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Endovascular treatment for carotid stenosis developing after neck radiotherapy

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ABSTRACT

Aims: One of the causes of carotid stenosis is radiation therapy to the neck area. Cervical irradiation is frequently used in the treatment of head and neck cancers. However; the ionizing effect of radiation causes arteritis, which can lead to acceleration of fibrosis or atherosclerosis, thrombosis, stenosis, or occlusion. Carotid stenosis due to radiation is relatively rare. Accordingly, in this study, our aim was to assess the feasibility, safety and preliminary efficacy of endovascular therapy for carotid stenosis developing after neck radiotherapy.

Methods: This study was a retrospective review of a prospectively maintained database of a consecutive unselected group of symptomatic and asymptomatic patients with carotid artery stenosis developing after neck radiotherapy. Data was collected from 2017 to 2023. A total of 17 patients who developed carotid stenosis due to neck radiotherapy were included in the study. Neck irradiation was applied in 76.5% of cases due to laryngeal cancer. All statistical analysis was performed using R version 4.2.1 (The R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org). Univariate analysis was performed using c2 and Wilcoxon tests. Cumulative survival estimates were assessed using the life-table method.

Results: One patient had a technical failure due to a difficult aortic arch. Because of the degree of stenosis (40≤) was not serious in conventional angiography of 2 patients, medical follow-up was decided. 3 patients were admitted to the emergency department due to acute ischemic stroke. Endarterectomy was performed in 4 patients due to the complex structure of the aortic arch and carotid arteries for carotid artery stending. The number of patients with stenosis in the right carotid was 10, while the number of patients with stenosis in the left carotid was 7. No restenosis was observed in patients with stent placement in follow-up carotid Doppler and CT angiography performed 3 months later. Additionally, no new neurodeficit was observed in the neurological examinations 3 months later.

Conclusion: This retrospective study demonstrates that endovascular treatment for carotid stenosis developing after neck radiotherapy is safe, effective and reliable.

Keywords: Carotid stenosis, neck radiotherapy, endovascular treatment, carotid stending, stroke

INTRODUCTION

Carotid artery stenosis is one of the important causes of ischemic stroke. One of the causes of carotid stenosis is radiation therapy to the neck area. Cervical irradiation is frequently used in the treatment of head and neck cancers. However; the ionizing effect of radiation causes arteritis, which can lead to acceleration of fibrosis or atherosclerosis, thrombosis, stenosis, or occlusion (Figure 1). It also causes fibrosis in soft tissue and skin (Figure 2).[1-3]

Radiation-induced carotid artery stenosis is a major high-risk entity for carotid endarterectomy. Open surgical therapy for patients with radiation-induced lesions has been associated with higher rates of stroke, cranial nerve damage, and problems with wound healing such as necrosis, infection, and skin breakdown. Therefore, endovascular treatment is more advantageous than open surgery.[4,5] However, high rates of restenosis and reintervention have been reported in patients with radiation-induced carotid stenosis.[6,7] Carotid stenosis due to radiation is relatively rare. Accordingly, in this study, our aim was to assess the feasibility, safety and preliminary efficacy of endovascular therapy for carotid stenosis developing after neck radiotherapy.

METHODS

Study Design

This study was a retrospective review of a prospectively maintained database of a consecutive unselected group of symptomatic and asymptomatic patients with carotid artery stenosis developing after neck radiotherapy. Data was collected

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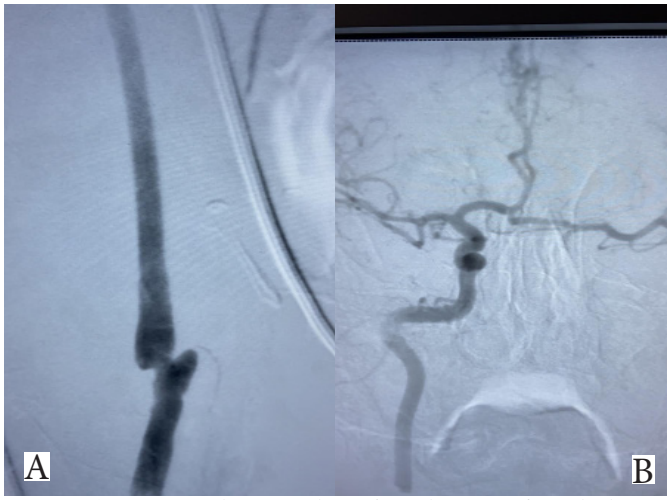

Figure 1. a) Conventional angiography performed 13 years after radiotherapy shows a decrease in carotid artery calibration and stenosis. b) Because of the same patient's left carotid is occluded, the entire anterior system filling with right carotid contrast material injection

Figure 2. A patient who received radiotherapy to the neck area due to laryngeal cancer. Atrophy, scar tissue on the skin and tracheostomy are observed in the neck area

from 2017 to 2023. This study was approved by the Selçuk University Ethics Committee with a waiver of informed consent (Date: 13.12.2023, Decision No: 2024/30). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients

