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Cryptic evidence on underreporting of mRNA vaccine-induced cardiomyositis in the elderly: a need to modify antihypertensive therapy

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Abstract

Background. Cardiomyositis has been considered a rare complication of COVID-19 vaccination that primarily affects young people. However, recent studies indicate under-reporting of cases in the elderly. Furthermore, post-mortem studies of five cases (median age 58) that died suddenly within 7 days of vaccination, indicate an autoimmune element. Albeit an individual case history, the author's unexpected personal evidence supports the latter studies.

Methods. Readings of blood pressure (BP) and pulse were taken twice daily.

Findings. Seven days after the fifth of a series of anti-COVID-19 vaccinations, a "stress test" (15 min jog) in an elderly subject exposed a cardiac problem – arrhythmia and a rapid fall of BP with slow recovery. The timing suggested myocarditis as a post-vaccination *early* side-effect that usually targets those more likely to exercise (i.e., the young). Thus, it is usually cryptic in the elderly. In addition, retrospective studies of his own BP readings during the vaccination period (2021-2023) revealed the sudden emergence of transient, but prolonged, falls of BP *several weeks* after each of his last four vaccinations. These hypotensive episodes were cryptic (asymptomatic) and likely not detected in shorter post-vaccination analyses.

Interpretation. Short-term post-vaccination side effects are distinct from those occurring after some weeks. The first category includes systemic or localized inflammatory responses that, in the case of the heart, might either trigger arrythmia and acute functional impairment, or remain cryptic. Localized responses could initiate tissue damage, culminating weeks later in the second category – asymptomatic but measurable functional impairment. Continuing regular dosages of antihypertensive medication during this period would likely intensify the hypotension. That this did not occur in the author's case is attributed to his two-decade-long practice of modulating dosage daily, based on BP readings. Failure to follow this protocol might explain some sudden home deaths. A parallel is drawn with his previous study that showed the need to modify antihypertensive therapy in response to external temperature changes.

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Introduction

Citing reports of the US Center for Disease Control (CDC), it was correctly concluded early in the COVID-19 pandemic that most adverse events of vaccination, including cardiomyositis, “were mild and short in duration”.[1] Among these was a 2021 report that cardiomyositis is more frequent in young versus old, in males versus females and in military males versus non-military males. It was *not* noted that the first mentioned in these pairs tend to exercise more, and that such exercise may reveal cardiac symptoms. However, exercise restriction was recommended for diagnosed cases.[2] An extensive Japanese population study has since concluded that there has been under-reporting of occurrences of cardiomyositis in the elderly.[3] Furthermore, German biopsy studies[4] and the post-mortems of five subjects (median age 58) that died suddenly at home within 7 days of vaccination,[5] indicate a cardiac autoimmune element.

There is little information on the nature of these sudden deaths. Thus, the account of an elderly authority in the field (the present author) of his own exercise-related “near death” experience, 7 days after a fifth (“booster”) dosage of an mRNA vaccine, might be helpful. It so happens that he also had available blood pressure (BP) readings for the vaccination period (2021-2023). These readings were part of a two-decade study of the treatment of his own mild hypertension with angiotensin II receptor antagonists (ARBs).[6] The continued use of these has been problematic for COVID-19 patients because they bind the receptor for angiotensin-II (AT_1R) and hence might influence the membrane-associated angiotensin converting enzyme 2 (ACE2), to which the SARS-CoV-2 virus binds.[7][8] The general conclusion has been, either that ARB usage should not influence case management,[9] or that it might help rather than hinder.[10]

However, this paper brings to light circumstances, probably less rare than generally thought, where hindrance is evident. While, through exercising, the author discovered within*days* of vaccination one, otherwise cryptic, cardiac symptom, his retrospectively examined BP readings indicate transient asymptomatic cardiac impairments *several weeks* after the last four of his five vaccinations. This period is much longer than the four-week cut-off employed in some studies,[11] as has recently been noted.[12][13]

He attributes the absence of symptoms (i.e., their crypticity) to his protocol of adjusting ARB doses daily according to BP readings (see Methods). This practice had previously brought to light the need to adjust doses according to environmental temperature.[6] Thus, although this journal does not usually publish what is essentially a personal case history, in this instance the editors have granted a waiver. Of importance in this respect is that the study was carried out with widely available BP monitors. Thus, using a “crowd sourcing” approach,[14] the results might readily be confirmed by some of the many millions of hypertensive subjects with a scientific background.

