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REVIEW ARTICLE

Characteristics of sudden hearing loss after different COVID-19 vaccinations: a systematic review and meta-analysis

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Abstract

Introduction COVID-19 vaccines are essential to prevent complications and reduce the burden of SARS-CoV-2. However, these vaccines showed side effects such as fatigue, pain, fever, and rarely hearing loss. In this review, we aim to summarize studies investigating hearing loss following COVID-19 vaccination and try to find the possible association and risk factors for this hazardous complication.

Methods We performed a comprehensive search of five electronic databases (PubMed, Scopus, Web of Science, google scholar, Cochrane) from inception until 9 October 2022. We finally included 16 studies after the first and second scans. We used SPSS to analyze the extracted data.

Results A total of 630 patients were identified, with a mean age of 57.3. Of the patients, 328 out of 609 vaccinated patients took the Pfizer-BioNTech BNT162b2 vaccine, while 242 (40%) took the Moderna COVID-19 vaccine. The mean time from vaccination to hearing impairment was 6.2, ranging from a few hours to one month after the last dose. The results found a significant difference between vaccine types in terms of incidence and prognosis of the condition, while they showed that the number of doses prior to the onset had no significance.

Conclusion SNHL has been reported in a small number of people who have received the COVID-19 vaccine, but it is unclear at this time whether the vaccine is directly causing this condition. However, the COVID-19 vaccine has been demonstrated to be safe and effective in preventing illness, and the benefits of vaccination are significant compared to any potential risks.

Protocol registration The protocol of this study was registered on Prospero CRD42022367180.

Keywords COVID-19 · Vaccine · Hearing loss · Side effects

Introduction

More than six and half million deaths were caused by severe acute respiratory distress syndrome 2 (SARS-Cov-2), caused by the new coronavirus disease that emerged in Wuhan in China in December 2019 (COVID-19) and spread massively, causing a pandemic [1–3].

Multiple therapeutic and preventive measures have been tried since the pandemic's start; unfortunately, the therapeutic options are still controversial, and no known therapy has been proven [4]. However, preventive measures seem to effectively

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reduce the transmission of the disease and decrease its severity [5]. In response to this idea (prevention is the best treatment), many vaccines against COVID-19 have been developed [6]. These vaccines make a dramatic change in the transmission velocity, severity, and mortality of the COVID-19 disease [7–9]. Till now, about five billion persons are fully vaccinated, and more than five billion and three hundred million persons have been vaccinated with at least one dose, according to WHO statistics [2].

Although these venerable benefits of COVID-19 vaccines, it has several side effects [10, 11]. The common side effects are injection site pain, swelling, pruritus, and redness. In the meantime, symptoms like fatigue, headache, muscle pain, fever, and stomach problems like stomach pain and diarrhea are common [11, 12]. However, multiple uncommon but significant side effects, including myocarditis, Guillain–Barré syndrome (GBS), and thrombosis with thrombocytopenia syndrome, have been documented during the SARS-CoV-2 immunization campaign [13]. Neurological complications of COVID-19 vaccines were rare, and serious side effects like GBS, acute inflammatory demyelinating polyneuropathy, transverse myelitis, and cerebral venous thrombosis were seen in less than 1 out of every 1,000,000 doses of vaccine [14, 15].

Hearing loss is generally classified as conductive hearing loss (CHL) and sensory-neural hearing loss (SNHL) [16]. In people with CHL, the threshold at which they detect sounds traveling through the bone is higher than when they encounter the same sounds traveling through the air. Most cases of CHL have outer and/or middle ear dysfunction but adequate functioning in the inner ear. SNHL is a kind of hearing impairment that may be brought on by injury to the cochlea or farther afield, either along the vestibulocochlear nerve or in the brain. Even when the middle ear and outer ear are healthy, SNHL may result in total hearing loss. The hearing thresholds of people with SNHL are the same via the air as though the bone [16, 17]. It has been reported that COVID-19 infection may affect the vestibular-hearing system causing dizziness, tinnitus, vertigo, and hearing impairment [18, 19]. However, other studies reported that COVID-19 did not lead to significant hearing impairment [20].

