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### ORIGINAL ARTICLE

# Cardiovascular effects of COVID-19 lockdown in professional football players

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#### ABSTRACT

BACKGROUND: The COVID-19 pandemic with the stay-at-home orders and lockdown has dramatically forced athletes to stop team training and competitions, causing deep changes in habits and lifestyle. Aim of this study was to evaluate in a retrospective single center study the cardiovascular (CV) health and fitness of elite football player after COVID-19 lockdown in Italy and to compare such findings with the 2019 off-season period, in order to identify potential differences in the CV features and outcomes.

METHODS: All 29 professional football players of the first male team were enrolled before resuming training and competition after COVID-19 lockdown and underwent several exams including physical examination, resting and stress electrocardiography (ECG), echocardiography, spirometry and blood tests.

RESULTS: Median age was 27 years (23; 31), with no athlete being COVID-19 positive at the time of the evaluation. In comparison with the usual off-season 2-month detraining, significant differences were found for left ventricular (LV) mass (189 g [172; 212] vs. 181 g [167; 206], P=0.024) and LV Mass Index for body surface area (94 g/m<sup>2</sup> [85; 104] vs. 88 g/m<sup>2</sup> [79.5; 101.5], P=0.017), while LV mass/fat free mass remained unchanged (2.8 g/kg [2.6; 2.9] vs. 2.9 g/kg [2.6; 3.2], P=0.222). Respiratory function and metabolic profile were improved, while no significant changes were found in ECG findings, at rest and during exercise.

CONCLUSIONS: Prolonged abstinence from training and competitions induced by lockdown elicited significant changes in comparison with off-season in parameters ascribable to detraining, as the changes in LV mass, in respiratory function and in metabolic profile.

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KEY WORDS: Athletes; Cardiovascular system; COVID-19; Quarantine.

The recent pandemic caused by the novel human coronavirus infection (COVID-19) had a great impact on the health care systems worldwide causing radical changes of common habits and lifestyles.<sup>1,2</sup> The recommendations proposed by several governments with rigorous containment measures (lockdown) forced athletes to stop team training and competing in order to promote the safeguarding of collective health. The health benefits of physical activity in reducing morbidity and mortality have been proved by several publications.<sup>3-5</sup> Nevertheless four-week suspension of physical activity in intensive-trained elite athletes may be sufficient to determine cardiovascular as well as structural and functional alterations at several level and organs, including muscles.<sup>6-8</sup> On the other hand, in elite football players after the competitive season at least 4- to 6-week transition or off-season period characterized by physical and psycho-

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logical rest and some multicomponent individual training (also practice of other sports) are needed.<sup>9</sup> The decrease of the specific training stimulus as during the off-season provides a detraining effect that may be apparently considered similar to what happens during the lockdown. However, the lockdown period can be considered different compared to the typical off-season period as players were not allowed to leave their house with a restriction of their movement possibilities; in addition and unlike the off-season period, a forced "de-training" abruptly stops the activities of the regular season and this restriction may lead to some psychological stress. "Detraining" involves a partial or complete loss of the physiological adaptations induced by intensive physical exercise.<sup>6-8</sup> Therefore, a decrease of physiological performances, compared to the usual post-off-season, is expected after the lockdown period. Several studies showed a reduction of cardiovascular function ventilatory efficiency after a period of detraining in elite athletes7 and football players.<sup>10</sup> The review of Mujika et al.<sup>6,7</sup> reported a decrease in stroke volume and cardiac output during exercises as well as in cardiac dimensions and ventilatory efficiency in athletes after 4 (or more) weeks of detraining. D'Ascenzi et  $al^{10}$  found a decrease in the left ventricular volume after 2 months of detraining in elite football players.

Despite the published scientific literature on detraining effect (or elite athletes) and the proposed athletes management algorithms for both COVID-19 negative or asymptomatic athletes, as well as COVID-19 positive athletes,<sup>11-16</sup> at present no studies have examined the effect of the COVID-19 lockdown on the cardiovascular (CV) health in elite football players.

Therefore, the aim of this study was to evaluate CV health of elite football player after COVID-19 lockdown in Italy and to compare the findings with the off-season 2019 period to identify potential differences in the CV outcomes.

#### Materials and methods

#### **Study population**

This retrospective study enrolled all the 29 professional Football athletes, from the first male team of a major Italian first league (Serie A) club. None of them was affected by Coronavirus infection (*i.e.* COVID-19) at the time of the enrollment, as proved by both the immunological analyses of IgM and IgG antibody titers and the nasopharyngeal swab. As requested by the Italian Federation of Sport Medicine (FMSI)<sup>17</sup> before being cleared for resuming training and competition all the players underwent a complete medical

protocol. Briefly, the COVID-19 negative athletes must undergo several exams before resuming training and competition, including physical examination, 12-lead resting and stress ECG, color Doppler echocardiography, spirometry and a set of hematological analyses. If an athlete resulted COVID-19 positive, also cardiopulmonary exercise test and thorax computed tomography (CT) were required to clear him for competition. The same set of exams are required by law to clear professional athletes for competition before the beginning of the season once a year. We retrospectively collected the results of the same exams obtained at the annual pre-participation screening performed in 2019 July-August for all athletes composing the first Football team, performed by the same medical staff in Villa Stuart Sports Clinic, FIFA Medical Center of Excellence.

