

Carcinome anaplasique de la thyroïde en Tunisie: A propos de 50 cas

Clinicopathological and Prognostic Features of Anaplastic Thyroid Carcinoma: A Tunisian Study of 50 Cases

Alia Methnani¹, Selmi Mariem¹, Jihen Houas⁴, Rim Braham¹, Mohamed Dhaha¹, Rim Abidi³, Chiraz Nasr³, Skander Kedous¹, Saoussen Dhambri¹

1. Université de Tunis El Manar, Faculté de Médecine de Tunis, 1007, Institut Salah Azaiz, Service d'Otolaryngologie et de Chirurgie Cervico-faciale, Tunis, Tunisie.
2. Université de Tunis El Manar, Faculté de Médecine de Tunis, 1007, Institut Salah Azaiz, Service d'Anatomopathologie, Tunis, Tunisie.
3. Université de Tunis El Manar, Faculté de Médecine de Tunis, 1007, Institut Salah Azaiz, Service de Radiothérapie Tunis, Tunisie.
4. Service ORL, Hôpital Universitaire Farhat Hached, Faculté de Médecine de Sousse, Sousse, Tunisie.

ABSTRACT

Introduction: Anaplastic thyroid carcinoma (ATC) is an exceptionally rare and aggressive malignancy.

Aim: This study aimed to evaluate the clinical features, therapeutic outcomes, and prognostic factors within a Tunisian multicenter cohort.

Methods: We conducted a retrospective multicenter analysis of 50 ATC cases treated between 1998 and 2021 at two tertiary referral centers in Tunisia.

Results: The mean age was 62 years with a female predominance (M/F ratio 0.61). The most common presenting symptom was rapid enlargement of a long-standing goiter (80%). At diagnosis, the mean tumor size was 62 mm, and all patients presented with stage IV disease: IVA (n=1), IVB (n=23), and IVC (n=26). Therapeutic interventions included tracheostomy (n=29), surgical resection (n=21, with R0/R1 achieved in 16), and palliative radiotherapy (n=21). Only five patients received full multimodal therapy. Univariate analysis identified slow symptom onset, early stages (IVA/IVB), absence of distant metastasis, R0/R1 resection, and multimodal treatment as significant factors for improved survival. Conversely, obesity and blood group B were associated with poorer outcomes. The mean overall survival was 3.85 months, and no patient was alive at the last follow-up.

Conclusion: ATC is associated with a particularly unfavourable prognosis, with an overall survival of less than one year. While multimodal management appears to marginally improve survival, early diagnosis and the integration of targeted therapies and immunotherapies are essential to change the therapeutic landscape.

Keywords: Anaplastic thyroid carcinoma , Targeted therapy , Immunotherapy , Radiotherapy , Chemotherapy

RÉSUMÉ

Introduction: Le carcinome anaplasique de la thyroïde (CAT) est une tumeur maligne rare et agressive.

Objectif: Cette étude visait à évaluer les caractéristiques cliniques, les résultats thérapeutiques et les facteurs pronostiques au sein d'une cohorte multicentrique tunisienne.

Méthodes: Nous avons mené une analyse rétrospective multicentrique de 50 cas de CAT traités entre 1998 et 2021 dans deux centres de référence tertiaires en Tunisie.

Résultats: L'âge moyen était de 62 ans avec une prédominance féminine (sex-ratio H/F de 0,61). Le symptôme révélateur le plus fréquent était l'augmentation rapide d'un goitre ancien (80 %). Au diagnostic, la taille tumorale moyenne était de 62 mm et tous les patients présentaient un stade IV : IVA (n=1), IVB (n=23) et IVC (n=26). Les interventions thérapeutiques comprenaient la trachéotomie (n=29), la résection chirurgicale (n=21, dont 16 résections R0/R1) et la radiothérapie palliative (n=21). Seuls cinq patients ont bénéficié d'un traitement multimodal complet. L'analyse univariée a identifié une installation lente des symptômes, les stades précoces (IVA/IVB), l'absence de métastases à distance, la résection R0/R1 et le traitement multimodal comme des facteurs significatifs d'amélioration de la survie. Inversement, l'obésité et le groupe sanguin B étaient associés à de mauvais résultats. La survie globale moyenne était de 3,85 mois et aucun patient n'était vivant au terme du suivi.

