ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2018; 4(12): 47-51
www.allresearchjournal.com
Received: 13-10-2018
Accepted: 15-11-2018

Sunil Kumar Agrawala
Associate Professor, Department of Surgical Oncology, IMS & SUM Hospital, Bhubaneswar, Odisha, India

Mahesh Chandra Sahoo
Assistant Professor, Medical Research Laboratory, IMS & SUM Hospital, Bhubaneswar, Odisha, India

Correspondence
Mahesh Chandra Sahoo
Assistant Professor, Medical Research Laboratory, IMS & SUM Hospital, Bhubaneswar, Odisha, India

Incidence of head and neck cancer associated with papillomavirus in relation to smoking at a tertiary care centre

Sunil Kumar Agrawala and Mahesh Chandra Sahoo

Abstract
The trends in head and neck cancer incidence and smoking prevalence are studied, discussing where such trends parallel but also how and why they may not. In the public health efforts at tobacco control and education have successfully reduced the prevalence of cigarette smoking, resulting in a lower incidence of head and neck cancer. Vigilance at preventing tobacco use and encouraging cessation should continue, and expanded efforts should target particular ethnic and socioeconomic groups. However, an unfortunate stagnation has been observed in oropharyngeal cancer incidence and likely reflects a rising attribution of this disease to oncogenic human papillomavirus, in particular type 16 (HPV-16). For the foreseeable future, this trend in oropharyngeal cancer incidence may continue, but with time the effects of vaccination of the adolescent and young adult female population should result in a lower viral prevalence and hopefully a reduced incidence of oropharyngeal cancer. To hasten the reduction of HPV-16 prevalence in the population, widespread vaccination of adolescent and young adult males should also be considered.

Keywords: Head and neck cancer, smoking, human papillomavirus, HPV-16

Introduction
Barring skin and thyroid malignant growths, for all intents and purposes all carcinomas that happen in the head and neck locale emerge inside the upper aero digestive tract and associated adenexal structures. Taken together, carcinomas of the upper aero digestive tract, likewise named head and neck disease, will represent just 45,660 new tumors in 2007 or just 3.2% of every single occurrence threat [1] The mind dominant part of these head and neck malignancies are squamous cell carcinomas (SCCHN) with the majority of the rest of salivary organ carcinomas. To more readily comprehend etiologic affiliations and clinical administration/results, head and neck malignant growths are subcategorized by their site of beginning and yearly record for roughly 17,000 tumors of the oral cavity, 10,000 of the larynx, 10,000 of the oropharynx, and 2500 of the hypopharynx [1-3]. In this study, we investigate slants in head and neck malignant growth rate and relationship with smoking patterns or scarcity in that department, and the clarifications and general wellbeing suggestions for these relations.

Materials and Methods
From 2013 to 12018, 391 patients with non-thyroid head-and-neck malignant growth conceded for RT were incorporated into a planned report examining the enlistment of radiation induced HT. A total of 391 patients were treated at IMS and SUM Hospital, Bhubaneswar. The RT was conveyed with high-vitality straight quickening agents utilizing 4– 8MeV photons, at 2 Gy/day, 5 days/week with no arranged breaks. All patients were dealt with utilizing three-dimensional computer based treatment arranging. At Radiumhemmet, the last tumor retained portion was commonly 64 Gy. At IMS and SUM Hospital, the portion was 54 Gy when radiation was managed preoperatively and 66 Gy if just RT was arranged. The assimilated portion to the thyroid depended on the independently created portion designs. In all cases some portion of the thyroid was inside the objective volume.
Before inception of RT, serum tests were taken for TSH, triiodothyronine (T3) and thyroxine (T4) or free T4 (fT4). Patients were assessed and pursued with blood tests toward the finish

