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رادیوبیولوژی و پرستاری انکولوژی
29-31 January 2025
Olympic hotel,Tehran ,IRAN

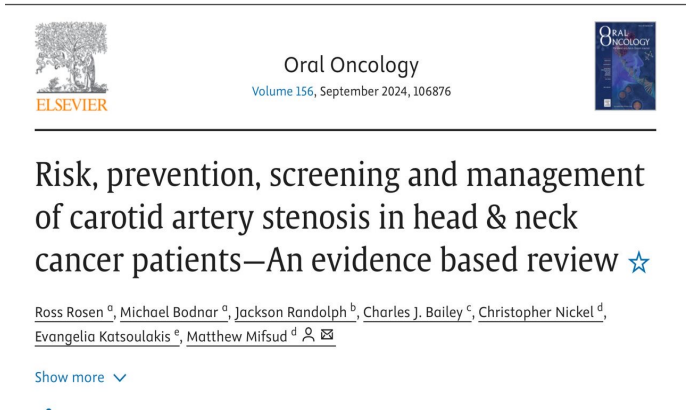
Peripheral artery disease in radiotherapy

Masoud sayad

Cardiologist, fellowship of cardio-oncology

References

- Braunwalds heart disease; textbook of cardiovascular medicine, 12th edition
- Herrmann cardio-oncology practice manual; 2022
- Washington manual of cardio-oncology; 2022
- ESC guideline of cardio-oncology; 2022
- ESC guideline of peripheral artery and aortic disease; 2024
- UpToDate; 2024



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Oral Oncology

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Risk, prevention, screening and management of carotid artery stenosis in head & neck cancer patients—An evidence based review ☆

Ross Rosen [a], Michael Bodnar [a], Jackson Randolph [b], Charles J. Bailey [c], Christopher Nickel [d], Evangelia Katsoulakis [e], Matthew Mifsud [d]

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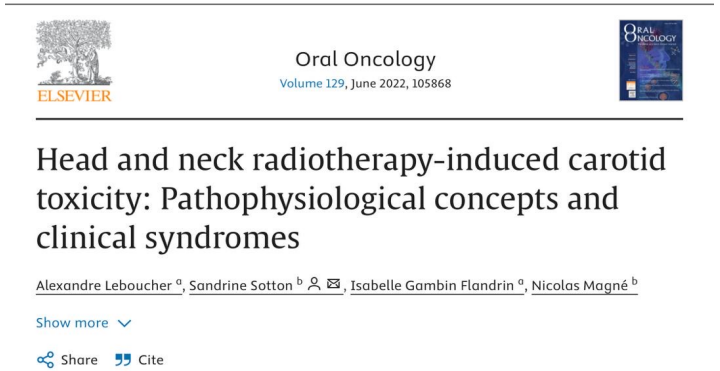

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Oral Oncology

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Head and neck radiotherapy-induced carotid toxicity: Pathophysiological concepts and clinical syndromes

Alexandre Leboucher [a], Sandrine Sotton [b], Isabelle Gambin Flandrin [a], Nicolas Magné [b]

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Introduction

- **PAD**: lower or upper extremity obstruction of arteries

but generally all arteries except coronary vasculature

- **PVD**: blood vessel (artery, vein, lymphatic) diseases (atherosclerosis, vasculitis, vasospasm,…)

- **Limb arteries**: 6P (pain, pallor, pulselessness, poikilothermia, paralysis, paresthesia)

Diagnosis: ABI

- **Mesenteric artery**: abdominal discomfort

Diagnosis: endoscopy, CTA , MRA , duplex ultrasound

- **Renal artery**: secondary HTN, malignant HTN , decreased renal function

Diagnosis: duplex ultrasound, CTA, challenge tests

Head and neck vessels

- **Carotid artery**: TIA, CVA, carotid artery rupture (carotid blowout syndrome)