Conclusion : Le CAT est associé à un pronostic particulièrement défavorable, avec une survie globale inférieure à un an. Bien que la prise en charge multimodale semble améliorer marginalement la survie, un diagnostic précoce et l'intégration des thérapies ciblées et de l'immunothérapie sont essentiels pour transformer le paysage thérapeutique.

Mots-clés: Carcinome anaplasique de la thyroïde, Thérapie ciblée, Immunothérapie, Radiothérapie, Chimiothérapie

Correspondance

Alia Methnani

Université de Tunis El Manar, Faculté de Médecine de Tunis, 1007, Institut Salah Azaiz, Service d'Otolaryngologie et de Chirurgie Cervico-faciale, Tunis, Tunisie.

Email: alia.methnani@fmt.utm.tn

INTRODUCTION

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive and lethal solid tumors in humans (1). Although it accounts for only 1% to 2% of all thyroid malignancies, it is responsible for more than 50% of thyroid cancer-related deaths (1,2). ATC is characterized by rapid growth, early local invasion, and a high propensity for distant metastasis, leading to a dismal prognosis with a median survival typically ranging from 3 to 5 months (3,4).

The management of ATC remains a major clinical challenge. While multimodal therapy combining radical surgery, radiotherapy, and chemotherapy has shown some efficacy in improving local control and marginally extending survival, many patients are diagnosed at advanced stages (Stage IVB or IVC), where only palliative care is feasible (2,5). Despite recent advances in targeted therapies and immunotherapy, the clinical outcomes in real-world settings, particularly in resource-limited environments, remain poorly documented.

In Tunisia, ATC represents a significant oncological burden, often arising from long-standing neglected goiters. This study aims to describe the clinicopathological features and therapeutic outcomes of a Tunisian multicenter cohort of 50 patients and to identify the primary prognostic factors influencing survival in our context.

METHODS

We conducted a retrospective multicenter study including 50 patients diagnosed with anaplastic thyroid carcinoma (ATC) over a 23-year period. To analyze clinical variations, the cohort was divided into two groups based on the timing of diagnostic confirmation:

- **Group 1:** Patients whose ATC diagnosis was established postoperatively following histopathological examination of the surgical specimen.
- **Group 2:** Patients with a primary suspicion of advanced local or metastatic disease, where the diagnosis was confirmed via initial biopsy.

Overall survival (OS) was calculated from the date of initial diagnosis until death or the last follow-up. Prognostic factors were evaluated using univariate and multivariate analyses. Statistical significance was defined as a p-value less than 0.05 ($p < 0.05$).

This study was conducted in accordance with the principles of the Declaration of Helsinki. Given its retrospective nature, individual informed consent was waived. Patient data were fully anonymized prior to analysis. This work is derived from a doctoral thesis previously approved by the institutional authorities of Faculty of Medicine of Sousse.

RESULTS

The study included 50 patients treated at two tertiary referral centers: 40 at the Salah Azaïz Institute and 10 at the Farhat Hached University Hospital. The mean age at diagnosis was 62 years (range: 27–89 years), with a peak frequency observed between 60 and 75 years. A female predominance was noted, with a sex ratio (M/F) of 0.61. Eight patients had a prior history of thyroid disorders, including seven with substituted hypothyroidism and one with balanced hyperthyroidism. Two patients had undergone thyroid surgery for benign disease more than 20 years ago, and one patient had a history of cervical radiation for Hodgkin lymphoma 25 years prior. No patients had a personal history of thyroid malignancy. Regarding general health, the WHO performance status was > 2 in 70% of the cohort, while only 12% maintained a status of 0. Body Mass Index (BMI) data, available for 22 patients, showed that 3 patients had a BMI > 30 kg/m², with no cases of malnutrition (BMI < 18 kg/m²) at diagnosis.