Methods

A BIOS BP and pulse monitor (model BD353; Thermor Ltd., Newmarket, Ontario) was purchased in 2020. The levels and

patterns of readings compared well with those of a model from another manufacturer. After resting (>10 min) the author took readings twice daily (approx. 8 am and 8 pm) from his own left arm. According to the results, dosages of antihypertensive agents (Losartan and recently Candesartan) were modulated (zero, half tablet, one tablet, etc.) with the aim of achieving values of 130 and 75 (mm Hg) for systolic and diastolic, respectively.

This protocol was implemented in 2000 when mild hypertension was diagnosed and later facilitated dosage management when BP values were seen to be influenced by environmental temperature.[6] While this “time in the therapeutic range” approach is now becoming more widely adopted,[15][16][17] the relative constancy of BP and pulse values means that agent dosages must act as *surrogate indicators* for what the BP values *might* have been. To smooth out random fluctuations, in the present work weekly averages are calculated. The author is not aware that, even in the era of machine learning, there yet exist simple devices that can automatically output from recorded BP and pulse measurements, suggested doses for named agents. For clarity, the author’s results are narrated here in the first person.

Results

Post-vaccination acute cardiac arrythmia

Table 1. COVID-10 vaccination schedule and short-term side effects

Date	mRNA vaccine	Side effect (wife)	Side effect	Organ	Post Vaccination Runs
7 Mar 2021	Pfizer	No	No	-	On days 2 and 5
25 June 2021	Pfizer	No	No	-	On days 2 and 8
23 Dec 2021	Moderna	No	No	-	On days 6 and 9
12 May 2022	Moderna	Systemic immune (day 1)	Local immune	Both Gums teeth (day 2)	None
8 Oct 2022	Moderna	Systemic immune (day 1)	Local immune	Heart (day 7)	On days 3 and 7

In my dotage, my love of running has moderated to 15-minute jogs twice weekly in a nearby park. I continued this after my first three vaccinations with no problems (Table 1). However, after my wife and I had our first “boosters” (fourth vaccination) two widely separated teeth (upper and lower jaws that my dentist had warned were problematic), became very painful. Assuming a local cytokine-release problem (my wife had a systemic one), I did not run. After the second booster (fifth vaccination), I was feeling well and jogged normally on day-3. But 10 minutes into my day-7 jog, I experienced a mild tightening in my chest and sat down. I detected a faint fluttering pulse. Recalling the reported “rare” incidence of postvaccination myocarditis,[1] I assumed atrial fibrillation and walked slowly home where I rested for a while and then took BP and pulse readings.

My pulse was 140/min and systolic pressure was 75 mm Hg (Fig. 1). It took three hours continued rest for my BP to return

to normal and several more hours for my pulse to follow likewise. Given the new knowledge,[3][4][5] and having never in my 84 years experienced an episode like this, it is unlikely that it was unrelated to the vaccination. Since then (15th Oct 2022) I have been well but have discontinued jogging pending formal cardiac investigations and my own research, which is the main topic of this paper.

