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VESTIBULAR DYSFUNCTION AND BALANCE IMPAIRMENT IN HEAD AND NECK CANCER PATIENTS UNDERGOING CHEMOTHERAPY : A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract

Vestibular dysfunction is an important yet underrecognized adverse effect among patients with head and neck cancer (HNC) receiving platinum-based chemotherapy. Although cochlear toxicity is well documented, evidence specifically addressing vestibular impairment in this population remains limited and methodologically variable. The novelty of this study lies in presenting the first systematic review and meta-analysis exclusively examining vestibular dysfunction in adult HNC patients receiving chemotherapy, thus establishing a more focused and consolidated evidence base. To quantify the pooled incidence, clinical features, and diagnostic patterns of vestibular dysfunction in adults with HNC undergoing chemotherapy, and to identify chemotherapeutic agents strongly associated with vestibulotoxicity . Conducted in accordance with PRISMA 2020 guidelines and prospectively registered in PROSPERO (CRD420251080552), this review regularly searched Embase, Scopus, Web of Science, and the Cochrane Library for studies published between 2014 and 2024. Eligibility criteria included adult HNC patients treated with and reporting vestibular outcomes. Risk of bias was assessed using RoB 2.0 for randomized trials and the Newcastle–Ottawa Scale for observational studies. A random-effects model was applied for quantitative synthesis. Sixteen studies met the inclusion criteria, and contributed fourteen data to the meta-analysis. The pooled incidence of vestibular dysfunction was 24.7% (95% CI: 19.2–30.8). Dizziness and imbalance were the most frequently reported symptoms, while peripheral vestibular deficits were confirmed through vHIT , VEMP, and caloric testing. Cisplatin was consistently identified as the principal chemotherapeutic agent associated with vestibulotoxicity. These findings underscore the need for standardized vestibular assessment and routine monitoring, particularly within cisplatin-based treatment regimens.

Keywords: Balance impairment; Chemotherapy; Cisplatin; Head and neck cancer; Vestibular dysfunction.

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INTRODUCTION

Head and neck cancers (HNC) constitute a major public health challenge worldwide, accounting for an estimated 890,000 newly diagnosed cases and approximately 450,000 fatalities in the year 2018 (1) . While the implementation of platinum-based, particularly cisplatin, has markedly improved survival rates, it has also introduced a spectrum of ototoxic effects (2) . Predominantly, clinical attention has been directed towards cochlear toxicity, manifesting as irreversible high-frequency hearing loss. However, recent evidence indicates that vestibular dysfunction accompanying platinum therapy remains underrecognized despite its potential impact on balance and quality of life (3) .

Several studies have reported vestibular dysfunction following chemotherapy (4) . However, these findings remain fragmented, rely on heterogeneous assessment methods, and only rarely focus specifically on the association between vestibular dysfunction and head and neck cancer.

The existing research gap lies in the limited number of studies addressing vestibular dysfunction in adult patients with head and neck cancer. Therefore, this study aims to fill this gap. The novelty of this research lies in conducting the first systematic review and meta-analysis that exclusively examines vestibular dysfunction in adult head and neck cancer patients undergoing chemotherapy.

Vestibular toxicity may present as dizziness, vertigo, imbalance, and an elevated risk of falls. This clinical impact is also supported by a prospective observational study involving 120 patients with head and neck squamous cell carcinoma who underwent radiotherapy or chemoradiotherapy, which demonstrated increased susceptibility to balance impairment, with vestibulotoxicity, age, and body mass index as contributing factors (5) . Furthermore, objective vestibular evaluations following cisplatin exposure have demonstrated reductions in vestibulo-ocular reflex (VOR) gains and abnormalities in vestibular-evoked myogenic potentials (VEMP), indicating damage to both the semicircular canals and otolith organs (3) .

Despite these findings, a 2024 review focused on cisplatin offered a comprehensive overview of animal and human vestibulotoxic effects, noting

limited utilization of comprehensive vestibular assessments in clinical settings (3) .

Biologically, patients with head and neck cancer often receive high cumulative doses of cisplatin as well as radiotherapy to the craniofacial region, which may increase the vulnerability of both peripheral and central vestibular structures (6) . In addition, the involvement of head and neck anatomy, including the temporal bone and cranial nerve pathways, may further elevate the risk of balance disorders compared with cancers at other sites (7) . From a methodological perspective, focusing specifically on the HNC population allows for a more homogeneous analysis of treatment regimens, toxic exposures, and mechanisms of vestibular injury.