of RT and from there on with interims of 3months for the principal year, at that point each 6 to a year. All patients were pursued for at least 3 months after RT was finished. Obvious HT was characterized as a blend of expanded S-TSH level (ordinary range, 0.1– 5.0 mIU/L; from July 2002, 0.2– 4.0 mIU/L) with diminished dimension of all out S-T4 level (60– 140 nmol/L) or S-fT4 (10– 22 pmol/L; from July 2002, 10– 20 pmol/L) or in mix with inception of thyroxine substitution treatment. Treatment with levothyroxine was begun in every patient who had persevering rise of the dimensions of TSH in blend with clinical side effects of HT. Additionally in patients without clinical indications, yet with raised S-TSH, such treatment was begun when the (free) T4 level was not exactly the ordinary range.

The time from the beginning of RT to HT or to the last follow-up was broke down similarly as death in normal survival examination. The noteworthiness of contrasts between gatherings was evaluated by the Mantel-Haenzel (logrank) test. Multivariate investigations just as univariate examinations of continous factors were broke down with Cox relapse.

Results

Of 391 patients, 27 patients with thyroid medical procedure or realized thyroid illnesses previously head-and-neck malignant growth finding, 15 patients who were not given RT and 41 patients with deficient follow-up were prohibited from this investigation, leaving an aggregate of 308 patients for assessment. The explanation behind a lacking follow-up was mainly because of an early disappointment (n _ 33; mean _ SD survival after beginning of RT _ 6.2 _ 4.7 months) or that patients moved to another region gathering (n _ 8). There was no huge distinction between patients who were incorporated and the individuals who were definitely not. The clinical attributes of the patients and tumors are set out in Table 1. The middle follow-up time was 4.2 years (go, 3 months to 10.9 years). At the season of the last development, 94 of the 308 assessed patients were as yet alive (30.5%). For the living patients the middle follow-up was 6.5 years (run, 7 months to 9.8 years), and for the dead patients the middle follow-up was 2.7 years (go, 3 months to 10.9 years). Their ages extended from 21 to 94 years (middle, 65 years) at the season of conclusion. The greater parts of the patients were male and had a past history of smoking. Mean TSH level in serum before RT was 1.5 _ 1.3 mIU/L (0.02– 14.0). Larynx was the most continuous essential tumor site, and the least regular site was the nasopharynx. Illness arrange was 0 – II in 37% and III– IV in 54% of the patients. One hundred forty-two patients (46%) got RT as it were. One hundred forty-six patients (47%) got RT in blend with medical procedure. Eight patients (3%)m got RT with the expansion of chemotherapy. Twelve patients (4%) got a mix of RT, medical procedure, and chemotherapy. The mean radiation portion to the essential site was 63.3 _ 3.8 Gy (40.0 – 68.0). The RT dose to the neck was two-sided in 230 patients (75%) and one-sided in 78 patients (25%). Generally, 150 patients (49%) experienced medical procedure. Thirty-four patients (11%) got medical procedure that included the thyroid organ, and 124 patients (40%) got nonthyroidal medical procedure.

