



**Management of pseudoaneurysm of internal carotid artery  
in post-irradiated nasopharyngeal carcinoma patients**

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Review

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3 **Management of pseudoaneurysm of internal carotid artery in post-**  
4 **irradiated nasopharyngeal carcinoma patients**  
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**Abstract**

*Objective:* Massive epistaxis due to ruptured pseudoaneurysm of internal carotid artery (ICA) is an often-fatal complication of radiation treatment for patients with nasopharyngeal carcinoma. We would like to review the clinical characteristic and predictors of survival in patients suffering from this serious complication after radiotherapy.

*Study Design.* Retrospective case series.

*Methods.* Review of the clinical records and radiological investigations of the post-irradiated NPC patients with ICA pseudoaneurysm diagnosed with digital subtraction angiogram in Queen Mary Hospital from January 2003 to December 2012. Risk factors analyzed for survival included gender, size of initial tumor, history of second course of radiotherapy, history of previous maxillary swing nasopharyngectomy, presence of persistent disease, successful initial haemostasis, successful airway control and endovascular treatment.

*Results.* Twenty-six were included in the analysis. 23 patients underwent endovascular treatment and 20 (87%) had successful control of the bleeding. 18 (69%) patients survived. Univariate analysis showed that successful temporary control of bleeding and airway control were associated with survival.

*Conclusion.* Prompt bleeding control and airway management is necessary to improve survival. Endovascular treatment is a good definitive treatment option with a high success rate.

**Key Words:** carotid blowout; carotid artery pseudoaneurysm; epistaxis, nasopharyngeal carcinoma, complication of radiotherapy

**Level of Evidence:** Level 4 (Case series)

## Introduction

Nasopharyngeal carcinoma (NPC) endemic in Southern China (WHO type II and III) is a highly radiosensitive malignancy and radiotherapy is the mainstay of curative treatment<sup>1</sup>. For advanced local recurrences, which are beyond surgical salvage, a second course of external radiotherapy is often administered, either for curative intent or for palliation.

However, radiotherapy can lead to undesirable complications in view of the close proximity of the nasopharynx to radiosensitive structures. These complications include ototoxicity, xerostomia, trismus, temporal lobe necrosis, osteoradionecrosis of the skull base and pseudoaneurysm of internal carotid artery (ICA)<sup>2,3</sup>. The detrimental effect would be even more pronounced after a second course of external radiotherapy, with the reported cumulative incidence of long-term post-reirradiation sequale of 24% and treatment mortality of 1.8%.

Rupture of pseudoaneurysm of ICA is a rare complication of radiotherapy treatment of NPC. However, it is associated with high morbidity and mortality. It is an ear, nose and throat (ENT) emergency because patients with rupture of ICA pseudoaneurysm would present with massive epistaxis, which is difficult to control. Joint efforts of the ENT surgeon, interventional radiologist and neurosurgeon are necessary for successful management of the condition<sup>4</sup>.

In the literature, there are few small retrospective studies and case reports on the disease condition<sup>5-10</sup>. Some studies are focused on the neurosurgical approach of management<sup>4,11-13</sup>. The aim of the current study is to review the clinical characteristics of post-irradiated NPC patients who suffered from rupture of ICA pseudoaneurysm and the factors for successful management, particularly from the

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3 ENT perspective. We would also try to identify survival predictors, in order to  
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5 improve the current management, and hence survival of this group of patients.  
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### 8 9 10 **Materials and Methods**

