

Myocardial Injury after COVID-19 mRNA booster vaccination

Investigator-initiated, industry-independent, active surveillance study

Professor Christian Mueller, University Hospital Basel, Switzerland

On behalf of the MACIS Investigators

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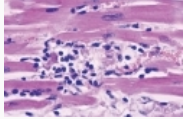
CRIB

Cardiovascular Research
Institute Basel

Disclosures: Research Support



Several diagnostic companies, Novartis, Idorsia



Background: Myocardial injury/Myocarditis

- Possible severe adverse event following mRNA COVID-19 vaccines
- Occurring mainly in young men a few days after vaccination
- **Using passive surveillance** following vaccination with BNT162b2-mRNA (Pfizer-BioNTech) or mRNA-1273 (Moderna), is currently considered **rare** (0.0035%).
- However, passive surveillance **detects only severe cases** requiring hospitalization.

Hypothesis:

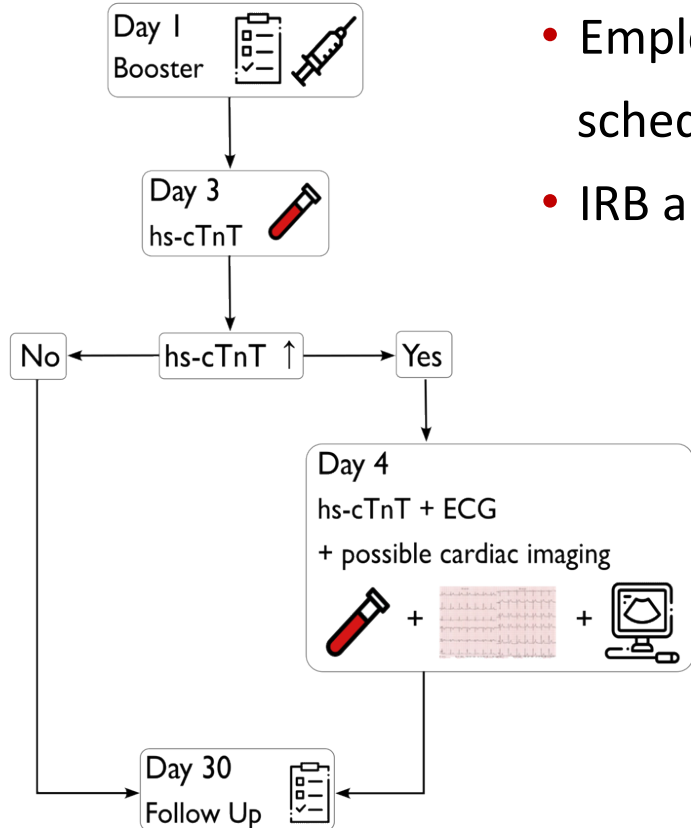
- Vaccine-associated myocardial injury is **much more common**, as symptoms may be mild & unspecific or even absent.
- Evaluating the true incidence is of major importance, as this information is required for informed decision making for patients, physicians, and public health authorities given the apparent **need for repetitive** (possibly yearly) **booster vaccinations** for billions of humans worldwide due to diminishing protection months after the last COVID-19 vaccination.

Prospective active surveillance study: 2 Aims

- 1) Evaluate **true incidence**
- 2) Provide a “**safety net**” for persons identified with vaccine-associated myocardial injury to allow early detection and preventive measures to avoid possible aggravation

METHODS

Screening for myocarditis



- Employees of the University Hospital Basel, Switzerland, scheduled to receive mRNA-1273 booster vaccination
- IRB approval, Written ICF

Exclusion criteria:

cardiac events or cardiac surgery 30d prior to vacc.

PE: Adjudicated acute myocardial injury >ULN (myocarditis), without evidence of an alternative cause

