

# The unseen connection: laryngeal carcinoma and thrombosis of the internal jugular vein

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## ABSTRACT

The occlusion of the internal jugular vein (IJV) in the context of laryngeal carcinoma is a rare but significant occurrence that may manifest at various stages of the disease. Laryngeal carcinoma, a form of cancer affecting the voice box, carries profound implications for individuals and society alike. Although the primary focus often lies in treating cancer, emerging research has uncovered an intriguing link between laryngeal carcinoma and jugular vein thrombosis (JVT), necessitating further investigation.

We conducted a retrospective study spanning from January 2020 to December 2023, analyzing data from 60 patients who underwent surgery for laryngeal carcinoma at the Ear, Nose and Throat Department of the University Clinical Center of Kosovo. Among them, 9 patients were identified with concurrent IJV thrombosis, discovered incidentally during computed tomography examinations or based on clinical symptoms. Logistic regression analysis revealed associations between laryngeal carcinoma and JVT, emphasizing the importance of vigilance in diagnosis and management. Our findings underscore the need for heightened awareness and preventive measures, particularly in high-risk patients, to mitigate the impact of this interrelated condition. Early detection and intervention are crucial in optimizing outcomes for individuals confronting the dual challenges of laryngeal carcinoma and JVT.

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## Introduction

Occlusion of the internal jugular vein (IJV) in the context of laryngeal carcinoma is a rare phenomenon observed across various stages of the disease. Laryngeal carcinoma, or cancer of the larynx, is a diagnosis with profound implications, particularly prevalent within head and neck cancers, imposing significant burdens on individuals and societies alike. This type of cancer affects the voice box, resulting in voice alterations and debilitating symptoms.<sup>1-5</sup> While treatment primarily focuses on addressing cancer itself, recent research has highlighted an unexpected association between laryngeal carcinoma and jugular vein thrombosis (JVT), a condition deserving thorough exploration.<sup>6,7</sup>

Laryngeal carcinoma is a malignant tumor arising in the larynx, where the vocal cords are located. Major risk factors include smoking, alcohol consumption, and exposure to certain chemicals. Early symptoms often include persistent hoarseness, difficulty swallowing, and throat discomfort. Diagnosis typically involves imaging studies such as computed tomography (CT) scans and magnetic resonance imaging (MRI), along with endoscopic procedures and biopsies to confirm cancerous cells.

JVT occurs when blood clots form within the IJV, a crucial vessel that returns deoxygenated blood from the brain,

face, and neck to the heart. Various factors can contribute to JVT, including prolonged use of central venous catheters, infections, trauma, or underlying medical conditions. This condition is not only painful but can also lead to serious complications.<sup>8,9</sup>

Recent studies have underscored the correlation between laryngeal carcinoma and JVT. The association between cancer and thromboembolic disorders has long been recognized, initially described by Trousseau in 1865.<sup>10,11</sup> While spontaneous thrombosis of the IJV is uncommon and often attributed to factors like intravenous drug use or medical procedures, it can also occur due to malignancy-related hypercoagulability, direct tumor invasion, or postsurgical changes following neck dissection.

Clinicians managing laryngeal cancer patients must be vigilant in recognizing and diagnosing these potential complications. Screening for JVT should be integrated into routine assessments, particularly for patients with advanced disease. Consideration of prophylactic measures, such as anticoagulant therapy and close monitoring, may be warranted in high-risk individuals.<sup>7</sup>

Should JVT develop, its management becomes crucial to optimizing cancer treatment outcomes. Diagnostic approaches typically involve imaging modalities like ultrasound, CT scans, MRI, and venography, with biopsy essential for confirming or ruling out malignancy. Spontaneous thrombophlebitis can serve as an initial indicator of an underlying neoplasm, necessitating comprehensive evaluation and follow-up in cases of venous thrombosis.

Understanding and addressing the intricate relationship between laryngeal carcinoma and JVT enables healthcare providers to deliver more effective care and improve patient outcomes.