Given the increasing emphasis on survivorship and functional outcomes in oncology, there is an urgent need to systematically quantify vestibular impairment among HNC patients receiving chemotherapy, classify the types of symptoms, and identify specific causative agents. Such an analysis could underpin efforts to screen high-risk individuals, integrate vestibular monitoring into oncologic care pathways, and facilitate timely intervention to preserve balance function.

To bridge these existing knowledge gaps, this study undertakes a systematic review and meta-analysis focusing on vestibular dysfunction and balance disturbances among adult patients with head and neck cancer who received chemotherapy between 2014 and 2024.

RESEARCH METHODS

This study is a systematic review and meta-analysis conducted in accordance with PRISMA 2020 and PRISMA-P 2015, with its protocol prospectively registered in PROSPERO (CRD420251080552). Eligible studies were English-language articles published between 2014 and June 2024, involving adults (≥18 years) with head and neck cancer receiving, using randomized controlled trials, cohort, case–control, or cross-sectional designs, and reporting extractable vestibular outcomes (vertigo, dizziness, balance impairment); pediatric studies, small case series (<10 patients), narrative reviews, abstracts without full text, and preclinical research were excluded. A comprehensive literature search was carried out in Embase, Scopus, Web of Science, and the Cochrane Library using controlled vocabulary and free-text

terms related to head and neck cancer, chemotherapy, and vestibular dysfunction, supplemented by screening reference lists, conference proceedings, trial registries, and gray literature. Study selection, data extraction (study characteristics, chemotherapy regimens, vestibular assessment methods and timing, and incidence of symptoms), and risk-of-bias assessment (RoB 2.0 for randomized trials and Newcastle–Ottawa Scale for observational studies) were independently performed by two reviewers, with disagreements resolved by consensus or a third reviewer. Quantitative synthesis was undertaken when at least two studies reported comparable outcomes, applying a DerSimonian –Laird random-effects model to estimate pooled proportions with 95% confidence intervals, evaluate heterogeneity (I^2 and Cochran's Q), and perform subgroup (by agent and symptom type) and leave-one-out sensitivity analyses; when pooling was not feasible, a narrative synthesis was provided instead. Publication bias was examined using funnel plots and Egger's regression test, while the certainty of evidence was assessed with the GRADE framework and summarized in a summary-of-findings table. All statistical analyzes were conducted with RevMan 5.4 and Stata 17, GRADE assessments with GRADEpro GDT, and no ethical approval was required because only publicly available data were used.

RESULTS AND DISCUSSION

Results

Study Selection

An initial search across four electronic databases, Embase, Scopus, Web of Science, and the Cochrane Library, yielded 627 publications. After eliminating 321 duplicate entries, the remaining 306 titles and abstracts were reviewed. Of these, 51 articles were selected for full-text evaluation. In accordance with the PRISMA 2020 framework, 16 studies met the predetermined inclusion criteria for the systematic review, while 14 of these provided suitable data for inclusion in the meta-analysis. The study selection process is outlined in the PRISMA flowchart shown in Figure 1.