Fifty-two of the patients (17%) were determined to have obvious HT. The combined number of patients with HT after 1, 3, 5 and 10 years was 20, 46, 49, and 52, separately. This relates to 38%, 88%, 94%, and 100% of the complete hazard at comparing years. The middle time to the advancement of HT was 1.8 years (run, 0.3 to 8.1 years). Table 1 demonstrates the HT occurrence of the diverse treatment gatherings. The Kaplan-Meier actuarial danger of HT at 1, 3, 5, and 10 years after treatment for all patients was 7%, 19%, 20%, and 27%, individually (Fig. 1). We performed both univariate and multivariate examinations. In the univariate investigation with all out variables (Table 1), the data if RT to the neck was given as two-sided or one-sided (log rank [LR] _ 4.5, p _ 0.033), and if there were a careful mediation (LR _ 17.1, p _ 0.001), had a measurably critical effect on HT. A pattern was found proposing that the female sex was related with a higher hazard (LR _ 3.6, p _ 0.058). Utilizing Cox relapse investigation in the univariate examinations for continous factors (Table 2), the pre-RT TSH esteem was a noteworthy factor (relative peril [RH] _ 49.5, p _ 0.001). Table 3 shows the aftereffect of a multivariate investigation. Just noteworthy covariates from the univariate evaluations were incorporated together with age and sex. An expanded starting TSH esteem was a huge hazard factor for HT (RH _ 1.58, p _ 0.001). In the event that RT to the neck was given as respective treatment, it was additionally a noteworthy hazard factor (RH _ 0.37, p _ 0.02). The data about careful mediation (by and large, p _ 0.001) had an outstanding factually huge effect on HT (Table 3). In the event that medical procedure included the thyroid organ, it was a solid hazard factor (RH _ 4.74, p _ 0.001), yet nonthyroid medical procedure did not vary from any medical procedure whatsoever (RH _ 1.44, p 0.305). The pattern connecting the female sex with an expanded hazard for HT in the univariate examination was saved as a pattern in the multivariate appraisal (RH_ 0.56, p _ 0.063).

Table 1: Patient and tumor attributes and univariate investigations as for all out components and the danger of hypothyroidism (HT)

Factors	N	HT (%)	LR	*P* Value
Sex		35(15.1)	3.6	0.058
Male	231	17(22.1)		
Female	77			
Smoking history	221	43(19.5)	2.2	0.142
Yes	61	8(13.1)		
No	26	1(3.9)		
Unknown Diagnosis				
Hypopharynx	25	5(20.0)	4.8	0.569
Larynx	92	16(17.4)		
Nasopharynx	11	0		
Oral cavity	67	13(19.4)		
Oropharynx	72	13(18.1)		
Major salivary glands	14	2(14.3)		
Other/unknown	27	3(11.1)		
AJCC stage				
0	6	0	7.9	0.097
I	42	3(7.1)		
II	66	13(19.7)		
III	59	15(25.4)		
IV	107	17(15.9)		
Not staged	28	4(14.3)		
Neck irradiation				
Bilateral	230	45(19.6)	4.5	0.033
Unilateral	78	7(9.0)		
Surgery				
No surgery	150	16(10.7)	17.1	<0.001
Involving thyroid gland	34	14(41.2)		
Nonthyroidal Surgery	124	22(17.7)		

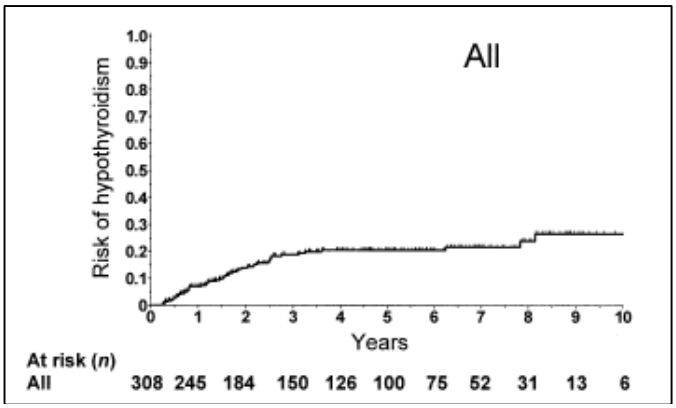

Fig 1: Kaplan-Meier curve of radiation-induced hypothyroidism in 308 head and neck cancer patients.

Discussion

In this investigation we affirm that HT is basic after outer RT for head-and-neck disease as portrayed already by

Table 2: Univariate examinations (Cox relapse) with deference to continuous factors and the danger of hypothyroidism

Factor	RH	CI	Wald	P value
Age	0.99	0.97-1.01	1.7	0.196
Initial TSH	1.51	1.35-1.70	49.5	<0.001
RT dose	0.97	0.91-1.03	1.2	0.274

Abbreviations: RH _ relative hazard; CI _ 95% confidence interval; Wald _ Wald statistic; TSH _ thyroid-stimulating hormone; RT _ radiotherapy.