The mean delay between the onset of the first symptom and the initial consultation was 1.6 months (range: 12 days–8 months). The primary clinical manifestation was the rapid "explosive" transformation of a long-standing goiter in 80% of cases. All patients presented with an anterior low-cervical mass (Figure 1), with a mean duration of evolution of 18 months (range: 1 month–24 years).

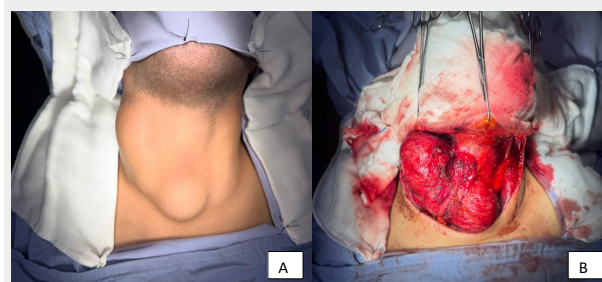


Figure 1. Clinical and intraoperative photographs of a patient with anaplastic thyroid carcinoma. (A) Preoperative view showing a large anterior cervical mass with erythematous skin changes and significant local swelling. (B) Intraoperative view demonstrating the extensive tumor bulk and local invasion encountered during surgical exploration.

Compression symptoms were highly prevalent, including dyspnea in 30 cases (60%), dysphonia in 29 (58%), dysphagia in 26 (52%), aspiration in 29 (58%), and cervical pain in 64% of cases. The mean tumor size on physical examination was 62.1 mm (range: 20–120 mm), with skin invasion observed in 7 cases (Figure 2). Palpable lateral cervical lymphadenopathy was found in 17 patients, with a mean size of 24.7 mm (range: 10–50 mm), typically hard and fixed to deep structures.



Figure 2. Clinical photograph showing a large anterior cervical mass with extensive skin invasion and ulceration in a patient with anaplastic thyroid carcinoma

The frequency of the main sonographic, radiological, endoscopic and laboratory findings is displayed in Figure 4. Signs of malignancy were present in 82% of cervical ultrasound examinations and in 84% of cervico-thoracic CT scans, performed in 46 patients (Figure 3); the mean thyroid mass size on CT was 62 mm (range: 20–120 mm). Nodal involvement was detected by ultrasound in 37 patients, with a mean size of 22.9 mm (range: 4–50 mm), involving the central compartment and/or mediastinum, and the lateral compartment in 18 cases. Thoraco-abdominopelvic CT, performed in 42 patients for distant staging, revealed metastases in 26 patients (62%), including pulmonary localizations (45%), bone and liver metastases, or combined pulmonary and bone involvement.

Panendoscopy under general anesthesia, conducted in 16 patients, revealed laryngeal paralysis in 13 cases, subglottic or tracheal invasion in 6 cases, and cervical esophageal invasion in 3 cases. The most frequent blood group was O Rh+ (34%), followed by group B, and calcitonin, measured in 5 patients, was normal in all cases.

Thyroid fine-needle aspiration (FNA) was performed in 31 patients. According to the Bethesda classification, results were non-diagnostic (Bethesda I) in 6 cases, benign (II) in 1 case, atypia of undetermined significance (III) in 8 cases, and suspicious for a follicular neoplasm (IV) in 4 cases. Fine-needle aspiration of lymph nodes was performed in 17 patients, revealing benign or reactive lymphadenopathy in 3 cases, malignancy or atypia in 5 cases, and metastases of thyroid origin in 9 cases. The definitive diagnosis of anaplastic thyroid carcinoma (ATC) was established in all cases through histopathological examination.