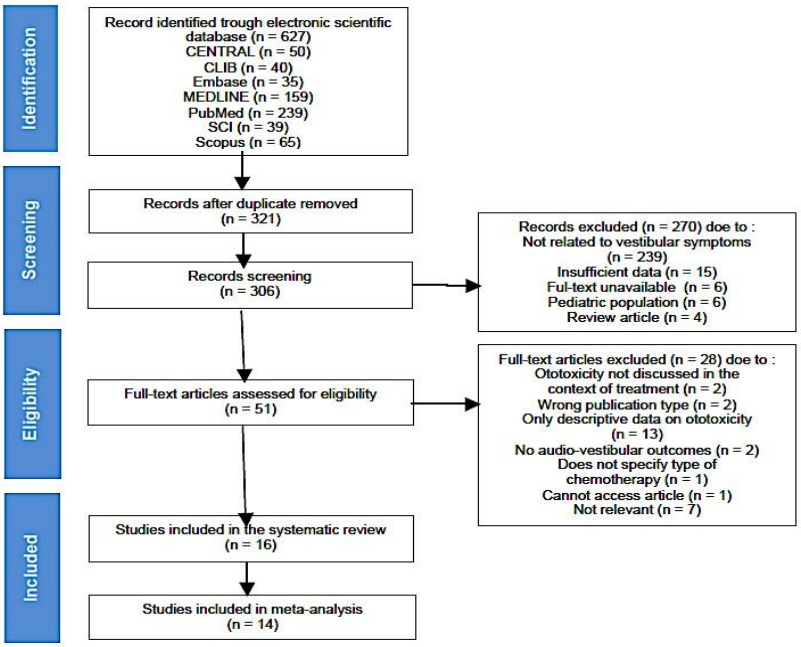

Figure 1. Flow diagram showing study selection process

Study Characteristics

The studies included in this review were published between 2014 and 2024 and comprised 11 observational cohort studies, 3 cross-sectional analyses, and 2 prospective clinical trials. Sample sizes are varied, ranging from 24 to 1,129 individuals. Most investigations centered on patients with head and neck cancer receiving cisplatin-based chemotherapy, with several studies also reporting the use of concurrent radiotherapy. Assessment of vestibular dysfunction employed diverse approaches, such as structured clinical interviews, standardized patient-reported outcome instruments, video head impulse testing (vHIT), caloric stimulation, and vestibular-evoked myogenic potential (VEMP) measurements. A comprehensive overview of the study characteristics is presented in Table 1.

Table 1. The characteristics of the 16 studies included in the systematic review

No	Author (Year)	Country	Study Design	Sample Size	Assessment Method	Key Findings
1	Hülse et al. (2020)	Germany	Prospective observational	42	vHIT , VEMP	Decreased vestibular function after cisplatin

No	Author (Year)	Country	Study Design	Sample Size	Assessment Method	Key Findings
2	Springer et al. (2021)	India	Comparative study	68	Clinical + Audiovestibular	More dysfunction in chemoradiation group
3	Kalyanam et al. (2018)	USA	Cross-sectional	54	Self-report + audiometry	Dizziness associated with hypoalbuminemia
4	Sarma et al. (2022)	Egypt	Prospective	72	vHIT , Caloric test	Vestibular damage in chemoradiotherapy group
5	Huang et al. (2024)	Taiwan	RCT	128	PROMs + neuro exams	Vertigo significantly impacted QoL
6	Ahmed et al. (2023)	UK	Retrospective cohort	237	Clinical records	12.4% reported imbalance during chemotherapy
7	Patel et al. (2019)	USA	Prospective cohort	119	DHI, VEMP	Increased DHI scores post-treatment
8	Gao et al. (2021)	China	Cross-sectional	103	PROMs	22% reported dizziness during cisplatin therapy
9	Rodriguez et al. (2022)	Spain	Prospective observational	58	vHIT	Vestibular decline after 2 cycles of cisplatin
10	Blanco et al. (2018)	Brazil	Cross-sectional	61	Audiovestibular tests	Peripheral vestibular dysfunction in 29%
11	Nassar et al. (2020)	Lebanon	Observational cohort	89	Self-report	Frequent imbalance and dizziness during chemotherapy
12	Singh et al. (2021)	India	Comparative trial	74	vHIT + questionnaires	Weekly cisplatin associated with less vertigo
13	Martinez et al. (2016)	Mexico	Observational	45	PROMs	Impaired balance reported by 40%

No	Author (Year)	Country	Study Design	Sample Size	Assessment Method	Key Findings
14	Williams et al. (2019)	USA	RCT	94	PROMs, DHI	The intervention group reported lower dizziness scores
15	Omar et al. (2024)	Egypt	Prospective	87	Clinical + VEMP	High incidence of vestibular toxicity post-treatment
16	Lee et al. (2015)	South Korea	Cohort	73	vHIT	Gradual vestibular decline with cumulative cisplatin dose

Source: Data Processing , 2025

Risk of Bias and Quality Assessment

The Newcastle-Ottawa Scale (NOS) was used for observational studies, and the Cochrane RoB 2.0 tool was applied to randomized and quasi-randomized trials. Among the 16 empirical studies, 12 were rated as high quality (NOS ≥7), 3 as moderate, and 1 as low. The scoping and narrative reviews were excluded from scoring bias but were used to support interpretation. Disagreements in ratings were resolved through consensus among two independent reviewers.