The retrospective study design was evaluated and approved by the Review Board of Villa Stuart Sports Clinic, FIFA Medical Center of Excellence. All athletes included in this study were fully informed of the type and nature of the evaluation and signed the consent form, pursuant to Italian law and the Clinic policy.

During the 7-week lockdown, 34 home-training sessions were prescribed to the athletes with the aim to reduce the de-training effects. Therefore, strengthening workouts targeting lower limb muscles (adductor, quadriceps, hamstring) and different type of jumps were prescribed twice/ week for all the lockdown period. Nineteen out of 34 sessions were designed as high-intensity interval training and prescribed using cycling (spinning) activity during the first 5 weeks. 15 out of 34 sessions were designed as core stability, proprioception and functional movements. However as soon as the movement restrictions were loosened, players were allowed to go out (around 100 m for their house maximum) and more specific training exercises as sprint running progressions (sprint from 10 to 50 m) were prescribed (week 6-7).

#### **Cardiovascular evaluation**

Physical examination and medical history were performed according to the recommendations after COVID-19 -lockdown.<sup>17</sup> The 12-lead electrocardiograms (ECGs) were recorded at rest in supine position using Cardioline Click-ECG (Cardioline, Trento, Italy) at paper speed of 25 mm/s, at a standard gain of 1 mV/cm and evaluated according to the current International Criteria.<sup>18</sup> The exercise ECG with continuous 12-lead ECG monitoring was performed in an upright position using a commercial bicycle ergometer (Cardioline XR400, Cardioline), with an incremental protocol of 50 W every 2 minutes until exhaustion, fol-

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lowed by 5-minute recovery. The perceived exertion rate was evaluated with the Borg CR10 Scale.

Transthoracic 2D color Doppler and tissue Doppler echocardiography was performed in all athletes using a commercial machine (Vivid S6, GE Healthcare, Chicago, IL, USA) according to the European recommendation.<sup>19</sup> Briefly, diameters and wall thickness were assessed by a combination of long- and short-axis two-dimensional views. Left ventricular (LV) ejection fraction was calculated by biplane Simpson's rule from 4- and 2-chamber apical view. LV mass was calculated on M-mode images using the corrected American Society of Echocardiography convention<sup>20</sup> and indexed for body surface area (BSA). The lean body mass was estimated by dual-energy X-ray absorptiometry (DXA) assessment using a standardized protocol.<sup>21</sup> Parameters of LV diastolic filling and relaxation were obtained with pulsed Doppler as early (E) and late (A) peakflow velocities and with tissue Doppler imaging (TDI) as early (e'), late (a') diastolic and systolic (s') peak velocities.

Respiratory function was assessed by pulmonary volumes, capacities and flows by spirometry using a two-way disposable mouthpiece connected to a pneumotachograph (MIR, USA) with nose occluded, according to current guidelines.<sup>22</sup> The following parameters were assessed in all the athletes: forced expiratory volume at the end of the first second of forced expiration [FEV<sub>1</sub>], peak expiratory flow [PEF], maximal voluntary ventilation [MVV], forced vital capacity [FVC], tidal volume [TV] and the FEV1/ FVC ratio.

#### Statistical analysis

Continuous variables are reported as median (1st; 3rd quartile), and categorical variables as count and proportion as appropriate. Differences were evaluated using Wilcoxon signed-rank test for repeated measurements and Kruskal-Wallis Test for unpaired variables. Unsupervised machine learning was performed after appraisal of linear correlation with Pearson Test, displayed with dendrograms and heatmaps. Specifically, two principal components were obtained and then used for hierarchical clustering using centroid linkage, selecting three clusters. In addition, kmeans clustering was performed for confirmatory purposes. Statistical significance was set at the two-tailed 0.05 level, without multiplicity adjustment. Computations were performed with R 3.6 (R Foundation for Statistical Computing, Vienna, Austria).

#### Results

#### **Demographic characteristics**

The athletes' median age was 27 years (23; 31), 100% males, none was COVID-19 positive. When comparing the time period after COVID-19 lockdown with after offseason 2019, no significant changes were found in athletes' demographic and clinical characteristics in terms of weight (despite a trend in weight increase, median weight 81 kg vs. 80 kg respectively), body surface area, and arterial blood pressure (Table I).