Active surveillance & Immediate response

Avoidance of exercise until hs-cTnT ↓

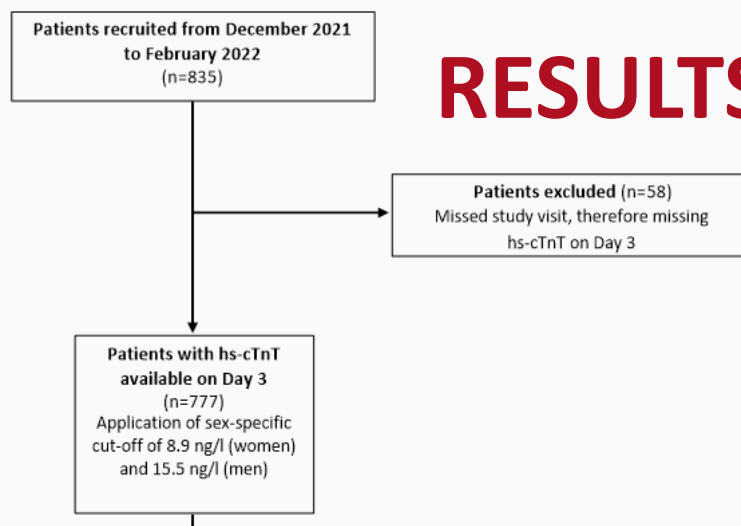
Methods

Secondary endpoint:

a) **acute cardiomyocyte injury** (as a continuous variable) **versus** age-, sex-, history of CAD/AMI-**matched controls** that had presented with acute chest discomfort to the ED in a multicenter study (NCT00470587) and were centrally adjudicated as having a non-cardiac cause

b) **Major adverse cardiac events (MACE) at 30d**: cardiac death, AHF, life-threatening arrhythmia, AMI

