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IMPROVED ACCURACY OF LONG COVID-19 PREDICTION IN HOSPITALIZED HYPERTENSIVE PATIENTS COMPARED TO THE GENERAL COHORT

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THE ROLE OF RIGHT VENTRICLE FUNCTIONALITY IN THE CARDIOPULMONARY STATUS OF HYPERTENSIVE PATIENTS HOSPITALIZED FOR SARS-COV-2 INFECTION

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Objective: There is little data concerning the impact of SARS-Cov-2 infection on the cardiopulmonary status and right ventricle (RV) function of patients with arterial hypertension (HTN). The purpose of our study was to investigate whether hospitalization for COVID-19 affects the functional status of hypertensive patients, using cardiopulmonary exercise test and echocardiographic parameters, 3 months after the infection onset.

Design and method: All subjects underwent cardiorespiratory exercise using Bruce or modified Bruce protocol where all cardiorespiratory parameters were evaluated. Echocardiographic parameters including right ventricle longitudinal strain were analyzed using an offline program. Subjects with a history of HTN were divided into two groups according to hospitalization for Covid-19 infection. Group I included 28 subjects who were hospitalized for Sars-Cov-2 infection and Group II included 34 subjects without the need for hospitalization.

Results: Out of a total population of 198 patients with COVID-19 infection, 62 subjects had a hypertension history (mean age: 61±10 years, 58.1% males, history of coronary artery disease: 16.1%) and they were evaluated 3 months after the symptoms' onset. Hospitalized patients were older (63±8 vs. 52±11 years, p<0.001). Analysis of cardiopulmonary test parameters, oxygen consumption both maximum (21±4 vs. 23.5±4, p: 0.01) and during the 1st minute of recovery (15.5±2 vs. 21±25, p: 0.02), VO₂_AT (17±4 vs. 27.5±32) and PETCO₂ (39±4 vs. 38±19 mmHg, p: 0.03) were impaired comparing to non-hospitalized subjects. Out of echocardiographic parameters, the diameter of the left atrium (mm), differed significantly between the two groups (41±6 vs. 38±5 p: 0.02). Furthermore, in hospitalized patients, the absolute mean value of right ventricle strain (RVLS, (%): 13±8 vs. 23±3, p:0.04) was impaired despite a similar left ventricle ejection fraction between the two groups. Finally, using linear regression analysis adjusted for age, gender, hypertension history, and hospitalization, hospitalization proved to be an independent predictive factor for RVLS in hypertensive patients.

Conclusions: To conclude our study highlighted the negative impact of hospitalization for Sars-Cov-2 infection in the capacity for exercise and in right ventricle functionality, implying the severity of the disease as a negative independent predictive factor in hypertensive patients.

IMPACT OF SARS-COV-2 INFECTION IN NEUROCOGNITIVE AND CARDIOPULMONARY FUNCTIONALITY OF HYPERTENSIVE PATIENTS

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Objective: Few data have been published regarding the holistic approach of post-Covid patients with a history of hypertension, examining both physical and mental health. The purpose of our prospective study was to follow up cardiorespiratory status, and mental and psychological health of hypertensive patients 3 months after the first day of infection.

Design and method: All patients with a history of Sars-Cov-2 infection and good functional status were assessed using cardiorespiratory test, transthoracic echocardiogram, and standardized questionnaires by a comprehensive team of experts (cardiologists, psychiatrists, and psychologists). The population was divided into two groups according to hypertension status.

Results: Out of total population of 198 patients (51±15 years, 44.4% males, 6.6% history of coronary heart disease) with COVID-19 infection were assessed. Hypertensives had higher BMI (p<0.001) and BSA (p<0.001) and they were hospitalized in higher percentage (p<0.01). Out of echocardiographic parameters, diastolic dysfunction parameters including left atrial diameter (p<0.001) and E/A ratio (p<0.001) differed significantly between the two groups. LVEF (%) was significantly impaired (56±10% vs. 58±9%, p:0.04) in hypertensives that was depicted in lower values of oxygen consumption (VO₂ (ml/kg/min)) both maximum (p<0.001) and during the 1st minute of recovery (p<0.006), metabolic equivalents

(METS) at peak, (p<0.001) and HR1st minute recovery (p< 0.001) comparing to normotensives. Systolic blood pressure (mmHg) at rest (p: 0.002), at peak (p: 0.01), and during the 1st minute of recovery (p: 0.001) as well as Borg scale score for dyspnea (p:0.02) were higher while the exercise duration was significantly lower (p<0.001) in hypertensives comparing to normotensives. Similarly, their psychometric tests (DASI METS (p:0.008), Functionality (p:0.036)) were also affected. Finally, using linear regression analysis adjusted for age, gender, hypertension status, and hospitalization, age (p: 0.001) proved to be an independent predictive factor for VO₂, VO₂_AT, and VO₂1st minute of recovery in hypertensive patients.

