RAPID COMMUNICATION

Cardiac side effects of RNA-based SARS-CoV-2 vaccines: Hidden cardiotoxic effects of mRNA-1273 and BNT162b2 on ventricular myocyte function and structure

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First published: 12 October 2023 https://doi.org/10.1111/bph.16262

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bph.16262.

Abstract

Background and Purpose

To protect against SARS-CoV-2 infection, the first mRNA-based vaccines, Spikevax (mRNA-1273, Moderna) and Comirnaty (BNT162b2, Pfizer/Biontech), were approved in 2020. The structure and assembly of the immunogen – in both cases, the SARS-CoV-2 spike (S) glycoprotein – are determined by a messenger RNA sequence that is translated by endogenous ribosomes. Cardiac side effects, which for the most part can be classified by their clinical symptoms as myo- and/or pericarditis, can be caused by both mRNA-1273 and BNT162b2.

Experimental Approach

As persuasive theories for the underlying pathomechanisms have yet to be developed, this study investigated the effect of mRNA-1273 and BNT162b2 on the function, structure, and viability of isolated adult rat cardiomyocytes over a 72 h period.

Key Results

In the first 24 h after application, both mRNA-1273 and BNT162b2 caused neither functional disturbances nor morphological abnormalities. After 48 h, expression of the encoded spike protein was detected in ventricular cardiomyocytes for both mRNAs. At this point in time, mRNA-1273 induced arrhythmic as well as completely irregular contractions associated with irregular as well as localized calcium transients, which provide indications of significant dysfunction of the cardiac ryanodine receptor (RyR2). In

Conclusions and Implications

Here we demonstrated for the first time, that in isolated cardiomyocytes, both mRNA-1273 and BNT162b2 induce specific dysfunctions that correlate pathophysiologically to cardiomyopathy. Both RyR2 impairment and sustained PKA activation may significantly increase the risk of acute cardiac events.

Supporting Information

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Filename	Description
bph16262-sup-	Video S1. Representative video sequences: A) untreated cardiac muscle cel
0001-	 – regular contraction; B) after BNT162b2 application – increased
Video_S1.mp4	contraction; C-F) after mRNA-1273 application – arrhythmic, irregular as
MPEG-4 video,	well as partly "peristaltic" contraction (C – top: non-beating but
14.8 MB	morphologically intact myocyte).
bph16262-sup-	Video S2. Visualization of calcium transients using Fluo-4, AM.
0002-	Representative video sequences: A,B) untreated cardiac muscle cell –
Video_S2.mp4	regular transients; C,D) after BNT162b2 application – regular transients
MPEG-4 video,	with increased intensity; E-G) after mRNA-1273 application – focal or
17.1 MB	irregular as well as arrhythmic transients (E – top, F – left: hypercontracted
	cardiac muscle cell with calcium overload).

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