Characteristics	After off-season	After COVID-19 lockdown	P value	
Weight, kg	80 (75; 86.5)	81 (77; 86)	0.138	
BSA, m <sup>2</sup>	2.04 (1.94; 2.12)	2.04 (1.96; 2.14)	0.332	
Systolic BP, mmHg	110 (102.5; 120)	110 (103.5; 113.5)	0.100	
Diastolic BP, mmHg	80 (70; 80)	70 (66; 78)	0.103	
Heart rate, bpm	60.5 (53; 70)	64 (57; 73.5)	0.502	
Training-related ECG findings	21 (72.4%)	21 (72.4%)	1.0	
Borderline ECG findings	1 (3.4%)	1 (3.4%)	1.0	
Abnormal ECG findings	0 (0%)	0 (0%)	1.0	
PQ interval, msec	158 (146; 184)	170 (148; 192)	0.049	
QRS axis, degree	72 (46; 86)	75 (61; 82)	0.698	
QRS duration, msec	96 (90; 103)	98 (89; 104)	0.920	
QT interval, msec	404 (379; 431)	396 (374; 423)	0.300	
QTc interval, msec	410 (400; 418)	407 (395; 417)	0.086	
Stress ECG				
Maximum workload, W	300 (250; 300)	300 (250; 300)	0.793	
Index maximum workload, W/kg	3.37 (3.16; 3.92)	3.41 (3.14; 3.91)	0.696	
Peak heart rate, bpm	170 (163; 172)	170 (163.5; 176)	0.212	
Peak systolic BP, mmHg	180 (163.5; 176)	180 (162.5; 195)	0.245	
Peak diastolic BP, mmHg	80 (70; 80)	80 (70; 80)	1.0	

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#### Electrocardiography and exercise ECG

No significant changes were found in ECG findings, both at rest and during exercise. As expected, the majority of the athletes (72.4%) showed training-related ECG findings, in particular sinus bradycardia and increased QRS voltage suggestive for LV hypertrophy; the unique borderline finding was left axis deviation in 1 athlete, both findings remained unchanged. No abnormal ECG findings were observed in the study population in both observations. No significant changes were found in the maximum workload reached during exercise ECG, or in peak heart rate and peak blood pressure. Median Borg scale evaluation during exercise ECG was 6 (5; 7) over 10.

#### **Echocardiography**

All athletes showed LV cavity size, wall thickness, both absolute and normalized LV mass within normal ranges for athletes and in line with the discipline practiced (mixed, non-endurance).<sup>23</sup> LV dimensions and volumes, wall thickness, parameters of systolic and diastolic function were unchanged after COVID-19 lockdown, remaining between normal limits in both evaluations (Table II). On the contrary, significant differences were found for LV mass (189 g [172; 212] *vs.* 181 g [167; 206], P=0.024), LV mass index for BSA (94 g/m<sup>2</sup> [85; 104] *vs.* 88 g/m<sup>2</sup> [79.5; 101.5], P=0.017), while LV mass/fat free mass remained unchanged (2.8 g/kg [2.6; 2.9] *vs.* 2.9 g/kg [2.6; 3.2], P=0.222).

Left atrial and aortic root dimensions fall within normal ranges in both examinations and no differences were observed for both dimensions over time. On individual analysis, no athletes showed an enlarged aortic root or a dilated left atrium ( $\geq$ 40 mm for aortic root and >40 mm for left atrium). In 9 (31%) athletes LV enddiastolic dimension ranged from 56 to 59 mm, without exceeding the arbitrary clinical cut-point of 60 mm limit.<sup>24</sup> LV wall thickness never exceeded the normal limit ( $\geq$ 12 mm).<sup>25</sup>

 TABLE II.—Echocardiographic data and pulmonary function of Football athletes after COVID-19 lockdown.

Parameter	After off-season	After COVID-19 lockdown	P value
Echocardiography			
LV end-diastolic diameter, mm	54 (51; 57)	53 (51; 56)	0.477
LV end-systolic diameter, mm	35.5 (33; 37)	35 (34; 37)	0.059
Septal LV thickness, mm	10 (9; 11)	10 (9; 10.2)	0.399
LV Posterior Wall, mm	9 (9; 9.5)	9 (8; 10)	0.968
RWT ratio	0.34 (0.32; 0.36)	0.34 (0.31; 0.37)	0.990
LV mass/BSA, g/m <sup>2</sup>	94 (85; 104)	88 (79.5; 101.5)	0.017
LV mass, g	189 (172; 212)	181 (167; 206)	0.024
LV mass/fat free mass, g/kg	2.8 (2.6; 2.9)	2.9 (2.6; 3.2)	0.222
LV end-diastolic volume, mL	141 (123; 160)	140 (126; 156)	0.589
LV end-systolic volume, mL	51 (44; 58)	53 (46; 63)	0.046
Left atrium, mm	35.5 (33; 39)	33.4 (30.1; 37)	0.089
Aortic root, mm	33 (30; 34)	33 (30; 34)	0.867
PW E-wave, cm/s	0.81 (0.68; 0.91)	0.71 (0.63; 0.80)	0.116
PW A-wave, cm/s	0.43 (0.39; 0.50)	0.43 (0.35; 0.56)	0.362
PW E/A ratio	1.7 (1.6; 2.0)	1.6 (1.3; 1.9)	0.071
TDI e-wave, cm/s	0.17 (0.13; 0.19)	0.17 (0.14; 0.19)	0.528
TDI a-wave, cm/s	0.07 (0.06; 0.08)	0.08 (0.07; 0.08)	0.205
TDI s-wave, cm/s	0.12 (0.11; 0.14)	0.13 (0.11; 0.15)	0.798
E/E' ratio	4.4 (3.9; 5.1)	4.3 (3.5; 5.2)	0.639
EF (%)	65 (60; 66)	61.6 (60; 64)	0.059
RV basal diameter, mm	34 (32; 38)	38 (36; 39)	0.134
Tricuspid TDI s-wave, cm/s	0.13 (0.12; 0.15)	0.14 (0.12; 0.15)	0.141
Pulmonary function			
FVC, L	6.1 (5.7; 6.8)	6.3 (5.7; 6.7)	0.007
FEV <sub>1</sub> , L	5.2 (4.7; 5.7)	5.2 (4.7; 5.7)	0.684
FEV <sub>1</sub> /FVC ratio	0.86 (0.83; 0.91)	0.83 (0.78; 0.88)	0.007
PEF, L/min	10.7 (9.8; 11.7)	11.0 (9.5; 12.2)	0.869
MVV, L/min	172 (163; 201)	206 (175; 230)	0.003
TV, L	6.1 (5.4; 6.6)	6.2 (5.6; 6.8)	0.023