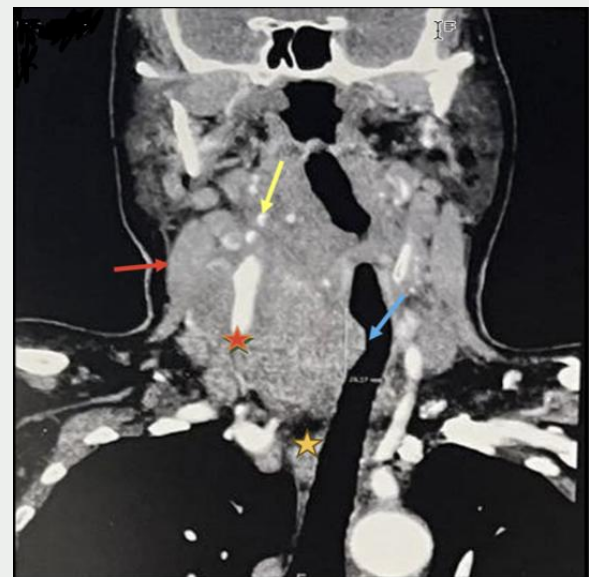


Figure 3. Contrast-enhanced chest and neck CT, coronal view, soft tissue window: Invasive and infiltrating right substernal goitre. The mass, originating from the right thyroid bed, is poorly defined and measures 54 mm. It features macro-calcifications (yellow arrow) and results in the following:

- Invasion of the ipsilateral sternocleidomastoid (SCM) muscle (red arrow).
- Infiltration of the right carotid sheath, with lateral displacement of the jugulo-carotid vessels (red star).
- Tracheal compression with a 26 mm long luminal narrowing (blue arrow).
- Infiltration of the fat pads at the level of the thoracic inlet (yellow star).

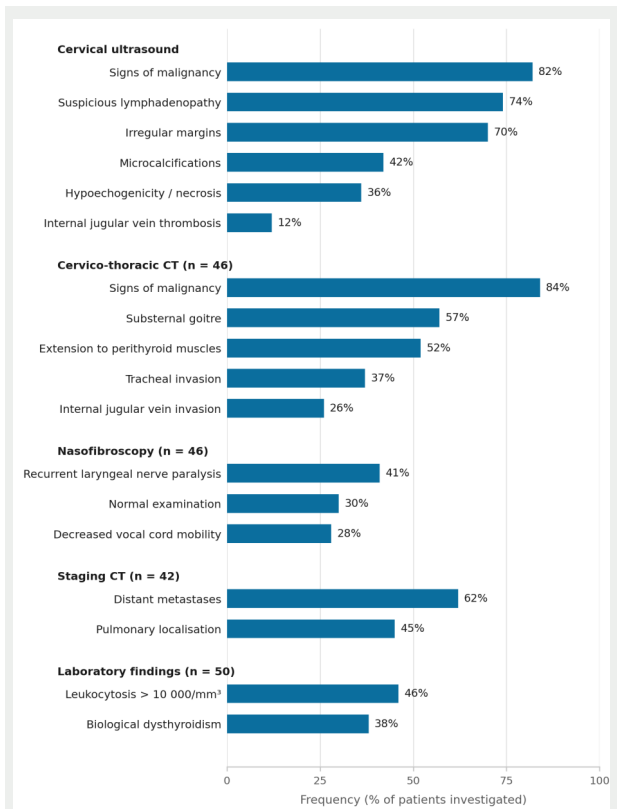


Figure 4. Frequency of the main paraclinical findings at diagnosis in 50 patients with anaplastic thyroid carcinoma. Percentages are expressed relative to the number of patients who underwent each investigation. CT: computed tomography.

Patients were categorized into two groups based on the diagnostic method: Group 1 (n = 21), where ATC was diagnosed on the surgical specimen, and Group 2 (n = 29), where ATC was diagnosed directly via surgical biopsy. Macroscopically, tumor specimens had a mean size of 48–56 mm and were typically hard, grayish-white or yellowish, with extensive areas of necrosis in most cases. Microscopically, the tumors consisted of undifferentiated proliferation with a high mitotic index, featuring highly atypical cells and a spindle-cell component in 62% of cases. An inflammatory infiltrate was noted in approximately 60% of specimens, and an associated papillary component was found in 9 cases, suggesting a transformation from a pre-existing differentiated carcinoma in some patients.