### Aim of the study

Venous thromboembolism is associated with significant morbidity and mortality in patients undergoing surgery, but conflicting data exist on venous thromboembolism risk in patients undergoing head and neck surgery for malignant conditions. The primary aim of this article is to investigate and elucidate the multifaceted relationship between laryngeal carcinoma and JVT, exploring the potential risk factors, clinical implications, and opportunities for improved patient care and management. By doing so, we aim to enhance the awareness and understanding of this association within the medical community and contribute to the development of preventive and therapeutic strategies for these interrelated conditions.

### Materials and Methods

We retrospectively performed a systematic analysis of present patient data from the Ear, Nose and Throat (ENT) Department of the University Clinical Center of Kosovo with the electronic patient record, considering the period from January 2020 to December 2023. Basic demographic factors, including age, sex, type of surgery (partial vs. total laryngectomy), duration of hospital stay, and histopathological results were studied. All patients have been preoperatively prepared with necessary laboratory tests and appropriate examinations for general anesthesia. During this time interval, we identified 60 patients who underwent surgery due to laryngeal carcinoma.

Among them, we subsequently identified patients in whom JVT was also detected concurrently. The discovery of JVT was incidental during the CT examination due to suspicion of laryngeal carcinoma as well as based on clinical symptoms, including neck and facial edema, and breathing difficulties, where a neck Doppler ultrasound was performed.

A positive vote from the Ethics Committee of the Kosovo Chamber of Doctors (no.03/2024) was obtained prior to the analysis.

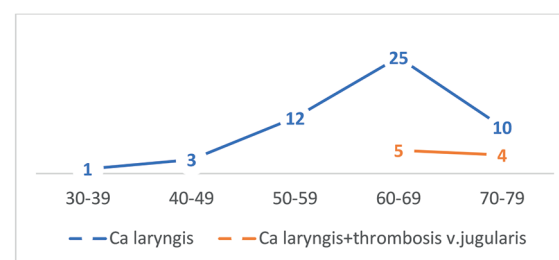
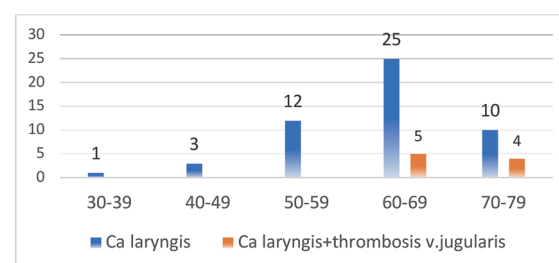
### Statistical analysis

This retrospective study was carried out in Prishtina (Kosovo), ENT Clinic from 2020 to 2023. Statistical analysis included calculating variables such as age, gender, type of carcinoma, and laryngeal carcinoma associated with JVT. The *t*-test, *p*-value, and average age of patients were calculated. Also, we compared results for each group with or without thrombosis. A *p*-value of less than 0.05 was considered significant. All data were analyzed using SPSS Statistics for Windows Version 24.0 (IBM, Armonk, NY, USA).

Factors of interest were included in logistic regression analysis to identify associations between laryngeal carcinoma and JVT. Odds ratios and 95% confidence intervals were reported for significant covariates detected *via* logistic regression.

### Results

This retrospective study includes a total of 60 patients with laryngeal carcinoma operated at the ENT Clinic between January 2020 and December 2023. Their demographics are reported in Table 1 and Figure 1. There were 51 men (100%) with laryngeal carcinoma and 9 patients with laryngeal carcinoma and JVT. The average age was 63.4 years. Based on our data, since out of 9 patients with laryngeal carcinoma accompanied by JVT, 6 patients (66.7%) were females, we consider

