

Effect of radical (chemo)radiotherapy on cardiovascular autonomic function in patients with head and neck cancer: a prospective observational study

Adil Ahmed Khan

96adil@gmail.com

AIIMS: All India Institute of Medical Sciences <https://orcid.org/0009-0007-6781-5836>

Shivam Kumar

AIIMS RISHIKESH

Sweety Gupta

AIIMS RISHIKESH

Deepa Joseph

AIIMS RISHIKESH

Poorvi Kulshrestha

AIIMS RISHIKESH

Prashant Kumar Saini

AIIMS RISHIKESH

Ashutosh Kashyap

AIIMS RISHIKESH

Ajit Singh

AIIMS RISHIKESH

Manoj Gupta

AIIMS RISHIKESH

Research Article

Keywords: Head and neck cancer, Autonomic nervous system, Carotid sinus, Neck irradiation, Chemoradiotherapy, Heart rate variability

Posted Date: October 22nd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11267884/v1>

Abstract

Purpose

Radiotherapy for head and neck cancer irradiates the carotid sinus, yet early effects on cardiovascular autonomic function are poorly described. We prospectively evaluated autonomic function before, at the end of, and six months after definitive radiotherapy with or without concurrent chemotherapy.

Methods

Thirty-one adults aged 18–74 years with squamous cell carcinoma of the oral cavity, oropharynx, larynx or hypopharynx underwent autonomic function testing at baseline, at the end of treatment and at six months. Each session included a ten-minute supine recording for heart rate and blood pressure variability, followed by deep breathing, Valsalva manoeuvre, lying-to-standing, isometric handgrip and cold pressor tests. Repeated-measures analysis of variance and paired t-tests were used; analyses were exploratory and unadjusted for multiple comparisons.

Results

Twenty-nine patients completed the end-of-treatment assessment and seventeen the six-month assessment. High-frequency power of heart rate variability was higher than baseline at the end of treatment ($P = 0.040$) and at six months ($P = 0.012$). Systolic and diastolic blood pressure and their low-frequency variability increased at the end of treatment but not at six months. Deep breathing, Valsalva, lying-to-standing and handgrip responses did not change. The cold pressor diastolic response showed no overall change ($P = 0.093$); an isolated baseline-to-six-month difference ($P = 0.049$) indicated a smaller pressor rise.

Conclusion

Within six months, conventional autonomic reflex tests showed no significant deterioration, and changes in resting variability were mostly transient. These exploratory findings do not establish baroreflex dysfunction; longer follow-up with direct measurement of baroreflex sensitivity is needed.

Introduction

Head and neck cancers (HNCs) arise predominantly from the oral cavity, pharynx, larynx and salivary glands and are frequently managed with multimodality treatment incorporating surgery, radiotherapy (RT) and systemic therapy [1]. Radiotherapy plays a central role in definitive and postoperative treatment, and irradiation of the cervical lymphatic regions is required for many patients because of the high incidence of regional nodal involvement. Consequently, structures within the carotid sheath and its

vicinity may receive substantial radiation exposure despite advances in conformal techniques such as intensity-modulated radiotherapy (IMRT). Complete sparing of the carotid arteries and adjacent neural structures is often not feasible when the cervical lymphatic compartments are treated.

The carotid sinus, located at the carotid bifurcation, contains mechanosensitive baroreceptors that detect changes in arterial wall stretch and initiate the afferent limb of the arterial baroreflex. Afferent signals travel predominantly through the glossopharyngeal nerve to the nucleus tractus solitarii in the medulla, where they are integrated with other visceral autonomic inputs. The result is reciprocal modulation of sympathetic and parasympathetic activity, providing beat-to-beat regulation of heart rate, vascular tone and arterial blood pressure [2]. Impairment of this reflex can produce abnormal heart rate variability (HRV) and blood pressure variability (BPV), impaired cardiovascular reflexes, orthostatic intolerance and, in severe cases, marked blood pressure lability.

Radiation-induced injury to the carotid sinus and its afferent pathways has been implicated in afferent baroreflex failure after treatment for HNC. Proposed mechanisms include radiation-associated vascular fibrosis and stiffening, structural changes in the carotid wall, and injury to small afferent nerve fibres traversing irradiated tissue [3–6]. Clinically overt baroreflex failure is uncommon and is generally recognised years after neck irradiation, presenting with labile blood pressure, episodic hypertension, orthostatic hypotension, tachycardia or bradycardia, dizziness and syncope [3, 5]. Published reports consist largely of case reports, small observational studies and retrospective evaluations, and the true incidence and natural history of radiation-associated autonomic dysfunction remain uncertain. Physiological studies have demonstrated abnormal baroreflex sensitivity and cardiovascular reflexes after neck irradiation even without overt baroreflex failure [4, 7, 8]. Studies in nasopharyngeal carcinoma have reported differences in cardiovascular autonomic parameters years after radiotherapy [9], and a nine-year prospective follow-up suggested that concurrent chemoradiotherapy is associated with accelerated cardiovascular autonomic dysfunction [10].