BSA: body surface area; FEV<sub>1</sub>: forced expiratory volume at the end of the first second of forced expiration; FVC: forced vital capacity; LV: left ventricular; MVV: maximal voluntary ventilation; PEF: peak expiratory flow; RV: right ventricular; TV: tidal volume.

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#### **Pulmonary function**

The FEV<sub>1</sub>, PEFMVV, FVCTV, and the FEV1/FVC ratio were over normal ranges for all athletes. In particular, when compared with published reference values in elite athletes<sup>26, 27</sup> the observed values were higher than what was previously reported values in football athletes (Table II), comparable with endurance athletes. After COVID-19 lockdown, FVC and MVV significantly improved (6.3 L [5.7; 6.7] *vs*. 6.1 L [5.7; 6.8] and 206 L/min [175; 230] *vs*. 172 L/min [163; 201], respectively, both P=0.007), as an adaptive change to the continued endurance activity during lockdown. FEV1 and PEF remained unchanged.

#### **Metabolic function**

Blood test showed a significant reduction in plasmatic glucose, total and HDL cholesterol (P=0.015, P=0.031 and P=0.003, respectively). Changes in white blood cells and in platelets, despite being statistically significant, were deemed not clinically significant, all values are presented in Table III.

#### Characteristics of football players at cluster analysis

Linear correlation among all considered parameter appraised with Pearson correlation was displayed with heatmaps (Figure 1) and dendrograms (Figure 2). Differences between all the variables included in the hierarchical cluster analysis identified three clusters of changes after lockdown, which are shown in Table IV and in Figure 3 and 4. *Post-hoc* comparisons after cluster analysis suggested that the greatest contributors to between-cluster differences were the following variables: age (P=0.032), play role (P=0.021), weight (P=0.011), FVC (P=0.012) and

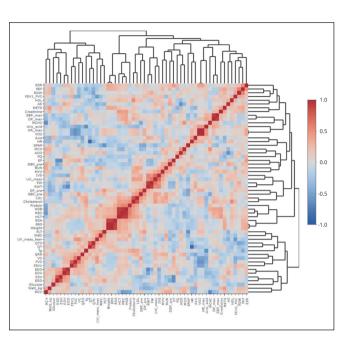


Figure 1.—Heat map of correlation between cardiovascular variables. Legend indicates strength of correlation coefficient (red: high correlation; blue: inverse correlation, white: no correlation). The dendrogram highlights the different clusters.

total cholesterol (P=0.004). Athletes falling in cluster #3 showed the most marked reduction in body weight, in LV mass and in total cholesterol.

#### Discussion

Our study demonstrated for the first time the effects of CO-VID-19 lockdown in professional first team male Football

 TABLE III.—Hematological and metabolic characteristics of football athletes after COVID-19 lockdown.

Parameter	After off-season	After COVID-19 lockdown	P value
Red blood cells, x10 <sup>6</sup> /µL	5.15 (5.0; 5.4)	5.05 (4.04; 6.09)	0.074
White blood cells, x10 <sup>3</sup> /µL	5.3 (4.6; 6.3)	5.0 (4.8; 5.4)	0.009
Platelets, x10 <sup>3</sup> /µL	189 (161.5: 231)	217 (163; 248)	0.004
Hemoglobin, g/dL	15 (14; 15)	14.7 (14.3; 15.3)	0.205
Hematocrit, %	44.5 (43; 46)	43.3 (42.2; 44.1)	0.015
Glucose, mg/dL	90 (83; 95)	84 (81; 88)	0.015
Blood urea nitrogen, mg/dL	37 (32; 43)	37 (30; 42)	0.424
Creatinine, mg/dL	1.0 (0.9; 1.1)	1.0 (1.0; 1.1)	0.194
Total protein, g/dL	7.3 (7.1; 7.6)	7.4 (7.2; 7.5)	0.600
Total cholesterol, mg/dL	189 (175; 223)	182 (159; 206)	0.031
HDL cholesterol, mg/dL	55 (51; 65)	51 (48; 57)	0.003
LDL cholesterol, mg/dL	117 (90; 129)	111 (93; 142)	0.142
Triglycerides, mg/dL	72 (46; 101)	70 (65; 86)	0.795
Uric acid, mg/dL	5.8 (5.0; 6.5)	5.6 (5.2; 6.5)	0.918
Body fat, %	12.6 (11.6; 14.6)	13.5 (12.1; 14.8)	0.421