Many studies in the literature have reported hearing loss as a complication of COVID-19 vaccines [21–23]. However, no systematic review or meta-analysis summarizes the literature on this topic. This systematic review aims to investigate and summarize the reported studies about hearing loss following COVID-19 vaccination and tries to find the possible association and risk factors for this hazardous complication.

Methods

We followed the PRISMA statement guidelines when reporting this systematic review and meta-analysis [24]. All steps were done in strict accordance with the Cochrane Handbook of Systematic Reviews and Meta-analysis of Interventions [25]. The steps of this study were prespecified, and the protocol was registered on PROSPERO (CRD42022367180).

Eligibility criteria

Studies were included in our review if they satisfied the following criteria:

Population studies on patients receiving any of the COVID-19 vaccines.

Intervention All types of COVID-19 vaccines.

Outcome Studies were reporting hearing loss following COVID-19 vaccines.

Study design We included case reports, case series, and prospective and retrospective observational studies.

We excluded review articles, studies whose data were not reliable for extraction and analysis, studies that were reported as abstracts only, studies whose complete full-texts were not available, and studies that were not published in the English language.

Information sources and search strategy

We performed a comprehensive search of five electronic databases (PubMed, Scopus, Web of Science, google scholar, Cochrane) from inception until 9 October 2022 using the following query: (Hearing loss OR Hypoacusis OR Hypoacuses OR Hearing Impairment OR Deafness) AND (Vaccine) AND (Coronavirus OR COVID-19 OR COVID 19 OR SARS-CoV-2 OR 2019-nCoV)". Further, the references of the included studies were manually searched for any potentially eligible studies.

Selection process

Endnote (Clarivate Analytics, PA, USA) was used to remove duplicates, and the references that were retrieved underwent a two-step screening process: first, the titles and abstracts of all identified articles were screened independently by two authors to determine their applicability to this systematic review and meta-analysis, and second, the full-text articles of the identified abstracts were screened to determine their final eligibility to systematic review and meta-analysis.

Data collection process and data items

Data were extracted to a uniform data extraction sheet. The extracted data included (1) characteristics of the included studies, (2) characteristics of the population of included studies, (3) risk of bias domains, and (4) outcome measures.

Assessing the risk of bias in the individual studies

To estimate the overall evidence from the study, we applied the National Institutes of Health (NIH) [26], Joanna Briggs Institute (JBI) [27], and The Newcastle–Ottawa Scale (NOS) [28] quality assessment tools for assessing for case series, case reports, and cross-sectional included studies, respectively. The assessment depends on a scoring system based on reporting different details for the cases of interest, such as case identification, clinical picture, diagnostic interventions, and treatment line and its effect on the clinical picture.

The categories of quality of evidence from (NIH) score either poor, fair, or good, while the scoring of (JBI) quality depends on percentages. Regarding the NOS, the categories of quality of evidence were Very Good, Good, Satisfactory, and Unsatisfactory Studies. Two authors independently assessed the quality of evidence, and the third author resolved the conflicts.

Statistical analysis

The data were analyzed using SPSS. Continuous and categorical variables were described using mean with standard deviation (SD) and numbers (N) with percentages (%), respectively. The Chi-square test was used to assess the difference between two or more categorical data. The results were considered significant when the P value was less than 0.05.

Results

We identified 227 records after searching the different databases. Thirty records were removed because they were duplicated, and 150 records were excluded by title/abstract screening. Finally, we included 16 studies after the second scan; Fig. 1

Demographics

A total of 630 patients were identified in the extracted case reports that described patients who developed hearing loss after the administration of COVID-19 vaccines, with a mean age of 57.3 that ranged from 15 to 93 years old. The majority of the patients were females, 339 (53.8%). In addition, 328 out of 609 vaccinated patients took the Pfizer-BioNTech BNT162b2 vaccine, while 242 (40%) took the Moderna COVID-19 vaccine. 625 out of 630 reported hearing loss as a chief complaint. The most common chief complaints were unilateral sudden hearing loss 583 (92.5), bilateral hearing loss 29 (4.6), tinnitus 24 (3.8), and dizziness 12 (1.9). The mean time from vaccination to hearing impairment was 6.2 days, ranging from a few hours to one month after the last dose. More details can be seen in Table 1. The characteristics of the patients included in the analysis can be seen in Supplementary File 1.