Cardiovascular autonomic consequences of HNC treatment may therefore lie on a spectrum from subclinical physiological abnormality to clinically manifest baroreflex failure. Relatively little prospective information describes the early post-treatment period in patients with tumours at several head and neck subsites treated with IMRT, and few studies have combined several complementary measures of autonomic cardiovascular function. We therefore undertook a prospective observational study to evaluate changes in cardiovascular autonomic regulation after radical (chemo)radiotherapy in patients with HNC, using HRV, BPV and cardiovascular reflex testing before treatment, at its completion and at six months, with the aim of identifying early physiological alterations that may precede overt radiation-associated baroreflex dysfunction.

Materials and methods

Study design and participants

This was a prospective longitudinal observational study conducted at a single institution and reported in accordance with the STROBE statement [11]. Patients were recruited between November 2022 and December 2023. Cardiovascular autonomic function was assessed at three time points: before treatment (baseline), at completion of radiotherapy (end of treatment) and at six months of follow-up.

Patients aged 18–74 years with biopsy-proven malignancy of the oral cavity, oropharynx, larynx or hypopharynx, stage I–IVB according to the eighth edition of the American Joint Committee on Cancer (AJCC) staging system [12], and planned for definitive radical radiotherapy, with concurrent chemotherapy where clinically appropriate, were eligible. Patients with recurrent or metastatic disease, radiological carotid artery encasement of more than 180°, previous surgery for the index malignancy, prior induction chemotherapy, diabetes mellitus, hypertension, known autonomic nervous system disorders or a tracheostomy in situ were excluded. In this paper, radiotherapy with or without concurrent chemotherapy is referred to as chemoradiotherapy (CRT).

The study was approved by the institutional ethics committee and written informed consent was obtained from all participants before enrolment.

Sample size

This was a time-bound study: the number of participants was determined by the recruitment window (November 2022–December 2023). Because no comparable prospective study was available, an exploratory calculation was used for planning (G*Power 3.1.9.4, Heinrich-Heine-Universität Düsseldorf, Germany; medium effect size 0.5, two-sided α 0.05, power 80%, anticipated attrition 10%). The final sample of 31 patients was governed by the recruitment period, and the study is not powered to detect small effects.

Treatment

Patients received definitive radiotherapy to a total dose of 70 Gy in 33 fractions or 66 Gy in 30 fractions using IMRT on a Halcyon linear accelerator with 6-MV flattening-filter-free photons, delivered five days per week over approximately 6–6.5 weeks. Concurrent systemic therapy, where given, was weekly cisplatin at 40 mg/m² or weekly carboplatin [@ AUC-2 for Cisplatin ineligible patients]. Before chemotherapy, baseline blood investigations, pure-tone audiometry and cardiac evaluation were performed.

Cardiovascular autonomic function testing

Autonomic function testing (AFT) was performed at each time point. Each assessment consisted of a 10-min resting recording followed by a standardised battery of cardiovascular reflex tests. Participants completed a pre-test questionnaire to identify conditions that could contraindicate or influence testing

(Online Resource 1). To standardise conditions, participants avoided caffeine and nicotine for at least 3–4 h and alcohol for at least 8 h before testing; sympathomimetic drugs were withheld for 24–48 h and anticholinergic drugs for 48 h where clinically permissible. Thirty minutes before testing, participants rested in a quiet room at controlled temperature and humidity, and were then oriented to the procedure with a 10-min practice session.

Participants were positioned supine and instrumented with three ECG electrodes, a respiratory belt around the chest, an upper-arm blood pressure cuff on the non-dominant arm and a Finometer MIDI finger cuff (Finapres Medical Systems, Enschede, The Netherlands) on the non-dominant hand. The Finometer provides continuous beat-to-beat estimates of systolic (SBP), diastolic (DBP) and mean arterial pressure by the volume-clamp method. ECG, arterial pressure and respiratory signals were acquired with PowerLab hardware and recorded with LabChart software (ADInstruments, Dunedin, New Zealand) (Fig. 1).

After instrumentation, ECG, respiration and beat-to-beat blood pressure were recorded for 10 min with the participant supine and at rest. The resting ECG was used for time- and frequency-domain HRV analysis and the resting blood pressure recording for BPV analysis. The reflex tests were then performed in the following order, with 2 min of rest between tests: deep breathing, Valsalva manoeuvre, lying-to-standing, cold pressor and sustained isometric handgrip. The protocol is summarised in Table 1 and follows the conventional tests described by Ewing and colleagues [13]; the full protocol is in Online Resource 1. The E:I ratio was the ratio of the longest R–R interval during expiration to the shortest during inspiration, and the Valsalva ratio the ratio of the longest R–R interval after the strain to the shortest during it [14]. The 30:15 ratio was the ratio of the longest R–R interval around the thirtieth beat to the shortest around the fifteenth beat after standing.