Table 3: Multivariate analysis (Cox regression) with respect to the risk of hypothyroidism

Factor	RH	CI	Df	Wald	P value
Age(years)	0.99	0.97-1.01	1	1.7	0.218
Male sex	0.56	0.31-1.03	1	3.4	0.063
Initial TSH	1.58	1.4-1.79	1	53.9	<0.001
Surgery*			2	18.1	<0.001
0 vs. 1	4.74	2.23-10.1	1	16.3	<0.001
0 vs. 2	1.44	0.72-2.88	1	1.1	0.305
Neck irradiation*	0.37	0.16-0.85	1	5.4	0.02

Abbreviations: RH _ relative hazard; CI _ 95% confidence interval; *df*_ degrees of freedom; Wald _ Wald statistic; TSH _thyroid-stimulating hormone.

Components incorporated into the multivariate examination were noteworthy variables from the univariate investigations, and sex and age.

* Type of medical procedure: 0 _ no medical procedure; 1 _ medical procedure including thyroid organ; 2 _ nonthyroidal medical procedure; neck portion: 0 _ two-sided, 1 _ one-sided. others (4, 5, 6, 7, 8, 9) and without anyone else's input (10). The in general rate of HT in the present examination was 17%, and expanded to 41% if medical procedure that incorporated the thyroid organ was performed. This is proportional to the frequency figures announced in past examinations. The occurrence of radiation induced HT has anyway changed generously between various reports and the subsequent periods are frequently restricted. In the present material with nonthyroid head-and-neck malignancy patients we could break down the occurrence of HT up to 10 years after RT. The Kaplan-Meier chance for HT following 5 years and 10 years post irradiation was 20% and 27%, separately. Checking confusions of malignancy treatment is basic in the subsequent method for all disease survivors [11]. Radiation-actuated HT is an outstanding reaction that can be dealt with securely with levothyroxine. Tests for distinguishing a hypo functional thyroid ought to in this manner be incorporated into the assessment of patients treated with RT for tumors in the head-and-neck zone. Considering the proceeding with danger of HT in these patients, a long lasting TSH testing is justified. In any case, HT brought about by illumination to the neck is undefined from that happening precipitously. Hypothyroidism is a regular condition in an arbitrary populace test, with a predominance of about 2% in females [12]. It is more typical in ladies than in men [24], and the commonness increments with age [13]. Past investigations on the take a huge risk light has demonstrated that HT is more incessant in ladies than in men [14, 4]. In any case, in our accomplice of patients neither age nor sex was of factual centrality. The vast majority of the HT in the present investigation happens before 3 years after RT, yet a couple of patients create HT at later occasions. The reaction to radiation is administered by the intrinsic cell radio sensitivity, the energy of the tissue, and the manner by which cells are composed in that tissue [15]. Be that as it may, it isn't completely known why ordinary tissues presented to radiation keep on working for quite a long while after light and after that logically lose their capacity. On account of 131I treatment for hyperthyroidism, HT may create inside the first months after such treatment or in years [16, 17]. A rate of 20%– 40% in the primary year after treatment and an aggregate yearly occurrence of 2.8%–7.7% there, after have been accounted for [16, 18]. The instruments of this idle period don't appear to depend essentially on the quick multiplication of cells. Late radiation harms happen transcendently in gradually multiplying tissues however are not confined to these gradually reestablishing cell frameworks. Clinically late impacts seem to depend more on the all out portion and volume of radiation [19] and the measure of the radiation part [20]. The endocrine components of the thyroid organ are returning postmitotic cells and are generally radiation safe [15]. As made a decision from endothelial cells of different locales, the endothelial cells of the thyroid may have expansion cycles shorter than those of the endocrine cells. Consequently, harm to the endothelial cells of the thyroid slender system might be a vital instrument in both early and postponed radiation damage [21]. A substitute theory recommends that the intense and the late impacts of radiation are brought about by exhaustion of foundational microorganisms of the focused on cell-reestablishment tissues. Intense impacts rely upon the harmony between cell executing and compensatory replication of the stem and proliferative cells. The improvement recently impacts necessitates that foundational microorganisms have just a restricted proliferative limit [22, 23]. Pay for broad or rehashed cell executing may deplete this limit, bringing about possible tissue disappointment [23, 24]. It has likewise been recommended that distinctions in cell radiation affectability would clarify the inconstancy between patients in the seriousness of ordinary tissue difficulties after RT [25, 26]. On the off chance that the enlistment of thyroid brokenness after illumination could be clarified by varieties in cell radio sensitivity isn't know, yet endeavors to think about this issue should be finished. The radiation portion for thyroid brokenness is critical [28, 27]. In the present examination, we couldn't find that a higher RT portion to the essential site