In order to report the fate of cases, a follow-up was initiated with a mean of 15.6 and a range of 2–63 days after the initiation of the treatment. A total of 17 patients recovered, and 5 reported no response. The mean age of recovered patients was 48.9 (17.4). According to Table 2, the percentage of recovered males was slightly higher than recovered females (40.9% and 36.3%, respectively). Eight cases of those who developed hearing loss after the second dose recovered, while only 9.1 recovered among those who developed this condition after the third dose.

Quality assessment

The overall estimation of the quality of evidence included case series based on the National Institutes of Health (NIH) score showed to be good. Seven included case series, five studies with scores ranging from (7–9) representing a good quality of evidence while two others have a fair quality of evidence with a score ranging from (4–6), Table 3. Estimation of quality of evidence of a total of eight included case reports according to the score of Joanna Briggs Institute (JBI) quality assessment tool showed to be good. Five included case reports have good evidence, with a score exceeding 70%, and three with fair evidence scoring more than 50%, Table 4. There is one cross-sectional study among the included studies, and it scored 6, representing

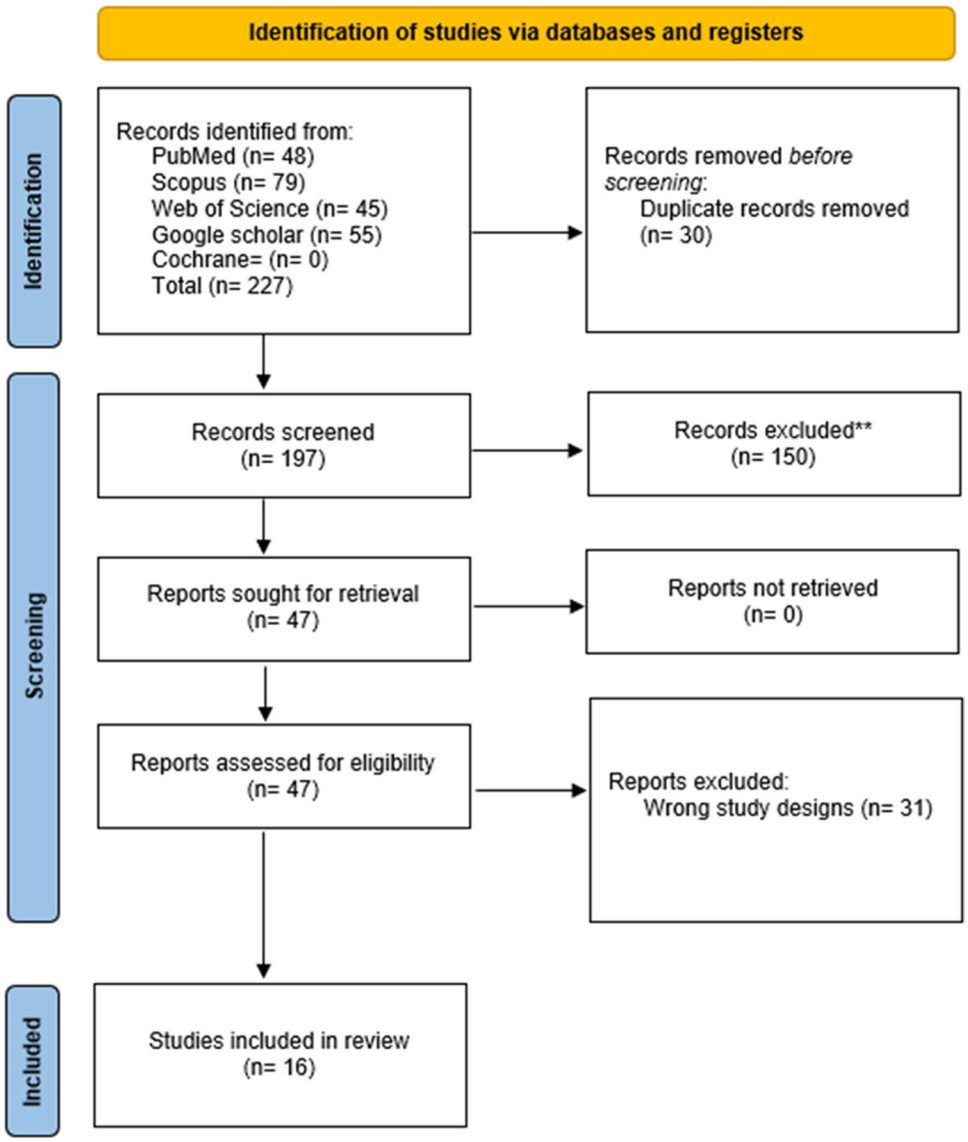

Fig. 1 PRISMA flow diagram of studies' screening and selection

satisfactory quality according to The Newcastle–Ottawa Scale (NOS).

Discussion

Our present study has investigated the potential association between the available COVID-19 vaccines and the suddenly reported sensorineural hearing loss (SNHL). The main findings could be summarized in (I) 23 records have reported a sudden SNHL in 630 patients who received different 5 vaccines, (II) a statistically significant increased incidence was detected in patients who received Pfizer-BioNTech or Moderna vaccines; however, a cross-sectional study conducted by Formeister et al. reported no association between Pfizer-BioNTech or Moderna vaccinations and SSHL [29], (III) patients with a past history of confirmed autoimmune disease have a higher chance to develop SNHL.

