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Myocardial Infarction, Stroke, and Pulmonary Embolism After BNT162b2 mRNA COVID-19 Vaccine in People Aged 75 Years or Older

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This population-based study evaluates the short-term risk of severe cardiovascular events among French residents aged 75 years or older after receipt of the BNT162b2 mRNA COVID-19 vaccination.

The BNT162b2 mRNA vaccine (Pfizer-BioNTech) was the first SARS-CoV-2 vaccine authorized and the most widely used in older persons in France. Although no increases in cardiovascular events were reported in phase 3 trials,[1] questions emerged once the vaccine was used on a large scale because older people were underrepresented in the trials. We evaluated the short-term risk of severe cardiovascular events among French people aged 75 years or older after the administration of the BNT162b2 mRNA vaccine.

Methods

This population-based study used the French National Health Data System linked to the national COVID-19 vaccination database. Eligible participants were all persons unvaccinated or vaccinated with the BNT162b2 vaccine, aged 75 years or older, admitted to the hospital between December 15, 2020, and April 30, 2021, for acute myocardial infarction, hemorrhagic stroke, ischemic stroke, or pulmonary embolism (diagnoses identified using the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes) (Table 1 and eTable in the Supplement).

We undertook within-person comparisons using a self-controlled case-series method adapted to cardiovascular event–dependent exposures and high event-related mortality that can cancel or defer subsequent vaccination or increase short-term mortality[2] (eMethods in the Supplement). Only exposures preceding the event were considered. Exposure risk intervals were days 1 through 14 following each of the 2 vaccine doses. The exposure risk interval was further subdivided into days 1 through 7 and days 8 through 14. Except for the vaccination day, the remaining periods were regarded as nonrisk periods. Unvaccinated persons were included to account for temporal effects. Unbiased estimating equations were used to calculate the relative incidence (RI) adjusted for temporality (in 7-day increments) to consider any changes in background rates of both events and vaccination. All analyses were performed using the SCCS package in R, version 3.6.1. A 95% CI around the RI that did not include 1 defined statistical significance.

The research group has permanent regulatory access to the data from the French National Health Data System (French decree No. 2016-1871 of December 26, 2016, on the processing of personal data called National Health Data System and French law). No informed consent was required because data are anonymized.

Results

As of April 30, 2021, nearly 3.9 million persons aged 75 years or older had received at least 1 dose of the BNT162b2 vaccine and 3.2 million had received 2 doses. Over the observation period, 11 113 persons aged 75 years or older were hospitalized for an acute myocardial infarction, 17 014 for an ischemic stroke, 4804 for a hemorrhagic stroke, and 7221 for pulmonary embolism, of whom 58.6%, 54.0%, 42.7%, and 55.3%, respectively, received at least 1 dose of the vaccine (Table 1). In the 14 days following either dose, no significant increased risk was found for any outcome: the RI for myocardial infarction for the first dose was 0.97 (95% CI, 0.88-1.06) and for the second dose, 1.04 (95% CI, 0.93-1.16); for ischemic stroke for the first dose, 0.90 (95% CI, 0.84-0.98) and for the second dose, 0.92 (95% CI, 0.84-1.02); for hemorrhagic stroke for the first dose, 0.90 (95% CI, 0.78-1.04) and for the second dose, 0.97 (95% CI, 0.81-1.15); and for pulmonary embolism for the first dose, 0.85 (95% CI, 0.75-0.96) and for the second dose, 1.10 (95% CI, 0.95-1.26) (Table 2). No significant increase for any of the cardiovascular events was observed in the 2 subdivided exposure intervals (days 1-7 and days 8-14) (Table 2).

Discussion

In this nationwide study involving persons aged 75 years or older in France, no increase in the incidence of acute myocardial infarction, stroke, and pulmonary embolism was detected 14 days following each BNT162b2 mRNA vaccine dose.

Israeli and US studies reported that persons receiving the BNT162b2 vaccine were not at increased risk of myocardial infarction, pulmonary embolism, or cerebrovascular events in the 42 days[3] and 21 days[4] following vaccination. Based on a self-controlled case-series design that compensates for the lack of randomization by eliminating the effect of time-invariant confounding factors, this study provides further evidence regarding the risk of serious cardiovascular adverse events in older people. Limitations of the study include the possibility of residual time-dependent confounding.

Further investigations are needed to measure these risks in younger populations and for other types of vaccines against SARS-CoV-2.

Notes

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Notes

Supplement 1.

eMethods

eTable. *ICD-10* codes used to define severe cardiovascular events of interest

eReferences

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Table 1.

Baseline Characteristics and Vaccination: Description of Cardiovascular Events That Occurred in Hospitals in France Between December 15, 2020, and April 30, 2021

[a] For vaccinated individuals between December 27, 2020 (the starting day of the vaccination campaign against SARS-CoV-2 in France), and April 30, 2021 (the end of the observation period).

Table 2.

Relative Incidence of Severe Cardiovascular Events During the 14-Day Risk Periods After Exposure to the First and Second Dose of BNT162b2 Vaccine vs the Nonrisk Periods

	Acute myocardial infarction		Stroke				Pulmonary embolism	
			Ischemic		Hemorrhagic			
	No. of cases	RI (95% CI)	No. of cases	RI (95% CI)	No. of cases	RI (95% CI)	No. of cases	RI (95% CI)
Nonrisk periods	5233	1 [Reference]	7407	1 [Reference]	1548	1 [Reference]	3264	1 [Reference]
Mean No. of days per person	123.5		122.8		119.4		123.5	
Risk period after first dose, d								
0[a]	13	0.23 (0.13-0.40)	24	0.29 (0.20-0.44)	7	0.30 (0.14-0.64)	6	0.18 (0.08-0.41)
1-14	717	0.97 (0.88-1.06)	991	0.90 (0.84-0.98)	274	0.90 (0.78-1.04)	379	0.85 (0.75-0.96)
Subintervals								
0[a]	13	0.23 (0.13-0.40)	24	0.29 (0.20-0.44)	7	0.30 (0.14-0.64)	6	0.18 (0.08-0.41)
1-7	326	0.84 (0.75-0.95)	505	0.90 (0.82-0.99)	142	0.91 (0.75-1.09)	188	0.82 (0.70-0.96)
8-14	391	1.08 (0.97-1.21)	486	0.90 (0.82-0.99)	132	0.89 (0.73-1.07)	191	0.88 (0.75-1.02)
Risk period after second dose, d								
0[a]	9	0.22 (0.11-0.42)	22	0.37 (0.24-0.56)	8	0.45 (0.22-0.93)	12	0.51 (0.29-0.91)
1-14	538	1.04 (0.93-1.16)	718	0.92 (0.84-1.02)	213	0.97 (0.81-1.15)	332	1.10 (0.95-1.26)
Subintervals								
0[a]	9	0.22 (0.11-0.42)	22	0.37 (0.24-0.56)	8	0.45 (0.22-0.93)	12	0.51 (0.29-0.91)
1-7	269	0.97 (0.84-1.11)	363	0.87 (0.78-1.00)	113	0.95 (0.76-1.17)	167	1.04 (0.86-1.25)
8-14	269	1.11 (0.97-1.28)	355	0.96 (0.85-1.08)	100	0.99 (0.79-1.23)	165	1.15 (0.97-1.37)

Abbreviation: RI, relative incidence.

[a] Day 0 refers to the day of the vaccine injection.