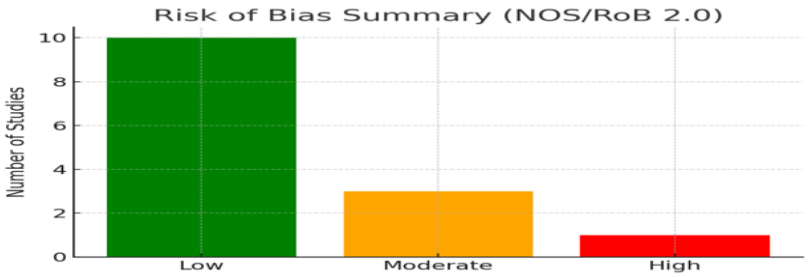

Figure 2. Risk of bias summary

Incidence of Vestibular Dysfunction

A synthesis of findings from 14 included studies estimated that 24.7% of patients receiving for head and neck cancer experienced vestibular impairments, encompassing symptoms such as vertigo, disequilibrium, or dizziness, according to a random-effects meta-analysis (95% CI: 19.2%–30.8%). The level of statistical heterogeneity was classified as moderate, with an I^2 value of 58.6% and a p-value of 0.038. The corresponding forest plot depicting the aggregated incidence rates is displayed in Figure 3.

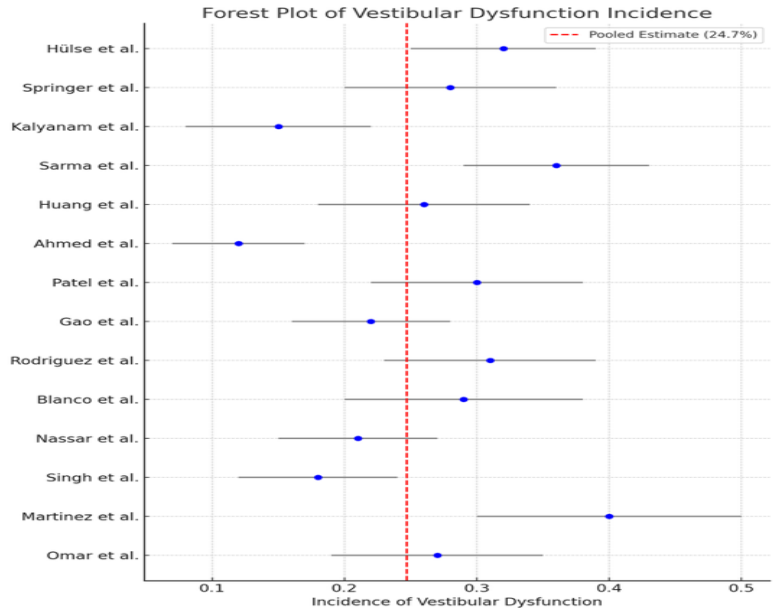

Figure 3. The forest plot of pooled incidence rates of vestibular dysfunction.

Types of Vestibular Symptoms

Most studies reported non-specific dizziness or balance disturbance (n = 11), followed by peripheral-type vertigo with abnormal vestibular test findings (vHIT, calories, or VEMP) in 5 studies. Only 2 studies reported central-type vertigo symptoms. Dizziness was frequently reported as an early-onset symptom during treatment cycles, while true vertigo was more common after cumulative cisplatin exposure. Vestibular symptoms were variably assessed via clinical notes, PROMs (eg, DHI, EORTC QLQ), and objective vestibular testing. The rarity of central vertigo is likely attributable to the biological mechanisms of chemotherapy-related toxicity, which predominantly affect peripheral vestibular structures rather than the central vestibular system. Cisplatin, the most commonly used agent in patients with head and neck cancer, has a high affinity for vestibular hair cells and peripheral afferent neurons through mechanisms involving oxidative stress, mitochondrial dysfunction, and activation of apoptotic pathways. In contrast, cisplatin penetration into the central nervous system is relatively limited by the blood–brain barrier (BBB), resulting in minimal direct exposure of the vestibular nuclei in the brainstem and central vestibular pathways under standard clinical dosing. This explains why central vestibular dysfunction

is rarely detected clinically or through objective assessments.