Although there are several cases confirmed to have SNHL after vaccination by other vaccines such as influenza, tetanus, diphtheria, meningococcus, and rabies, there is no exact etiology to explain [30, 31]. A study could detect circulating antibodies and cytokines that can induce an immunologic and inflammatory response and release further antibodies directed to the cochlea [32]. Yanir et al. suggested that vaccine booster dose might be associated with an increased risk of SSHL due to its stimulation and activation of the immune system earlier [33]. This is contrary to our findings as the

Table 1 Shows the characteristics of the included patients

		Frequency (n^a)	Percentage (%[b])
Characteristics (n = 630)			
Age, mean (range)	57.3 (15–93)		
Gender	Male	291	46.2
	Female	339	53.8
Comorbidities[c]	AD	6	0.95
	HTN	2	0.3
	AF	1	0.15
	OSAS	1	0.15
	Hyperlipidemia	1	0.15
	NR[d]	617	98
Vaccines			
Type of given vaccine	Pfizer-BioNTech BNT162b2 vaccine	328	54
	Moderna COVID-19 vaccine	242	40
	Janssen/Johnson & Johnson vaccine	28	5
	Oxford, AstraZeneca vaccine	9	1.5
	Sinovac-CoronaVac COVID-19 vaccine	2	0.3
Doses triggering the onset	One dose	12	2
	Two doses	9	1.4
	Three doses	3	0.5
	NR[d]	606	96.2
Diagnostic tools			
MRI		2	0.3
Pure tone audiometry		71	11.3
NR[d]		557	88.4
Treatment			
Methylprednisolone		5	0.8
Dexamethasone		14	2.2
Prednisone		17	2.7
Ginkgo biloba extract		2	0.3
Batroxobin		2	0.3
Betahistine		1	0.15
Cyclophosphamide		1	0.15
Salvage		1	0.15
Vestibular physiotherapy		1	0.15
NR[d]		588	93.3
Chief complain			
Hearing loss		625	99.2
Unilateral progressive hearing loss		9	1.4
Unilateral sudden hearing loss		583	92.5
Bilateral hearing loss		29	4.6
Dizziness		12	1.9
Tinnitus		24	3.8
Ear tightness		1	0.15
Ear fullness		2	0.31
Vertigo		8	1.3
Nausea		2	0.31
Visual field defect		2	0.31
Diplacusis		1	0.15
Dysphagia		1	0.15
Hematuria		1	0.15