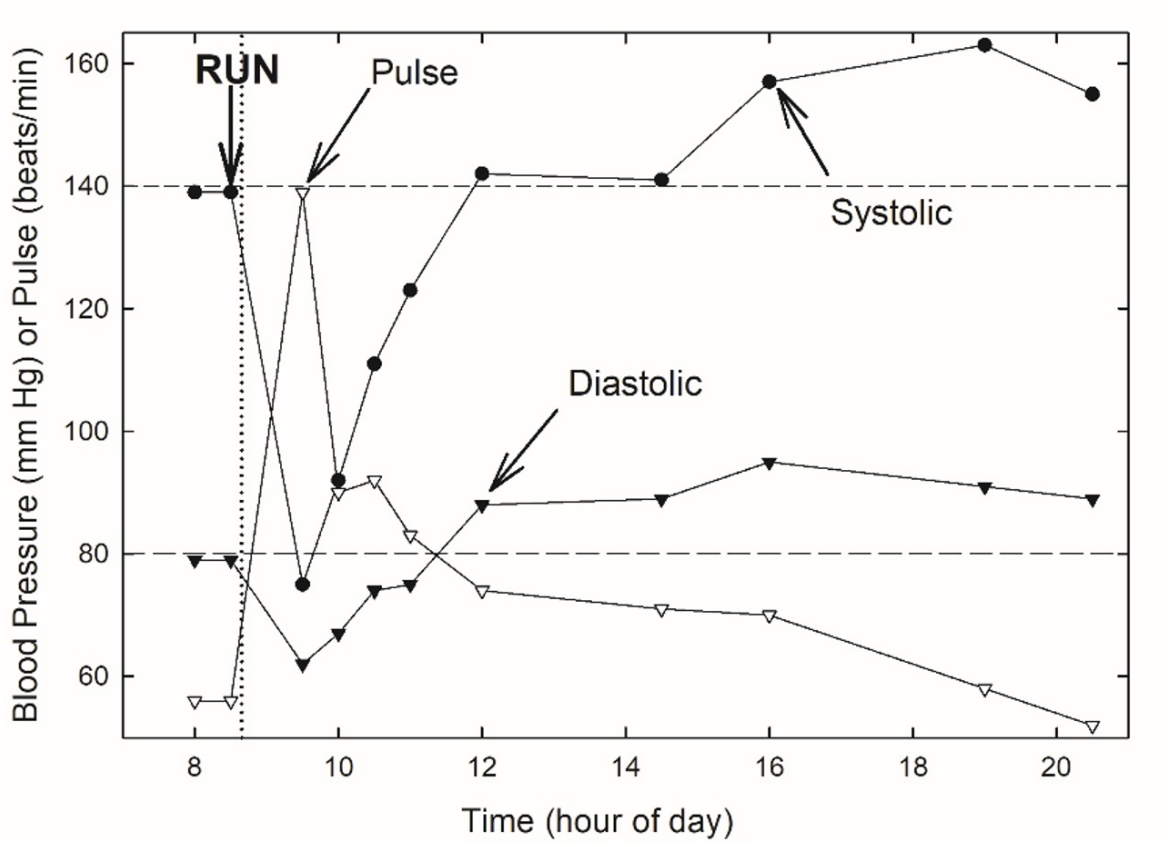

Figure 1. Changes in BP and pulse following a hypotensive episode while gently running seven days after a 5 th COVID-19 vaccination (second mRNA "booster"). Horizontal dashed lines indicate baseline values prior to running. The values corresponding to the start point ("RUN") are a repeat of those of 8-00 am, assuming minimal change in the interim (30 min). The vertical dotted line indicates the time of onset of tachycardia (approx. 10 min into the run). The long duration of the period from this to the first determination of BP and pulse values, should be noted. Pulse (open triangles); systolic BP (filled circles); diastolic BP (filled triangles).

Formal investigations (January 2023) included echocardiograms and electrocardiographic monitoring during a treadmill "stress test" where speed increased slowly and my pulse achieved 130 beats/minute without undue breathlessness. Most blood tests were considered satisfactory, but atrial natriuretic peptide (NT-proBNP) was increased (182 ng/litre; normally <125 ng/litre). This was intriguing for various reasons. First, because its elevation can be a sign of cardiac failure.[18] Second, because its blood levels are influenced by ARBs. Third, because my own mild hypertension has long been treated with this class of antihypertensive agent.[6] And finally, because the cardiomyocyte-secreted hormone was discovered by a recently deceased colleague.[19] Nevertheless, my cardiologist advised that jogging could resume. Subsequent reexamination of my own BP records suggested caution in this respect.