Table 1 Cardiovascular autonomic reflex test protocol		
Test	Protocol	Primary parameters
Deep breathing	Six breaths/min for 1 min; 5 s inspiration, 5 s expiration	Δ HR; E:I ratio
Valsalva manoeuvre	40 mmHg for 15 s, supine	Valsalva ratio
Lying-to-standing	Standing in three steps over 3 s, maintained for 5 min; serial HR/BP	30:15 ratio; Δ SBP
Cold pressor	Hand immersed to the wrist in 10°C water for 1 min	Maximum Δ DBP
Isometric handgrip	30% of maximal voluntary contraction for up to 4 min	Maximum Δ DBP

HR heart rate; E:I expiration-to-inspiration; SBP systolic blood pressure; DBP diastolic blood pressure; Δ change from pre-test value.

Heart rate and blood pressure variability

HRV was analysed from normal-to-normal R–R intervals of the 10-min resting ECG using Nevrokard HRV analysis software, version 9.1.0 (Medistar, Ljubljana, Slovenia), according to published standards [15]. Time-domain parameters were mean NN interval, standard deviation of NN intervals (SDNN), coefficient of variation of R–R intervals (CV RR), mean heart rate, standard deviation of heart rate (SDHR), root mean square of successive differences (RMSSD) and pNN50. Frequency-domain parameters (low frequency [LF] 0.04–0.15 Hz, high frequency [HF] 0.15–0.40 Hz) were total power (TP), LF power, HF power and the LF/HF ratio.

BPV was analysed from beat-to-beat SBP, DBP and mean arterial pressure recorded during the same period [16, 17]. Time-domain parameters were the mean, median, standard deviation, standard deviation of successive differences (SDSD) and RMSSD of each pressure; frequency-domain parameters were LF power, HF power and the LF/HF ratio for each pressure (Fig. 2).

Statistical analysis

Analyses were performed with IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA). Data were normally distributed and are presented as mean $\pm$ standard deviation; categorical variables are presented as numbers and percentages. Changes across the three time points were tested with repeated-measures analysis of variance. Baseline was compared with end of treatment and with six months using paired t-tests, using all patients with paired data at each time point ($n = 29$ and $n = 17$, respectively); baseline means therefore differ between the two comparisons. A two-sided $P < 0.05$ was considered statistically significant. Because many autonomic parameters were tested and no correction for multiple comparisons was applied, the analysis is exploratory and nominal P values should be interpreted accordingly.

Use of artificial intelligence tools

A large language model (ChatGPT, OpenAI) was used to assist in drafting and editing parts of the manuscript text. The authors checked all content against the study data and take full responsibility for the manuscript.

Results

Participants

Thirty-one patients were enrolled and completed baseline assessment. Two patients died from tumour-related bleeding before completing treatment, so 29 patients completed the end-of-treatment assessment. Seventeen patients completed the six-month assessment: of the remaining 12, seven died (four from pulmonary causes, two from poor nutrition and one from a cardiac cause), three defaulted

from follow-up and three did not attend for autonomic testing but remained under routine clinic follow-up. Baseline characteristics are shown in Table 2. Thirty patients (96.8%) were men, most had locally advanced disease (stage IVA or IVB in 74.2%) and 19 (61.3%) had oropharyngeal primaries. Twenty-five patients received 70 Gy in 33 fractions and six received 66 Gy in 30 fractions. Twenty-one patients received concurrent systemic therapy (cisplatin 15, carboplatin 6) and 10 received radiotherapy alone; of those treated with chemotherapy, 13 received more than four cycles and 8 received four or fewer.

Table 2
Baseline patient, tumour and treatment characteristics (N = 31)

Characteristic	n (%)
Age < 65 years / 65–74 years	28 (90.3) / 3 (9.7)
Sex: male / female	30 (96.8) / 1 (3.2)
ECOG performance status 0 / 1 / 2	7 (22.6) / 20 (64.5) / 4 (12.9)
Primary site: oropharynx / larynx / hypopharynx / oral cavity	19 (61.3) / 5 (16.1) / 5 (16.1) / 2 (6.5)
Histology: well / moderately / poorly differentiated SCC	3 (9.7) / 23 (74.2) / 5 (16.1)
T stage: T2 / T3 / T4a / T4b	6 (19.4) / 9 (29.0) / 13 (41.9) / 3 (9.7)
N stage: N0 / N1 / N2a / N2b / N2c / N3b	6 (19.4) / 9 (29.0) / 4 (12.9) / 2 (6.5) / 5 (16.1) / 5 (16.1)
Stage group: III / IVA / IVB	8 (25.8) / 17 (54.8) / 6 (19.4)
Radiotherapy dose: 70 Gy/33 / 66 Gy/30 fractions	25 (80.6) / 6 (19.4)
Concurrent systemic therapy: none / cisplatin / carboplatin	10 (32.3) / 15 (48.4) / 6 (19.4)
Chemotherapy cycles (n = 21): >4 / ≤4	13 (61.9) / 8 (38.1)

ECOG Eastern Cooperative Oncology Group; SCC squamous cell carcinoma.