had a critical connection with the danger of creating HT. Notwithstanding, when gathering the patients as per one-sided or two-sided neck light, we found a huge contrast, demonstrating that the volume illuminated is of significance for radiation-initiated HT. It has recently been recommended that immunologic parameters could be engaged with the pathogenesis of HT after RT [29, 30]. In the present investigation, we found that a high TSH esteem before RT, that may demonstrate immune system thyroid sickness, is a critical factor for the advancement of HT. Along these lines, thyroid hormones, as well as thyroid autoantibodies ought to be incorporated into the testing strategy before RT to the neck. In the most recent decade the indicative technique for utilizing TSH estimations has changed because of affectability upgrades in these examines, and it is presently perceived that serum TSH estimation is a more touchy test than serum fT4 for identifying marginal hypothyroidism or hyperthyroidism [31]. Expanding proof likewise demonstrates that plain HT as well as subclinical HT can have vital clinical impacts and prognostic ramifications on wellbeing [32]. This change did not influence our outcomes, as the most recent patient in our examination with HT was analyzed in December 2001. In the event that extra patients in our examination had been determined to have obvious HT and treated with thyroxine substitution treatment with this new reference interim isn't know. Speculatively an expanded rate could have happened bringing about an underestimation of the genuine HT frequency level. Another part of subclinical HT might be the conceivable danger of thyroid malignancy after corresponding TSH incitement of the illuminated organ. Assuming this is the case, levothyroxine substitution of patients with subclinical HT after RT to the neck appears to be reasonable. Additionally a low serum convergence of TSH is by all accounts a noteworthy hazard factor for different sicknesses, e.g., the improvement of dementia [33], expanded mortality as a result of cardio-vascular infections [34], and for breaks of the hip and vertebrae [35]. The proposed suggestion is presently that serum TSH fixations amid substitution treatment ought to be held inside the lower some portion of the wellbeing related reference interim (0.5 to 2.0 mIU/L) [36]. A past specialist has attempted unsuccessfully to diminish the rate of radiation-actuated HT with organization of thyroxine amid outside RT [37]. Besides, Zoberi *et al*. [38] have portrayed an imminent report plan with s.c.amifostine prophylaxis to patients with head-and-neck disease before every radiation division to diminish the long haul occurrence of HT. No outcome has yet been introduced yet the methodology is intriguing. Another method for diminishing the frequency of HT may theoretically be if the radiation portion to the thyroid could be constrained. The point of RT to head-and neck tumors is to convey fractionated RT that slaughters disease cells while saving ordinary tissue work. For instance, force tweaked RT guarantees exceptionally conformal portion disseminations around tumor focuses at the saving of generous segments of the basic organs included [39]. These basic organs frequently limit portion levels to the tumor. Given the consistently expanding frequency recently term radiation-initiated HT for patients with head-and-neck malignant growth, we suggest long lasting TSH screening after RT to the neck. Early thyroid hormone substitution treatment in patients getting to be hypothyroid is vital for keeping up ideal life quality in malignant growth survivors.