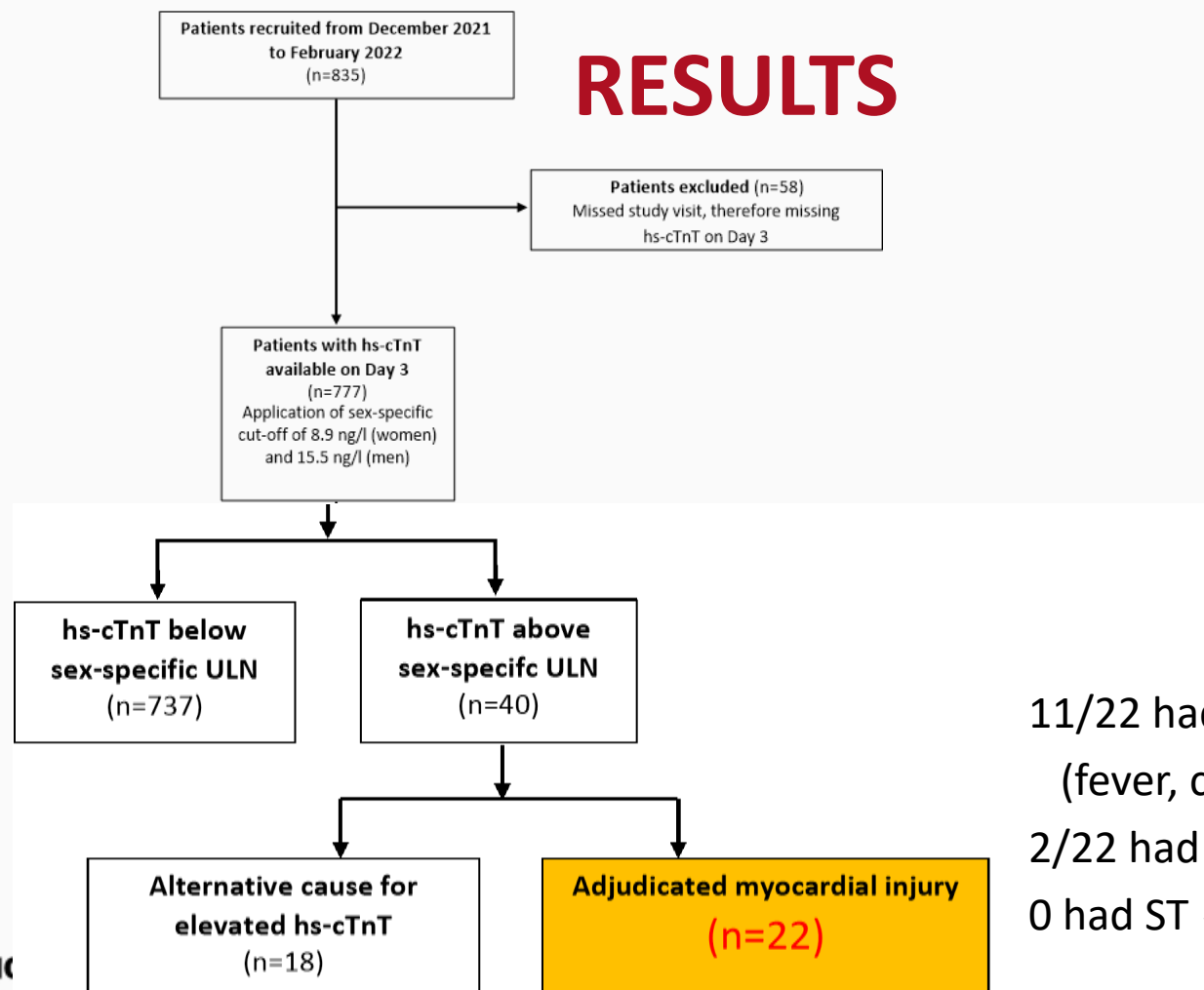
RESULTS



RESULTS

Variable	Overall
N	777
Age, median [IQR]	37.0 [30.0, 50.0]
Women, n (%)	540 (69.5)
Number of previous COVID vaccines, n (%)	
One vaccination	1 (0.1)
One vaccination after COVID infection	37 (4.8)
Two vaccinations	714 (92.0)
Two vaccinations after COVID infection	24 (3.1)
Days since last vaccination, median [IQR]	206.0 [188.0, 230.0]
History of coronary artery disease, n (%)	3 (0.4)
History of acute myocardial infarction, n (%)	1 (0.1)
History of heart surgery, n (%)	3 (0.4)
History of myocarditis, n (%)	5 (0.6)
History of chronic heart failure, n (%)	2 (0.3)

RESULTS

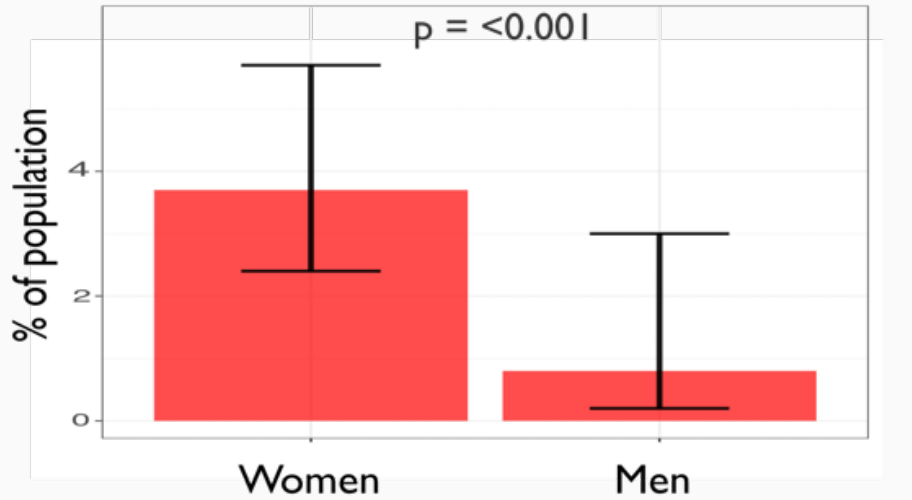


11/22 had **unspecific symptoms**
(fever, chills, myalgia)
2/22 had **chest pain**
0 had ST ↓

