

Adverse Side Effects of COVID-19 Vaccines in Older Adults: A Comprehensive Review of Current Research

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Abstract

The purpose of this research review was to examine current scientific literature on COVID-19 vaccine-induced side effects in older adults. We reviewed studies focusing on side effects categorized into cardiologic, immunologic, neurologic, and ocular groups. Cardiologic side effects included myocarditis, pericarditis, and myocardial infarction. Immunologic conditions examined were anaphylaxis and vaccine-induced immune thrombotic thrombocytopenia. Neurologic side effects included Guillain-Barré syndrome and Bell's Palsy. Ocular side effects covered ocular swelling, submacular hemorrhage, and corneal graft rejection after keratoplasty and Descemet membrane endothelial keratoplasty. Additionally, less common side effects in older adults were reviewed but found to be statistically rare. Overall, COVID-19 vaccine-induced side effects in elderly populations were rare. We concluded that the vaccine's efficacy in preventing excess deaths due to COVID-19 is significant, and the risk of these rare side effects does not justify foregoing vaccination in at-risk individuals. Patients at higher risk for these side effects should be informed, and additional considerations should be made by their treating physician. This review aims to increase awareness of rare vaccine-induced side effects to encourage further studies, enhancing understanding of their etiology and prevalence in at-risk older adult populations.

Keywords

COVID-19 Vaccine, Adverse Side Effects, Older Adults, Vaccine Safety

1. Introduction

The COVID-19 pandemic is one of the most impactful events of the 21st century.

The 2020 outbreak and subsequent lockdowns have caused major changes in administration worldwide. A significant body of research has demonstrated major adverse side effects associated with COVID-19, many of which are debilitating and chronic [1].

The speed at which COVID-19 vaccinations were developed and brought to market is unprecedented in medical history. To address the global morbidity and mortality of COVID-19, the vaccine development process was expedited by conducting clinical trials in parallel rather than sequentially [2]. The first COVID-19 vaccines available in the United States were developed and sold by Pfizer and Moderna, marking the first mRNA-based vaccines approved for human use [3]. The Pfizer-BioNTech COVID-19 Vaccine BNT162b2, sold as Comirnaty, was the first to receive regulatory approval from the Food and Drug Administration [4]. This vaccine was collaboratively developed by the U.S. pharmaceutical firm Pfizer and the German biotechnology company BioNTech. The Pfizer-BioNTech vaccine received emergency use authorization from the FDA in December 2020, with the authorization expanded to include ages 12 and older in May 2021 [4]. Comirnaty received full regulatory approval from the FDA in August 2021. Since December 2020, more than 4.6 billion doses of BNT162b2 have been distributed globally [5].

The second COVID-19 vaccine available in the United States was developed by Moderna, an American pharmaceutical corporation. The Moderna COVID-19 vaccine, mRNA-1273, branded as Spikevax, received emergency regulatory approval from the U.S. Food and Drug Administration on December 18, 2020 [4]. The original variant of this vaccine is now known as Spikevax 0. Moderna began producing an updated COVID-19 vaccine, mRNA-1273.222, starting in 2022 to combat the Omicron variant [6]. The Moderna vaccine is designed to be stored and transported at a standard refrigerator temperature of 2 to 8 degrees Celsius, compared to the ultra-cold temperature requirements of -90 to -60 degrees Celsius for the Pfizer-BioNTech BNT162b2 vaccine [7]. Because of this, Moderna vaccinations were preferentially distributed to rural communities in the United States and exported to nations lacking deep refrigeration capabilities. The relative geographic distribution of the different vaccines is important to consider when studying their side effects at a community level.

Viral-vector COVID-19 vaccines have been marketed and distributed in the United States and abroad. Adenovirus viral vector vaccines have been developed and used to combat COVID-19, though their efficacy in preventing its spread has been debated [8]. The Sputnik V COVID-19 vaccine was the first adenovirus viral vector vaccine, receiving regulatory approval from the Russian Ministry of Health in August 2020 [9].¹ This made it the first publicly available COVID-19 vaccine

¹Sputnik V was the first widely available COVID-19 vaccine in the world, but does not feature prominently in this publication. This is because the premise of our work focuses primarily on medium to long-term effects, and data from the Russian Federation and partner nations on the side effects and efficacy of Sputnik V is largely unavailable. The Chinese Sinopharm vaccine does not feature in this review for the same reason.

worldwide. However, Sputnik V has never been marketed in the United States and has not received FDA approval. The Oxford-AstraZeneca COVID-19 vaccine, ChAdOx1, developed in the United Kingdom, also uses an adenovirus viral vector approach toward SARS-CoV-2 [10]. It was approved by the UK's Medicines and Healthcare Products Regulatory Agency on December 30, 2020, and later by the European Medicines Agency. Notably, the Oxford-AstraZeneca vaccine did not gain regulatory approval in the United States and is not sold there [11]. The Janssen COVID-19 vaccine, Ad26.COV2.S, marketed as JCovden, was developed by the Belgian pharmaceutical company Janssen and received emergency use authorization from the U.S. FDA in February 2021 [12].