11 From January 2003 to December 2012, post-irradiated NPC patients who  
12 presented with significant epistaxis to the Queen Mary Hospital and were diagnosed  
13 to have ICA pseudoaneurysm on angiogram were included in the review. All patients  
14 were subjected to digital subtraction angiography (DSA), which was performed via  
15 femoral artery catheterization. Angiograms of both carotid and vertebrobasilar arteries  
16 were performed. Those who did not receive an angiogram were excluded.  
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19 Our management protocol of post-irradiated NPC patients with suspected ICA  
20 pseudoaneurysm rupture is as follows. First, the patient would be admitted to the  
21 hospital for an urgent ENT assessment and management. The ENT surgeon would  
22 estimate the amount of blood loss and assess the site of bleeding (anterior or  
23 posterior). The bleeding may stop spontaneously as sentinel bleeding. If the bleeding  
24 was persistent, he would then try to control the bleeding temporarily by anterior and  
25 posterior packing with nasal tampon and balloon of the urinary catheter. If there were  
26 risk of aspiration and airway compromise from the massive epistaxis, he would decide  
27 whether to proceed to intubation, cricothyroidotomy or tracheostomy for airway  
28 protection. If pseudoaneurysm bleeding was suspected, an urgent angiogram would  
29 be jointly performed by the interventional radiologist and neurosurgeon to locate the  
30 source of bleeding. Once the diagnosis of pseudoaneurysm of the internal carotid  
31 artery was confirmed, they would decide on the definitive treatment. Definitive  
32 treatment included endovascular treatment in the same session or open extracranial-  
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3 intracranial bypass. Figure 1 is the flow chart of the management algorithm of  
4 suspected ICA pseudoaneurysm rupture in post-irradiated NPC patients in our center.  
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7 Retrospective review of the clinical records and radiological investigations of  
8 this group of patients were performed. The demographic data, NPC stage at initial  
9 presentation, treatment regimen, number of courses radiotherapy, type of radiotherapy  
10 received and history of maxillary swing nasopharyngectomy were retrieved. Details  
11 on the management from the initial epistaxis and airway control to the definitive  
12 treatment with endovascular or open surgical procedures were reviewed.  
13 Radiological features of the pseudoaneurysm were also recorded. The patients'  
14 outcome including mortality and morbidity, either from the rupture of  
15 pseudoaneurysm or treatment related, were analyzed.  
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27 Statistical analysis was performed with the Statistical Package for Social  
28 Sciences (version 21.0; SPSS Inc, Chicago, IL). Chi-square test was used for  
29 univariate comparisons of survival predictors. A p-value of  $< 0.05$  was taken as  
30 statistically significant.  
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## 39 **Results**

### 40 Demographics and initial tumor staging

41  
42 Twenty-six post-irradiated nasopharyngeal carcinoma patients with  
43 pseudoaneurysm of internal carotid artery were identified during the study period.  
44 The median age was 53.5 years (41 – 70 years). The male sex was more affected with  
45 the male to female ratio of 21:5. Five patients had T1 NPC at presentation, 8 with T2,  
46 10 with T3 and 3 with T4 diseases. Eleven patients had received concurrent  
47 chemotherapy during the primary radiotherapy treatment.  
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3 All patients had received radiotherapy with curative intent. Twenty-four  
4 patients had the conventional 2-dimensional (2D) radiotherapy. Two patients had the  
5 intensity-modulated radiotherapy (IMRT). The mean radiation dosage received was  
6 67.2Gy (62 – 70Gy). The mean duration of epistaxis presentation with ruptured  
7 pseudoaneurysm from the completion of primary radiotherapy treatment was 101.5  
8 months (3 – 308 months).  
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16 Eighteen patients (70%) had local NPC recurrence. Eight patients (32%) with  
17 recurrence were treated with another course of radiotherapy only. The other ten (38%)  
18 patients had undergone maxillary swing nasopharyngectomy, which would be offered  
19 to patients with resectable local recurrence in our center, and adjuvant radiotherapy.  
20 Hence, all these eighteen patients underwent a second course of radiotherapy. The  
21 mean additional radiation dosage received was 44.8Gy (42 – 60Gy). The mean  
22 duration of bleeding from the second radiotherapy treatment was 65.4 months (3 –  
23 164 months).  
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#### 37 Disease status

38 Eight patients (31%) were known to have biopsy-proven local NPC recurrence  
39 at the time of pseudoaneurysm rupture. Five of them previously received a second  
40 course of radiotherapy and two had maxillary swing nasopharyngectomy and adjuvant  
41 radiotherapy. However, these 7 patients developed further recurrence despite re-  
42 treatment of curative intent. Only one patient had extensive local recurrence and was  
43 not offered either another course of radiotherapy or surgery.  
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#### 55 General health

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3 None of the patients in the group had history of stroke or was put on  
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5 antiplatelet or anticoagulation medications. Six patients (23.1%) had hypertension and  
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7 were on anti-hypertensive for control. Two patients (7.7%) had diabetes mellitus.  
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#### 10 11 12 ENT management

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14 With regard to the ENT management, successful temporary control of  
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16 bleeding was achieved in 17 patients (65%). Among which, 10 patients require  
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18 posterior nasal packing. There were 9 patients (35%) who had failed control of  
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20 bleeding despite anterior and posterior packing.  
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23 Interventions for airway protection were performed on 17 patients. Among  
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25 which, 9 patients were intubated and 8 required cricothyroidotomy or tracheostomy  
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27 because of severe trismus after radiotherapy. Seven out of the seventeen patients had  
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29 failed or delayed airway control despite attempted airway protection intervention.  
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31 Nine patients did not require any interventions.  
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#### 34 35 36 Definitive management