Cardiovascular autonomic reflex tests

There was no significant longitudinal change in the conventional reflex tests. During deep breathing, neither Δ HR ($P = 0.175$) nor the E:I ratio ($P = 0.219$) changed over time, and the Valsalva ratio was stable ($P = 0.302$). In the lying-to-standing test, neither Δ SBP ($P = 0.432$) nor the 30:15 ratio ($P = 0.218$) changed, and pairwise comparisons showed no differences between baseline and end of treatment or six months. The Δ DBP during isometric handgrip did not differ across time points ($P = 0.656$), nor between baseline and end of treatment ($P = 0.614$) or six months ($P = 0.652$).

For the cold pressor test, the overall change in Δ DBP over time was not significant ($P = 0.093$). On pairwise comparison, Δ DBP fell from 11.17 ± 9.74 to 7.90 ± 9.89 mmHg at the end of treatment ($P =$

0.199) and from 12.94 ± 9.95 to 6.24 ± 8.27 mmHg at six months ($P = 0.049$) (Table 3). This is a nominally significant pairwise result in the absence of a significant overall effect.

Table 3
Cold pressor test: change in diastolic blood pressure (Δ DBP, mmHg), baseline versus follow-up

Comparison	n	Baseline	Follow-up	t	P
Baseline vs end of treatment	29	11.17 ± 9.74	7.90 ± 9.89	1.316	0.199
Baseline vs 6 months	17	12.94 ± 9.95	6.24 ± 8.27	2.136	0.049

Mean $\pm$ standard deviation; paired t-test.

Heart rate variability

Most resting HRV parameters were stable. Significant longitudinal changes were seen in CV RR ($P = 0.048$), TP ($P = 0.049$) and HF power ($P = 0.005$). Pairwise, HF power increased from 33.51 ± 18.58 at baseline to 44.94 ± 17.17 at the end of treatment ($P = 0.040$) and from 28.50 ± 18.20 to 40.91 ± 16.74 at six months ($P = 0.012$); no other HRV parameter differed significantly from baseline at either time point.

Blood pressure variability

Resting BPV showed several changes at the end of treatment (Table 4). Longitudinal changes were significant for mean SBP ($P = 0.041$), median SBP ($P = 0.041$) and LF-SBP power ($P = 0.020$), and for LF-DBP power ($P = 0.002$) and the LF/HF ratio of DBP ($P = 0.010$). Pairwise, SBP, DBP and LF power increased at the end of treatment. None of the SBP or DBP variability parameters differed significantly between baseline and six months; for example, mean SBP was 119.62 ± 26.30 mmHg at baseline and 126.57 ± 24.40 mmHg at six months ($P = 0.315$).

Table 4
Resting blood pressure variability: baseline versus end of treatment (n = 29)

Parameter	Baseline	End of treatment	P
Mean SBP (mmHg)	115.89 ± 26.42	139.34 ± 39.38	0.015
Median SBP (mmHg)	112.92 ± 31.59	139.27 ± 40.13	0.018
LF-SBP power	37.72 ± 23.54	49.46 ± 16.41	0.004
Mean DBP (mmHg)	50.89 ± 18.90	62.04 ± 19.24	0.023
Median DBP (mmHg)	50.31 ± 19.96	60.83 ± 16.24	0.022
LF-DBP power	38.64 ± 21.02	53.73 ± 17.61	0.002
LF/HF ratio of DBP	1.57 ± 1.14	2.65 ± 2.09	0.015

Mean $\pm$ standard deviation; paired t-test. LF low frequency; HF high frequency. No parameter differed significantly between baseline and six months.

Summary of findings

Conventional reflex tests showed no significant deterioration during the first six months after treatment. Selected resting HRV and BPV parameters changed, chiefly at the end of treatment. The BPV changes were not present at six months, whereas the increase in HF power persisted. The isolated cold pressor finding at six months should be interpreted cautiously given the non-significant overall analysis.

Discussion

In this prospective longitudinal study, cardiovascular autonomic function was assessed before treatment, at its completion and at six months in patients with HNC receiving definitive radical (chemo)radiotherapy, using resting HRV and BPV and a battery of reflex tests. Earlier reports have mostly been retrospective or cross-sectional evaluations of patients months to years after treatment, or case series. Goyal et al. compared 15 patients more than six months after chemoradiotherapy with 15 healthy controls and reported abnormal HRV and autonomic responses to stressors [8]. Autonomic disturbance also follows surgical disruption of the carotid region: bilateral carotid body tumour resection is associated with overt or subclinical baroreflex dysfunction [18]. A long-term prospective study in nasopharyngeal carcinoma has linked concurrent chemoradiotherapy with accelerated autonomic dysfunction [10], and our study adds early-phase data across several head and neck subsites, including reflex testing.