The rapidly developed vaccines helped combat the pandemic. A common trait among all first-generation COVID-19 vaccines is the speed with which they were developed and distributed.² Less than a year passed from the first reported cases of COVID-19 to the distribution of the first doses of the COVID-19 vaccine in the United States. The distribution of COVID-19 vaccines saved an estimated 14.4 million lives globally in 2021 alone, increasing to 19.3 million lives saved when excess deaths due to pandemic knock-on effects are included [13]. Vaccines against COVID-19 also accelerated the end of global lockdown policies and reduced the economic and social burdens associated with excess deaths and prolonged shelter-in-place orders. Public vaccination campaigns were considerably more cost-effective than shelter-in-place orders. In Israel, the cost of preventing each excess death due to COVID-19 using shelter-in-place methods was \$9,700,000 USD, while each death prevented using primary vaccination efforts was just \$57,000 USD [14].³ The effectiveness of vaccination is demonstrated by CDC data collected from thirteen U.S. districts between April 9 and June 19, 2021: a mortality rate of 1.6 per 100,000 for unvaccinated individuals compared to 0.1 per 100,000 for fully vaccinated individuals [15].⁴

Vaccines significantly improve the survival rate of patients who become infected with COVID-19 [15]. However, it is important to objectively study and assess the known side effects of COVID-19 vaccines. The rapid development of these vaccines has raised questions about their side effects. These side effects are now better studied due to the abundance of clinical reports and data available over time. Concerns about vaccine-induced side effects are common among the public and are often cited as reasons for vaccine hesitancy [16]. Proper documentation and assessment of these side effects are crucial to increasing public confidence in the safety of COVID-19 vaccines. This will provide individuals and healthcare providers with the necessary information to make informed decisions for longterm health outcomes.

The purpose of this article is to review and document the latest research and

 ²First-generation is defined as vaccines developed to treat the original strain of Sars-Cov-2.
 ³Prices are converted from Israeli Shekels to United States Dollars.

⁴Geographic areas of data collection were Alabama, Arizona, Colorado, Indiana, Los Angeles (California), Louisiana, Maryland, Minnesota, New Mexico, New York City (New York), North Carolina, Seattle (Washington), and Utah.

case studies demonstrating adverse side effects of COVID-19 vaccines in elderly populations. Our research is divided into sections that assess the side effects of bodily systems. Our goal is to highlight commonly cited vaccine-induced side effects of COVID-19 vaccines currently marketed in the Western world. We aim to increase awareness of the potential risks these vaccines may pose to elderly individuals and to facilitate a comprehensive risk-reward analysis by individuals and clinicians considering their use.

2. COVID-19 Vaccine-Associated Cardiological Symptoms in Elders

Multiple studies have found significant variation in the presentation of cardiological dysfunction following the administration of COVID-19 vaccines. Pericarditis is a commonly reported side effect associated with mRNA-based COVID-19 vaccines in elderly populations.

Box-1. **Pericarditis** is inflammation of the pericardial sac and is the most common pathological process involving the pericardium. The pericardium is a double-layered, fibroelastic sac surrounding the heart. Pericardial inflammation often leads to increased fluid accumulation within the pericardial sac, forming a pericardial effusion, which may be serous, hemorrhagic, or purulent [17].

Myocarditis is an inflammation of the myocardium. It typically occurs in young patients but can happen at any age. It most commonly results from a viral illness but can also be due to non-infectious causes. The clinical presentation varies and may include febrile illness, mild chest pain, arrhythmias, heart failure, cardiogenic shock, or death [18].

Atrial fibrillation is the most common type of cardiac arrhythmia. It results from abnormal electrical activity within the atria of the heart, causing them to fibrillate. It is characterized as a tachyarrhythmia, meaning the heart rate is often fast. Due to its irregular rhythm, blood flow through the heart becomes turbulent, increasing the risk of forming a thrombus (blood clot), which can dislodge and cause a stroke [19].

Diaz *et al.* conducted a study between February and May 2021 using data from 2,000,287 patients across 40 U.S. hospitals. Their research found that 15 patients developed pericarditis after one dose of the COVID-19 vaccine, and 22 developed it after two doses [20]. The mean onset of symptoms was 20 days post-vaccination. Seventy-three percent of reported cases were male, with the average age of onset being 59 years. The mean monthly number of pericarditis cases in the same locality during the pre-vaccine era (January 2019 to January 2020) was 49.1 (95% CI, 46.4 - 51.9), compared to 78.8 (95% CI, 70.3 - 87.9) in the post-vaccine era (February to May 2021). This data demonstrates a statistically significant increase in cases following the availability of the COVID-19 vaccine, suggesting an increased prevalence of pericarditis post-vaccination. Further studies are necessary to determine if a direct causal relationship exists. The high average age of onset is significant, as there may be a correlation between the age at vaccination and the onset of post-vaccination pericarditis.

Myocarditis is a commonly reported side effect associated with COVID-19 vaccines. This condition has also been reported as a side effect of smallpox and influenza vaccines [21]. Myocarditis following COVID-19 vaccination with mRNA-type vaccines has a significantly higher incidence rate among adolescent and young adult males [1]. The incidence of myocarditis reported in young adult males under 40 ranges from 8.1 to 39 cases per 100,000 doses given [22]. Cases of COVID-19 vaccine-induced myocarditis have also been observed in elderly populations. Duke University Medical Center conducted a study on patients vaccinated against COVID-19 who later developed myocarditis [23]. Of the 7 patients hospitalized with myocarditis during the study, 3 did not receive a COVID-19 vaccine. Of the seven patients hospitalized with myocarditis during the study, three had not received a COVID-19 vaccine. Among the vaccinated patients, three were young males, with two vaccinated with BNT162b2 and one with mRNA-1273. The only elderly patient was a 70-year-old female hospitalized with myocarditis after her second vaccine dose. Her Troponin I level peaked at 2.34 ng/dL, and she had a left ventricular ejection fraction of 40%. The episode resolved after 12 hours, and she was discharged four days later. The researchers determined that her myocarditis was likely associated with her vaccination status. The study concluded that myocarditis is a rare side effect of mRNA COVID-19 vaccines but noted limitations in their study. While myocarditis has been observed in elderly patients following COVID-19 vaccination, the side effect does not show a clear preference for older individuals [22]. Further studies are needed to determine the prevalence of COVID-19 vaccine-induced myocarditis in elderly populations.