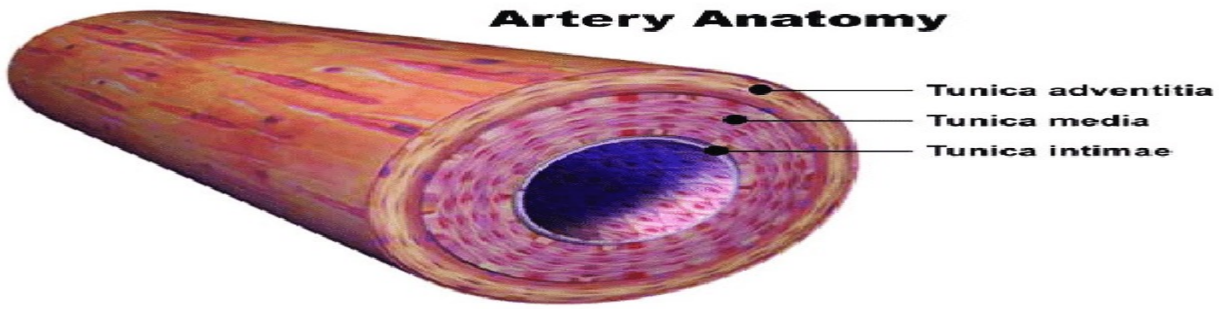
- **Cerebral vessels**: children are more susceptible to radiation-induced cerebral vasculopathy

Specially supraclinoid region of ICA and circle of Willis

Can occur both focal arteriopathy or moyamoya arteriopathy

Pathogenesis

- Large sized arteries are composed of 3 layers:



1) Tunica intima
2) Tunica media
3) Tunica adventitia

- Radiation induces endothelial damage, apoptosis and necrosis of endothelium
- Epithelial tissues undergo early toxicity

Loosening of endothelium → expression of adhesion molecules → inflammatory cells → oxidized LDL → atheromatous plaque, thrombosis, ulceration

- This process can be stopped and then restart by a second trigger
- Radiation damages all 3 layer
- Adventitia damage causes fibrosis
- Radiation is a potent injurious stimulus
- Radiation dose ≥2 Gy can alter endothelial cell function
- RT-induced atherosclerosis is often diffused and in uncommon locations

Risk factors

- Smoking
- DM
- HTN
- Hyperchlosterolemia
- CKD
- Insulin resistance
- CRP
- Radiation

- Up to 30% of patients develop significant CAS after head and neck radiation
- Canadian cancer registry showed 6% of patients with head and neck RT had stroke
- 7% of patients with RT for HL have carotid stenosis after 20 years and 4% develop stroke 5.6 years with median dose of 44 Gy
- In patients with head and neck cancer with higher dose(>50 Gy), CAS as high as 79% at a median of 9.5 years

Table 6 High-risk populations for carotid artery stenosis

Population	Prevalence of carotid stenosis (%)
>60 years + CVRFs (hypertension, CAD, current smoking, first-degree family history of stroke)[210]	Two CVRFs: 14% Three CVRFs: 16% Four CVRFs: 67%
Hypertension + cardiac disease[211]	22%
HD[212]	• In HD patients, prevalence of carotid stenosis is high, and is associated with high peri-operative and long-term stroke or death rates • Carotid stenosis is a predictor of death in patients with long-term dialysis and aged ≥70 years at time of surgery • Lower risk if previous renal transplant.
PAD[213]	23.2%
Severe CAD (before CABG)	• Almost 20%[214] • Carotid bruit and T2DM: increased predictive value[215] • Carotid stenosis = risk factors for peri-operative stroke.[215]
Carotid bruit[216]	31%
Previous neck irradiation[217]	21.7% (70%–99% stenosis)

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CVRFs, cardiovascular risk factors; HD, haemodialysis; PAD, peripheral arterial disease; T2DM, type 2 diabetes mellitus.

- Risk of stroke after neck RT increases 5-6 times higher than general population

➢Traditional cardiovascular risk factors (can be indirect consequence of cancer and its therapy)

➢Radiation dose>30-35 Gy

➢Dose-response relationship, as low as 10 Gy

➢Age>35 y/o

➢Time since radiation

➢Other drug therapies may contributing vascular disease:

✓ICIs: GCA with adventitia inflammation

✓BCR-ABL TKI: Nilotinib, Ponatinib

✓Platinium-based chemotherapies

✓Stroke was higher among brain tumor patients who received both RT and alkylating agents

❖Radiation field:

Circle of Willis confer higher rates of cerebrovascular events than focal brain radiation

Radiation fields that include lower CCA in breast cancer radiation have not been associated with increased incidence of stroke

- HPV status: increased inflammation and can procede atherosclerosis

❖RT techniques:

Preserving large vessels is not perform in planning

Carotid artery can deliver more radiation by IMRT rather than 3D-CRT

Accelerated fractionation reirradiation techniques was associated with carotid blowout syndrome