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38 All patients were confirmed to have ruptured pseudoaneurysm of the internal  
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40 carotid artery on digital subtraction angiography. Twenty-three patients had  
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42 endovascular treatment with stenting or coiling. Twenty patients (87%) had  
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44 successful control of the bleeding after endovascular treatment. Two died from  
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46 failure to control the epistaxis and one patient had minor intracerebral hemorrhage.  
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48 However, six of the twenty patients (30%) with successful control of hemorrhage  
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50 developed cerebral infarction after the procedure. Figure 2 and 3 showed the  
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52 angiography of an illustrative case of ICA pseudoaneurysm before and after  
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54 endovascular treatment.  
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5 The remaining three patients underwent emergency extracranial-intracranial  
6 (EC-IC) bypass surgery because of the severe stenosis of the internal carotid artery,  
7 which posed difficulties in endovascular treatment and very high risk of subsequent  
8 arterial and stent thrombosis. Of all the three patients who had undergone bypass  
9 surgery, one patient had successful control, one patient failed and one patient suffered  
10 from extensive intracranial hemorrhage.  
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18 Three out of the twenty-three patients with endovascular treatment required  
19 subsequent elective extracranial-intracranial (EC-IC) bypass surgery due to stent  
20 occlusion and inadequate blood supply from the contralateral circulation.  
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### 27 Outcomes

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29 Eighteen patients (69%) survived the rupture of the pseudoaneurysm of ICA  
30 and eight patients (31%) died from failed control of bleeding or complications of  
31 treatment within one month of presentation. Three out of the eighteen patients who  
32 survived the bleeding suffered from significant cerebral ischemia due to stent  
33 occlusion with severe neurological consequences. No patient had rebleeding after  
34 successful treatment of the ICA pseudoaneurysm.  
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### 45 Survival predictors

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47 Table 1 showed the result of the univariate analysis of factors predicting  
48 survival. Successful temporary control of bleeding and successful airway control  
49 were the two statistically significant factors, which predicted survival in this group of  
50 patients. T staging of the initial tumor, sex, presence of re-irradiation, known NPC  
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3 recurrence, history of maxillary swing nasopharyngectomy or use of endovascular  
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5 treatment were not associated with survival.  
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## 8 9 **Discussion**