Immunohistochemistry, performed in 21 patients, showed positivity for cytokeratins in 74% of cases, EMA in 56%, and PAX8 in 40%. Conversely, thyroglobulin was negative in 66% of cases, TTF1 in 74%, and calcitonine was negative in all cases where it was sought. The Ki67 index reached up to 100%, and p53 was overexpressed in several cases, confirming the high grade and aggressiveness of these tumors.

Based on the TNM classification (8th edition), all patients were stage IV at diagnosis: 1 patient was stage IVA (intrathyroidal tumor without nodal or distant metastasis), 23 were stage IVB (loco-regional extra-thyroidal extension), and 26 were stage IVC (distant metastasis). Initial supportive care was required for 42 patients (84%), including 29 tracheotomies (13 performed urgently), 10 gastrostomies, and the placement of a nasogastric tube in 30 patients. Only 8 patients did not require a specific initial intervention.

Patients were managed according to two distinct clinical scenarios based on the timing of diagnostic confirmation. Group 1 (n = 21) consisted of non-metastatic patients (1 Stage IVA, 20 Stage IVB) whose diagnosis was established postoperatively. Group 2 (n = 29) included patients with advanced disease (7 cases of skin permeation and/or 26 cases of distant metastasis) diagnosed via initial biopsy. Multidisciplinary team meetings (MDT) recommended concomitant chemoradiotherapy for all patients, although its completion was often limited by disease progression. The patients in Group 1 had a mean age of 65 years and experienced a mean overall survival of 4.5 months. Within this group, surgical management included total thyroidectomy (n=8), lobe-isthmectomy (n=8), subtotal lobectomy (n=4), and subtotal thyroidectomy (n=1). Neck dissection was performed in the majority of cases, primarily targeting the mediastinal-recurrent compartment (n=20), followed by selective level III-IV dissection (n=6) and bilateral functional dissection (n=1). Despite this aggressive surgical approach, R0 resections remained exceptional, as most margins showed either microscopic (R1) or macroscopic (R2) involvement.

Adjuvant therapies were initiated with varying degrees of completion. Adjuvant radiotherapy was administered to 14 patients using a Cobalt-60 conformational technique, delivering a mean cumulative dose of 13 Gy (range: 6–30 Gy) with a mean postoperative delay of 64 days for palliative and decompressive purposes.

Adjuvant chemotherapy was initiated in five patients, utilizing either a doxorubicin-cisplatin (n=2) or a taxane-carboplatin (n=3) regimen, with a mean surgery-to-chemotherapy interval of 30.2 days.

Group 2 (n = 29) comprised patients with the most advanced clinical presentations, including 26 cases with distant metastases (Stage IVC) and seven cases with skin invasion at the time of diagnosis. The mean age in this subgroup was 64 years. Due to the high prevalence of upper airway obstruction, initial management focused primarily on palliative stabilization. Airway management required tracheostomy in 24 patients (83%), with 13 of these performed as life-saving emergency procedures upon admission. Furthermore, nutritional support was necessary for 22 patients, provided via gastrostomy (n = 10) or nasogastric tube placement (n = 12).

Given the extensive local invasion and metastatic spread, curative-intent surgery was not feasible for any patient in this group, limiting management to palliative modalities. Decompressive radiotherapy (Cobalt-60) was administered to seven patients with a mean delivered dose of 9 Gy (range: 4–20 Gy); however, treatment was frequently interrupted due to rapid clinical deterioration. Similarly, only four patients were fit enough to initiate palliative chemotherapy (Doxorubicin-Cisplatin). The median number of cycles completed was two, as progressive disease or poor performance status precluded further treatment.

The univariate analysis identified several key determinants significantly associated with improved overall survival. Regarding patient-specific characteristics, a Body Mass Index (BMI) below 30 kg/m² (p = 0.013) and non-B blood groups (p = 0.031) emerged as favorable indicators. From a clinical perspective, a less abrupt onset of symptoms (p = 0.01) and a tumor size limited to 5 cm or less (p = 0.051) were linked to a less fulminant disease course.