Reexamination of blood pressure records

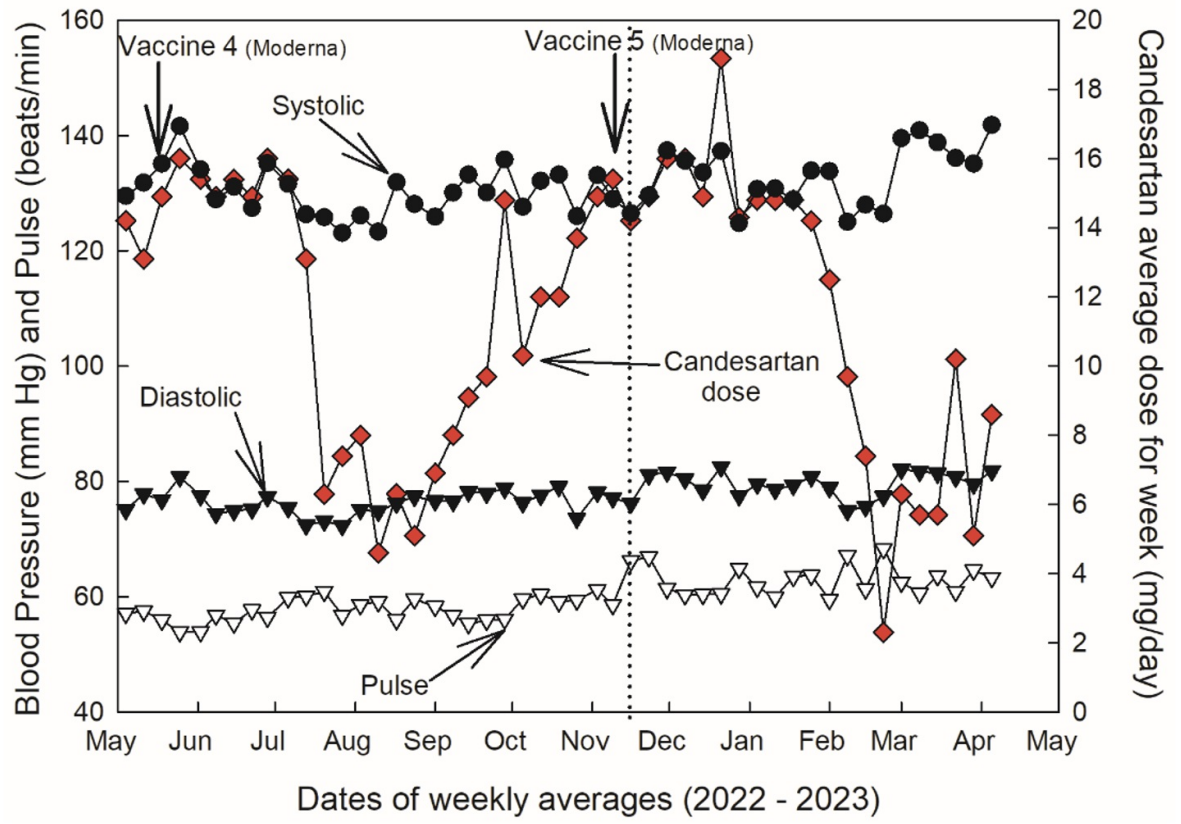

Figure 2. Influence of 4th and 5th COVID-19 mRNA vaccinations on BP, pulse, and required Candesartan dosages. Values of systolic BP (filled circles), diastolic BP (filled trianges), and pulse (open trianges), being kept relatively constant, the required dosage of Candesartan (red diamonds) acts as a *surrogate indicator* of what systolic blood pressure *might* have been. Vertical arrows indicate times of vaccinations. The vertical dotted line indicates the time of onset of tachycardia while running one week after the 5th vaccination (see Fig. 1). Individual data points indicating 7-day averages (ordinate), correspond to central Wednesdays with three days on either side (abscissa). The number of weeks between events can be approximated by counting the number of data points between them. Pulse values increased slightly (linear regression slope = 0·025; r^2 = 0·54; P < 0·0001).

In the 1960s I was house-physician to the hypertension research unit at a London teaching hospital. I subsequently explored other research avenues, but the diagnosis of mild hypertension in 2000 rekindled my interest, and my BP has been well-controlled with low ARB doses. Attempting to emulate normal baroreceptor-mediated controls, BP reading are recorded twice daily, and doses varied accordingly (see Methods). Given the above considerations, I retrospectively examined my records corresponding to the 2021-2023 period of COVID-19 vaccination.

Figure 2 refs to the 4th and 5th vaccinations. The hypotensive episode 7 days after the latter (Fig. 1), is noted by a vertical dotted line. As intended, systolic and diastolic BPs remained relatively constant around 130 and 75 (mm Hg), respectively. To maintain this constancy, Candisartan doses were modulated twice daily, decreasing when BP tended to rise, and increasing when BP tended to fall. Pulse values were also relatively constant, but linear regression showed a significant

slight increase.

Unexpectedly, seven weeks after the fourth vaccination (first booster), recorded BP values began to fall. The lower required candesartan dosages show that the fall would have been sustained for several weeks and then, should I have survived the episode, return to normal over the following ten weeks. During the latter part of this period, the fifth vaccination (second booster) was administered, but did not influence this recovery. However, thirteen weeks after this fifth vaccination, the required candesartan dosage showed an even greater decrease over a five-week period, from which, happily, a recovery may be in progress at the time of this writing.