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11 To the best of author's understanding, this is the largest retrospective study on  
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13 the management of pseudoaneurysm of internal carotid artery in post-irradiated  
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15 nasopharyngeal carcinoma patients. There have been a number of case reports on the  
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17 management of one to a few patients with ruptured pseudoaneurysm. Wong et al.<sup>4</sup>  
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19 reported their series of 11 patients from the perspective of neurosurgeon and focused  
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21 on the angiographic findings and endovascular treatment used. Our current cohort  
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23 would like to review the management of this group of patients with the focus on the  
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25 clinical characteristics and the initial management from the ENT perspective.  
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29 It is impossible to accurately determine the true incidence of ICA  
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31 pseudoaneurysm rupture as some patients of the current cohort had their primary  
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33 treatment done in other centers. On average, our hospital treats around 100 patients  
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35 with NPC per year. The current cohort had only 26 patients, accounting for less than  
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37 3% of the treated NPC patients.  
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41 The etiology of ICA pseudoaneurysm formation was believed to be  
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43 multifactorial. Radiation damage is one important factor<sup>1</sup>. Subclinical infection from  
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45 osteoradionecrosis of skull base<sup>3</sup> may also contribute the formation. Those with a  
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47 second course of radiotherapy have higher radiation damage to surrounding tissue and  
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49 are more prone to skull base osteoradionecrosis. In our series, 70% of our patients  
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51 had a second course of radiotherapy. Second course radiotherapy is a risk factor for  
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53 developing the potential fatal complication. Although the incidence is low, with  
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55 approximately 2-3 cases per year in our tertiary referral center, patients who would  
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3 receive a second course of radiotherapy should be informed this rare but potentially  
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5 life-threatening complication.  
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7 The majority of patients (92%) had conventional 2-dimensional (2D)  
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9 radiotherapy. Intensity-modulated radiotherapy (IMRT), instead of conventional 2D  
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11 radiotherapy with external beam radiation, has been universally adopted for NPC  
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13 treatment since 2007 in our hospital. IMRT, with the use of computed tomography-  
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15 assisted planning and radiation delivery, allows an accurate conformation to the tumor  
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17 shape<sup>14,15</sup>. Its ability to minimize the toxicities to surrounding normal tissues is  
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19 another advantage<sup>15</sup>. We postulate that IMRT may reduce the risk of  
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21 pseudoaneurysm formation by two mechanisms. First, IMRT enabled a better  
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23 coverage of the tumor and leads to less local recurrence, reducing the need for second  
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25 radiation. The reduction in the need for second irradiation may lead to less incidence  
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27 of ICA pseudoaneurysm rupture in the future. Secondly, for patients with local  
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29 recurrence occurring inside the high dose area (in-field failure), re-irradiation with  
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31 IMRT may be able to reduce the dose to the petrous apexes and internal carotid  
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33 arteries, especially in centrally located recurrences.  
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38 The mean duration of presentation of ruptured pseudoaneurysm was about 8.5  
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40 years after the primary radiotherapy in our series. It is too early to conclude that  
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42 IMRT would reduce the incidence of pseudoaneurysm formation in the ICA.  
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45 We have identified that successful temporary control of bleeding and airway  
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47 control were associated with survival in the univariate analysis, although both of them  
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49 were not statistically significant survival predictors in the multivariate analysis due to  
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51 the small number of cases. Such results have implied the clinical importance of the  
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53 initial ENT management. First, all ENT surgeon should have a high index of  
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55 suspicion of ruptured ICA pseudoaneurysm when a post-irradiated NPC patient  
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3 presents with massive epistaxis. Particular attentions have to be paid to the initial  
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5 bleeding control and airway management. It is difficult to achieve temporary control  
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7 of bleeding as the bleeding from ruptured pseudoaneurysm of ICA is usually  
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9 torrential and the anatomy of nasopharynx prevents good packing. In our center, both  
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11 anterior and posterior packing are used. Similarly, it is difficult to secure the airway  
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13 in this group of patients because they usually have trismus as the complication of  
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15 radiotherapy to the head and neck region. Orotracheal intubation may not be feasible.  
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17 The ENT surgeon may have to resort to cricothyroidotomy or tracheostomy in the  
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19 emergency setting for airway protection to prevent aspiration. Prompt bleeding  
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21 control and airway management is essential to buy time for the subsequent angiogram  
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23 assessment and definitive treatment.  
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28 One limitation of the study is the heterogeneity of the treatment (open surgery  
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30 and different endovascular treatment methods) and this affects the survival data  
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32 analysis. Throughout the past 10 years, there have been significant advances in the  
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34 imaging and endovascular treatment techniques<sup>12,16-18</sup>. Various endovascular  
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36 treatment options had been used in our center, including coiling and different stents.  
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38 As the focus of the study was not on the various endovascular treatment options, we  
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40 have grouped different endovascular treatment methods together for analysis. We  
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42 failed to demonstrate the superiority of one particular definitive treatment methods  
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44 over the others due to the small number of cases.  
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48 Our results with emergency EC-IC bypass surgery are not encouraging. We  
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50 have only 33% success in controlling the bleeding without significant neurological  
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52 complications or death. Performing this operation in an emergency setting, where the  
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54 patient may already be anemic and hypovolemic, might increase the risk of cerebral  
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3 hypoperfusion and complications. Further investigation would be required to define  
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5 the role of this surgery on the management of ICA pseudoaneurysm rupture.  
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### 9 10 **Conclusion**

11 Rupture of pseudoaneurysm of internal carotid artery is a rare complication of  
12 radiotherapy for NPC and is associated with high morbidity and mortality. There  
13 should be a high index of suspicion of the condition when post-irradiated NPC patient  
14 presents with massive epistaxis. Prompt initial management with regard to the  
15 bleeding and airway control is necessary. Endovascular treatment is a good definitive  
16 treatment option with a high rate of successful control of bleeding, though the  
17 procedure is associated with risk of cerebral ischemia. The value of emergency EC-  
18 IC bypass surgery needs further investigation.  
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Table 1: Factors predicting survival in the univariate analysis

	Relative Risk	p-value (chi-square test)
<b>Female sex</b>	1.25	0.26
<b>Early initial T stages (T1/T2)</b>	3.78	0.29
<b>Second course of radiotherapy</b>	0.78	0.38
<b>Previous maxillary swing nasopharyngectomy</b>	1.54	0.42
<b>Persistent disease</b>	0.25	0.97
<i>Successful hemostasis</i>	5.95	0.015
<i>Successful airway control</i>	10.28	0.001
<b>Endovascular treatment (Definitive treatment)</b>	2.23	0.14

**Figure Legends**

Figure 1. Flow chart showing management algorithm for suspected internal carotid artery pseudoaneurysm rupture in post-irradiated nasopharyngeal carcinoma patients.