The extent of the disease at the time of presentation proved to be a critical factor: a less advanced tumor stage (p < 0.001) and the absence of distant metastases (p = 0.04) were significantly associated with better outcomes. Furthermore, at the histopathological level, the presence of a co-existing papillary component within the anaplastic proliferation was identified as a favorable prognostic feature (p = 0.038).

In terms of therapeutic interventions, our results emphasize the importance of aggressive management. The completion of a full multimodal protocol—incorporating surgery, radiotherapy, and chemotherapy—was the most significant therapeutic factor (p < 0.001). Achieving a macroscopically complete surgical resection (R0/R1, p = 0.02) and the administration of radiotherapy (p = 0.018) also provided a survival advantage. However, multivariate analysis revealed that only the initial tumor stage remained a significant independent prognostic factor (p = 0.007; 95% CI: 0.000–2.687). This finding confirms that the disease extent at diagnosis is the primary determinant of the clinical outcome, largely overshadowing the impact of subsequent therapeutic efforts.

DISCUSSION

Anaplastic thyroid carcinoma (ATC) remains one of the most aggressive malignancies, with a prognosis that has seen little improvement over several decades (1,3). Our multicenter study confirms this grim reality, showing a mean overall survival of only 3.85 months. This aggressive course is primarily driven by the "explosive" nature of the tumor, which in our series presented as a rapid transformation of a long-standing goiter in 80% of cases. The distinction we established between Group 1 (postoperative diagnosis) and Group 2 (preoperative diagnosis) highlights a critical diagnostic challenge. In Group 1, the incidental discovery of ATC during surgery for a supposedly differentiated or benign disease suggests that some forms of ATC may "masquerade" initially, or arise from a pre-existing differentiated thyroid carcinoma (DTC). This theory is supported by the identification of a papillary component in 18% of our specimens, a finding consistent with the literature regarding the dedifferentiation process (2,6,7). While Group 1 patients had a slightly better survival (4.5 vs. 3.4 months), the high rate of R1/R2 margins underscores that even in apparently limited forms, ATC is deeply infiltrative from the outset.

The management of Group 2 patients illustrates the palliative reality of ATC in advanced stages. With 83% of these patients requiring tracheostomy often as an emergency window for curative-intent multimodal therapy is extremely narrow (8). Our univariate analysis identified the completion of a full multimodal protocol (surgery, radiation, and chemotherapy) as a significant prognostic factor ($p < 0.001$). However, the rapid deterioration of the WHO performance status in our cohort meant that only 10% of all patients could actually complete such a regimen.

Consistent with international data, our multivariate analysis confirmed that the initial tumor stage is the only independent prognostic factor ($p = 0.007$). This finding emphasizes that survival is largely dictated by the extent of the disease at the time of first consultation. Therefore, in a context where neglected goiters are frequent, early clinical suspicion and rapid referral to tertiary centers are paramount (3-9).

The management of anaplastic thyroid carcinoma requires an immediate and highly coordinated multidisciplinary approach (Figure 5). Upon clinical suspicion characterized by a rapidly enlarging cervical mass and compressive symptoms an emergency diagnostic work-up must be initiated. This includes a contrast-enhanced CT scan of the neck, chest, abdomen, and pelvis to assess both local resectability and distant staging (Stage IVC), alongside a core-needle biopsy (10,11). A pivotal step in the modern management of ATC is the early integration of molecular profiling. We propose that mutational analysis, particularly for the BRAF V600E mutation, as well as RET fusions, should be requested at the time of initial biopsy (12,13). This genomic search is no longer optional; it is a critical determinant of the therapeutic strategy, as the presence of targetable mutations can transform an unresectable tumor into a candidate for neoadjuvant or

palliative targeted therapy with significantly improved response rates (12-13).