These results were obtained with the Moderna mRNA vaccine. The second and third mRNA vaccinations included a different version (Table 1). Figure 3 shows that a less extreme fall in required dosage occurred four weeks after administration of the Pfizer version. This was sustained for ten weeks, followed by what appeared to be a recovery over ten weeks, which just preceded the third vaccination with a Moderna version. Surprisingly, the fall following this third vaccination occurred with little delay and was much smaller, being sustained for three weeks, followed by a recovery over seven weeks. As with Figure 2, the targeted values for systolic and diastolic BPs were sustained throughout this study period, but there was again a small progressive increase in pulse values.

Over these periods (Figs. 2, 3) Candesartan was the ARB of choice. However, at the time of the first vaccination, the medication was Losartan, which had been employed since 2000. Figure 4 shows for early 2021 that increasing dosages were needed to sustain the target BP values over that study period. There was a hint, but no clear evidence, that the Pfizer vaccine had induced a dip a few weeks after injection. Overall, figures 2-4 indicate increasing vulnerability to vaccine-induced hypotension over the study period.

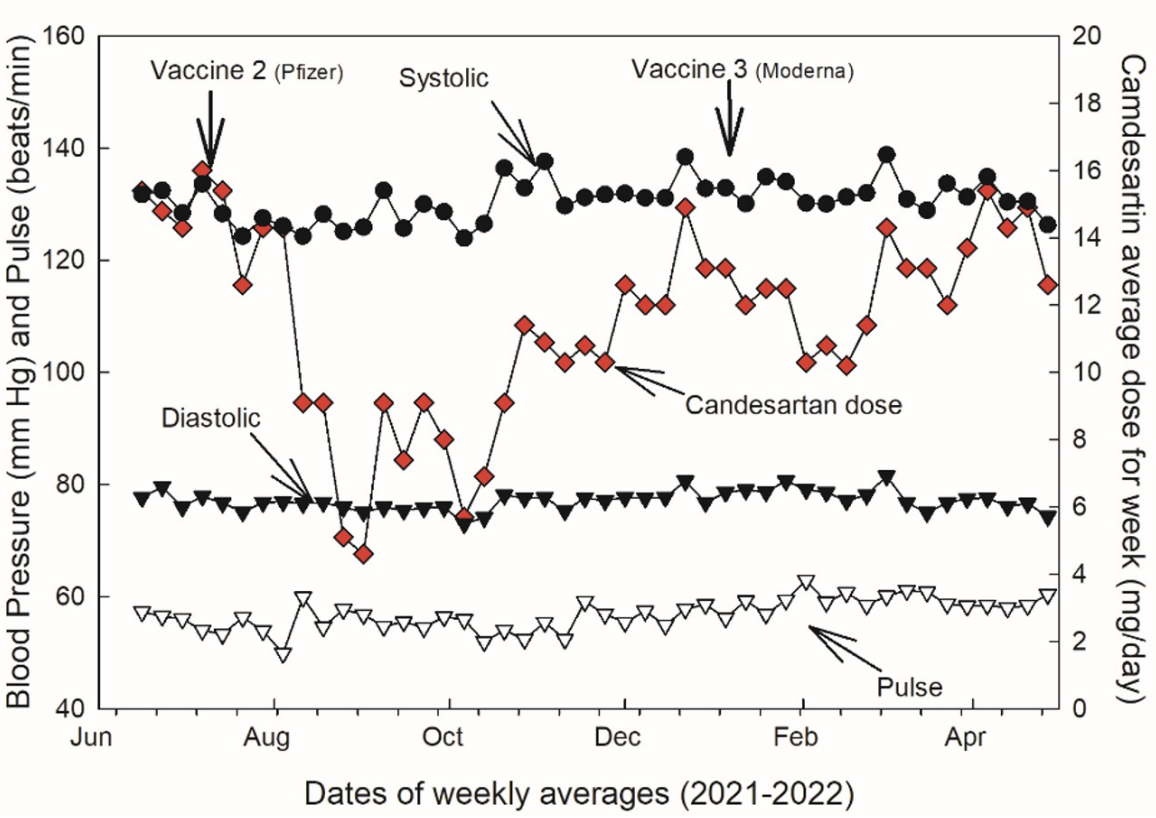

Figure 3. Influence of 2nd and 3rd COVID-19 mRNA vaccinations on BP, pulse, and required Candesartan dosage. Details are as in Fig. 2. Pulse values increased slightly (linear regression slope = 0·018; r^2 = 0·38; $P < 0·0001$).