Figure 2. Digital subtraction angiography showing a pseudoaneurysm of the paraclival segment of the internal carotid artery.

Figure 3. Digital subtraction angiography showing the absence of contrast filling of the pseudoaneurysm after successful deployment of an endovascular stent.

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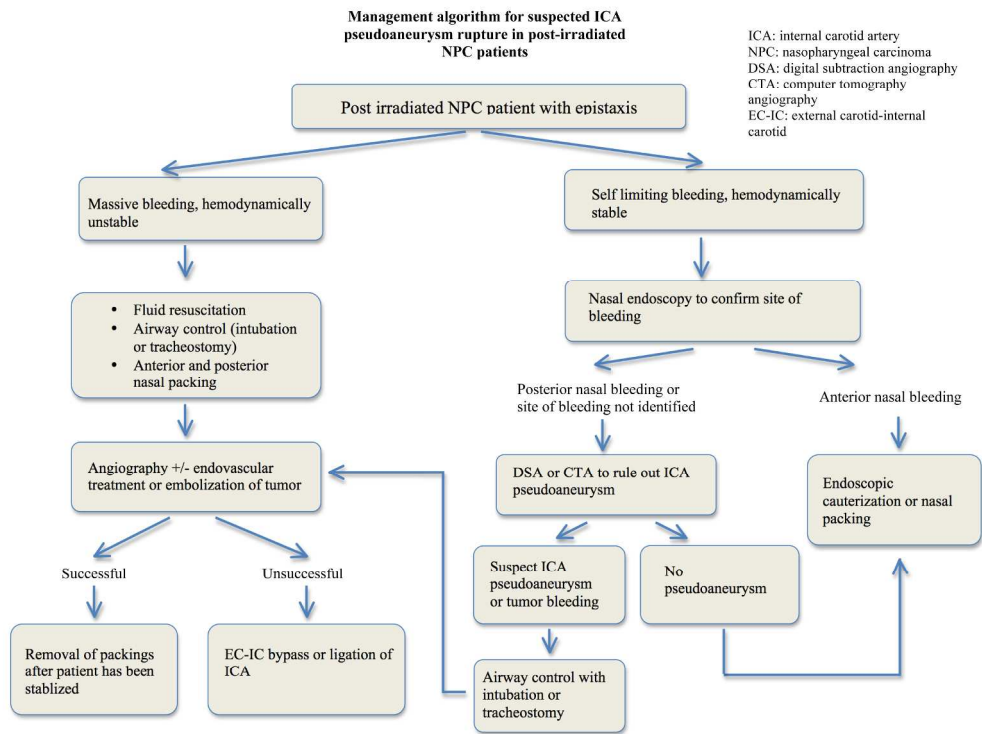
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Table 1: Factors predicting survival in the univariate analysis

	Relative Risk	p-value (chi-square test)
<b>Female sex</b>	1.25	0.26
<b>Small initial tumor*</b>	3.78	0.29
<b>Second course of radiotherapy</b>	0.78	0.38
<b>Previous maxillary swing nasopharyngectomy</b>	1.54	0.42
<b>Persistent disease</b>	0.25	0.97
<b><i>Successful hemostasis</i></b>	<i>5.95</i>	<i>0.015</i>
<b><i>Successful airway control</i></b>	<i>10.28</i>	<i>0.001</i>
<b>Endovascular treatment</b>	2.23	0.14

\* Small initial tumor included the initial T1-T2 tumor.



Flow chart showing management algorithm for suspected internal carotid artery pseudoaneurysm rupture in post-irradiated nasopharyngeal carcinoma patients.  
279x215mm (300 x 300 DPI)

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Digital subtraction angiography showing a pseudoaneurysm of the paraclival segment of the internal carotid artery.  
86x86mm (300 x 300 DPI)

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Digital subtraction angiography showing the absence of contrast filling of the pseudoaneurysm after successful deployment of an endovascular stent.  
86x86mm (300 x 300 DPI)