For patients with resectable disease (Stage IVA or early IVB), the goal remains urgent surgical debulking via total thyroidectomy and comprehensive neck dissection, aiming for R0/R1 margins (1,3). However, given the high risk of rapid recurrence, adjuvant multimodal therapy combining radiotherapy and chemotherapy (Taxane or Platinum-based) should ideally commence within four weeks post-surgery (2,4). In contrast, for patients presenting with unresectable or metastatic disease (Stage IVB/IVC), the focus shifts toward rapid stabilization and systemic control. In these advanced cases, the role of targeted therapies such as the combination of Dabrafenib and Trametinib for BRAF-mutated tumors has emerged as a new standard of care, often offering superior outcomes compared to conventional chemotherapy (5,14). For patients without targetable mutations, palliative radiotherapy and chemotherapy remain the backbone of treatment to manage local symptoms. Throughout this process, early integration of palliative care is essential to address respiratory distress and maintain quality of life, reflecting the clinical reality that ATC management is a race against time where every diagnostic and therapeutic day counts (3,15).

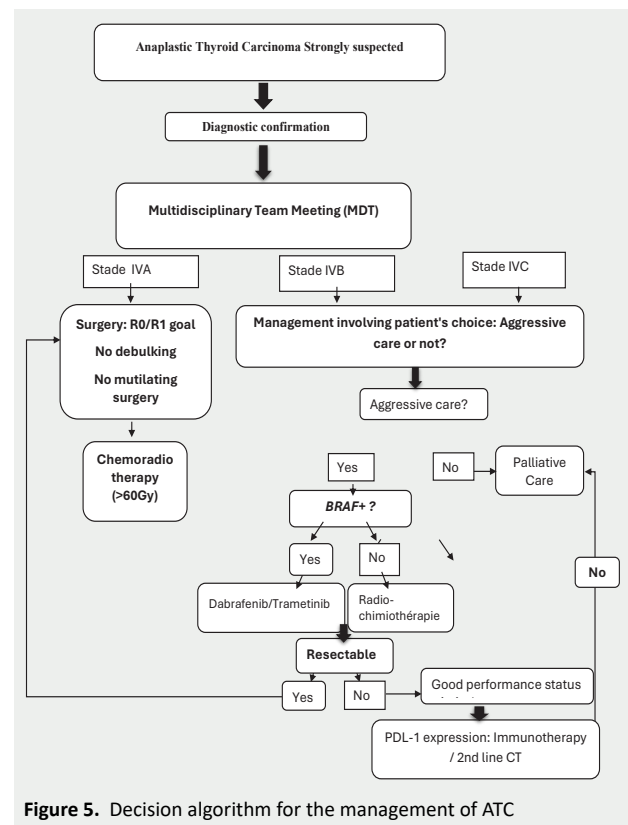


Figure 5. Decision algorithm for the management of ATC

CONCLUSION

Anaplastic thyroid carcinoma remains one of the most challenging entities in head and neck oncology. Our multicentre study confirms a particularly unfavourable prognosis, with an overall survival of less than one year (mean overall survival: 3.85 months). The "explosive" clinical presentation of these tumors, often arising from

long-standing goiters, frequently leads to a delayed diagnosis at an advanced, unresectable stage. Our findings emphasize that while the initial tumor stage is the primary independent prognostic factor, a rapid and aggressive multimodal therapeutic approach remains the only strategy capable of offering even a marginal survival advantage.

However, the therapeutic landscape is currently undergoing a paradigm shift. The integration of systematic molecular profiling and the emergence of targeted therapies, particularly for BRAF-mutated cases, offer a glimmer of hope in what was previously a strictly palliative field. In Tunisia, improving the prognosis of ATC will require the establishment of "fast-track" diagnostic circuits to ensure that every patient can benefit from genomic analysis and innovative therapies as early as possible.