Resting autonomic function

HRV reflects the dynamic interaction of sympathetic and parasympathetic influences on the sinoatrial node and can be assessed in the time and frequency domains [15]. Most resting HRV parameters did not change significantly. CV RR, TP and HF power changed in the overall analysis, and HF power was the only parameter significantly different from baseline both at the end of treatment and at six months.

This HF increase should be interpreted cautiously. HF power is predominantly influenced by respiration-related vagal modulation, but no HRV component is a direct or exclusive measure of one autonomic branch, and the result should not be read as increased sympathetic activity. It indicates a change in cardiac autonomic modulation that warrants evaluation in larger cohorts with respiratory control and fuller autonomic assessment. Respiratory signals were recorded, but respiratory rate was not incorporated into the HRV analysis.

BPV characterises short-term fluctuations in arterial pressure [16]. Mean and median SBP and DBP, LF-SBP and LF-DBP power and the DBP LF/HF ratio increased at the end of treatment but were not sustained at six months. Blood pressure changes during head and neck radiotherapy have been described previously [19], and blood pressure and its variability are influenced by hydration, nutritional

status, pain, physical activity, psychological stress, medications (including antiemetics and corticosteroids) and the acute effects of cancer treatment. The BPV changes therefore cannot be attributed to radiation-induced carotid baroreceptor injury. They suggest that cardiovascular regulation may fluctuate during and just after treatment, without evidence of persistent autonomic failure during the period studied.

Responses to physiological stressors

No single test captures autonomic function, so a battery is used. The Ewing battery comprises the Valsalva manoeuvre, deep breathing, orthostatic testing and isometric exercise [13]; we added the cold pressor test as a predominantly sympathetic stimulus. Heart rate responses to deep breathing, Valsalva and standing mainly reflect parasympathetic (cardiovagal) function, whereas blood pressure responses to Valsalva, standing, handgrip and cold mainly reflect sympathetic vasomotor function [20, 21]. None of the deep breathing, Valsalva, lying-to-standing or handgrip measures changed significantly, so we found no demonstrable deterioration in cardiovagal or sympathetic vasomotor reflexes over the first six months. This matters because clinically significant baroreflex dysfunction may present as orthostatic hypotension or exaggerated blood pressure fluctuation [2].

The cold pressor Δ DBP fell numerically over time, but the overall analysis was not significant ($P = 0.093$). The baseline-to-six-month comparison ($P = 0.049$) was nominally significant, yet it is an isolated finding among many parameters tested, in only 17 patients, and does not by itself establish autonomic impairment. Δ DBP is the peak pressor rise during the test and does not measure recovery; a smaller rise is more consistent with a blunted sympathetic vasoconstrictor response than with impaired recovery. Established afferent baroreflex failure would more typically be expected to produce exaggerated rather than reduced pressor responses [2, 3].

Delayed radiation-associated dysfunction and clinical implications

Clinically overt baroreflex failure after neck irradiation is uncommon and has been reported as a delayed complication, often years after treatment [3, 5]. Radiation-related carotid wall thickening, calcification and atherosclerosis also develop progressively after radiotherapy [6]. The short follow-up in our study may therefore explain the absence of major reflex abnormalities, and the absence of abnormality at six months should not be taken to mean that long-term autonomic consequences do not occur. Prior neck surgery and tumour-related factors can also contribute to carotid sinus injury, making attribution to radiotherapy alone difficult [5].

The clinical significance of early autonomic change after CRT remains uncertain. Our findings do not support pharmacological intervention on the basis of the observed HRV, BPV or reflex-test changes. Their principal implication is the potential value of prospective autonomic surveillance: a baseline assessment provides a reference for later comparison, especially in patients receiving substantial

cervical irradiation, and longer follow-up may show whether early changes in cardiovascular variability predict later symptomatic autonomic dysfunction.

Strengths and limitations

Strengths include the prospective longitudinal design with a pre-treatment baseline and the combination of resting HRV, BPV and reflex testing. Limitations are as follows. The sample was small, set by the recruitment period rather than by a formal power calculation, and only 17 of 31 patients completed the six-month assessment; because seven of the 12 who did not complete it had died, the six-month group is a survivor-selected subset. There was no non-irradiated control group, and treatment was heterogeneous (10 patients had radiotherapy alone and chemotherapy was cisplatin or carboplatin), so radiation effects cannot be separated from those of chemotherapy, tumour burden, nutrition and other treatment-related factors. Baroreflex sensitivity was not measured directly [22], so the findings do not assess carotid baroreceptor sensitivity itself, although it carries prognostic value in other settings [23]. Very-low-frequency indices were not analysed. Age, sex, body mass index, diet, physical activity, psychological stress, medication use, human papillomavirus status and tobacco and alcohol exposure were not incorporated into the analysis. No dosimetric data for the carotid sinus were analysed, so dose–response relationships could not be assessed. Many parameters were tested without correction for multiple comparisons, and pairwise comparisons used different patient subsets. Almost all patients were men, and the study was conducted at one institution. Future studies should combine longer follow-up, larger samples, carotid dosimetry, validated baroreflex sensitivity measurement and control for clinical and metabolic confounders.