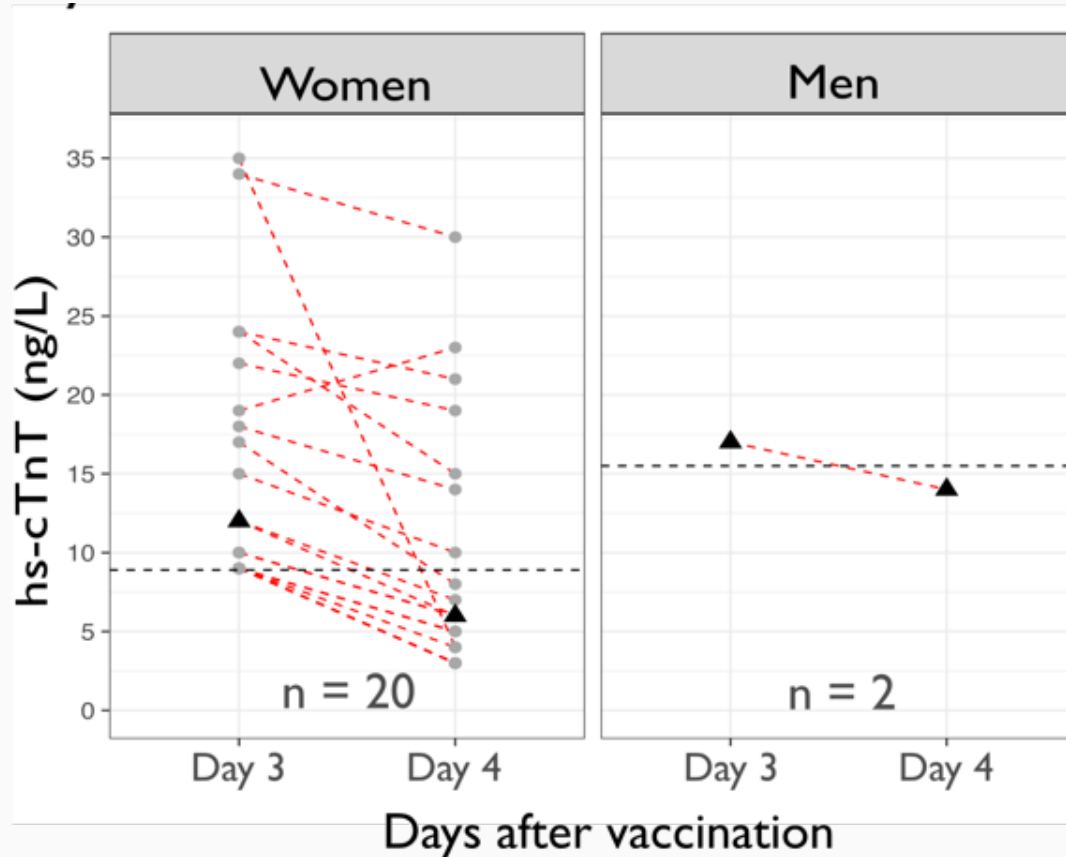
RESULTS

Incidence of myocardial injury: **2.8%** [95%CI, 1.7-4.3%]

3.7% vs. **0.8%**



RESULTS



RESULTS

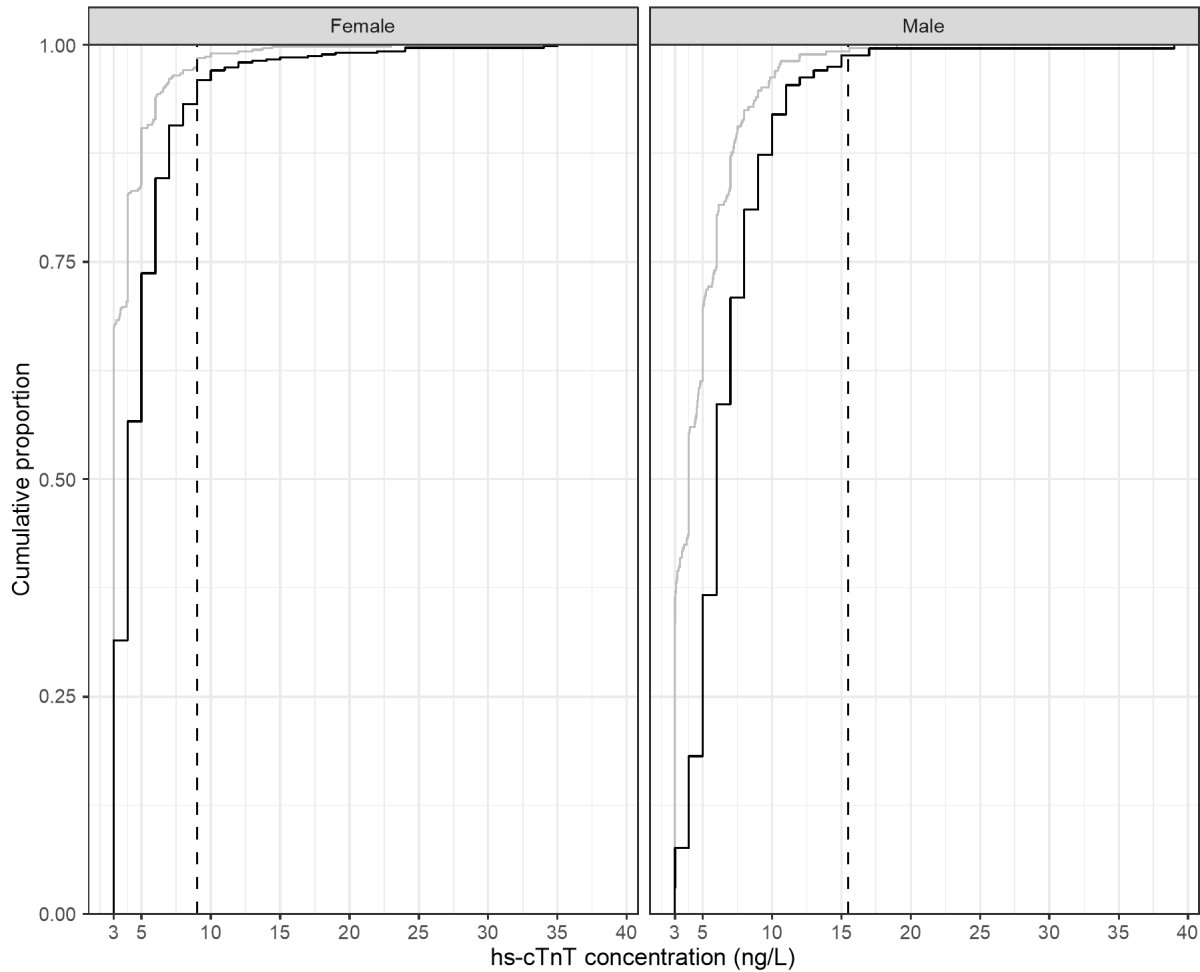
Variable	Overall	No Myocardial Injury	Myocardial Injury	p
n	777	755	22	
Age, median [IQR]	37 [30, 50]	37 [29, 50]	46 [33, 54]	0.11
Sex				0.03
Male, n (%)	237 (30.5)	235 (31.1)	2 (9.1)	
Female, n (%)	540 (69)	520 (69)	20 (91)	
No of previous COVID vacc., n (%)				0.20
One vaccination	1 (0.1)	1 (0.1)	0 (0.0)	
One vaccination after COVID-inf	37 (4.8)	37 (4.9)	0 (0.0)	
Two vaccinations	714 (92.0)	694 (92.0)	20 (90.9)	
Two vaccinations after COVID	24 (3.1)	22 (2.9)	2 (9.1)	
days since last vacc., median [IQR]	206 [188, 230]	205 [188, 229]	222 [187, 253]	0.14
History of CAD, n (%)	3 (0.4)	3 (0.4)	0 (0.0)	1.00
History of AMI, n (%)	1 (0.1)	1 (0.1)	0 (0.0)	1.00
History of heart surgery, n (%)	3 (0.4)	3 (0.4)	0 (0.0)	1.00
History of myocarditis, n (%)	5 (0.6)	5 (0.7)	0 (0.0)	1.00
History of chronic HF, n (%)	2 (0.3)	2 (0.3)	0 (0.0)	1.00