Myocardial infarction (MI) is a potential complication of COVID-19 vaccines. Most cases associated with MI were STEMIs linked to the Oxford-AstraZeneca ChAdOx1 viral-vector vaccine [11]. However, a direct population-level link between MI and COVID-19 vaccination status has not been found. A French study evaluating the short-term side effects of the Pfizer-BioNTech BNT162b2 mRNAbased vaccine found no increased risk of MI for patients over the age of 75 [24]. Of the 3.9 million French nationals over 75 who had received at least one dose of BNT162b2, 11,113 had been hospitalized for MI, representing a relative incidence of 0.97 (95% CI, 0.88 - 1.06) for those who had received one dose and 1.04 (95% CI, 0.93 - 1.16) for those who had received two doses. Although this correlation was considered by some in the medical community, the data does not indicate a significant link between COVID-19 vaccines and the onset of MI in the elderly. However, while population-level data does not suggest a correlation, further studies considering ethnic and genetic backgrounds, individual medical history, and risk factors are necessary to rule out the absolute age-related risk of developing COVID-19 vaccine-induced MI.

Atrial fibrillation is a COVID-19 vaccine-induced side effect studied in elderly populations. Kumar *et al.* conducted a comprehensive review of the VAERS (Vaccine Adverse Event Reporting System) co-managed by the CDC and FDA [25].

The study found 2,611 events of atrial fibrillation, split between 1,328 men and 1,245 women, the majority of whom were over 40 years old. The data showed that the rate of atrial fibrillation onset among the vaccinated public was 5 in 1,000,000. Importantly, this side effect shows a propensity for older populations, with most cases occurring in middle-aged and elderly individuals.

3. COVID-19 Vaccine-Associated Immunological Symptoms in Elders

Anaphylaxis is a COVID-19 vaccine-induced side effect that affects elderly populations. The reported incidence rate of post-vaccine anaphylaxis is currently 1 in 100,000 individuals [26].

Box-2. **Anaphylaxis** is a common medical emergency and a life-threatening acute hypersensitivity reaction. It is defined as a rapidly evolving, generalized, multi-system allergic reaction. Without treatment, anaphylaxis is often fatal due to its rapid progression to respiratory collapse [27].

It is important to note that COVID-19 vaccine-induced anaphylaxis shows no preference for elderly patients and is reported at statistically equal rates among both young and elderly individuals [26]. However, the risk of anaphylaxis is often greater in elderly individuals due to more severe presentations stemming from age-related immune hypersensitivity [28]. Vaccine guidance literature recommends monitoring patients for at least 15 minutes to ensure they can receive rapid assistance if symptoms of anaphylaxis occur. Hives, pruritus, flushing, and angioedema are common initial symptoms of vaccine-induced allergic reactions that must be monitored following the administration of COVID-19 vaccines [29]. These symptoms may be treated with antihistamines and glucocorticoids, with continued monitoring for 4 hours. Severe symptoms such as syncope, swollen tongue, or shortness of breath should be immediately treated with an epinephrine auto-injection [26].

Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) is an immunologic condition reported as a side effect of the COVID-19 vaccine. Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by low platelet counts (<100,000 platelets/µL blood) that cannot be explained by any other etiology [30]. COVID-19 vaccines interact with platelets or platelet factor 4 (PF4) in the blood serum, potentially resulting in VITT [31]. The Oxford-AstraZeneca COVID-19 vaccine, ChAdOx1, came under international scrutiny for its association with VITT [32]. COVID-19 vaccine-induced VITT is reported in just 1 in 500,000 patients [32].

Saluja *et al.* conducted a systematic review of reported cases of VITT in Medline, Embase, and Ebsco up to June 2022 [33]. A total of 66 cases of COVID-19 vaccine-induced VITT were reported. The mean time from vaccination to presentation was 8.4 days, and the mean patient age was 63 years, with 60.6% of cases being female. Patients were treated with steroids, intravenous immunoglobulins (IVIG), or both. There were no reported deaths, suggesting promising treatment outcomes. The data suggests a higher incidence of VITT in elderly populations, which is notable since ITP typically presents in younger female populations [34]. This implies an unknown mechanism in COVID-19 vaccine-induced immune thrombotic thrombocytopenia leading to a higher prevalence among the elderly. Further investigation is needed to understand the age disparity in the presentation of COVID-19 VITT compared to standard ITP.

4. COVID-19 Vaccine-Associated Neurologic Symptoms in Elders

Guillain-Barré syndrome (GBS) is a reported side effect of COVID-19 vaccination currently under investigation.

Box-3. **Guillain-Barré syndrome** is a rare immune-mediated disease characterized by damage to the peripheral and autonomic nervous systems. It is one of the leading causes of flaccid paralysis worldwide. Although relatively rare, it can be life-threatening and debilitating [35].

Bell's palsy is the most common peripheral paralysis of the seventh cranial nerve, characterized by a rapid and unilateral onset. This idiopathic condition causes partial or complete weakness of one side of the face, along with changes in taste, sensitivity to sound, and alterations in lacrimation and salivation [36].