References

1. Jemal A, Seigel R, Ward E *et al*. Cancer statistics, 2007. CA Cancer J Clin. 2007; 57:43-66.
2. Carvalho AL, Nishimoto IN, Califano JA, Kowalski LP. Trends in incidence and prognosis for head and neck cancerin the United States: a site-specific analysis of the SEER database. Int. J Cancer. 2005; 114:806-808.
3. Jemal A, Seigel R, Ward E *et al*. Cancer statistics, 2006. CA Cancer J Clin. 2006; 56:106-130.
4. Vrabec DP, Heffron TJ. Hypothyroidism following treatmentfor head and neck cancer. Ann Otol Rhinol Laryngol. 1981; 90:449-453.
5. Mercado G, Adelstein DJ, Saxton JP *et al.* Hypothyroidism: A frequent event after radiotherapy and after radiotherapy with chemotherapy for patients with head and neck carcinoma. Cancer. 2001; 92:2892–2897.
6. Grande C. Hypothyroidism following radiotherapy for headand neck cancer: Multivariate analysis of risk factors. Radiother Oncol. 1992; 25:31-36.
7. Tami TA, Gomez P, Parker GS *et al.* Thyroid dysfunction after radiation therapy in head and neck cancer patients. Am JO to laryngol. 1992; 13:357-362.
8. Leon X, Gras JR, Perez A *et al.* Hypothyroidism in patientsLong-term incidence of radiation-induced hypothyroidism ● R. TELL *et al.* 399treated with total laryngectomy. A multivariate study. Eur Arch Otorhinolaryngology. 2002; 259:193-196.
9. Colevas AD, Read R, Thornhill J *et al.* Hypothyroidism incidence after multimodality treatment for stage III and IV squamous cell carcinomas of the head and neck. Int J Radiat Oncol Biol Phys. 2001; 51:599-604.
10. Tell R, Sjodin H, Lundell G *et al.* Hypothyroidism after external radiotherapy for head and neck cancer. Int J Radiat Oncol Biol Phys. 1997; 39:303-308.
11. Kattlove H, Winn RJ. Ongoing care of patients after primary treatment for their cancer. CA Cancer J Clin. 2003; 53:172-196.
12. Tunbridge WM, Evered DC, Hall R *et al.* The spectrum ofthyroid disease in a community: The Whickham survey. Clin Endocrinol (Oxf). 1977; 7:481-493.
13. Petersen K, Lindstedt G, Lundberg PA *et al.* Thyroid diseasein middle-aged and elderly Swedish women: Thyroid-related hormones, thyroid dysfunction and goitre in relation to ageand smoking. J Intern Med. 1991; 229:407-413.
14. Posner MR, Ervin TJ, Miller D, *et al.* Incidence of hypothyroidism following multimodality treatment for advanced squamous cell cancer of the head and neck. Laryngoscope. 1984; 94:451-454.
15. Hall EJ. Clinical response of normal tissues. In: Radio biology for the radiologists. 5th ed. Philadelphia: Lippincott, William sand Wilkins; 2000, 339-360.
16. Nofal MM, Beierwaltes WH, Patno ME. Treatment of hyperthyroidism with sodium iodide I-131. Jama. 1966; 197:605-610.
17. Willemsen UF, Knesewitsch P, Kreisig T, *et al.* Functional results of radioiodine therapy with a 300-Gy absorbed dose in Graves' disease. Eur. J Nucl Med. 1993; 20:1051-1055.
18. Holm LE, Lundell G, Israelsson A *et al.* Incidence of hypothyroidism occurring long after iodine-131 therapy for hyperthyroidism. J Nucl Med. 1982; 23:103-107.