Table 1 (continued)

		Frequency (n^a)	Percentage (%[b])
Follow-up time, mean (range)		15.6 (2–63)	
Outcome			
Incidence of post-vaccination hearing loss features			
Unilateral sensorineural	Rt sensorineural	11	1.7
	Lt sensorineural	6	0.95
	Not specified	576	91.4
	Total	593	94.1
Bilateral sensorineural		3	0.5
Rt mixed		3	0.5
Lt mixed		1	0.15
Prognosis			
Recovered		17	2.7
Not improved		5	0.8
NR[d]		608	96.5
Time (in days) from vaccination to hearing impairment, mean (SD)			
Type of vaccine	Pfizer-BioNTech BNT162b2 vaccine	6.2 (1.3)	
	Moderna COVID-19 vaccine	6.3 (1.1)	
	Janssen/Johnson & Johnson vaccine	6 (0)	
	Oxford, AstraZeneca vaccine	1.5 (0.7)	
	Sinovac-CoronaVac COVID-19 vaccine	4 (0)	
Number of doses prior to the attack	One dose	8.9 (9.6)	
	Two doses	5 (4.2)	
	Three doses	NR[d]	

[a]N: counts; [b]%: percentages; [c]comorbidities: autoimmune diseases (AD), hypertension (HTN), atrial fibrillation (AF), obstructive sleep apnea syndrome (OSAS), hyperlipidemia; [d]NR: not reported; MRI: magnetic resonance imaging; Rt: right; Lt: left

first vaccination dose is more associated with this adverse event; this could be explained by the delay in diagnosis and treatment during the pandemic in addition to patient reluctance and structural barriers to health care [34]. However, the abrupt onset of hearing loss within a few days of the booster dose agrees with the immunogenic theory that demonstrates a booster effect that stimulates and activates the immune system earlier.

Moreover, thrombosis and vasospasm of the internal auditory artery are both considered the main causes of idiopathic sudden sensorineural hearing loss [23, 35]. Recent reports showed that there are some safety concerns about the increased risk for thrombotic events in the Oxford-AstraZeneca COVID-19 vaccine [36], which may contribute to the pathogenesis. Additionally, the sudden onset nature of this event raises the suspension of such vascular etiology.

The majority of patients reported a sudden unilateral hearing loss after about 6 days of receiving their first COVID-19 vaccination shot. High-dose steroids were generally used in order to manage such cases. Intratympanic dexamethasone and oral prednisolone were the most frequently prescribed medications; however, less than 5% of patients whose treatment responses were reported demonstrated a partial or complete recovery.

The role of glucocorticoids in treating SNHL cases was described in several reports [34, 37, 38]. Glucocorticoids activate all steroid receptors in the cochlea, which activates Na and K-ATPase and changes cell osmolarity. There is a correlation between the level of glucocorticoids in the

Table 2 Represents the factors that may be associated with the prognosis of the patients

Variables ($n=22$)	Recovered		No improvement	
	N^a	$\%^b$	N^a	$\%^b$
Gender				
Male	9	40.9	4	18.2
Female	8	36.3	1	4.5
Age in years, mean (SD)	48.9 (17.4)		38.6 (26.8)	
Vaccine type				
Pfizer-BioNTech BNT162b2 vaccine	8	36.3	2	9.1
Moderna COVID-19 vaccine	2	9.1	0	0
Janssen/Johnson & Johnson vaccine	0	0	0	0
Oxford, AstraZeneca vaccine	7	31.8	1	4.5
Sinovac-CoronaVac COVID-19 vaccine	0	0	2	9.1
NR[c]	13	59	8	36.3
Number of doses				
One dose	7	31.8	2	9.1
Two doses	8	36.3	1	4.5
Three doses	2	9.1	1	4.5
Comorbidities ($n=11$)				
AD	6	54.5	0	0
HTN	2	18.2	0	0
AF	1	9.1	0	0
OSAS	1	9.1	0	0
Hyperlipidemia	1	9.1	0	0
Treatment ($n=44$)				
Methylprednisolone	2	4.5	3	6.8
Dexamethasone	14	31.8	0	0
Prednisone	17	38.6	0	0
Ginkgo biloba extract	0	0	2	4.5
Batroxobin	0	0	2	4.5
Betahistine	1	2.3	0	0
Cyclophosphamide	1	2.3	0	0
Salvage	1	2.3	0	0
Vestibular physiotherapy	1	2.3	0	0