Ogunjimi et al. conducted a meta-analysis of data on PubMed to investigate the prevalence of GBS following COVID-19 vaccination [37]. Their study found a prevalence of 8.1 (95% CI 30 - 220) cases per 1,000,000. The mean age of onset for GBS in vaccinated patients was 56.8 years, with the greatest occurrence in males aged 40 - 60. Viral vector COVID-19 vaccines were associated with an increased risk of developing GBS, while mRNA COVID-19 vaccines were not. Demyelinating type GBS was the most common neurophysiological type secondary to COVID-19 vaccination. More than 80% of the patients developed GBS within 21 days following their first dose of a viral vector vaccine [37]. Facial nerve paralysis can occur in isolation or as part of autoimmune diseases such as Guillain-Barré syndrome, polyneuritis, or other forms of autoimmune neuropathy [38]. Keh et al. reported a spike in GBS cases above the 2016-2020 average in March-April 2021, with 198 cases occurring within 6 weeks of the first dose of the COVID-19 vaccine in the United Kingdom [39]. GBS is now considered a well-established side effect of COVID-19 vaccines, with development favoring older populations, as indicated by the mean onset age of 56.8 years.

Bell's palsy (BP) is a neurological condition identified as a potential side effect of the COVID-19 vaccine. Albakri *et al.* conducted a systematic review of Pub-Med, SCOPUS, and EBSCO from the start of COVID-19 vaccination efforts through October 2022 to determine the prevalence of COVID-19 vaccine-associated Bell's palsy [40]. Their study found a prevalence of 25 cases per 1,000,000, with 62.8% of cases presenting with unilateral facial paralysis [40]. The majority of cases occurred after the first dose of the COVID-19 vaccine, with hypertension being the most common comorbidity among the patients studied. The average onset time was 1 - 1.6 days post-vaccination. The mechanism by which COVID-19 vaccines may cause Bell's Palsy remains unclear. However, 69.2% of patients in the study made a full recovery. Cases of vaccine-induced Bell's Palsy are rare, and further studies are needed to determine its true clinical association. The onset appears to favor elderly populations based on the available data.

5. COVID-19 Vaccine-Associated Ocular Symptoms in Elders

Several COVID-19 vaccine-induced ocular symptoms disproportionately affect elderly populations. Acute eyelid swelling is a commonly reported side effect with a higher occurrence rate in elderly patients. Al-Khames *et al.* conducted a study on reported side effects in 1,736 patients and found that acute eyelid swelling immediately following the COVID-19 vaccine had a prevalence of 1,150 per 1,000,000 doses [41]. Lee and Huang found the average age of COVID-19 vaccine-induced eyelid swelling to be 57.7 years (range 44 - 67), indicating an increased prevalence in older individuals. The mechanism by which this side effect occurs remains unclear but is believed to be associated with an immunological response to the vaccine [42].

Box-4. **Submacular hemorrhage** (SMH) is a potentially blinding complication of macular neovascular (MNV) diseases. The retinal pigment epithelium and the neurosensory retina, particularly the photoreceptor layer, can be severely compromised by the deposited blood [43].

Acute transplant rejection is a condition that occurs within days to months after transplantation when the recipient's immune system identifies the grafted organ as foreign and mounts a defense. The etiology, pathophysiology, presentation, and management of this common transplantation complication are complex. Diagnosis is based on clinical features involving the grafted organ and is confirmed by diagnostic laboratory studies, including tissue biopsy [44].

Submacular hemorrhage is another COVID-19 vaccine-induced side effect documented in ocular studies. Park *et al.* conducted a clinical study on patients experiencing ocular side effects from the COVID-19 vaccine and found 21 individuals who met the study criteria, with an average age of 77 years [45]. Fifty-two percent of reported cases involved submacular hemorrhage, with the average time to onset being 2 days. All patients were negative for anti-PF4 antibodies, suggesting the findings were not secondary to VITT [31]. The average age of patients with submacular hemorrhage in Park's study was 81, indicating a greater prevalence in elderly individuals. Interestingly, COVID-19 vaccine-induced submacular hemorrhage showed a propensity for mRNA-type vaccines, with 73% of cases receiving mRNA vaccines [45]. The cause of this side effect is not yet known, and the author recommends further studies with larger subject pools. Corneal surface manifestations have been documented as side effects induced by the COVID-19 vaccine. Lee and Huang conducted a review of these ocular side effects in a clinical study. They found the average onset of ocular surface manifestations to be at 68.5 years (range 56 - 83), indicating a significant prevalence in elderly patients [42]. Corneal graft rejection after keratoplasty (PKP) following the COVID-19 vaccine was documented in half of the patients. The average patient age was 64.5 years (range 56 - 73). Graft failure onset ranged from 13 to 21 days post-vaccination, with findings evenly distributed between mRNA and viral vector vaccines. Ravichandran and Natarajan proposed that COVID-19 vaccines may cause an immune response inducing Class II MHC complex antigens in the grafted cornea [46]. This effect has been documented with influenza vaccines, but it is unclear if the same mechanism affects tissue rejection with COVID-19 vaccines [47]. The presentation in elderly individuals could be due to age-related immune hypersensitivity often seen in this age group [28].

Corneal graft rejection after Descemet membrane endothelial keratoplasty (DMEK) occurred in half of all patients with corneal surface manifestations in Lee and Huang's study [42]. The average patient age was 74.5 years (range 66 - 83), with symptoms appearing 7 to 21 days post-vaccination. Similar to cases of PKP, symptoms showed no preference for a specific vaccine type. The mechanism of onset for vaccine-induced DMEK cases is speculated to be similar to those of COVID-19 vaccine-induced PKP [48]. The exact mechanism of COVID-19 vaccine-induced graft rejection is still debated, and further studies are needed to determine causality conclusively.