Risk stratification

Cancer carries a 2-fold higher risk of arterial thromboembolism

- Baseline CV risk assessment should be estimated by risk scores
- ECG: AF (a mjor cause of stroke)
- BP measurement
- Lab tests (lipid panel, BS, HbA1C)

- Duplex ultrasound for baseline assessment ⟶ not recommended, just for patients with neurological signs and symptoms

- Use available CT scans for atherosclerotic changes

Prevention and prophylaxis

- LDL lowering agents: improve outcomes even with no known coronary or cerebrovascular disease
- High risk patients (concurrent platinium) need primary prevention with high dose of statins
- Selection of statins that are not metabolized by CYP3A4 is recommended
- BP keep< 130/80 with ACEIs or ARBs
- BS controle with cardiocentric approach

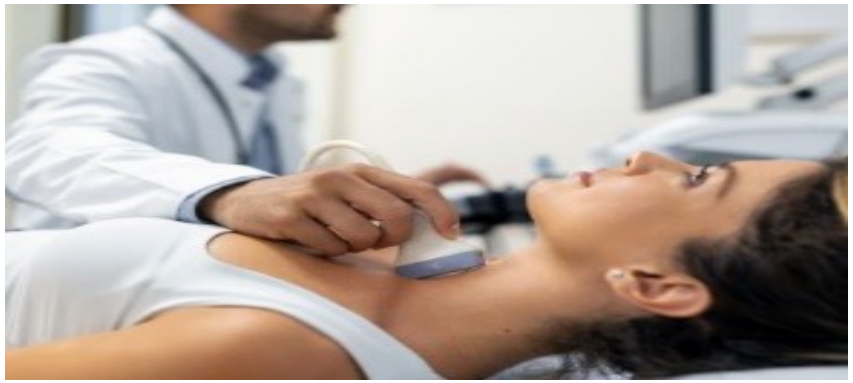
- Smoking is absolutely prohibited
- Emphasise on activity
- Keep body weight normal
- Diet rich in food and vegetables
- Patients with prior vessel hemorrhage should refer to neurology/neurosurgery specialist for risk assessment
- Patients with prior stroke should receive ASA
- In lower exterimity PAD, Clopidogrel is prefered

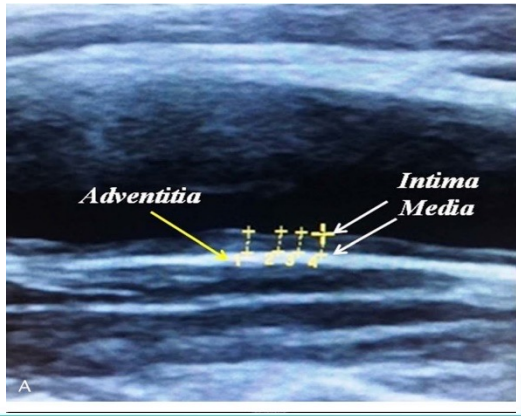
Screening

- Many patients with stenosis remain asymptomatic, so routine screening has been suggested
- Modalities:

✓**Ultasound**: significant increased arterial stiffness post-RT

IMT: the mainstay of screening, >0.9 is abnormal

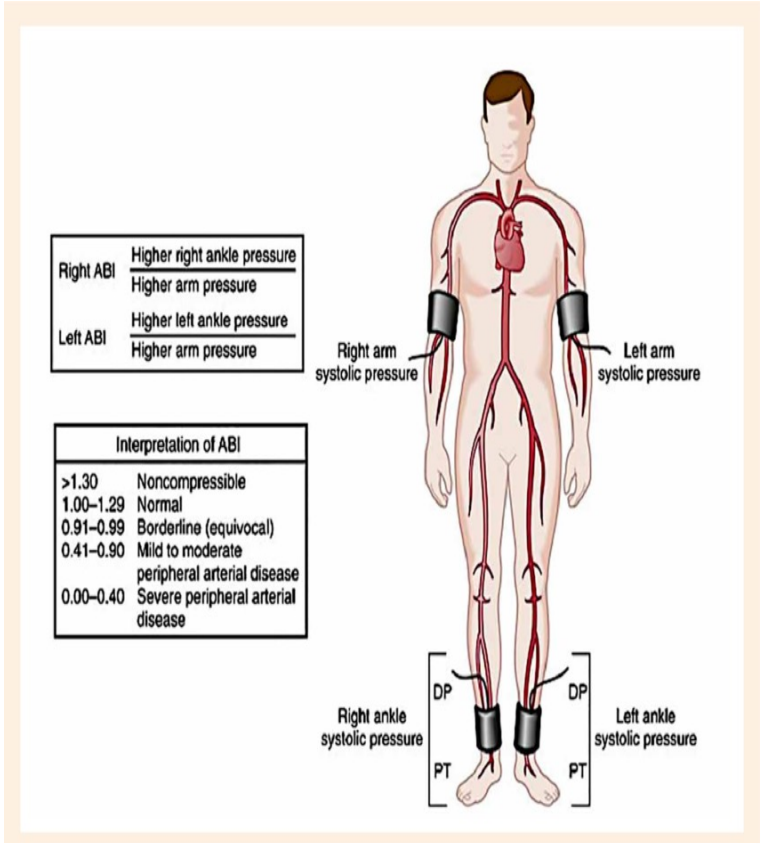




- ✓**ABI**: for lower extremities

  every 6-12 months for patients received RT to major vessels of lower exterimity

- ✓**CTA , MRA**: for exact estimation of stenosis



Surveillance

- UpToDate: carotid sonography 2 years after completion of RT and then every 3 years

- Herrmann: carotid sonography 1 year after completion of RT in **high risk patients** (determined by radiation dose and cardiovascular risk) and repeated every 2 years

Recommendation in childhood cancer survivors with cranial radiation:

- **Neuroimaging** in high risk patients (radiation field include circle of Willis, whole radiation dose≥ 24 Gy):

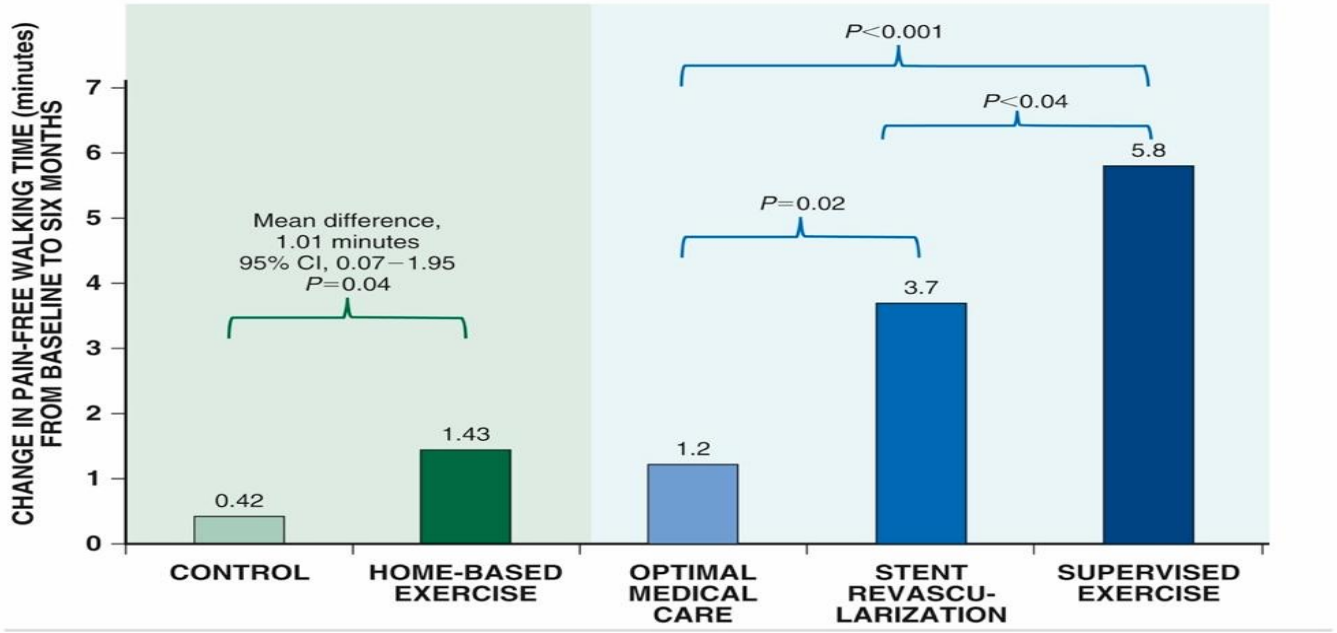
  5 years after RT and every 5 years indefinitely with both brain MRI and MRA.