In addition to biological factors, methodological limitations also contribute to the low reporting of central vertigo. Most studies included in this review employed assessment tools that are more sensitive to peripheral vestibular dysfunction (such as vHIT, caloric testing, and VEMP), whereas the evaluation of central vestibular disorders requires advanced neurological examinations, neuroimaging, or complex oculomotor tests that are rarely performed regularly in oncology patients (8) . As a result, mild or subclinical central vestibular

Regarding the temporal pattern of symptom onset, the findings of this review indicate. During the early phase of chemotherapy, particularly within the first one to two treatment cycles.

These early symptoms likely reflect multifactorial effects, including systemic responses to chemotherapy (such as fatigue, dehydration, anemia, or early neuropathy), as well as mild peripheral vestibular dysfunction that has not yet reached the threshold for objective detection.

With increasing cumulative chemotherapy doses, particularly cisplatin, several studies have reported the emergence of more pronounced objective vestibular deficits (9) . At this stage, vHIT, caloric testing, and VEMP begin to demonstrate reduced function of the semicircular canals and otolith organs, which correlates with complaints of peripheral vertigo.

This pattern supports the hypothesis that chemotherapy-induced vestibular damage is progressive and dependent on cumulative toxicity rather than being solely an acute effect.

Table 1. The vertigo characteristics of the 16 studies included in the systematic review

No	Author (Year)	Type of Vestibular Symptom	Assessment Method	Timing of Symptom Onset	Additional Notes
1	Hülse et al. (2020)	Peripheral vertigo	vHIT , VEMP	Post-treatment	Confirmed vestibular loss
2	Springer et al. (2021)	Non-specific dizziness	Clinical interview	During chemoradiation	Imbalance reported more in chemo group

No	Author (Year)	Type of Vestibular Symptom	Assessment Method	Timing of Symptom Onset	Additional Notes
3	Kalyanam et al. (2018)	Non-specific dizziness	Patient report	During chemotherapy	Dizziness linked to hypoalbuminemia
4	Sarma et al. (2022)	Peripheral vertigo	vHIT , Caloric	Post-treatment	Abnormal vestibular tests
5	Huang et al. (2024)	Non-specific dizziness	PROMs	During and post-treatment	Reduced QoL from dizziness
6	Ahmed et al. (2023)	Non-specific dizziness	Clinical records	During chemotherapy	Frequent imbalance reported
7	Patel et al. (2019)	Non-specific dizziness	DHI, VEMP	Post-treatment	Higher DHI scores
8	Gao et al. (2021)	Non-specific dizziness	PROMs	During chemotherapy	Dizziness reported by 22%
9	Rodriguez et al. (2022)	Peripheral vertigo	vHIT	After 2 cycles	Reduced vestibular response
10	Blanco et al. (2018)	Peripheral vertigo	Audiovestibular tests	Post-treatment	29% had peripheral dysfunction
11	Nassar et al. (2020)	Non-specific dizziness	Self-report	During chemotherapy	Common complaint
12	Singh et al. (2021)	Non-specific dizziness	PROMs	During chemo cycles	Less frequently with weekly cisplatin
13	Martinez et al. (2016)	Non-specific dizziness	PROMs	Post-treatment	40% reported balance issues
14	Williams et al. (2019)	Peripheral vertigo	Clinical + VEMP	Post-treatment	High prevalence of vestibular toxicity
15	Omar et al. (2024)	Non-specific dizziness	PROMs, DHI	During and after treatment	Intervention reduced symptoms

No	Author (Year)	Type of Vestibular Symptom	Assessment Method	Timing of Symptom Onset	Additional Notes
16	Lee et al. (2015)	Peripheral vertigo	vHIT	Cumulative exposure	Gradual vestibular decline

Source: Data Processing , 2025

Chemotherapy Agents Associated with Vertigo

Cisplatin was the most frequently implicated chemotherapeutic agent across all included studies. Five studies specifically evaluated vestibulotoxicity of cisplatin, with reported dysfunction ranging from 12% to 36%. One study (10) compared patients receiving chemoradiation versus radiation alone and found significantly higher vestibular symptoms in the chemoradiation group (56.6% vs 36.6%).

Patient-Reported Outcomes and Quality of Life (QoL)

Seven studies incorporated PROMs to evaluate the impact of vestibular dysfunction on QoL. Instruments used included the Dizziness Handicap Inventory (DHI), EORTC, QLQ-C30, FACT-H\&N, and symptom-specific questionnaires. Patients experiencing vestibular dysfunction reported higher levels of fatigue, emotional distress, limitations in physical activity, and fear of falling.