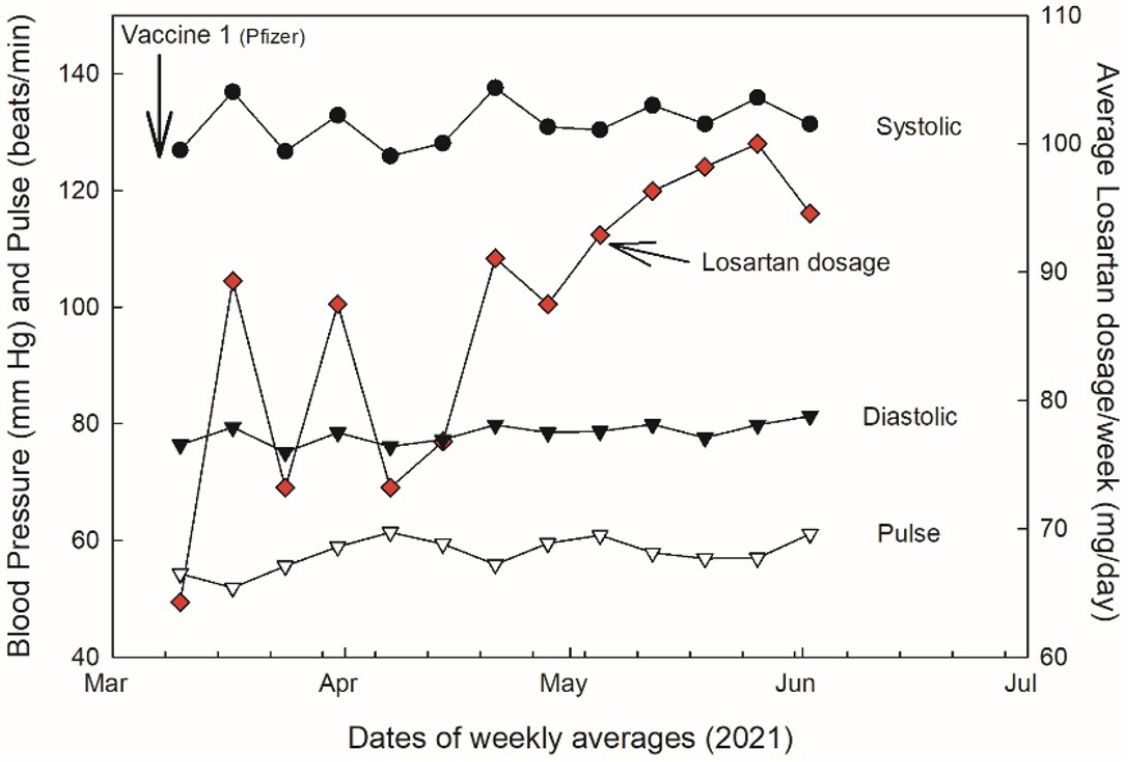

Figure 4. Influence of the 1st COVID-19 mRNA vaccination on pulse, BP and required Losartan dosage. Details are as

in Fig. 2. Pulse values increased slightly (linear regression slope = 0·05; r^2 = 0·26; P = 0·07).

Discussion

Despite an incomplete awareness of possible side-effects, the basic research of Katalin Karikó and others made mRNA-based vaccines available on time to save many lives in the COVID-19 pandemic.[20] The acceleration of research post-2020 was so rapid that preprint postings became the norm for many of us working in the field.