[a]N: counts; [b]%: percentages; [c]comorbidities: autoimmune diseases (AD), hypertension (HTN), atrial fibrillation (AF), obstructive sleep apnea syndrome (OSAS), hyperlipidemia; [d]NR: not reported; MRI: magnetic resonance imaging; Rt: right; Lt: left

blood plasma and the concentration of Na, K-ATPase in the inner ear. They change the physicochemical properties of the cellular membrane, stabilizing it by controlling phospholipase A2 production, leukotrienes, and thromboxane [39, 40].

Despite this complication is still rare, as reported by most COVID-19 vaccination investigating reports [41], it is a serious and resistant-to-treat adverse event and affects the patient's quality of life. Thus, this raised the concern of discovering a sensitive screening and follow-up biomarker in order to prophylactically detect such a vulnerable population with past autoimmune history before developing that irreversible complication. In fact, this could be an interesting field to develop and explore the associated biomarkers related to post-COVID-19 vaccination SNHL.

Table 3 Risk of bias assessment of the included case series using NIH

NIH quality assessment tool for case series studies criteria met	Study ID						
	Zhao et al. 2021	Formeister et al. 2022	Ekobena et al. 2022	Jeong and Choi, 2021	Medina and Gomez, 2022	Wichova et al. 2021	Zoccali et al. 2022
Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the study population clearly and fully described including a case definition?	Yes	Yes	Yes	No	Yes	Yes	Yes
Were the cases consecutive?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the subjects comparable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the intervention clearly described?	Yes	Yes	Yes	Yes	Yes	NR	Yes
Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	No	Yes
Was the length of follow-up adequate?	Yes	NR	Yes	NR	Yes	No	Yes
Were the statistical methods well-described?	No	No	Yes	No	Yes	NR	Yes
Were the results well-described	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Quality (total score)	Good	Good	Good	Fair	Good	Fair	Good

Table 4 Risk of bias assessment of the included case reports using JBI

The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports	Study ID							
	Shalabi et al. 2022	Kim et al. 2022	Chen et al. 2022	Shirai et al. 2022	Poli et al. 2022	Kahn et al. 2021	Pisani et al. 2021	Tsetsos et. al. 2021
Were the patient's demographic characteristics clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the patient's history clearly described and presented as a timeline?	No	Yes	Yes	No	Yes	Yes	Yes	Yes
Was the current clinical condition of the patient on presentation clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the current clinical condition of the patient on presentation clearly described?	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Were adverse events (harms) or unanticipated events identified and described?	No	Yes	No	No	No	Yes	No	No
Does the case report provide takeaway lessons?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Quality (total score)	75%	100%	75%	62%	88%	100%	88%	88%

Conclusion

SNHL has been reported in a small number of people who have received the COVID-19 vaccine, but it is unclear at this time whether the vaccine is directly causing this condition. Despite this, the COVID-19 vaccine has been demonstrated to be safe and effective in preventing illness caused by the virus, and the benefits of vaccination are significant compared to any potential risks.

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Author contribution EA created the idea and checked its validation, MHN and MDG did the screening, KA, and AS extract the data, YJA, BH, and SC did the quality assessment, OAA, KA, and AS wrote the manuscript, YJA did the analysis and wrote the results, and OAA and KA revised and finalized the manuscript.

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Availability of data and materials The datasets used and/or analyzed during the current study are available as MS Excel files (.xlsx) and RevMan file (.rm5) from the corresponding author upon reasonable request.

Declarations

Conflict of interest All authors have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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