6. Conclusions

Our review identified various COVID-19 vaccine-induced side effects in older adults, with cardiological, immunological, neurological, and ocular symptoms being the most prevalent. Common side effects included myocarditis, pericarditis, anaphylaxis, Guillain-Barré syndrome, Bell's Palsy, and ocular conditions like submacular hemorrhage and corneal graft rejection. While these side effects are rare, they highlight the need for careful monitoring, especially in older, high-risk populations.

Despite these concerns, the efficacy of COVID-19 vaccines in preventing severe illness and death in elderly populations remains clear. The benefits of vaccination outweigh the risks of rare side effects. Future research should focus on the underlying mechanisms of these side effects and strategies for mitigating risks, ensuring continued vaccine safety and effectiveness across all age groups.

7. Case Studies

7.1. Atrial Fibrillation Post-Vaccination

A 55-year-old woman with a history of paroxysmal atrial fibrillation, mild mitral prolapse, and hypertension presented to the emergency room with palpitations, chest pain, and dyspnea three days after receiving her first dose of mRNA-1273

[49]. Her echocardiogram indicated normal left ventricular ejection fraction, severe tricuspid regurgitation, and severe mitral regurgitation. Permanent atrial fibrillation was diagnosed after failing to restore normal cardiac rhythm. She underwent tricuspid valve annuloplasty, mitral valve repair surgery, and bilateral maze ablation 14 days after admission. Chen reviewed five additional cases of atrial fibrillation post-mRNA-1273 vaccination, noting that three patients were over 55, all female, and experienced onset within eight days of their first vaccination with an mRNA-type COVID-19 vaccine. The study concluded that fibrillary cardiac disorders may be a rare vaccine-associated side effect requiring further investigation to establish causality.

7.2. Myocarditis Presentation

A 66-year-old male with a history of hyperlipidemia, hypertension, and type II diabetes mellitus was admitted to the emergency room three months after his second dose of BNT162b2. Testing showed elevated Troponin-I, peaking at 4.96 ng/dL eight hours after admission, and a 44% left ventricular ejection fraction [21]. The patient had spontaneous resolution within 24 hours, attributed to a late presentation of myocarditis due to BNT162b2 exposure.

7.3. Hyperthyroidism Post-Vaccination

A 67-year-old male was admitted to the hospital 18 days after his second dose of the COVID-19 vaccine, presenting with hypertension, frequent atrial extra beats, fever, weight loss, and neck pain. Examination revealed an enlarged thyroid with poorly defined echogenic regions and pseudo-nodules. Serum TSH was low (0.005 uIU/mL) and T4 was elevated (2.87 ng/dL). Symptoms gradually improved, and thyroid hormones stabilized within two months. Physicians suspected vaccine-induced hyperthyroidism [50]. Further studies are needed to confirm the causa-tive relationship of COVID-19 vaccines with acute onset hyperthyroidism and its remission.

7.4. Acute CHF Exacerbation

A 67-year-old male presented to the emergency room six hours after his second COVID-19 vaccine dose, experiencing shortness of breath, fever, and chills. He later developed nausea, orthopnea, and fatigue. His medical history included hypertension, type 2 diabetes mellitus, hyperlipidemia, coronary artery disease, and congestive heart failure (CHF) with preserved ejection fraction. He was diagnosed with acute CHF exacerbation post-vaccination [51]. Treatment with diuretics and supplemental oxygen led to significant symptom improvement over the next two days. Further research is needed to determine the causative relationship between COVID-19 vaccines and CHF exacerbation.

7.5. Retinal Vascular Occlusion

An 82-year-old woman visited her ophthalmologist two weeks after her second

dose of the BNT162b2 COVID-19 vaccine, complaining of sudden reduced visual acuity. With no history of hypertension or vascular occlusion, her visual acuity was 20/63. An ophthalmic examination revealed inferotemporal branching retinal vein occlusions, edema, and retinal hemorrhage, leading to a diagnosis of probable COVID-19 vaccine-induced retinal vascular occlusion [52]. The patient was treated with steroids, and follow-up showed symptom resolution and improved visual acuity to 20/40. Further investigation is needed to determine the etiology of retinal vascular occlusion in relation to COVID-19 vaccination.

Conflicts of Interest

The authors have no financial stake in any organization or corporation that may benefit from the results of this study. They declare no conflicts of interest regarding the publication of this paper.

