, Schultz L, Poisson L. Factors Associated With Risk of Postdischarge Thrombosis in Patients With COVID-19. JAMA Netw Open. 2021 Nov 1;4(11):e2135397.



A study on high blood pressure progression in type 2 diabetes mellitus indicated by metabolomic analysis of human serum.

Metabolomics is defined as a non-invasive analysis of easily accessible human body fluids that includes a full quantitative and qualitative analysis of all metabolites in blood. Type 2 diabetes mellitus (T2DM) is a common metabolic illness that causes high blood sugar levels. Between 80 and 90 percent of T2DM patients develop high blood pressure (HBP), which exacerbates irreversible organ damage. Understanding the metabolic basis of high blood pressure is critical for early detection and treatment of diabetes complications.

When high-resolution mass spectrometry (HRMS) is combined with traditional mass spectrometry (MS), structural information is provided for metabolite identification. Due to its excellent sensitivity and reproducibility, ultrahigh-performance liquid chromatography quadrupole time-of-flight mass spectrometry (UHPLC-Q-TOF MS) has recently been popular in metabolomics studies.

This study aimed to understand the metabolic differences between T2DM and T2DM+HBP compared with HC and to predict the metabolites marking the progression from T2DM to T2DM+HBP using metabolomics on the ground of UHPL. In this study, a total of 4298 subjects (3062 men and 1236 women) were screened. An automatic biochemical analyzer was used to assess total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), aspartate transaminase (AST), and alanine aminotransferase (ALT) in the serum. From the physical examination participants, 34 patients with T2DM who developed HBP within a year were chosen.

The study examined the metabolomic profiles of 30 healthy controls and 30 patients using ultrahigh-performance liquid chromatography quadrupole time-of-flight metabolomic analysis (UHPLC-Q-TOF MS) in positive and

negative modes using electrospray ionisation (ESI). Before any statistical analysis, the original data set was separated into a training set (90, percent) and a test set (10 percent). For parameter selection, no samples from the test set were used. When using orthogonal projection to latent structure with discriminant analysis with electrospray ionisation modes, the results revealed a strong distinction in metabolomic profiles between T2DM and T2DM+HBP.C-Q-TOF MS.

Optimization of the chromatographic separation protocol was vital because of the high number of chromatographic peaks. In the end, the 15-minute gradient approach was used to analyse samples from the entire cohort of people. With our in-house reference standard library and HMDB, we gathered 6680 spectrum characteristics of each serum sample, 783 annotated metabolites in positive electrospray ionisation mode (ESI+), and 268 metabolites in negative electrospray ionisation mode (ESI). The PCA score plot revealed intergroup metabolic disparities, with each point representing a serum metabolome and the distance between data points reflecting the magnitude of metabolic differences. In ESI+ and ESI, all samples were evaluated using UHPLC-Q-TOF MS.

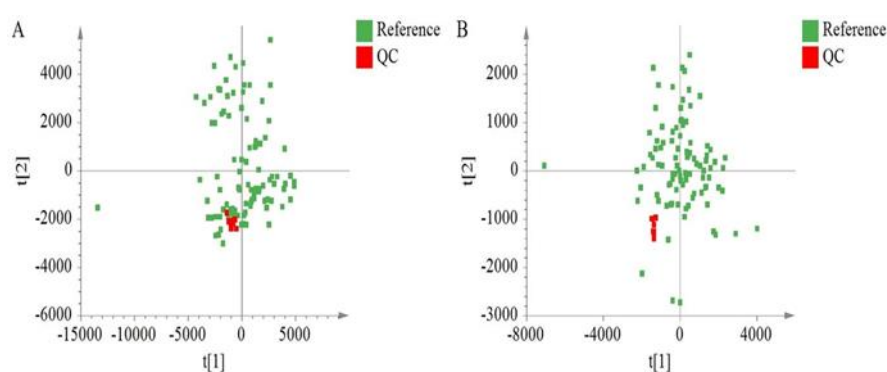


Figure 3: Score plots of principal components analysis models generated from the UHPLC-MS analyses of human serum displaying the biological samples and the quality control samples (QC; n=10, red)

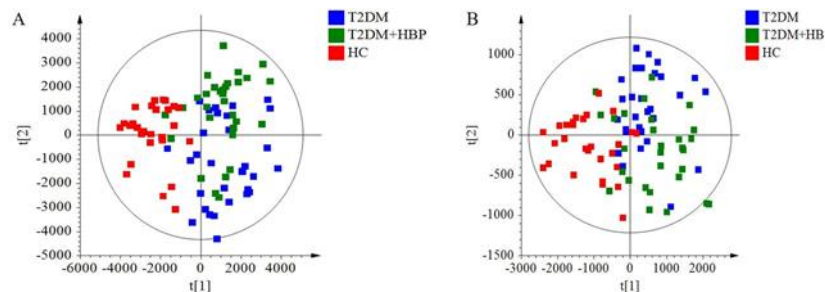


Figure 4: Score plot with partial least squares-discriminant analysis (PLS-DA) of serum metabolites in type 2 diabetes mellitus (T2DM; n=34, blue)

During illness progression, eight distinct metabolites changed significantly: L-isoleucine, L-glutamic acid, pyroglutamic acid, and linoleic acid dropped, while sphinganine, Cer(d18:0/16:0), Cer(d18:0/18:0), and citric acid increased. The -glutamyl cycle, tricarboxylic acid cycle, and ceramide metabolism are all linked to these metabolites.