Underreporting, especially in the elderly

Following the first report of Watanabe and Hana on the post-vaccination mortality risk of cardiomyositis becoming increasingly evident (October 18th, 2022), there was a lively debate in the comments column of the *medXriv* preprint server, accompanied by an amazing number of tweets (>10,000; unusual for that server). Their conclusions were repeated in a subsequent posting (December 22nd 2022): [3]

> *SARS-CoV-2 vaccination was associated with higher risk of myocarditis death, not only in young adults but also in all age groups including the elderly. Considering healthy vaccinee effect, the risk may be 4 times or higher than the apparent risk of myocarditis death. Underreporting should also be considered. Based on this study, risk of myocarditis following SARS-CoV-2 vaccination may be more serious than that reported previously.*

With increasing recognition of shortcomings of earlier studies,[11] there is now a growing consensus in the field regarding this conclusion.[12][13] An important recent advance is the detection of vaccination-induced circulating viral spike protein in 16 young non-cryptic cardiomyositis cases, but not in 45 age-matched asymptomatic vaccinated controls.[21]

Implications of the present study

Although a case report, the present identification of cryptic factors likely to have contributed to the author's cardiomyositis further supports Watanabe and Hana.[3] Special support came from his retrospective monitoring of BP responses to ARBs over past decades,[6] that included the period of the pandemic. Although confined to this class of antihypertensive agent, it is likely that the results will be found to apply to other classes. However, ARBs have played a more complex role in the pandemic as outlined in the Introduction to this paper, so caution must be exercised.

From the present study, a distinction can be drawn between short-term post-vaccination side effects occurring in the days immediately after vaccination and those occurring much later. The first category would include systemic and/or localized inflammatory responses (Table 1) which, in the case of a heart under stress, might trigger arrythmia and acute functional impairment (Fig. 1). Localized responses could initiate tissue damage, culminating, sometimes after several weeks, in measurable functional impairment (Figs. 2,3). Whether short or long term, when cryptic (e.g., as when not provoked by exercise), these cardiomyositis side-effects could be the source of unexplained deaths among vaccinated persons, some

of whom may have had preexisting cardiac problems.

Regarding mechanism, when heart failure is due to elevated peripheral vasoconstriction an appropriate remedy is to decrease the vasoconstriction with conventional antihypertensive medications. In this circumstance, there is usually a *reciprocal* relationship between systolic BP and pulse. As the BP increases the pulse decreases, and vice-versa. However, hearts can fail for central cardiac reasons. When this is the primary cause, baroreceptor reflexes may promote heart rate (pulse). In this circumstance, BP and pulse may be coordinately *increased*. Antihypertensive treatment could then lead to an uncompensatable degree of hypotension. A similar problem has been identified previously in relation to a peripheral cause, namely the relaxation of vasculature in response to high environmental temperatures, which seemed to be explicable on the basis of differential signaling by countervailing receptors.[6] As is now increasingly recognized, this circumstance dictates decreasing antihypertensive dosage below that employed with normal temperatures.[15]

These considerations bring us back to the above-mentioned elevated level of the author's blood levels of atrial natriuretic peptide,[19] whose receptor associates with a regulator of G-protein signaling serendipitously identified in his laboratory.[22] A link to hypertension was later established by Heximer and colleagues![23] Consistent with the results presented here, Daya and coworkers reported in 2023[18] that: "We observed elevated mortality among those with high NT-proBNP in lower categories of BP, suggesting that NTproBNP can 'unmask' elevated risk in uncontrolled BP." Nevertheless, they conclude that: "Our results suggest that NT-proBNP provides insight into possible end-organ damage and thus the need for early initiation of hypertension treatment." However, when that end-organ is a heart that is reflexly attempting to sustain BP, the *cessation* of ongoing hypertension treatment may be more important. Simply stated, if you are in a hole, be it from primary cardiac failure or the external influence of tropical temperatures, do not keep digging. A recent review by Maeda et al. provides insightful discussion of possible underlying physiology.[24]

While vaccination against coronavirus infection has, and will continue, to save the lives of millions, in the long-term, investigations of specific vulnerabilities, both of viruses and their hosts, are warranted. Viral vulnerabilities should be clarified so as to focus chemotherapeutic agents to specific target regions,[25] and the ancestral histories of different host groups should work to guide choices among those agents.[7]

Research in context

Evidence before this study

After general safety tests, COVID-19 mRNA vaccines were approved. Reports of side-effects, some extending beyond the "rare" category, have since emerged. The present work builds on the author's previous study of the potential danger of not lowering dosage of antihypertension medication in hot climates.

Added value of this study

An unsuspected relationship between mRNA vaccination and hypotension is revealed.

Implications of the available evidence

Post-vaccination deaths of those on antihypertensive medication might have been avoided. The simple methodology might facilitate “crowd source” confirmation. The “time in therapeutic range” (TTR) approach to BP medication might be more widely appreciated.

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Declaration of interests

The author declares no competing interests.

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