HDL: high-density lipoprotein; LDL: low-density lipoprotein

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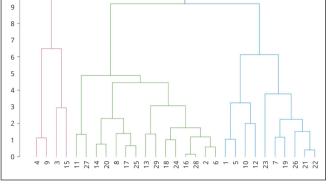
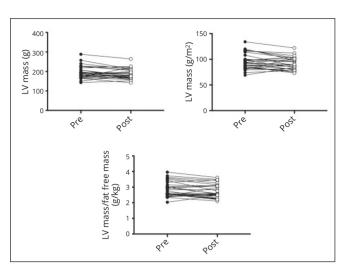


Figure 2.—Dendrogram highlighting the hierarchical clustering following computation of Euclidean distance of subjects in light of changes of selected variables after lockdown period in comparison with off-season period. Numberings in the x axis refer to the anonymized identifier of study subjects, whereas colored lines represent the different clusters.



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Figure 3.—Assessment of left ventricular (LV) mass, both absolute and scaled by body surface area (BSA) and fat-free mass (FFM) after 2019 off-season (pre) and after 2020 lockdown (post).

Characteristics	Cluster #1 (N.=10)	Cluster #2 (N.=15)	Cluster #3 (N.=4)	P value
Age, years	31.5 (27; 33)	24 (22; 27)	29 (23; 36)	0.032
Play role		~ / /		0.021
Goalkeeper	0 (0%)	2 (7%)	2 (7%)	
Defender	5 (17%)	5 (17%)	2 (7%)	
Midfielder	2 (7%)	8 (28%)	0 (0%)	
Forward	3 (10%)	0 (0%)	0 (0%)	
Weight, kg	-0.25 (-2; 1)	1.0 (0.0; 4.0)	-1.0 (-6.7; 1.0)	0.011
Body Mass Index, g/m <sup>2</sup>	-0.08 (-0.5; 0.3)	0.3 (0.0; 1.1)	-0.005 (-0.07; 0.02)	0.008
Body surface area, m <sup>2</sup>	-0.02 (-0.04; 0.02)	0.03 (0.0; 0.04)	-0.005 (-0.07; 0.02)	0.014
Systolic BP, mmHg	- 6 (-14; 4)	0.0 (-11; 7)	-14 (-20; -2)	0.185
Diastolic BP, mmHg	-1.5 (-10; 10)	-5 (-12; 1)	-6.5 (-10; -1)	0.686
Heart rate, bpm	15 (-2; 25)	-3 (-8; 9)	-1 (-6; 1)	0.105
FVC, L	0.06 (-0.4; 0.4)	0.2 (-0.1; 0.5)	0.7 (0.1; 2.0)	0.012
FEV <sub>1</sub> , L	-0.03 (-0.5; 0.2)	-0.05 (-0.1; 0.3)	0.2 (-0.3; 0.3)	0.488
FEV <sub>1</sub> /FVC	-0.014 (-0.04; 0.002)	-0.03 (-0.06; 0.01)	-0.08 (-0.2; -0.04)	0.094
PEF, L/min	0.2 (-1.2; 2.1)	-0.15 (-1; 0.8)	-1.3 (-3; 0.0)	0.338
MVV, L/min	35 (-5; 51)	45 (14; 63)	-2.2 (-19; 26)	0.153
Maximum workload, W	0.0 (-2; 0.1)	0.0 (-0.2; 0.0)	-3.2 (-4.4; -0.6)	0.092
Index maximum workload, W/kg	0.01 (-0.25; 0.26)	-0.03 (-0.2; 0.45)	-0.2 (-0.4; 1.2)	0.838
Peak heart rate, bpm	1.5 (-2.2; 8)	2.0 (-2; 6)	-4.0 (-10; 0.5)	0.138
Peak systolic BP, mmHg	-20 (-30; 1)	0.0 (-10; 20)	-20 (-31; -5)	0.136
LV mass, g	-6.5 (-32; 11)	-6 (-22; 6)	-27 (-41; -21)	0.112
Index LV mass, g/m <sup>2</sup>	- 4 (-13; 7)	-3 (-12; 2)	-12 (-20; -7)	0.185
LV mass/fat free mass, g/kg	-0.11 (-0.21; 0.04)	-0.05 (-0.5; 0.12)	0.24 (-0.19; 0.43)	0.413
Glucose, mg/dL	-4.5 (-11; 6)	-8 (-11; -2)	2 (-10; 13)	0.287
Blood urea nitrogen, mg/dL	-1.8 (-5.3; 2.5)	-1.4 (-5; 3.4)	-0.8 (-3.5; 4.8)	0.919
Creatinine, mg/dL	0.03 (-0.01; 0.06)	0.05 (-0.1; 0.1)	-0.04 (-0.2; 0.14)	0.566
Total protein, g/dL	-0.1 (-0.3; 0.02)	0.1 (0.0; 0.2)	-0.05 (-0.25; 0.1)	0.054
Total cholesterol, mg/dL	-23 (-42; -1)	4 (-13; 13)	-54 (-56; -13)	0.004
HDL cholesterol, mg/dL	- 6.5 (-11; 1.2)	-2 (-7; 3)	-16 (-22; -4)	0.164
LDL cholesterol, mg/dL	-3.5 (-15; 16)	11 (0.0; 32)	-10 (-25; 3)	0.066
Triglycerides, mg/dL	-3 (-63; 12)	11 (-3; 28)	-6 (-17; 13)	0.127
Uric acid, mg/dL	0.25 (-0.12; 1.1)	-0.1 (-1.0; 0.6)	-0.4 (-0.8; 0.12)	0.117
Fat free mass, %	-1.0 (-2.2; 1.0)	0.2 (-0.8; 1.4)	-0.7 (-1.8; 0.85)	0.473