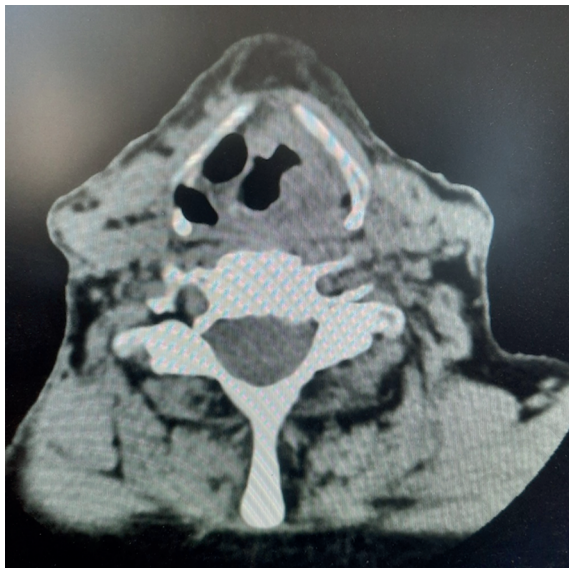


**Figure 1.** Demographics of the patients with laryngeal carcinoma and thrombosis of the internal jugular vein. Ca laryngis, carcinoma laryngis; v.jugularis, vena jugularis.

that in these patients, JVT has been a revealing factor of laryngeal carcinoma. The difference is considered to be not quite statistically significant.

The average age of the group with laryngeal carcinoma was 62.5 and 68.5 for laryngeal carcinoma with jugular thrombosis, in total 8.7. The standard deviation for the first group (laryngeal carcinoma) was 8.8 and 5.9 for the second group (laryngeal carcinoma with jugular vein carcinoma), in total 8.7. The *t*-test for the group with laryngeal carcinoma was 1.9088 and *df*=58. The *p*-value was 0.0612 for the second group and the standard error was 3.091. The average medication for the first group was 28.8, for the second one was 23.7, and the total was 28.0.

The main histopathological form was laryngeal squamous cell carcinoma, which has also been documented in the literature to be highly resistant to chemotherapy. The average length of hospitalization was 28 days.



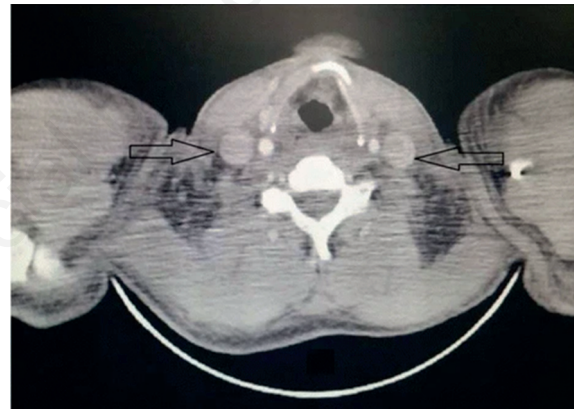
**Figure 2.** Native computed tomography of a patient with laryngeal carcinoma.

## Discussion

Venous thrombosis typically affects the legs, as the veins in the head and neck, being mostly valueless, are less prone to thrombosis due to gravity aiding drainage in the upright position. However, thrombosis remains a significant complication and a leading cause of death in patients with neoplasms. Bilateral JVT cases are rare and often associated with deep head and neck infections, sepsis, central venous catheterization, or neck injuries.<sup>12</sup>

JVT can occur spontaneously or secondary to various factors such as infections, surgeries, venous catheterization, or drug abuse. It is a rare condition that can be easily missed or misdiagnosed. Malignancies, although uncommonly documented as a cause of JVT, are reported in 29.7% of cases, highlighting the importance of thorough history-taking, physical examination, and investigation to detect hidden malignancies in patients presenting with spontaneous thrombophlebitis (Figures 2 and 3).<sup>2</sup>

In terms of gender differences, laryngeal cancer incidence



**Figure 3.** Computed tomography scan of a patient with bilateral thrombosis of the internal jugular vein. Reproduced from: Leci Tahiri *et al.* (2018).<sup>2</sup>