Conclusions: To conclude, the current study highlighted the reduced ability to exercise and fragility of patients with a history of hypertension. Age proved to be an independent negative predictor of functionality. Therefore, the need for a more comprehensive approach to the rehabilitation of post-covid patients is mandatory.

COMPREHENSIVE PRE-DISCHARGE SYMPTOMS ASSESSMENT IN HYPERTENSIVE PATIENTS HOSPITALIZED FOR COVID-19 ALLOWS TO PREDICT PERSISTENCE OF SYMPTOMS AT 3 MONTHS

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Objective: To study the prognostic value of survey-based respiratory, physical, emotional, and cognitive symptoms assessment in hypertensive patients hospitalized for COVID-19 in prediction of symptoms persistence at 3 months after discharge.

Design and method: 88 hospitalized patients with COVID-19 and a history of hypertension (mean age 57.8±11.8 years, 53% female) underwent a comprehensive survey-based symptoms assessment 1-2 days prior to discharge that included MRC Dyspnea scale, CAT and CCQ questionnaires, HADS, the physical symptoms subscale of the EFTER-COVID questionnaire, and the Memory, Thinking, and Communication subscale of the SBQ-LC questionnaire. Marginal effects in logistic regression analysis were used to gauge the predictive value of resulting scores and separate symptoms. 500 SANN-based classification models were subsequently trained for various combinations of significant predictors, with an automatic ranging of obtained models by their predictive accuracy.

Results: 77% of participants have reported an incomplete recovery at 3 month after hospital discharge. In the order of decreasing predictive value for persistence of symptoms, significant (p < 0,05) risk factors included EFTER-COVID physical symptoms score (Somers' D-statistic = 0,63), HADS depression subscale (D = 0,58), SBQ-LC Memory, Thinking, and Communication score (D = 0,52), MRC dyspnea class (D = 0,45), and CAT score (D = 0,30); among the specific symptoms, significant predictors included dyspnea (D = 0,42), dizziness (D = 0,38), muscles and joints pain (D = 0,38), and difficulties in remembering things (D = 0,40).

Out of the derived machine-learning based classification models, the optimal performance was observed for the one using gender, pre-discharge MRC dyspnea class, and summary scores on EFTER-COVID physical symptoms and SBQ-LC Memory, Thinking, and Communication subscales. The model exhibited a 100% predictive accuracy in classifying the pre-specified test/validation subset of the study group into those who would subsequently report persistence of symptoms or complete recovery.

Conclusions: Survey-based pre-discharge assessment of symptoms in hypertensive patients hospitalized for acute COVID-19 yields a high prognostic value. The combination of gender and survey-based measures of dyspnea, physical and cognitive symptoms may be used in this setting to predict the persistence of symptoms at 3 months after hospital discharge.

IMPROVED ACCURACY OF LONG COVID-19 PREDICTION IN HOSPITALIZED HYPERTENSIVE PATIENTS COMPARED TO THE GENERAL COHORT

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Objective: The accuracy of prediction of Long COVID-19 development is currently suboptimal. Phenotyping a general post-COVID-19 population based on simple clinical and anamnestic criteria may be used to address this problem.

The purpose of this study was to identify the early predictors of Long COVID-19 syndrome at 3 months after discharge in hospitalized patients with a history of hypertension (HT).

Design and method: 221 hospitalized patients with COVID-19 (mean age 53.4±13.6 years, 53% female, 40% with a history of hypertension) underwent compre-

hensive transthoracic echocardiography and a 6-minute walk test (6MWT) 1-2 days prior to discharge and after 1 month. A combination of logistic regression analysis and unsupervised machine learning was used to derive predictive models of self-assessed Long COVID-19 at 3 months after discharge (166 patients who have completed all visits comprised the final cohort).