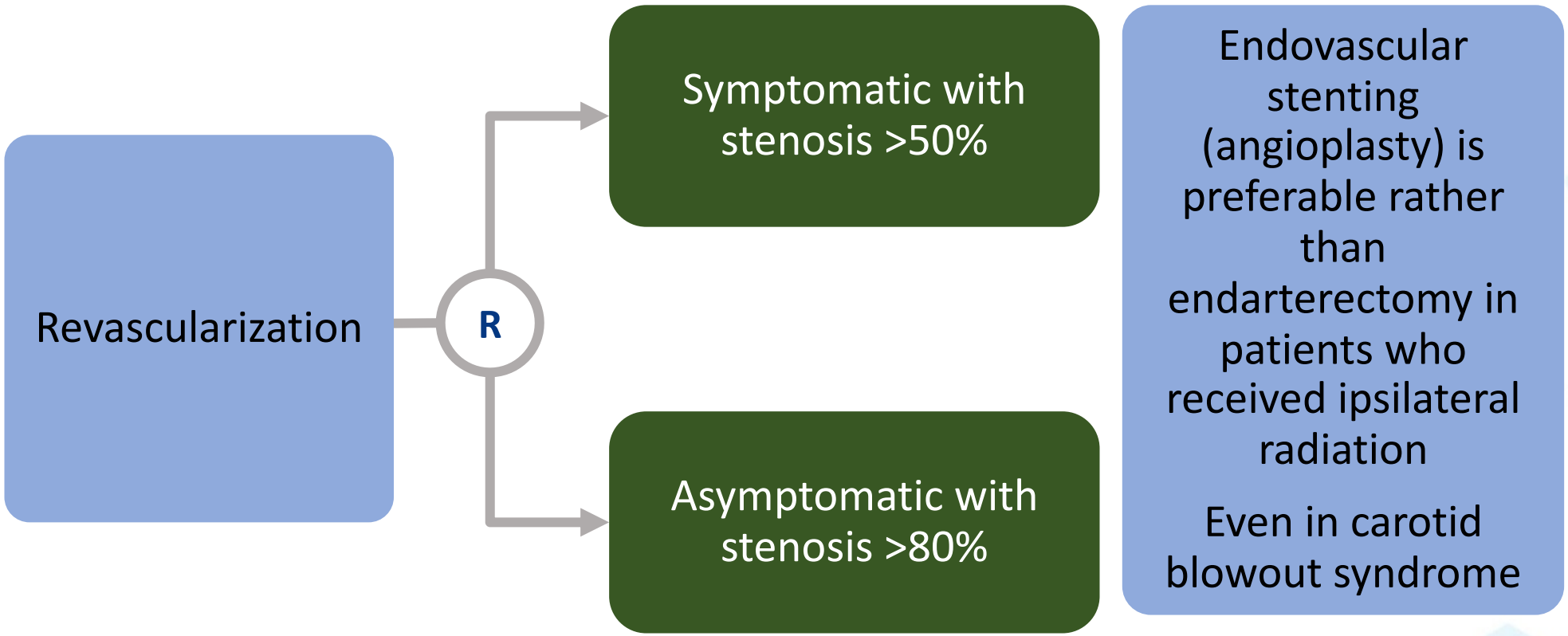
- **Lab testing** (lipid panel, BS, HbA1C) for modifiable risk factors of stroke

Treatment

- High dose of statin: very low LDL target (<70 mg/dl) , if target was not achieved combination therapy recommended
- Antiplatelets:
  - PLT>10000 : monotherapy with ASA
  - PLT>30000 : DAPT
  - PLT>50000 : anticoagulation
  - PLT>100000 : fibrinolytic

- Vasodilators (nitrates, pentoxifyllin, cilostazol) not recommended
- Supervised and home-based exercise training




Revascularization
R
Symptomatic with stenosis >50%
Asymptomatic with stenosis >80%
Endovascular stenting (angioplasty) is preferable rather than endarterectomy in patients who received ipsilateral radiation
Even in carotid blowout syndrome

Take home messages

- PAD is a common vascular damge after radiotherapy
- IMT is mainstay of screening for carotid artery stenosis
- Modifiable cardiovascular risk factors should be managed aggressively prior, during, ad after cancer treatment
- Statins are recommended in all patients who received radiation
- High dose statin is recommended in high risk patients with target LDL <70 mg/dl

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Thanks for your attention