A total of 17 patients who developed carotid stenosis due to neck radiotherapy were included in the study. Neck irradiation was applied in 76.5% of cases due to laryngeal cancer. The number of patients who received radiotherapy due to hematological and other cancers such as parotid, thyroid of the neck area was 23.5%. Consecutive patients with carotid stenosis developing after neck radiotherapy based on computed tomography angiography, magnetic resonance imaging angiography or carotid artery doppler ultrasound were included in this study. The degree of carotid artery stenosis was assessed on conventional angiography according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. The choice of CAS was made based on the individual judgment of the treating practitioner, based on clinical experience and the learning curve, as well as the patient's anatomical considerations regarding the feasibility of carotid artery stending (CAS). During the study period, 11 patients with carotid artery stenosis after neck irradiation were selected for carotid artery stending. We applied medical treatment to 2 patients while 4 patients were give to open surgery. The choice of carotid artery stending was made based on the individual judgment of the treating practitioner, based on clinical experience and the learning curve, as well as the patient's anatomical considerations regarding the feasibility of carotid artery stending and the contraindication to carotid open surgery. Modified Rankin Score (mRS) of the patients was checked at admission and at the 3-month follow-up.

Mean age was 60.7± (SD) 15.8 (range, 37-84 years), and 82.4% were men. Demographic and clinical characteristics are listed in Table 1. We did not apply general anesthesia to any patient during the procedure.

Table 1. Demographic and clinical characteristics in patients with carotid stenosis developing after neck radiotherapy

Characteristic	Value n (%)
Age, mean±SD years (range)	60.7±(SD)15.8 (range, 37-84)
Sex, number (%)	
Male	14 (82.4)
Female	3 (17.6)
Risk factors, number (%)	
Hypertension	8 (47.1)
Diabetes	4 (24.5)
Smoking	14 (82.4)
Hypercholesterolemia	3 (17.6)
Coronary disease	6 (35.3)
Patients with laryngeal cancer	13 (76.5)

SD: Standard deviation

Technique and the Device Description

All of the endovascular interventions were performed with a 6-8F sheath (short or long) via femoral, radial or brachial artery puncture. The guiding catheters (7F or 8F) were used more often than long sheaths. One or more treatment strategies were applied for the carotid stenosis (carotid stenting and/or balloon angioplasty). Protégé RX Self-expanding, Balton® Carotid self-expanding stent with delivery system RX, MER device were used for carotid stenosis. Stent models, diameters and lengths vary significantly depending on the characteristics of the carotid lesion and the operator's preferences. Digital subtraction angiography was performed to evaluate carotid stenosis. Carotid angiographic images were obtained from anterior to posterior angles, and multiple images were taken. It was also focused to improve stenosis image quality.

Statistical Analysis

All statistical analysis was performed using R version 4.2.1 (The R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org). Univariate analysis was performed using c2 and Wilcoxon tests. Cumulative survival estimates were assessed using the life-table method.

RESULTS

The smoking rate of these patients was 82.4%. Hypertension was the second most common condition with 42.1% (Table 1).

One patient had a technical failure due to a difficult aortic arch. Because of the degree of stenosis (40≤) was not serious in conventional angiography of 2 patients, medical follow-up was decided. 3 patients were admitted to the emergency department due to acute ischemic stroke. Endarterectomy was performed in 4 patients due to the complex structure of the

aortic arch and carotid arteries for carotid artery stending. We performed all angiography procedures under local anesthesia, including patients taken from the emergency department. We did not use a cerebral protection device in any of the patients in whom we performed carotid stenting. None of the patients had stent thrombosis during the procedure. Additionally, no patient developed dissection or major stroke.

The number of patients with stenosis in the right carotid was 10, while the number of patients with stenosis in the left carotid was 7. No restenosis was observed in patients with stent placement in follow-up carotid Doppler and CT angiography performed 3 months later. Additionally, no new neurodeficit was observed in the neurological examinations 3 months later. There were 3 patients taken from the emergency department to the angiography suite due to stroke. Before the procedure, mRS was between 1-3. At their 3-month follow-up, the neurological examination of 2 patients was normal. The mRS of 1 patient decreased from 3 to 1 (Table 2). Medical follow-up decision was made for 2 patients. The neurological examination of these patients 3 months later was normal. Additionally, there was no increase in the degree of stenosis in control imaging.