Results: Self-assessed Long COVID-19 at 3 months was detected in 50 (77%) of hypertensive and 74 (73%) of normotensive participants, $p = 0,597$. In the general cohort, a modest performance of 83% was observed in the validation subset for the derived pre-discharge predictors-based ML classification model, which only constituted to re-classification of 1/3 of otherwise false-positive cases compared to the assumption of 100% prevalence of Long COVID, with a total net reclassification improvement (NRI) of 8%. Phenotyping the general cohort based on the presence of hypertensive anamnesis significantly improved the predictive accuracy for the HT-positive subgroup: 100% accuracy was observed in the validation subset with an NRI of 23% vs baseline assumption. Chi-square test $P < 0,001$ vs the general cohort model confusion matrix. The derived models used sex, MRC dyspnea class, Charlson comorbidity index, and either (1) pre-discharge systolic BP and mitral E to left ventricular global longitudinal strain ratio, or (2) peak D-dimer, pre-discharge 6-minute walk distance, and peak capillary oxygen desaturation during the 6MWT.

Conclusions: History of hypertension can be used as a phenotyping criterion to improve the accuracy of Long COVID-19 prediction among hospitalized patients: the derived ML-based classification models yielded a 100% predictive accuracy in the pre-specified validation subset of hypertensive patients hospitalized for acute COVID-19.

BIOMARKERS OF ENDOTHELIAL DYSFUNCTION AND CLOTTING DYSREGULATION POST COVID-19- A SUBSTUDY OF CARTESIAN

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Objective: Multiple mechanisms may contribute to a hypercoagulation state in patients with COVID-19. Endothelial cells play a key role in cellular adhesion, coagulation, smooth muscle cell proliferation, and vascular wall inflammation. We aimed to describe the activation of the coagulation system, specifically thrombin generation, plasma release of endothelial factors and NETosis, and their association with kidney function following the resolution of the acute phase of SARS-CoV-2 infection.

Design and method: Plasma samples were collected from adults 3 to 9 months after a confirmed episode of COVID-19 (COVID+, hospitalized or not, n=22) or after negative testing for COVID-19 in individuals who remained free of COVID-19 (COVID-, n=22). The coagulation system was assessed using in-vivo markers such as D-dimers (ng/ml). Thrombin generation assay estimated the thrombin-generating capacity in platelet-rich and platelet-poor plasma to provide information on soluble coagulation factors and the role of platelets in this process. Plasma release of endothelial factors was assessed by the levels of procoagulant factor VIII (FVIII) and Von Willebrand factor (VWF), and NETosis was determined using DNA-histone complexes levels. Spearman and linear regressions were used, when appropriate, to assess relationships between coagulation biomarkers and clinical and demographic characteristics of the population, such as kidney function (eGFR) calculated with the CKD-EPI equation (ml/min/1.73m²).

Results: The COVID+ group was older (mean age 53.8± 17.6 years vs 40.6 ± 17.2 years, $p=0.031$). Compared to the controls, the COVID+ group had higher DNA-histone levels (Spearman $\rho = 0.311$, $p=0.040$) and lower platelet counts (Spearman $\rho = -0.334$, $p=0.033$), but these differences were no longer significant after adjustment for age. However, we observed a significant association between eGFR and D-dimers, VWF and FVIII. Among them, only the association of D-dimers with eGFR was independent of age ($\beta=4.59$, $p=0.030$).

Conclusions: These findings do not support a persistent long-term dysregulation of coagulation and endothelial dysfunction following the resolution of COVID-19. However, they show a significant increase in D-dimers associated with renal function, independent of both age and COVID-19.

LONG-TERM CHANGES IN ARTERIAL STIFFNESS AFTER COVID-19

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Objective: To assess if COVID-19 is associated with increase in arterial stiffness using a long-term follow-up study.

Design and method: 53 patients hospitalized for COVID-19 in 2021 and 53 age and sex-matched subjects from a proportional cohort were examined. COVID-19 convalescents were evaluated twice; the first visit was 10-16 months after hospitalization, followed by a second visit 6 months after (n=44). The VaSera device (Fukuda Denshi, Japan) was used to measure vascular age, cardio-ankle vascular index (CAVI) and ankle brachial index (ABI).

