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## Short term blood pressure alterations in recently COVID-19 vaccinated patients

### ARTICLE INFO

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#### Dear Editor,

The global medical community supports that vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is crucial for reaching the herd immunity threshold needed to curb the pandemic and return to normal life. Till now, a rapid development of coronavirus disease 2019 (COVID-19) vaccines has occurred and 7.45 billion doses have already administered worldwide. Although the efficacy and safety of COVID-19 vaccines have been tested in randomised clinical trials [1–3], some concerns have been raised based on very limited data regarding a non-immediate hypertensive response post vaccination. Mild to moderate elevated arterial blood pressure (BP) levels have been documented a few days after a single or two-doses vaccine [4,5]. The present study sought to investigate this observation in patients with known hypertension (HTN) and healthy controls.

A total of 100 patients between the age of 50 to 70 years old were studied. They were randomly assigned to one of the approved and available vaccines (Pfizer, Astra Zeneca, Moderna or Johnson & Johnson). Half of them were hypertensives under medical treatment and half of them were not. All participants had systolic BP <140 mmHg and diastolic BP <90 mmHg before vaccination and volunteered for standard daily home BP measurements (HBPM) and ambulatory BP measurements (ABPM) between the 5th and the 20th day after considered fully COVID-19 vaccinated.

Taking under consideration the BP recordings, all patients, hypertensives or not, had at some point a recorded hypertensive response defined as systolic BP values  $\geq 140$  mmHg and/or diastolic BP values  $\geq 90$  mmHg between day 5 and day 20 post vaccination irrespective of vaccine type. Hypertensives were older and with higher body mass index. Five of 50 hypertensive patients received additional medication whereas some of the non-hypertensive patients started life modification changes and systematic BP measurements for a possible diagnosis of HTN (Table 1).

These preliminary results were in accordance with two recently published studies that included patients receiving a messenger RNA (mRNA) based vaccine against COVID-19. The first one was a prospective survey of 113 health workers with apparently normal home BP vaccinated with Pfizer from Italy. Among them, six participants (5.3%) reported a rise in the average self-measured home systolic or diastolic BP by at least 10 mmHg within the first five days following the first dose of vaccine. Four subjects required modification of antihypertensive

treatment and two patients experienced a BP rise after the second dose as well. Notably, previous exposure to SARS-CoV-2 was correlated with a higher probability of a BP rise post vaccination [4]. The second one was a case series of nine patients with previous well controlled HTN conducted in a vaccination centre in Lausanne in Switzerland. Systolic and diastolic BP increased above the values of 180 mmHg and 110 mmHg, respectively, within minutes following vaccination with Pfizer or Moderna [5].

The potential pathophysiological link between COVID-19 vaccination and BP rise remains unclear. Regarding the mRNA-based vaccines it has been noted that mRNA encodes the Spike protein of SARS-CoV-2 in the cells reached by the vaccine. In turn, the Spike proteins congregate into the cytoplasm and migrate to the cell surface to protrude with a native-like conformation and be recognized by the immune system. Moreover, the Spike proteins circulate in the blood as free-floating proteins after cells being destroyed and interact with the angiotensin-converting enzyme 2 (ACE2) receptors resulting in the internalization and the degradation of the receptors. The loss of ACE2 receptors activity and the inactivation of angiotensin II decrease the production of angiotensin 1–7. The subsequent imbalance between angiotensin II (overactivity) and angiotensin 1–7 (deficiency) might have a role in the pathogenesis of HTN after COVID-19 vaccination. An alternative explanation could be a potential hypertensive response to the ingredients of the vaccines including polyethyleneglycol or tromethamine. Last but not least, emotional factors, stress, pain response, the white coat effect or even undiagnosed HTN might be hypothesized as triggers of this reaction in vaccinated subjects [6].

It is well known that SARS-CoV-2 interacts with ACE2 in order to enter the host's cells including cardiac myocytes and alveolar epithelial cells. Initial reports suggested that HTN might be involved in the pathogenesis of COVID-19 and should be considered as a clinical predictor of disease severity in infected patients. A pooled analysis of 13 studies from China pointed out that HTN was correlated with a nearly 2.5-fold higher risk for severe or fatal COVID-19, particularly in the elderly [7]. Therefore, it was recommended patients with cardiac diseases treated with ACE inhibitors or angiotensin II receptor blockers (ARBs) to be close monitored. Contrary to this hypothesis, the European Society of Cardiology (ESC) supports the unstopable use of renin-angiotensin system (RAS) inhibitors in hypertensive patients with COVID-19 that are already on these drugs due to the substantial better survival compared to those not on these drugs [8].

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**Table 1.**  
BP measurements after COVID-19 vaccination in study population.

	Hypertensives (n = 50)	Healthy controls (n = 50)	p-value
<b>Age (years)</b>	64±7.2	58±8.2	0.007
<b>Male gender</b>	25	25	0.1
<b>BMI (kg/m<sup>2</sup>)</b>	28.3 ± 4.5	27.8 ± 1.5	0.02
<b>Home BP mean</b>	SBP 174.7 ± 39.8	157.6 ± 44.1	0.001
	DBP 97.3 ± 5.8	95.8 ± 7.3	0.05
<b>24-hour BP mean</b>	SBP 176.7 ± 42.4	155.6 ± 35.9	0.001
	DBP 98.3 ± 8.1	93.8 ± 5.7	0.06

BMI: body mass index; BP: blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure.

Several side effects that have been reported after COVID-19 vaccination include haematological and vascular events, myocarditis, pericarditis or hyperglycaemia in short time intervals after the first or second dose. However, the frequency is unclear and the exact pathophysiological mechanisms are still inconclusive. Of note, the risks of these adverse events are significantly lower compared to those correlated with SARS-CoV-2 infection [9,10]. The present study implies a potential effect of COVID-19 vaccination on BP rather than a new side effect.

To conclude, vaccination for COVID-19 seems to be related with a short period of hypertensive response. This phenomenon was partial and mostly observed in older overweight hypertensives. Probably, BP should be systematically measured at home at least a week prior and after vaccination. However, the overall benefits of COVID-19 vaccination outweigh the risk of these observations.

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