References

- Razzaque, M.S. (2024) Can Adverse Cardiac Events of the COVID-19 Vaccine Exacerbate Preexisting Diseases? *Expert Review of Anti-infective Therapy*, 22, 131-137. <u>https://doi.org/10.1080/14787210.2024.2311837</u>
- [2] Li, Y., Chi, W., Su, J., Ferrall, L., Hung, C. and Wu, T.-C. (2020) Coronavirus Vaccine Development: From SARS and MERS to Covid-19. *Journal of Biomedical Science*, 27, Article No. 104. <u>https://doi.org/10.1186/s12929-020-00695-2</u>
- [3] Mirtaleb, M.S., Falak, R., Heshmatnia, J., Bakhshandeh, B., Taheri, R.A., Soleimanjahi, H., et al. (2023) An Insight Overview on COVID-19 mRNA Vaccines: Advantageous, Pharmacology, Mechanism of Action, and Prospective Considerations. *International Immunopharmacology*, **117**, Article 109934. https://doi.org/10.1016/j.intimp.2023.109934
- [4] Parums, D.V. (2021) Editorial: First Full Regulatory Approval of a COVID-19 Vaccine, the BNT162b2 Pfizer-BioNTech Vaccine, and the Real-World Implications for Public Health Policy. *Medical Science Monitor*, 27, e934625. <u>https://doi.org/10.12659/msm.934625</u>
- [5] van den Ouweland, F., Charpentier, N., Türeci, Ö., Rizzi, R., Mensa, F.J., Lindemann, C., et al. (2024) Safety and Reactogenicity of the BNT162b2 COVID-19 Vaccine: Development, Post-Marketing Surveillance, and Real-World Data. *Human Vaccines & Immunotherapeutics*, 20, Article 2315659. https://doi.org/10.1080/21645515.2024.2315659
- [6] Tseng, H.F., Ackerson, B.K., Sy, L.S., Tubert, J.E., Luo, Y., Qiu, S., et al. (2023) mRNA-1273 Bivalent (Original and Omicron) COVID-19 Vaccine Effectiveness against COVID-19 Outcomes in the United States. *Nature Communications*, 14, Article No. 5851. <u>https://doi.org/10.1038/s41467-023-41537-7</u>
- Murthy, B.P., Sterrett, N., Weller, D., Zell, E., Reynolds, L., Toblin, R.L., *et al.* (2021) Disparities in COVID-19 Vaccination Coverage between Urban and Rural Counties —United States, December 14, 2020–April 10, 2021. *Morbidity and Mortality Weekly Report*, **70**, 759-764. <u>https://doi.org/10.15585/mmwr.mm7020e3</u>
- [8] Lee, C., Kuo, H., Liu, Y., Chuang, J. and Chou, J. (2024) Population-Based Evaluation of Vaccine Effectiveness against SARS-CoV-2 Infection, Severe Illness, and Death, Taiwan Region. *Emerging Infectious Diseases*, **30**, 478-489. <u>https://doi.org/10.3201/eid3003.230893</u>

- [9] Akrami, M., Hosamirudsari, H., Faraji, N., Behnush, B., Goudarzi, F., Hesari, E., *et al.* (2023) Sputnik V Vaccine-Related Complications and Its Impression on Inflammatory Biomarkers in Healthcare Providers. *Indian Journal of Medical Microbiology*, 43, 79-84. <u>https://doi.org/10.1016/j.ijmmb.2022.10.012</u>
- [10] Cross, S., Rho, Y., Reddy, H., Pepperrell, T., Rodgers, F., Osborne, R., *et al.* (2021) Who Funded the Research behind the Oxford-Astrazeneca COVID-19 Vaccine? *BMJ Global Health*, 6, e007321. <u>https://doi.org/10.1136/bmigh-2021-007321</u>
- [11] Zafar, U., Zafar, H., Ahmed, M.S. and Khattak, M. (2022) Link between COVID-19 Vaccines and Myocardial Infarction. *World Journal of Clinical Cases*, **10**, 10109-10119. <u>https://doi.org/10.12998/wjcc.v10.i28.10109</u>
- [12] Wagner, A.L., Zhang, F., Kerekes, S., Shih, S. and Zhao, L. (2023) COVID-19 Vaccination Preferences during a Pause in Johnson & Johnson Vaccine Administration. *Vaccine: X*, **15**, Article 100373. <u>https://doi.org/10.1016/j.jvacx.2023.100373</u>
- Watson, O.J., Barnsley, G., Toor, J., Hogan, A.B., Winskill, P. and Ghani, A.C. (2022) Global Impact of the First Year of COVID-19 Vaccination: A Mathematical Modelling Study. *The Lancet Infectious Diseases*, 22, 1293-1302. https://doi.org/10.1016/s1473-3099(22)00320-6
- [14] Arbel, R. and Pliskin, J. (2022) Vaccinations versus Lockdowns to Prevent COVID-19 Mortality. *Vaccines*, 10, Article 1347. <u>https://doi.org/10.3390/vaccines10081347</u>
- [15] Scobie, H.M., Johnson, A.G., Suthar, A.B., Severson, R., Alden, N.B., Balter, S., *et al.* (2021) Monitoring Incidence of COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Status—13 U.S. Jurisdictions, April 4-July 17, 2021. *Morbidity and Mortality Weekly Report*, **70**, 1284-1290. <u>https://doi.org/10.15585/mmwr.mm7037e1</u>
- [16] Han, Q., Zheng, B., Abakoumkin, G., Leander, N.P. and Stroebe, W. (2022) Why Some People Do Not Get Vaccinated against COVID-19: Social-Cognitive Determinants of Vaccination Behavior. *Applied Psychology: Health and Well-Being*, 15, 825-845. <u>https://doi.org/10.1111/aphw.12411</u>
- [17] Dababneh, E. and Siddique, M.S. (2023) Pericarditis. StatPearls Publishing. <u>https://www.ncbi.nlm.nih.gov/books/NBK431080/</u>
- [18] Al-Akchar, M., Shams, P. and Kiel, J. (2023) Acute Myocarditis. StatPearls Publishing. <u>https://www.ncbi.nlm.nih.gov/books/NBK441847/</u>
- [19] Nesheiwat, Z., Goyal, A. and Jagtap, M. (2023) Atrial Fibrillation. StatPearls Publishing. <u>https://www.ncbi.nlm.nih.gov/books/NBK526072/</u>
- [20] Diaz, G.A., Parsons, G.T., Gering, S.K., Meier, A.R., Hutchinson, I.V. and Robicsek, A. (2021) Myocarditis and Pericarditis after Vaccination for Covid-19. *Journal of the American Medical Association*, **326**, 1210-1212. https://doi.org/10.1001/jama.2021.13443
- [21] Gautam, N., Saluja, P., Fudim, M., Jambhekar, K., Pandey, T. and Al'Aref, S. (2021) A Late Presentation of COVID-19 Vaccine-Induced Myocarditis. *Cureus*, 13, e17890. <u>https://doi.org/10.7759/cureus.17890</u>
- [22] Knudsen, B. and Prasad, V. (2023) Covid-19 Vaccine Induced Myocarditis in Young Males: A Systematic Review. *European Journal of Clinical Investigation*, 53, e13947. <u>https://doi.org/10.1111/eci.13947</u>
- [23] Kim, H.W., Jenista, E.R., Wendell, D.C., Azevedo, C.F., Campbell, M.J., Darty, S.N., et al. (2021) Patients with Acute Myocarditis Following mRNA COVID-19 Vaccination. JAMA Cardiology, 6, 1196-1201. <u>https://doi.org/10.1001/jamacardio.2021.2828</u>
- [24] Jabagi, M.J., Botton, J., Bertrand, M., Weill, A., Farrington, P., Zureik, M., et al. (2022) Myocardial Infarction, Stroke, and Pulmonary Embolism after BNT162b2 mRNA