RÉFÉRENCES

1. Kitahara CM, McCullough ML, Franceschi S, Rinaldi S, Wolk A, Neta G, et al. Anthropometric Factors and Thyroid Cancer Risk by Histological Subtype: Pooled Analysis of 22 Prospective Studies. *Thyroid*. 2016 Feb;26(2):306-18. doi: 10.1089/thy.2015.0319
2. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. *Med Sci Monit*. 2015 Jan 22;21:283-91. doi: 10.12659/MSM.892035.
3. Stamatiou A, Herrera-Gómez RG, Szturz P, et al. Carcinome anaplasique de la thyroïde : nouvelles approches thérapeutiques. *Rev Med Suisse*. 2021 May 19;17(739):962-966. PMID: 34009754
4. Bible KC, Kebebew E, Brierley J, Brito JP, Cabanillas ME, Clark TJ Jr, Di Cristofano A, Foote R, Giordano T, Kasperbauer J, Newbold K, Nikiforov YE, Randolph G, Rosenthal MS, Sawka AM, Shah M, Shaha A, Smallridge R, Wong-Clark CK. 2021 American Thyroid Association Guidelines for Management of Patients with Anaplastic Thyroid Cancer. *Thyroid*. 2021 Mar;31(3):337-386. doi: 10.1089/thy.2020.0944.
5. Houlihan OA, Moore R, Jamaluddin MF, Sharifah A, Redmond HP, O'Reilly S, et al. Anaplastic thyroid cancer: outcomes of trimodal therapy. *Rep Pract Oncol Radiother*. 2021;26(3):416-22. doi : 10.5603/RPOR.a2021.0042
6. Mohebbati A, DiLorenzo M, Palmer F, Patel SG, Pfister D, Lee N, et al. Anaplastic Thyroid Carcinoma: A 25-year Single-Institution Experience. *Ann Surg Oncol*. 2014 May;21(5):1665-70. DOI: 10.1245/s10434-014-3545-5
7. Hundahl SA, Cady B, Cunningham MP, et al. Initial results from a prospective cohort study of 5583 cases of thyroid carcinoma treated in the United States during 1996. *Cancer*. 2000 Jul 1;89(1):202-17. doi: 10.1002/1097-0142(20000701)89:1<202::AID-CNCR27>3.0.CO;2-A
8. Hvilsum GB, Londero SC, Hahn CH, et al. Anaplastic thyroid carcinoma in Denmark 1996-2012: A national prospective study of 219 patients. *Cancer Epidemiol*. 2018 Apr;53:65-71. doi: 10.1016/j.canep.2018.01.011.
9. Smallridge RC, Copland JA. Anaplastic thyroid carcinoma: pathogenesis and emerging therapies. *Clin Oncol (R Coll Radiol)*. 2010 Aug;22(6):486-97. doi: 10.1016/j.clon.2010.03.013
10. Saini S, Tulla K, Maker AV, Burman KD, Prabhakar BS. Therapeutic advances in anaplastic thyroid cancer: a current perspective. *Mol Cancer*. 2018 Oct 23;17(1):154. doi: 10.1186/s12943-018-0903-0.
11. Kebebew E, Greenspan FS, Clark OH, Woeber KA, McMillan A. Anaplastic thyroid carcinoma. Treatment outcome and prognostic factors. *Cancer*. 2005 Apr 1;103(7):1330-5. doi: 10.1002/cncr.20936.
12. Are C, Shaha AR. Anaplastic thyroid carcinoma: biology, pathogenesis, prognostic factors, and treatment approaches. *Ann Surg Oncol*. 2006 Apr;13(4):453-64. doi: 10.1245/ASO.2006.05.042.
13. Haigh PI, Ituarte PH, Wu HS, et al. Completely resected anaplastic thyroid carcinoma combined with adjuvant chemotherapy and irradiation is associated with prolonged survival. *Cancer*. 2001 Jun 15;91(12):2335-42. doi: 10.1002/1097-0142(20010615)91:12<2335::AID-CNCR1266>3.0.CO;2-1
14. Subbiah V, Kreitman RJ, Wainberg ZA, Cho JY, Schellens JHM, Soria JC et al. Dabrafenib plus trametinib in patients with BRAF V600E-mutant anaplastic thyroid cancer: updated analysis from the phase II ROAR basket study. *Ann Oncol*. 2022 Apr;33(4):406-415. doi: 10.1016/j.annonc.2021.12.014.
15. Glaser SM, Mandish SF, Gill BS, Balasubramani GK, Clump DA, Beriwal S. Anaplastic thyroid cancer: Prognostic factors, patterns of care, and overall survival. *Head Neck*. 2016 Apr;38 Suppl 1:E2083-90. doi: 10.1002/hed.24384.