CV EFFECTS OF COVID LOCKDOWN IN PRO FOOTBALLERS

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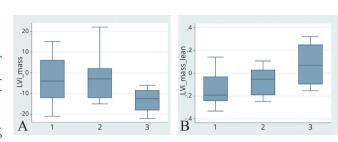


Figure 4.—Cluster-wise comparison of changes in left ventricular (LV) mass scaled by body surface area (LVi\_mass) (A) and for LV mass indexed for lean body mass (LVi\_mass\_lean) (B) based on the hierarchical cluster analysis comparing data after COVID-19 lockdown and after 2019 off-season.

players, evaluating clinical, cardiovascular, respiratory and metabolic parameters and compared them with the detraining due to off-season. D'Ascenzi et al.10 demonstrated that after a 2-month detraining a reverse remodeling of the LV exists, in terms of LV mass, which is comparable with the pre-season observation. A similar trend was demonstrated for fat-free mass, while heart rate remained unchanged. In our study, which analyzed an unprecedented period of lockdown in high-level athletes, we observed the most significant changes related to LV mass, both absolute and values indexed to BSA, and to respiratory function in comparison with the usual 2-month detraining due to off-season. Those changes may be ascribed not only to the home training prescribed to athletes to counteract the detraining imposed by the sport-restriction adopted during CO-VID-19 lockdown, which was different from usual training and competition. In fact, the athletes were subjected to endurance training, in particular cycling, while football is a mixed sport activity where running is the main locomotion performed at different speeds and static and dynamic components are alternated. Players usually cover a total distance between 10 to 12 km with 1-11% of sprinting activity<sup>28</sup> and 1-3 km at high-intensity running.<sup>29</sup> In addition, matches are full of short activities as accelerations, decelerations, change of directions and speed, jumping, kicking within the range of 1000-1400 events performed every 4-6 seconds.<sup>28</sup> Lockdown training was designed to limit the detraining effects (both aerobic and anaerobic), but also to limit the increase in fat mass and the decrease in muscle mass. Given the need to home training with the impossibility to leave houses the aim of the prescribed program was to limit the detraining effect targeting different aspects anecdotally important for the performance (i.e. metabolic and neuromuscular aspects) through general and not footballspecific exercises. The improvement in respiratory function found after lockdown is totally ascribed to the positive

adaptive changes to endurance training. On the other side, the changes in LV mass may be interpreted differently, in terms of a change of both LV wall thickness and LV dimensions and volumes, as an adaptive mechanism to endurance training, while fat-free mass (FFM) remained unchanged during detraining and lockdown. In fact, Pressler et al.30 demonstrated that cardiac dimensions and LV mass are substantially influenced by body composition, in particular FFM which was the best predictor of LV mass, showing the strongest correlation, better than age, height, weight or BSA.<sup>31</sup> Different authors reported<sup>10, 32, 33</sup> that there is a linear relationship between LV mass and FFM, which might explain the increase of LV mass in relation to increased FFM due to training in athletes. In this study, we demonstrated that despite the significant differences in absolute LV mass and LV mass scaled by BSA, the home training was effective in preventing a massive detraining due to lockdown and movement restriction. In fact, lockdown and quarantine are traditionally associated with emotional stress, blue mood, anxiety, unhealthy diet and food excess, associated with reduced physical activity. Altogether these habits may carry long-term negative effects in enhancing cardiovascular risk, even in healthy individuals.<sup>34, 35</sup> With the aim to reduce the dramatic effects of quarantine on the general population, the WHO released the guide for quarantine "Stay physically active during self-quarantine" new line for people in self-quarantine without any symptoms or diagnosis of acute respiratory illness.36 For competitive and professional athletes the anxiety and frustration of the lockdown, together with uncertainty of sport resumption and the need to maintain fitness to return to competition in the foreseeable future induced the need for supervised or unsupervised training schedules, even if the recommended exercise program was not fully in agreement with the type of sport practiced, as in this case. Unexpectedly, this study demonstrated that, despite the expectations, the prescribed endurance home training, coupled with a healthy diet at home was effective not only to counteract detraining, but also to induce the metabolic changes seen at blood test and the improvement in the respiratory function.