**Table 1.** Demographics of the patients with laryngeal carcinoma and thrombosis of the internal jugular vein.

| Age group          | Laryngeal carcinoma |       | Diagnosis |          | Total |      |
|--------------------|---------------------|-------|-----------|----------|-------|------|
|                    | N                   | %     | N         | %        | N     | %    |
| Total              | 51                  | -     | 9         | -        | 60    | -    |
| F                  | -                   | -     | 6         | 66.7     | 6     | 10.0 |
| M                  | 51                  | 100.0 | 3         | 33.3     | 54    | 90.0 |
| 30-39              | 1                   | 2.0   | -         | -        | 1     | -    |
| 40-49              | 3                   | 5.9   | -         | -        | 3     | -    |
| 50-59              | 12                  | 23.5  | -         | -        | 12    | -    |
| 60-69              | 25                  | 49.0  | 5         | 55.6     | 30    | -    |
| 70-79              | 10                  | 19.6  | 4         | 44.4     | 14    | -    |
| Average age        | 62.5                | -     | 68.4      | -        | 63.4  | -    |
| SD                 | 8.9                 | -     | 5.9       | -        | 8.7   | -    |
| t-test             | t=1.9088            | df=58 | p=0.0612  | SE=3.091 | -     | -    |
| Average medication | 28.8                | -     | 23.7      | -        | 28.0  | -    |

F, female; M, male; SD, standard deviation; *df* is 58, *df*=(*n*1+*n*2)-2; *df*=(6+54)-2=58; SE, standard error; IJV, internal jugular vein.

is significantly higher in males, accounting for approximately 90%, consistent with the findings in our study and supported by literature data, potentially due to greater exposure to risk factors. In females, laryngeal cancer mostly occurs post-menopause or in older age, suggesting a possible protective effect of estrogen.

Laboratory findings may reveal elevated D-dimer levels, a fibrin degradation product sensitive but nonspecific for venous thrombosis, which can also be elevated in malignancies, sepsis, recent surgeries, trauma, or pregnancy. In our study, the D-dimer level was not analyzed, as it was a retrospective study and not included as part of the investigation.

The incidence of venous thromboembolic disease is approximately one in 1000 people annually, with thrombosis in the superior mediastinum and neck veins less frequent and typically caused by direct trauma, drug use, or neck surgery. Pulmonary embolism, occurring in 2.7% of JVT cases, is a severe complication along with septic emboli, septicemia, cerebral edema, and cerebral pseudotumor. Squamous cell carcinoma accounts for over 90% of head and neck cancers, predominantly associated historically with tobacco and alcohol use but increasingly recognized with human papillomavirus infection, particularly in tongue cancers.<sup>13</sup>

Treatment for JVT includes anticoagulation with low molecular weight heparin followed by warfarin to prevent thromboembolic events. Additional therapies depend on individual circumstances, such as antibiotics for infections, removal of central venous catheters, or chemo-radiation for malignancies. According to the American Society of Clinical Oncology guidelines, hospitalized cancer patients generally require thromboprophylaxis, especially those undergoing chemotherapy.

Cancer cells can induce hypercoagulation, compounded by chemotherapy-associated thrombotic risks, making cancer patients up to 6.5 times more likely to develop thromboembolic events compared to the general population. Aggressive management to minimize complications like venous thromboembolism, pneumonia, surgical infections, and anemia may improve long-term survival outcomes, as evidenced by prolonged hospital stays of up to 28 days observed in our study and supported by prior research.

## Conclusions

Especially in young patients without other health conditions, JVT can sometimes be the initial manifestation of an underlying malignancy. The emerging association between laryngeal carcinoma and JVT underscores the intricate interplay of medical conditions and emphasizes the need for a comprehensive healthcare approach. Diagnosis of JVT may be challenging due to nonspecific symptoms, necessitating a high index of suspicion, as complications like pulmonary embolism or intracranial thrombus extension can be life-threatening. When thrombosis occurs without an inflammatory cause, malignancy should be considered. Collaboration between clinicians and researchers aims to deepen our understanding of this relationship, enhancing management and outcomes for patients dealing with both conditions.<sup>14,15</sup>

Our study identifies risk factors such as immobility, advanced cancer stages, histopathological cancer type, systemic therapy, and cancer surgery, highlighting the importance of implementing preventive measures as a standard practice in

clinical settings. Vigilance for thrombosis symptoms including neck swelling, pain, or discoloration is crucial for early intervention and improved outcomes. Treatment and prognosis depend on the extent of thrombosis, stage of laryngeal carcinoma, and overall health status, necessitating a multidisciplinary approach involving oncologists, hematologists, and vascular specialists to deliver comprehensive care. Early detection and appropriate management can significantly enhance survival rates and quality of life for individuals facing this complex dual challenge.

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