RESULTS

Baseline characteristics before matching				Baseline characteristics after matching		
Variable	Booster	Controls	SMD	Booster	Controls	SMD
n	777	3716		777	777	
Age, y (median [IQR])	37 [30, 50]	54 [43, 66]	1.059	37 [30, 50]	39 [31, 50]	0.071
Male, n (%)	237 (31)	2349 (63)	0.694	237 (31)	266 (34)	0.080
Known CAD, n (%)	3 (0)	750 (20)	0.689	3 (0)	3 (0)	<0.001
Previous AMI, n (%)	1 (0)	540 (15)	0.575	1 (0)	1 (0)	<0.001

SMD: standardized mean difference; CAD: coronary artery disease; AMI: acute myocardial infarction

— Controls — Booster



Cumulative distribution curve of cardiomyocyte injury as quantified by hs-cTnT concentrations stratified by sex. The dashed lines indicate the sex-specific upper reference limits.

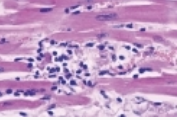
Discussion

- Hypothesis **confirmed!** Incidence **2.8%**, **>800-times** estimated
- **Mild**, no MACE within 30 days within the safety net
- Impact of mRNA vaccine-associated myocardial injury on the long-term risk of cardiac arrhythmias and HF is unknown.
- Small extent of acute myocardial injury (1/4 of spontaneous myocarditis) suggests favourable long-term outcome
- Possibly yearly booster vaccinations → cumulative burden of myocardial injury

Limitations

1. Blood draw only at d3 → underestimate true incidence
2. No CMR (as hs-cTnT < Limit of detection of CMR \approx 70-100ng/L)
3. ? mechanisms of myocyte injury (inflammation/myocarditis, cardiotoxic)
4. ? to what extent early detection and management contributed to the excellent outcomes at d30
5. We did not assess vaccine-induced pericarditis as it seems a benign condition

Conclusions



Using active surveillance **mRNA-1273 vaccine-associated myocardial injury** –likely indicating myocarditis- was found to be **much more common** than previously thought.

It occurred in **one out of 35 persons**, was **mild**, and **more frequent in women** versus men.