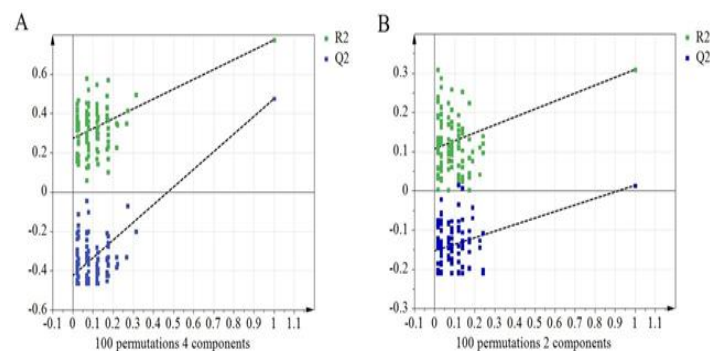


Figure 5: Permutation test results of the PLS-DA model in the positive (A) and negative ion modes (B). The R2Y value represents the goodness of fit of the model.

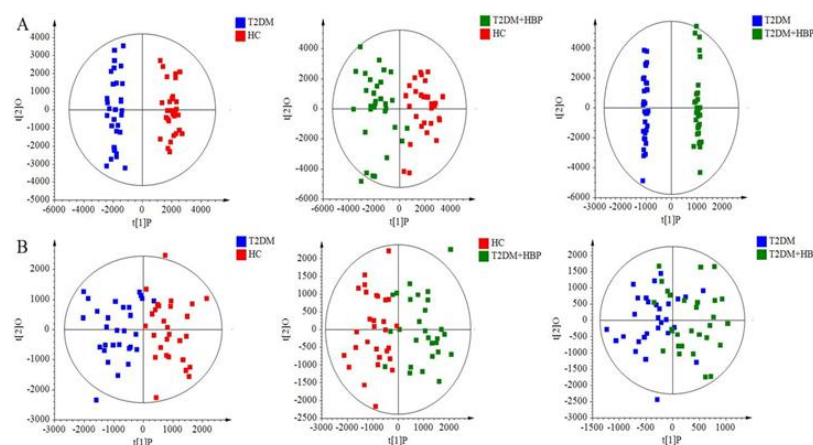


Figure 6: Scores plot of the orthogonal projection to latent structure with discriminant analysis (OPLS-DA) model built to discriminate between patients diagnosed with T2DM and those diagnosed with HBP.



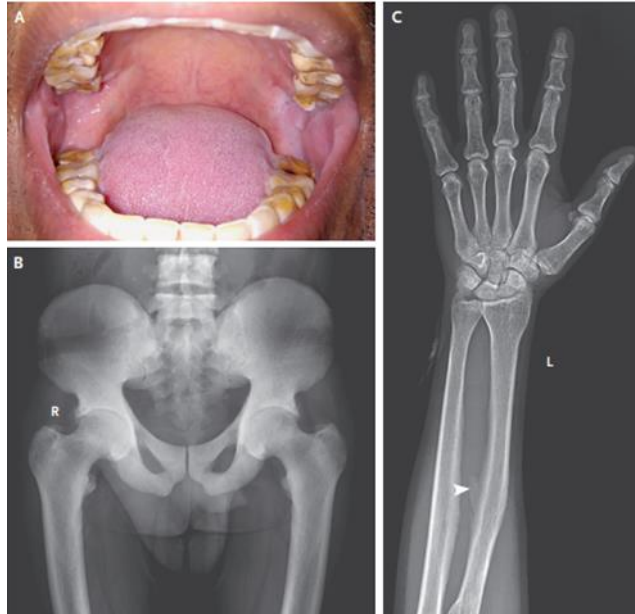
To detect clusters of T2DM related metabolite alterations, researchers used a metabolomics strategy based on UHPLC-Q-TOF MS in conjunction with contemporary multivariate statistical tools. The prior metabolites were linked to the TCA cycle, ceramide metabolism, and -glutamyl cycle, and their modifications showed the metabolic differences between HC and T2DM, who eventually developed T2DM+HBP.

These metabolic changes could be important in future clinical diagnosis, treatment, and evaluation of the therapeutic benefit of T2DM combined with HBP treatments.

Reference: Zhang Y, Zhao H, Liu B, Shu H, Zhang L, Bao M, Yi W, Tan Y, Ji X, Zhang C, Zhao N, Pang G, He D, Wang Y, Li L, Yi J, Lu C. Human serum metabolomic analysis reveals progression for high blood pressure in type 2 diabetes mellitus. *BMJ Open Diabetes Res Care*. 2021 Oct;9(1):e002337.

Hampton's Hump – Case Report

A 28-year-old lady with a 3-day history of dry cough and pleuritic chest pain presented to the emergency department. She suffered ulcerative colitis and pulmonary embolism in the past. While breathing ambient air, her heart rate was 87 beats per minute and her oxygen saturation was 99 percent. Fine crackles may be heard in the right lower lung during physical examination. The legs were perfectly symmetrical. Troponin, d-dimer, and N-terminal pro-B-type natriuretic peptide levels were all within normal limits. Deep S waves in lead I and T-wave inversions in lead III were seen on an ECG. Even though her vital signs and laboratory values were normal, a chest radiograph revealed a dome-shaped, pleural-based opacity in the right lung, consistent with Hampton's hump, raising concerns of recurrent pulmonary embolism.



Filling defects in the right lower lobar pulmonary artery and its segmental branches, as well as a peripheral wedge-shaped consolidation, were discovered during computed tomographic pulmonary angiography, confirming the diagnosis of pulmonary embolism with distal pulmonary infarction. In individuals with pulmonary embolism, Hampton's hump, a radiographic indication of pulmonary infarction, is a rare occurrence. Her symptoms improved after she began anticoagulant therapy, which she planned to continue for the rest of her life.

Reference:

de Almeida Mendes I, Neves VO. Hampton's Hump. N Engl J Med. 2021 Nov 4;385(19):1796.



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