COVID-19 Vaccine in People Aged 75 Years or Older. *Journal of the American Medical Association*, **327**, 80-82. <u>https://doi.org/10.1001/jama.2021.21699</u>

- [25] Kumar, A., Shariff, M., Bhat, V., DeSimone, C. and Deshmukh, A. (2022) Atrial Fibrillation after Vaccination for COVID-19: Analysis of the Vaccine Adverse Event Reporting System. *Journal of Interventional Cardiac Electrophysiology*, 65, 1-2. https://doi.org/10.1007/s10840-022-01263-4
- [26] Bousquet, J., Agache, I., Blain, H., Jutel, M., Ventura, M.T., Worm, M., et al. (2021) Management of Anaphylaxis Due to COVID-19 Vaccines in the Elderly. Allergy, 76, 2952-2964.
- [27] McLendon, K. and Sternard, B.T. (2023) Anaphylaxis. StatPearls Publishing. <u>https://www.ncbi.nlm.nih.gov/books/NBK482124/</u>
- [28] Ventura, M.T., Boni, E., Cecere, R., Buquicchio, R., Calogiuri, G.F., Martignago, I., *et al.* (2018) Importance of Hypersensitivity in Adverse Reactions to Drugs in the Elderly. *Clinical and Molecular Allergy*, **16**, Article No. 7.
- [29] Urakawa, R., Isomura, E.T., Matsunaga, K. and Kubota, K. (2023) Multivariate Analysis of Adverse Reactions and Recipient Profiles in COVID-19 Booster Vaccinations: A Prospective Cohort Study. *Vaccines*, **11**, Article 1513. <u>https://doi.org/10.3390/vaccines11101513</u>
- [30] Onisâi, M., Vlădăreanu, A., Spînu, A., Găman, M. and Bumbea, H. (2019) Idiopathic Thrombocytopenic Purpura (ITP)—New Era for an Old Disease. *Romanian Journal* of Internal Medicine, 57, 273-283. <u>https://doi.org/10.2478/rjim-2019-0014</u>
- [31] Ichhpujani, P., Parmar, U.P.S., Duggal, S. and Kumar, S. (2022) COVID-19 Vaccine-Associated Ocular Adverse Effects: An Overview. *Vaccines*, 10, Article 1879. <u>https://doi.org/10.3390/vaccines10111879</u>
- [32] Sunder, A., Saha, S., Kamath, S. and Kumar, M. (2022) Vaccine-Induced Thrombosis and Thrombocytopenia (VITT); Exploring the Unknown. *Journal of Family Medicine and Primary Care*, **11**, 2231-2233. <u>https://doi.org/10.4103/jfmpc.jfmpc_2259_21</u>
- [33] Saluja, P., Amisha, F., Gautam, N. and Goraya, H. (2022) A Systematic Review of Reported Cases of Immune Thrombocytopenia after COVID-19 Vaccination. *Vaccines*, 10, Article 1444. <u>https://doi.org/10.3390/vaccines10091444</u>
- [34] Lambert, M.P. and Gernsheimer, T.B. (2017) Clinical Updates in Adult Immune Thrombocytopenia. *Blood*, **129**, 2829-2835.
 <u>https://doi.org/10.1182/blood-2017-03-754119</u>
- [35] Aldeeb, M., Okar, L., Mahmud, S.S. and Adeli, G.A. (2022) Could Guillain-Barré Syndrome Be Triggered by COVID-19 Vaccination? *Clinical Case Reports*, **10**, e05237. <u>https://doi.org/10.1002/ccr3.5237</u>
- [36] Warner, M.J., Hutchison, J. and Varacallo, M. (2023) Bell Palsy. StatPearls Publishing. <u>https://www.ncbi.nlm.nih.gov/books/NBK482290/</u>
- [37] Ogunjimi, O.B., Tsalamandris, G., Paladini, A., Varrassi, G. and Zis, P. (2023) Guillain-Barré Syndrome Induced by Vaccination against COVID-19: A Systematic Review and Meta-Analysis. *Cureus*, 15, e37578. <u>https://doi.org/10.7759/cureus.37578</u>
- [38] Hampton, L.M., Aggarwal, R., Evans, S.J.W. and Law, B. (2021) General Determination of Causation between Covid-19 Vaccines and Possible Adverse Events. Vaccine, 39, 1478-1480. <u>https://doi.org/10.1016/j.vaccine.2021.01.057</u>
- [39] Keh, R.Y.S., Scanlon, S., Datta-Nemdharry, P., Donegan, K., Cavanagh, S., Foster, M., et al. (2022) COVID-19 Vaccination and Guillain-Barré Syndrome: Analyses Using the National Immunoglobulin Database. *Brain*, 146, 739-748. <u>https://doi.org/10.1093/brain/awac067</u>