Results: Groups did not differ by gender, smoking status, presence of hypertension or diabetes, but the control group and the second visit group differ by age (Table 1). There was no difference between the control group and COVID-19 group in vascular age and CAVI, however, there was a difference between the control group and the second visit in ABI ($p=0.002$). To assess the effect of COVID-19 on arterial stiffness; age, arterial hypertension, diabetes, smoking status, and systolic blood pressure were considered during analysis of covariance (ANCOVA) (Table 2). Patients in the control group and COVID-19 group did not differ in vascular age and CAVI after adjustment, but there was a trend toward increasing statistical significance at different visits. Patients in the control group and COVID-19 group differed in ABI, with statistical significance increasing at the later visit.

Table 1. Characteristics of the patients.

	Control group	COVID-19 group (1 visit)	COVID-19 group (2 visit)	p value
Age, yr	53.7±9.3	58.6±12.6	60.8±11.4	0.004
Female sex, no	32	29	25	0.82
Smoking status, no				0.99
Never smoker	29	27	22	
Former smoker	18	19	17	
Current smoker	6	6	5	
Hypertension, no	35	35	32	0.83
Diabetes, no	7	9	8	0.79
Vascular age, yr	55.5±16.2	56.4±17.1	60.3±14.1	0.47
CAVI	8.1±1.3	8.2±1.5	8.6±1.6	0.40
ABI	1.09±0.08	1.12±0.08	1.14±0.07	0.003

Table 2. Baseline adjusted ANCOVA.

	Control group - COVID-19 group (1 visit)	Control group - COVID-19 group (2 visit)
Vascular age, yr	F (1, 88) = 0.042, p = 0.837	F (1, 79) = 0.983, p = 0.324
CAVI	F (1, 90) = 0.087, p = 0.768	F (1, 80) = 1.321, p = 0.254
ABI	F (1, 90) = 5.331, p = 0.023	F (1, 78) = 12.659, p = 0.001

Conclusions: There is an elevation in ABI in patients hospitalized with COVID-19 compared to those not affected by COVID-19. This effect becomes more pronounced over time. No statistical significance was observed for vascular age and CAVI, although an upward trend was noted. Longer follow-up is needed to provide accurate conclusions as to whether these parameters may increase after COVID-19.

HYPERRENINISM - A COMMON PHENOMENON IN HOSPITALIZED COVID-19 PATIENTS

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Objective: Since the beginning of the worldwide pandemic the interaction of SARS-CoV2 on renin-angiotensin-aldosterone system is discussed intensively. Since ACE-2 was identified as the cellular receptor of SARS-CoV-2, the debate started with the question, whether treatment with ACE-inhibitors (ACE-I) and angiotensin receptor blockers (ARB) should be discontinued during the pandemic. In contrast, current studies investigate a potential benefit by ACE-I, ARB and mineralocorticoid receptor antagonists. However, data on renin and aldosterone concentrations in patients with COVID-19 are sparse.

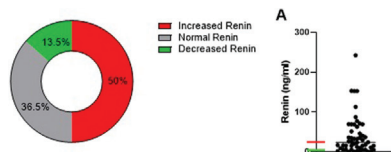


Figure 1: Distribution of plasma renin concentrations of hospitalized for moderate COVID-19. Definition of increased renin concentration: >23.9ng/ml, normal renin concentration: 1.68-23.9ng/ml, decreased renin concentration <1,68ng/ml
 Figure 2: A: Scatter dot plot of plasma renin concentrations. B: Scatter dot plot of aldosterone concentrations. Black bars: Median. Green and red bars: Upper and lower reference limit.

Table 1: Population characteristics

Total study population n=52	
Age	70 (IQR 45.5-80.8)
Body mass index (kg/m ²)	25.4 (IQR 20.8-35.4)
Female	9 (18.1%)
Male	22 (55.9%)
eGFR (ml/min)	88.5 (IQR 17-109.3)
Hypertension	20 (39.2%)
RR (sys) on admission (mmHg)	130 (IQR 116.8-140)
Oxygen support on admission	32 (62.7%)
Potassium (mmol/l)	3.9 (IQR 3.25-4.2)
Hyppokalemia	5 (9.6%)
Angiotensin receptor blocker	6 (11.5%)
Angiotensin converting enzyme inhibitor	5 (9.6%)
Loop-diuretic	8 (17.3%)

Design and method: We performed a cross-sectional study in 52 patients hospitalized for moderate COVID-19 (peripheral ward, no intensive care) assessing