Conclusion

In this prospective study of patients with head and neck cancer treated with definitive radical (chemo)radiotherapy, conventional cardiovascular autonomic reflex tests showed no significant deterioration during the first six months. Several resting HRV and BPV parameters changed, mainly at the end of treatment, and most BPV changes were not sustained at six months. An isolated baseline-to-six-month difference in the cold pressor response was not supported by the overall analysis. These findings do not show established autonomic failure or baroreflex dysfunction in the first six months, and the observed changes in resting variability may represent early alterations of uncertain clinical significance. Because radiation-associated baroreflex dysfunction is usually reported years after treatment, longer prospective follow-up with direct baroreflex sensitivity measurement and carotid dosimetry is needed.

Declarations

Funding: No funding received

Competing interests: The authors have no conflicting interests to disclose

Ethics approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the institutional ethics committee.

Consent to participate: Written informed consent was obtained from all individual participants included in the study.

Author contributions: Conceptualization- Dr Manoj Gupta, Dr Poorvi Kulshreshtha
Methodology- Dr Adil Ahmed Khan, Ajit Singh, Dr Shivam Kumar, Investigation- Dr Adil Ahmed Khan, Analysis- Dr Prashant Kumar Saini, Dr Ashutosh Kashyap, Data curation- Dr Adil Ahmed Khan, Writing(original draft)- Dr Adil Ahmed Khan, Writing(review and editing)- Dr Sweety Gupta, Supervision- Dr Deepa Joseph

Data availability: The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

References

1. Johnson DE, Burtneess B, Leemans CR, Lui VWY, Bauman JE, Grandis JR (2020) Head and neck squamous cell carcinoma. *Nat Rev Dis Primers* 6:92. <https://doi.org/10.1038/s41572-020-00224-3>
2. Biaggioni I, Shibao CA, Diedrich A, Muldowney JAS 3rd, Laffer CL, Jordan J (2019) Blood pressure management in afferent baroreflex failure: JACC review topic of the week. *J Am Coll Cardiol* 74:2939–2947. <https://doi.org/10.1016/j.jacc.2019.10.027>
3. Sharabi Y, Dendi R, Holmes C, Goldstein DS (2003) Baroreflex failure as a late sequela of neck irradiation. *Hypertension* 42:110–116. <https://doi.org/10.1161/01.HYP.0000077441.45309.08>
4. Timmers HJLM, Karemaker JM, Wieling W, Kaanders JHAM, Folgering HTM, Marres HAM, Lenders JWM (2002) Arterial baroreflex and peripheral chemoreflex function after radiotherapy for laryngeal or pharyngeal cancer. *Int J Radiat Oncol Biol Phys* 53:1203–1210. [https://doi.org/10.1016/S0360-3016\(02\)02827-4](https://doi.org/10.1016/S0360-3016(02)02827-4)
5. Shah-Becker S, Pennock M, Sinoway L, Goldenberg D, Goyal N (2017) Baroreceptor reflex failure: review of the literature and the potential impact on patients with head and neck cancer. *Head Neck* 39:2135–2141. <https://doi.org/10.1002/hed.24857>
6. Kim BJ, Kang HG, Lee SW, Jung J, Lee MH, Kang DW, Kim JS, Kwon SU (2018) Changes in the common carotid artery after radiotherapy: wall thickness, calcification, and atherosclerosis. *J Clin Neurol* 14:35–42. <https://doi.org/10.3988/jcn.2018.14.1.35>
7. Shapiro MH, Ruiz-Ramon P, Fainman C, Ziegler MG (1996) Light-headedness and defective cardiovascular reflexes after neck radiotherapy. *Blood Press Monit* 1(1):81–85
8. Goyal M, Shukla P, Gupta D, Bisht S, Verma NS, Tiwari S, Bhatt ML (2017) Cardiovascular sequel of neck irradiation in head and neck cancer patients. *Int J Radiat Biol* 93:711–716. <https://doi.org/10.1080/09553002.2017.1303217>