- [40] Albakri, K., Khaity, A., Atwan, H., Saleh, O., Al-Hajali, M., Cadri, S., *et al.* (2023) Bell's Palsy and COVID-19 Vaccines: A Systematic Review and Meta-Analysis. *Vaccines*, 11, Article 236. <u>https://doi.org/10.3390/vaccines11020236</u>
- [41] Al Khames Aga, Q.A., Alkhaffaf, W.H., Hatem, T.H., Nassir, K.F., Batineh, Y., Dahham, A.T., *et al.* (2021) Safety of COVID-19 Vaccines. *Journal of Medical Virol*ogy, **93**, 6588-6594. <u>https://doi.org/10.1002/jmv.27214</u>
- [42] Lee, Y. and Huang, Y. (2021) Ocular Manifestations after Receiving COVID-19 Vaccine: A Systematic Review. *Vaccines*, 9, Article 1404. <u>https://doi.org/10.3390/vaccines9121404</u>
- [43] Chakraborty, S. and Sheth, J.U. (2022) Management of Submacular Hemorrhage Using Intravitreal Brolucizumab with Pneumatic Displacement: A Case Series. *Case Reports in Ophthalmology*, **13**, 947-953. <u>https://doi.org/10.1159/000527073</u>
- [44] Vaillant, A.A., Misra, S. and Fitzgerald, B.M. (2024) Acute Transplantation Rejection. StatPearls Publishing. <u>https://www.ncbi.nlm.nih.gov/books/NBK535410/</u>
- [45] Park, H.S., Byun, Y., Byeon, S.H., Kim, S.S., Kim, Y.J. and Lee, C.S. (2021) Retinal Hemorrhage after Sars-Cov-2 Vaccination. *Journal of Clinical Medicine*, **10**, Article 5705. <u>https://doi.org/10.3390/jcm10235705</u>
- [46] Ravichandran, S. and Natarajan, R. (2021) Corneal Graft Rejection after COVID-19 Vaccination. *Indian Journal of Ophthalmology*, 69, 1953-1954. <u>https://doi.org/10.4103/ijo.ijo_1028_21</u>
- [47] Solomon, A. and Frucht-Pery, J. (1996) Bilateral Simultaneous Corneal Graft Rejection after Influenza Vaccination. *American Journal of Ophthalmology*, **121**, 708-709. <u>https://doi.org/10.1016/s0002-9394(14)70638-5</u>
- [48] Phylactou, M., Li, J.O. and Larkin, D.F.P. (2021) Characteristics of Endothelial Corneal Transplant Rejection Following Immunization with Sars-Cov-2 Messenger RNA Vaccine. *British Journal of Ophthalmology*, **105**, 893-896. <u>https://doi.org/10.1136/bjophthalmol-2021-319338</u>
- [49] Chen, C., Hsieh, M., Wei, C. and Lin, C. (2023) Atrial Fibrillation after mRNA-1273 Sars-Cov-2 Vaccination: Case Report with Literature Review. *Risk Management and Healthcare Policy*, 16, 209-214. <u>https://doi.org/10.2147/rmhp.s402007</u>
- [50] Şahin Tekin, M., Şaylısoy, S. and Yorulmaz, G. (2021) Subacute Thyroiditis Following COVID-19 Vaccination in a 67-Year-Old Male Patient: A Case Report. *Human Vaccines & Immunotherapeutics*, 17, 4090-4092.
 <u>https://doi.org/10.1080/21645515.2021.1947102</u>
- [51] Deb, A., Abdelmalek, J., Iwuji, K. and Nugent, K. (2021) Acute Myocardial Injury Following COVID-19 Vaccination: A Case Report and Review of Current Evidence from Vaccine Adverse Events Reporting System Database. *Journal of Primary Care* & Community Health, 12, Article 21501327211029230. https://doi.org/10.1177/21501327211029230
- [52] Vujosevic, S., Limoli, C., Romano, S., Vitale, L., Villani, E. and Nucci, P. (2022) Retinal Vascular Occlusion and Sars-Cov-2 Vaccination. *Graefe's Archive for Clinical* and Experimental Ophthalmology, 260, 3455-3464. https://doi.org/10.1007/s00417-022-05707-5

Abbreviations

BP: Bell's Palsy
CDC: Centers for Disease Control and Prevention
COVID-19: Coronavirus Disease 2019
DMEK: Descemet's Membrane Endothelial Keratoplasty
FDA: Food and Drug Administration
GBS: Guillain-Barré syndrome
ITP: Immune thrombocytopenic purpura
IVIG: Intravenous Immunoglobulin
MI: Myocardial Infarction
MNV: Macular Neovascular (Diseases)
PF4: Platelet Factor 4
PKP: Penetrating keratoplasty
SMH: Submacular Hemorrhage
VAERS: Vaccine Adverse Event Reporting System
VITT: Vaccine-Induced Immune Thrombotic Thrombocytopenia