Table 2. The endovascular procedures and clinical characteristics in patients with carotid stenosis developing after neck radiotherapy

Treatment selection	**Value n (%)**
Medical	2 (11.8)
Stending	11 (64.7)
Open surgery	4 (23.5)
Mortality	none (0)
Use of cerebral protection device	none (0)
Anesthesia in angiography	
Local	17 (100)
General	none (0)
Side	
Right	10 (58.8)
Left	7 (41.2)
Symptomatic stenosis, mRS score, mean±SD (range)	5 (29)
mRS before treatment	0.4±0.94 (0-3)
mRS after treatment	0.06±0.25 (0-1)

mRS: Modified rankin score, SD: Standard deviation

DISCUSSION

No patient died after 3 month. Also no patient developed a major or minor stroke. This study showed that the result of endovascular treatment for carotid artery stenosis after neck irradiation can be considered satisfactory. The Stent-Protected Percutaneous Angioplasty and Carotid Endarterectomy and EVA-3S studies showed stroke and death rates of 7.7% and 9.6%, respectively.[8] Our results were better compared to this large-scale study. However, it should be emphasized that all patients in this study presented with symptomatic tight atherosclerotic stenosis, which is associated with a higher risk of embolism during endovascular treatment. In our study, only 29% of the patients were symptomatic and the stenoses were non-atherosclerotic lesions. In another multicenter study, the combined stroke and death rates were 1.5% after 1 month.[5] The results in this study were much better, similar to ours.

We could not place the stent in only one patient. The technical success rate of endovascular treatment in our study was good according to intention-to-treat analysis. Other studies had a similarly high success rate.[5,8] Endovascular treatment may sometimes not be perform due to vascular access problems, extensive aortoiliac occlusive disease or the complex anatomy of the aortic arch. In our patient, the aortic arch prevented intervention from both the arm and femoral access.

Our clinical results were satisfactory at the end of the 3th month as well as at the end of the process. In addition, no occlusion or restenosis was observed in the control Doppler and CT angiography performed at the end of the 3th month. Favre et al.[5] stated that statin use positively affects long-term results in stenting carotid stenosis that develops after radiation. Therefore, they recommended the use of statins in patients receiving neck radiotherapy. In their study, the survival rate without developing new neurological deficits was 93% at 3-year follow-up. The number of patients in whom the procedure failed or who developed restenosis during the 3-year follow-up was 27. In our study, we did not use statins in any patient who did not have atherosclerosis. But it should also be emphasized that; while they presented their 3-year results, we presented their 3-month results.

Radiotherapy applied to head and neck region damages artery walls through three mechanisms.[9] The first mechanism is that radiation causes ischemia by causing occlusion in the vasa vasorum. Thus, fibrous tissue develops instead of elastic tissue and muscular fibers layers. This process leads to focal sclerosis. The second mechanism is that fibrous tissue causes occlusion in the artery lumen. Muzaffar et al.[10] demonstrated that a significant increase in arterial wall thickness within the first year after radiotherapy. These two mechanisms are important reasons for the development of restenosis after carotid stenting. The other mechanism is the acceleration of atherosclerosis process. The time interval the flow pattern in the carotids deteriorates after radiation is variable. In our study, it ranged from 3 to 22 years. In general, this interval varies between 2 and 30 years in studies.[4,11] The neck radiotherapy does not always lead to carotid artery occlusion or stenosis. It varies depending on the type of cancer in the neck area. Carotid stenosis is more common in the laryngeal carcinoma and nasopharyngeal. It has also been associated with age, coronary artery disease and smoking. It is observed more frequently in local cancers originating from the neck region than in hematological diseases.[9] In most of our patients, the reason was radiotherapy due to laryngeal cancer. Some studies claim that radiotherapy-induced ischemia also causes atherosclerosis in the carotid artery. However; there are studies suggesting that there is no relationship between radiotherapy and atherosclerosis.[5] Stenosis due to radiotherapy is observed especially in the common carotid arteries. Stenosis due to atherosclerosis develops especially at the origin and proximal segment of the internal carotid artery. In our study, common carotid involvement was also high. The cause of death of patients with carotid stenosis due to radiotherapy after stenting was usually cancer recurrence. Stroke or heart attack were less common causes of death. It is remarkable that in our study, no one died due to cancer, cerebrovascular or heart disease at the end of the 6-month follow-up. The question of when to intervene in carotid stenosis in cancer patients who have received radiotherapy is unclear. Stent placement is recommended for stroke prevention in patients with potentially severe stenosis. But it still needs to be evaluated according to the patient. The death and ischemic-hemorrhagic stroke have been reported

in large series studies using open surgery. There were also restenosis, nerve injury, and delays in wound healing.[12] The treatment outcomes of our patients were better compared to these patients who underwent open surgery. Additionally, our results were better than the mid-term results of open surgery. Other carotid stenting studies comparing with open surgery have similar results.[5] Therefore, it seems possible to recommend carotid artery stending as the primary treatment for stenosis occurring after neck irradiation. We did not use a cerebral protection device in our study. In other studies, different amounts of cerebral protection devices were used. Cerebral protection device is used against embolism complication. We think that the risk of embolism is reduced in these patients because they do not have atherosclerosis. Therefore, there is no need to use a cerebral protection device in the treatment of radiotherapy-related stenosis.

Limitations

This study has several limitations, including the relatively small sample size, its retrospective design and the we did not have a control group of medically treated carotid stenosis occlusions.

CONCLUSION

This retrospective study demonstrates that endovascular treatment for carotid stenosis developing after neck radiotherapy is safe, effective and reliable.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Selçuk University Ethics Committee (Date: 16.01.2024, Decision No: 2024/30).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution and analysis of the paper and that they have approved the final version.

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