9. Huang C-C, Huang T-L, Hsu H-C, Chen H-C, Lin H-C, Chien C-Y et al (2013) Long-term effects of neck irradiation on cardiovascular autonomic function: a study in nasopharyngeal carcinoma patients after radiotherapy. *Muscle Nerve* 47:344–350. <https://doi.org/10.1002/mus.23530>
10. Huang CC, Lai YR, Chiu WC, Fang FM, Hsieh DY, Lien CY, Cheng BC, Chien CY, Huang TL, Kung CT, Lu CH (2022) Concurrent chemoradiation therapy is associated with an accelerated risk of cardiovascular autonomic dysfunction in patients with nasopharyngeal carcinoma: a 9-year prospective follow-up study. *Radiother Oncol* 170:129–135. [10.1016/j.radonc.2022.03.004](https://doi.org/10.1016/j.radonc.2022.03.004)
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 370:1453–1457. [https://doi.org/10.1016/S0140-6736\(07\)61602-X](https://doi.org/10.1016/S0140-6736(07)61602-X)
12. Amin MB, Edge SB, Greene FL et al (eds) (2017) *AJCC Cancer Staging Manual*, 8th edn. Springer, New York
13. Ewing DJ, Martyn CN, Young RJ, Clarke BF (1985) The value of cardiovascular autonomic function tests: 10 years experience in diabetes. *Diabetes Care* 8:491–498. <https://doi.org/10.2337/diacare.8.5.491>
14. Sandroni P, Benarroch EE, Low PA (1991) Pharmacological dissection of components of the Valsalva maneuver in adrenergic failure. *J Appl Physiol* 71:1563–1567. <https://doi.org/10.1152/jappl.1991.71.4.1563>
15. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation* 93:1043–1065. <https://doi.org/10.1161/01.CIR.93.5.1043>
16. Parati G, Saul JP, Di Rienzo M, Mancia G (1995) Spectral analysis of blood pressure and heart rate variability in evaluating cardiovascular regulation: a critical appraisal. *Hypertension* 25:1276–1286. <https://doi.org/10.1161/01.HYP.25.6.1276>
17. Omboni S, Parati G, Frattola A, Mutti E, Di Rienzo M, Castiglioni P, Mancia G (1993) Spectral and sequence analysis of finger blood pressure variability: comparison with analysis of intra-arterial recordings. *Hypertension* 22:26–33. <https://doi.org/10.1161/01.HYP.22.1.26>
18. Ghali MGZ, Srinivasan VM, Hanna E, DeMonte F (2017) Overt and subclinical baroreflex dysfunction after bilateral carotid body tumor resection: pathophysiology, diagnosis, and implications for management. *World Neurosurg* 101:559–567. [10.1016/j.wneu.2017.02.073](https://doi.org/10.1016/j.wneu.2017.02.073)
19. Pandit PN, Patil RA, Palwe VS et al (2021) Patterns of blood pressure changes in patients with head and neck cancer receiving radiotherapy or chemo-radiotherapy at a tertiary cancer centre. *Head Neck* 43:1280–1288. <https://doi.org/10.1002/hed.26590>
20. Mathias CJ (2003) Autonomic diseases: clinical features and laboratory evaluation. *J Neurol Neurosurg Psychiatry* 74(Suppl 3):iii31–iii41. https://doi.org/10.1136/jnnp.74.suppl_3.iii31
21. Jaradeh SS, Prieto TE (2003) Evaluation of the autonomic nervous system. *Phys Med Rehabil Clin N Am* 14:287–305. [10.1016/S1047-9651\(02\)00113-2](https://doi.org/10.1016/S1047-9651(02)00113-2)

22. Pinna GD, Maestri R, La Rovere MT (2015) Assessment of baroreflex sensitivity from spontaneous oscillations of blood pressure and heart rate: proven clinical value? *Physiol Meas* 36:741–753. <https://doi.org/10.1088/0967-3334/36/4/741>
23. La Rovere MT, Bigger JT Jr, Marcus FI, Mortara A, Schwartz PJ (1998) Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. *Lancet* 351:478–484. [https://doi.org/10.1016/S0140-6736\(97\)11144-8](https://doi.org/10.1016/S0140-6736(97)11144-8)