These results highlight the importance of a dedicated home training in the unprecedented situation of quarantine or a national lockdown at every level, ranging from sedentary to active individuals to competitive or professional athletes.

#### Limitations of the study

Our study has all the limitations of retrospective studies; we limited our evaluations to the protocol suggested by the

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Italian Sports Medicine Federation so we did not evaluate other important parameters, as those obtained by the ergospirometry nor data on the psychology of the athletes. Our sample is limited to a first male Football team, so our results cannot be directly applied to other team or sports type or female athletes, but they can serve as a guidance to elicit the important differences existing after the lockdown period in comparison with the standard off-season period.

#### Conclusions

The comprehensive cardiovascular evaluation for Football players performed after the prolonged abstinence, as recommended by the Italian Sports Medicine Federation (FMSI), enlightened significant changes in parameters ascribable to detraining, as the changes in LV mass, both absolute and scaled to BSA, while an improvement was noted in the respiratory function and the metabolic profile. During quarantine it is pivotal to maintain fitness with dedicated training programs even if a change in the usual training is necessary.

#### References

**1.** Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, *et al.* Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. J Am Coll Cardiol 2020;75:2352–71.

**2.** Biondi Zoccai G, Landoni G, Carnevale R, Cavarretta E, Sciarretta S, Frati G. SARS-CoV-2 and COVID-19: facing the pandemic together as citizens and cardiovascular practitioners. Minerva Cardioangiol 2020;68:61–4.

**3.** Kokkinos P, Myers J, Kokkinos JP, Pittaras A, Narayan P, Manolis A, *et al.* Exercise capacity and mortality in black and white men. Circulation 2008;117:614–22.

**4.** Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. CMAJ 2006;174:801–9.

**5.** Peruzzi M, Sanasi E, Pingitore A, Marullo AG, Carnevale R, Sciarretta S, *et al.* An overview of cycling as active transportation and as benefit for health. Minerva Cardioangiol 2020;68:81–97.

**6.** Mujika I, Padilla S. Detraining: loss of training-induced physiological and performance adaptations. Part I: short term insufficient training stimulus. Sports Med 2000;30:79–87.

7. Mujika I, Padilla S. Detraining: loss of training-induced physiological and performance adaptations. Part II: Long term insufficient training stimulus. Sports Med 2000;30:145–54.

**8.** Sousa AC, Neiva HP, Izquierdo M, Cadore EL, Alves AR, Marinho DA. Concurrent Training and Detraining: brief Review on the Effect of Exercise Intensities. Int J Sports Med 2019;40:747–55.

**9.** Silva JR, Brito J, Akenhead R, Nassis GP. The Transition Period in Soccer: A Window of Opportunity. Sports Med 2016;46:305–13.

**10.** D'Ascenzi F, Pelliccia A, Cameli M, Lisi M, Natali BM, Focardi M, *et al.* Dynamic changes in left ventricular mass and in fat-free mass in top-level athletes during the competitive season. Eur J Prev Cardiol 2015;22:127–34.

**11.** Hull JH, Loosemore M, Schwellnus M. Respiratory health in athletes: facing the COVID-19 challenge. Lancet Respir Med 2020;8:557–8.

**12.** Phelan D, Kim JH, Chung EH. A Game Plan for the Resumption of Sport and Exercise After Coronavirus Disease 2019 (COVID-19) Infection. JAMA Cardiol 2020;5:1085–6.

**13.** Bhatia RT, Marwaha S, Malhotra A, Iqbal Z, Hughes C, Börjesson M, *et al.* Exercise in the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) era: A Question and Answer session with the experts Endorsed by the section of Sports Cardiology & Exercise of the European Association of Preventive Cardiology (EAPC). Eur J Prev Cardiol 2020;27:1242–51.

**14.** Pelliccia A. Return to play after the COVID-19 pandemic: a commentary by the Editor in Chief. J Sports Med Phys Fitness 2020;60:675–6.

**15.** Gervasi SF, Pengue L, Damato L, Monti R, Pradella S, Pirronti T, *et al.* Is extensive cardiopulmonary screening useful in athletes with previous asymptomatic or mild SARS-CoV-2 infection? Br J Sports Med 2021;55:54–61.