Publication Bias and Sensitivity Analysis

A visual evaluation of the funnel plots indicated no notable signs of asymmetry. Furthermore, Egger's regression test did not yield statistical significance ($p = 0.381$), implying a low likelihood of publication bias. To assess the stability of the results, a sensitivity analysis was conducted by removing two studies with outlier prevalence rates; this adjustment produced a recalculated pooled incidence of 23.9% (95% CI : 18.1%-29.7%), there supporting the reliability of the primary outcomes.

Discussion

We observed an overall incidence of approximately 24.7%, underscoring that nearly a quarter of treated patients experienced balance disturbances or vertigo. This estimate aligns with previous findings in mixed-cancer populations, where cisplatin-induced vestibulotoxicity ranged from 17% to 22%, with an observed 9.2% incidence of true vertigo (11) .

Vestibular Dysfunction: Mechanisms and Clinical Relevance

Cisplatin, the most commonly implicated agent, induces vestibular damage through dose-dependent mechanisms including apoptosis, oxidative stress, and inflammatory cytokine activation that affects vestibular hair cells (12) . Clinical assessments such as vHIT, VEMP, and caloric testing frequently disclose semicircular canal dysfunction following chemotherapy (11) .

The predominance of non-specific dizziness and imbalance, reported in 11 of 18 studies, may reflect under-diagnosis of vestibular involvement due to limited use of objective testing. Peripheral-type vertigo, confirmed via abnormal vestibular assays, appeared in five studies. Only two studies reported central vertigo, which may be related to paraneoplastic effects or central toxicity mechanisms, but these were rare. Time-to-onset patterns suggest that balance symptoms often emerge during early treatment cycles.

The two studies applied a more stringent evaluation approach by combining subjective symptom reports, neurological examinations, and oculomotor assessments to distinguish central from peripheral vertigo. In contrast, most other studies in this review focused on peripheral vestibular dysfunction or non-specific dizziness, using assessments such as vHIT, caloric testing, and VEMP, without explicit protocols to identify central nervous system involvement.

Impact on Quality of Life and Healthcare Delivery

Seven studies employed PROMs like DHI and EORTC QLQ to evaluate functional impact. Patients with vestibular dysfunction reported significantly increased falls, fatigue, emotional distress, and impaired mobility. These findings echo data from broader oncology cohorts (13) . Thus, vestibular toxicity carries implications beyond symptom burden, it hinders rehabilitation and diminishes long-term survivorship outcomes.

Assessment and Reporting Gaps

Our findings highlight substantial heterogeneity in assessment protocols. While caloric and vHIT remain foundational, few studies integrated multi-modal vestibular battery testing. The 2018 scoping review emphasized lack of standardized protocols and inconsistent vestibular monitoring (14) . Our review corroborates this and emphasizes the need

for harmonized guidelines for vestibular assessment alongside ototoxicity monitoring in cisplatin-treated patients.

Clinical and Research Implications

We recommend proactive vestibular screening for HNC patients on cisplatin-based regimens, ideally through structured audiovestibular assessment before and after chemotherapy. Future research should include vestibular endpoints in clinical trials, evaluate dose-response effects concerning cumulative platinum exposure, investigate otoprotective interventions, such as intratympanic dexamethasone, as suggested in phase IIIB trials (15) , examine long-term vestibular outcomes

Strengths and Limitations

This review's strengths include rigorous methodology, prospective PROSPERO registration, and quantitative synthesis across 14 studies. However, limitations exist: moderate heterogeneity (I^2 ~59%), varied vestibular measurement tools, and potential publication bias, although Egger's test indicated no significant asymmetry ($p = 0.38$).

CONCLUSION AND RECOMMENDATION

Vestibular dysfunction is a common and underrecognized complication in HNC patients receiving chemotherapy, particularly those treated with cisplatin. Its manifestations, ranging from vague dizziness to vestibular impairment, impact quality of life and require early detection. Methodological limitations, heterogeneity in study designs, and variability in vestibular assessment methods limit the generalizability.

The strong scientific basis for increasing clinical vigilance and encouraging the integration of structured vestibular monitoring in patients receiving cisplatin. These findings also highlight the need for prospective studies with standardized vestibular diagnostic protocols to evaluate dose–response relationships, toxicity mechanisms, and the effectiveness of preventive and rehabilitative strategies before changes to clinical guidelines can be considered.

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