Figures

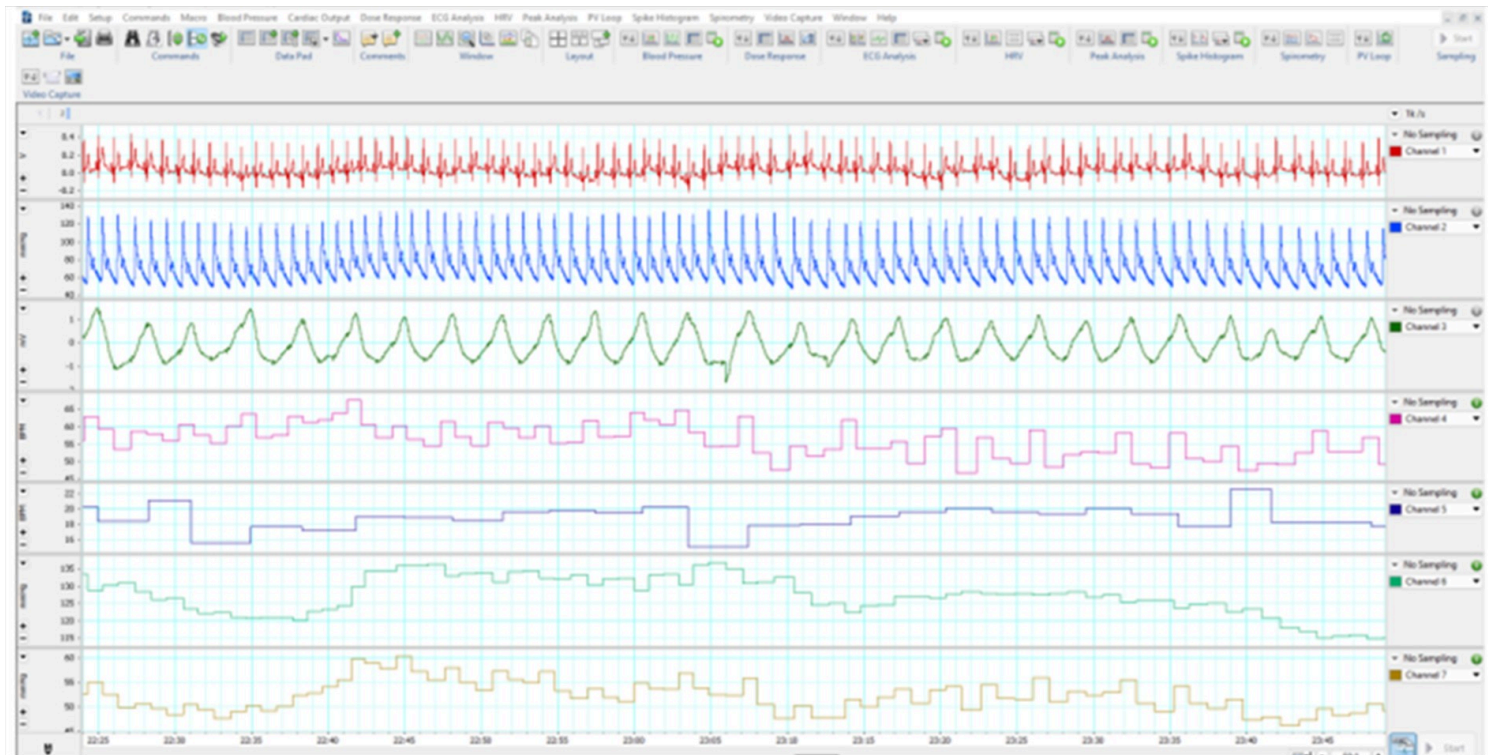


Figure 1

Representative LabChart recording of ECG, continuous arterial pressure, respiration and derived heart rate and blood pressure channels.

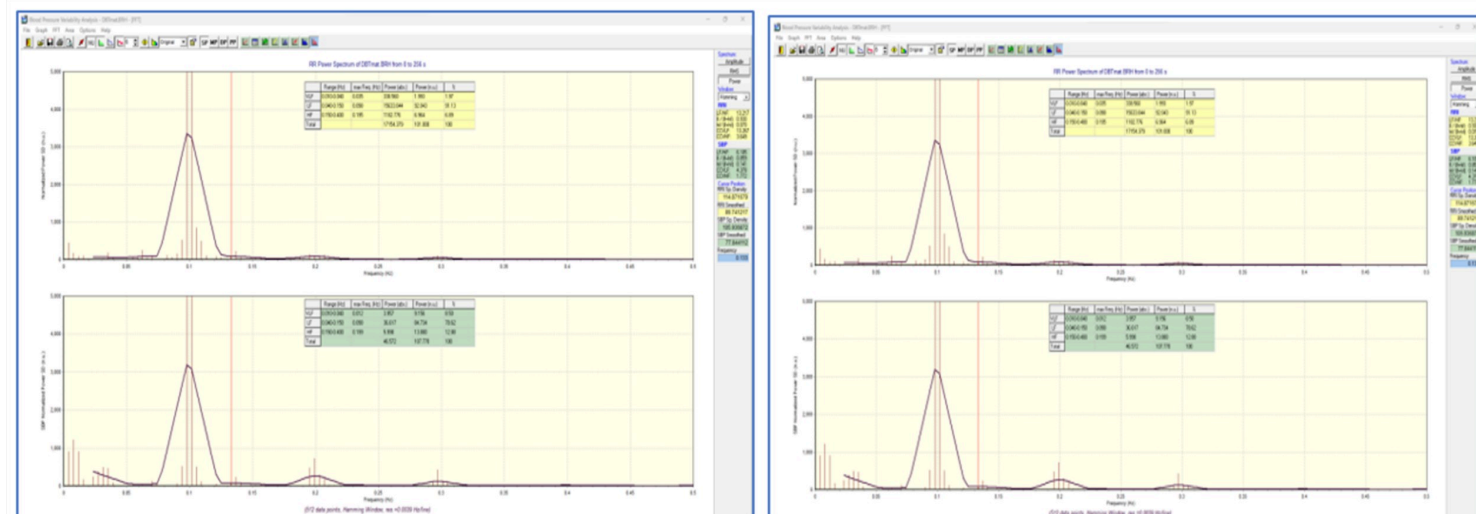


Figure 2

Nevrokard spectral analysis of heart rate variability (left) and blood pressure variability (right).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [APPENDIX.docx](#)