19. Withers HR, Taylor JM, Maciejewski B. Treatment volume and tissue tolerance. Int. J Radiat Oncol Biol Phys. 1988; 14:751-759.
20. Thames HD, Jr, Withers HR, Peters LJ *et al.* Changes in earlyand late radiation responses with altered dose fractionation: Implications for dose-survival relationships. Int. J Radiat Oncol Biol Phys. 1982; 8:219-226.
21. Fajardo LF, Berthrong M, Anderson RE. Thyroid. In: Radiation pathology: Oxford University Press; 2001, 337-343.
22. Botnick LE, Hannon EC, Hellman S. Multisystem stem cellfailure after apparent recovery from alkylating agents. Cancer Res. 1978; 38:1942–1947.
23. Hellman S, Botnick LE. Stem cell depletion: an explanation of the late effects of cytotoxins. Int. J Radiat Oncol Biol Phys. 1977; 2:181-184.
24. Weichselbaum RR, Dahlberg W, Little JB. Inherently radio resistant cells exist in some human tumors. Proc Natl Acad Sci, USA. 1985; 82:4732-4735.
25. Johansen J, Bentzen SM, Overgaard J *et al.* Relationship between the *in vitro* radio sensitivity of skin fibroblasts and thee expression of subcutaneous fibrosis, telangiectasia, and skin erythema after radiotherapy. Radiother Oncol. 1996; 40:101-109.
26. Burnet NG, Wurm R, Nyman J *et al.* Normal tissue radio sensitivity-how important is it? Clin Oncol (R Coll Radiol). 1996; 8:25-34.
27. Hancock SL, McDougall IR, Constine LS. Thyroid abnormalities after therapeutic external radiation. Int. J Radiat Oncol Biol Phys. 1995; 31:1165-1170.
28. Constine LS, Donaldson SS, McDougall IR *et al.*, Thyroid dysfunction after radiotherapy in children with Hodgkin's disease. Cancer. 1984; 53:878-883.
29. Cutuli B, Quentin P, Rodier JF *et al.* Severe hypothyroidism after chemotherapy and locoregional irradiation for breast cancer. Radiother Oncol. 2000; 57:103-105.
30. Lundell G, Holm LE. Hypothyroidism following 131I therapyfor hyperthyroidism in relation to immunologic parameters. Acta Radiol Oncol. 1980; 19:449-454.
31. Demers LM, Spencer CA. Thyrotropin/thyroid stimulating hormone (TSH) measurement. Thyroid. 2003; 13:33-44.
32. Biondi B, Palmieri EA, Lombardi G *et al.* Effects of subclinical thyroid dysfunction on the heart. Ann Intern Med. 2002; 137:904-914.
33. Kalmijn S, Mehta KM, Pols HA *et al.* Subclinical hyperthyroidism and the risk of dementia. The Rotterdam study. Clin Endocrinol (Oxf). 2000; 53:733-737.
34. Parle JV, Maisonneuve P, Sheppard MC *et al.* Prediction of all-cause and cardiovascular mortality in elderly people from one low serum thyrotropin result: A 10-year cohort study. Lancet. 2001; 358:861-865.
35. Bauer DC, Ettinger B, Nevitt MC *et al.* Risk for fracture in women with low serum levels of thyroid-stimulating hormone. Ann Intern Med. 2001; 134:561-568.
36. Lindstedt G, Nystrom E. Increased risk of bone-fragility related fractures in TSH-suppressive thyroxine treatment. La¨kartidningen. 2002; 99:2844-2845.
37. Bantle JP, Lee CK, Levitt SH. Thyroxine administration durin gradiation therapy to the neck does not prevent subsequent thyroid dysfunction. Int J Radiat Oncol Biol Phys. 1985; 11:1999-2002.
38. Zoberi I, Wasserman TH, Chao KS. A prospective, nonrandomized study of the impact of amifostine on subsequent hypothyroidism in irradiated patients with head and neck cancers. Semin Radiat Oncol. 2002; 12:14-17.
39. Brahme A. Optimized radiation therapy based on radiobiological objectives. Semin Radiat Oncol. 1999; 9:35-47.