**16.** Mohr M, Nassis GP, Brito J, Randers MB, Castagna C, Parnell D, *et al.* Return to elite football after the COVID-19 lockdown. Manag Sport Leis 2020. [Epub ahead of print]

**17.** Casasco M, Pigozzi F, Porcelli S, Beltrami G, Agnello L, Parisi A, *et al.* FMSI guidelines for return to physical activity after coronavirus pandemics lockdown. Med Sport 2020;73:167.

**18.** Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, *et al.* International recommendations for electrocardiographic interpretation in athletes. Eur Heart J 2018;39:1466–80.

**19.** Pelliccia A, Caselli S, Sharma S, Basso C, Bax JJ, Corrado D, *et al.*; Internal reviewers for EAPC and EACVI. European Association of Preventive Cardiology (EAPC) and European Association of Cardiovascular Imaging (EACVI) joint position statement: recommendations for the indication and interpretation of cardiovascular imaging in the evaluation of the athlete's heart. Eur Heart J 2018;39:1949–69.

**20.** Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2015;16:233–70.

**21.** Prior BM, Cureton KJ, Modlesky CM, Evans EM, Sloniger MA, Saunders M, *et al.* In vivo validation of whole body composition estimates from dual-energy X-ray absorptiometry. J Appl Physiol 1997;83:623–30.

**22.** Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, *et al.*; ATS/ERS Task Force. Standardisation of spirometry. Eur Respir J 2005;26:319–38.

**23.** Cavarretta E, Maffessanti F, Sperandii F, Guerra E, Quaranta F, Nigro A, *et al.* Reference values of left heart echocardiographic dimensions and mass in male peri-pubertal athletes. Eur J Prev Cardiol 2018;25:1204–15.

**24.** Pelliccia A, Culasso F, Di Paolo FM, Maron BJ. Physiologic left ventricular cavity dilatation in elite athletes. Ann Intern Med 1999;130:23–31.

**25.** Pelliccia A, Maron BJ, Spataro A, Proschan MA, Spirito P. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. N Engl J Med 1991;324:295–301.

**26.** Cheng YJ, Macera CA, Addy CL, Sy FS, Wieland D, Blair SN. Effects of physical activity on exercise tests and respiratory function. Br J Sports Med 2003;37:521–8.

**27.** Durmic T, Lazovic Popovic B, Zlatkovic Svenda M, Djelic M, Zugic V, Gavrilovic T, *et al.* The training type influence on male elite athletes' ventilatory function. BMJ Open Sport Exerc Med 2017;3:e000240.

**28.** Stølen T, Chamari K, Castagna C, Wisløff U. Physiology of soccer: an update. Sports Med 2005;35:501–36.

**29.** Mohr M, Krustrup P, Bangsbo J. Match performance of high-standard soccer players with special reference to development of fatigue. J Sports Sci 2003;21:519–28.

**30.** Pressler A, Haller B, Scherr J, Heitkamp D, Esefeld K, Boscheri A, *et al.* Association of body composition and left ventricular dimensions in elite athletes. Eur J Prev Cardiol 2012;19:1194–204.

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**31.** Foster BJ, Gao T, Mackie AS, Zemel BS, Ali H, Platt RW, *et al.* Limitations of expressing left ventricular mass relative to height and to body surface area in children. J Am Soc Echocardiogr 2013;26:410–8.

**32.** Khoury PR, Mitsnefes M, Daniels SR, Kimball TR. Age-specific reference intervals for indexed left ventricular mass in children. J Am Soc Echocardiogr 2009;22:709–14.

**33.** De Castro S, Pelliccia A, Caselli S, Di Angelantonio E, Papetti F, Cavarretta E, *et al.* Remodelling of the left ventricle in athlete's heart: a three dimensional echocardiographic and magnetic resonance imaging study. Heart 2006;92:975–6.

34. Mattioli AV, Sciomer S, Cocchi C, Maffei S, Gallina S. Quarantine during COVID-19 outbreak: changes in diet and physical activity increase the risk of cardiovascular disease. Nutr Metab Cardiovasc Dis 2020;30:1409-17.

**35.** Infusino F, Marazzato M, Mancone M, Fedele F, Mastroianni CM, Severino P, *et al.* Diet Supplementation, Probiotics, and Nutraceuticals in SARS-CoV-2 Infection: A Scoping Review. Nutrients 2020;12:1718.

**36.** World Health Organization. Stay physically healthy during selfquarantine; 2020 [Internet]. Available from: https://www.euro.who.int/ en/health-topics/health-emergencies/coronavirus-covid-19/publicationsand-technical-guidance/noncommunicable-diseases/stay-physicallyactive-during-self-quarantine#:~:text=Physical%20activity%20and%20 relaxation%20techniques,or%20a%20combination%20of%20both [cited 2022, Feb 3].

Conflicts of interest.—Giuseppe Biondi-Zoccai has been a consultant for Cardionovum (Bonn, Germany), Innovheart (Milan, Italy), Meditrial (Rome, Italy), and Replycare (Rome, Italy). All other authors have no conflicts of interests regarding the publication of this article.

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