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Orbital Radiotherapy For Thyroid Eye Disease

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ABSTRACT

Background: The management of thyroid eye disease (TED) has evolved significantly over the past decade, reflecting a growing understanding of its pathophysiology and treatment options. **Literature Review:** Early foundational work highlighted the necessity of a multidisciplinary approach and the implications of uncontrolled thyroid function on ocular manifestations (D Bothun et al., 2009). As research progressed, it became evident that traditional therapies often failed to adequately modify the disease trajectory, leading to a call for innovative treatments that could address both the physical and psychosocial burdens of TED. A notable advancement in the therapeutic landscape is the introduction of teprotumumab, a monoclonal antibody targeting the insulin-like growth factor 1 receptor, which has shown promise in modifying disease activity and improving patient outcomes [ref: b86ce04c-838d-4659-9853-4f46137ce1c7; ref: 9490db16-9cf1-482f-94ad-b0ce8637f064]. However, the role of orbital radiotherapy remains critical, particularly in addressing the inflammatory processes associated with TED. Recent studies indicate that radiotherapy can effectively reduce proptosis and improve ocular symptoms, although the variability in patient responses necessitates further investigation to optimize treatment protocols (Barbesino et al., 2022). The literature emphasizes the importance of individualized treatment strategies, taking into account the severity of the disease and the patient's quality of life. The need for comprehensive care that addresses both physical symptoms and psychosocial impacts is a recurrent theme [ref: c09ded44-e51d-4309-95d0-6772ea287f5b; ref: 6e31a688-4819-48f7-9c41-7840d75117d4]. Smoking cessation and careful management of thyroid function are also highlighted as essential components of effective TED management (D Bothun et al., 2009). **Conclusion:** In conclusion, the body of literature on TED illustrates a shift towards more targeted and personalized treatment approaches, with orbital radiotherapy playing a vital role in the management of ocular symptoms. The integration of novel therapies such as teprotumumab alongside traditional modalities signifies a promising direction for improving patient outcomes in TED.

Keyword: Orbital Radiotherapy, Thyroid Eye Disease

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INTRODUCTION

The management of thyroid eye disease (TED) has evolved significantly over the past decade, reflecting a growing understanding of its pathophysiology and treatment options. The early work by (D Bothun et al., 2009) emphasized the importance of a multidisciplinary approach for managing patients with Graves' ophthalmopathy, highlighting that uncontrolled thyroid function correlates with more severe ophthalmic manifestations. They noted that while antithyroid drugs and surgical interventions may not alter the course of TED, the use of steroids during radioiodine therapy could mitigate exacerbations, particularly in high-risk patients. This foundational research set the stage for subsequent explorations into more effective therapeutic strategies.

In 2019, (Wang et al., 2019) expanded on the complexities of TED, identifying the need for disease-modifying treatments that could effectively address the autoimmune nature of the disease. They pointed out that while immune suppression strategies exist, they often do not alter the disease trajectory, thus underscoring the necessity for innovative therapies that balance efficacy and safety. This call for advancement was echoed in the 2021 work by (S. Douglas et al., 2021), who reviewed the traditional focus on achieving euthyroidism and surgical intervention. Their findings revealed that standard therapies frequently fail to reliably modify proptosis and strabismus, while high-dose steroids present significant risks, suggesting a critical need for alternative options.

(Wang et al., 2021) further contributed to the discourse by examining the quality of life impacts of TED from a physician's perspective in the United States. Their insights highlighted the substantial burden TED places on patients, reinforcing the urgency of developing effective treatment modalities that address both the physical and psychosocial aspects of the disease. This concern about quality of life was echoed by (Sook Yoon & O. Kikkawa, 2022), who provided a comprehensive overview of TED's pathogenesis and treatment landscape. They noted that recent

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advances in understanding the disease's immunopathogenesis have led to the introduction of targeted therapies, including teprotumumab, which was approved by the FDA in early 2020.

The ongoing evolution of TED management is further illustrated by (Barbesino et al., 2022), who reviewed contemporary translational studies and clinical trials, emphasizing the promising directions in research that could reshape therapeutic approaches. In the same vein, (Lora Kossler et al., 2022) discussed the emergence of teprotumumab as a significant advancement in the treatment landscape, attributed to new insights into the role of the insulin-like growth factor 1 receptor in TED pathophysiology. Their review underscored the transition from traditional steroid regimens to novel biologic therapies, highlighting teprotumumab's potential to offer a more effective and targeted treatment option for patients suffering from this debilitating condition.

Together, these articles illustrate a trajectory of increasing sophistication in the understanding and treatment of TED, with a clear shift towards targeted therapies that promise to enhance patient outcomes and quality of life.

LITERATURE REVIEW

The article "Update on thyroid eye disease and management" by (D Bothun et al., 2009) provides a comprehensive overview of the management strategies for patients with Graves' ophthalmopathy, also known as thyroid eye disease (TED). The authors emphasize the importance of a multidisciplinary approach involving primary care physicians, endocrinologists, and ophthalmologists who possess specialized expertise in TED management. This coordinated care is crucial, particularly since uncontrolled thyroid function is linked to more severe manifestations of the disease.

A significant insight from the article is the impact of radioiodine therapy on TED. The authors note that while radioiodine is a common treatment for Graves' disease, it can exacerbate ophthalmic symptoms. This exacerbation risk can be mitigated

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through the administration of steroids during and after radioiodine therapy, which is particularly effective for patients with active TED. Conversely, in patients with inactive TED, the authors assert that the risk of exacerbation following radioiodine treatment is minimal. This distinction is essential for clinicians when determining the timing and appropriateness of radioiodine therapy in relation to the ocular manifestations of the disease.

The article also highlights the necessity of individualized treatment plans that consider the patient's quality of life and the psychosocial effects of TED. For patients with mild and early disease, the authors recommend a conservative management approach, which may include symptomatic treatments such as lubricating eye drops and temporary prisms for diplopia. This approach allows for careful monitoring of disease progression without immediate invasive interventions.

In cases of moderately severe to severe TED, particularly when there is a risk to sight due to optic neuropathy or corneal breakdown, the article advocates for urgent referral for 'rescue' therapy. This may include glucocorticoid administration and/or orbital decompression, underscoring the need for timely intervention in critical situations.

The authors also stress the importance of smoking cessation throughout the management of TED, as smoking is identified as a modifiable risk factor that can worsen outcomes. This recommendation aligns with the broader understanding of lifestyle factors influencing disease severity and management efficacy.

The article "Thyroid Eye Disease: How A Novel Therapy May Change The Treatment Paradigm" by (Wang et al., 2019) offers a comprehensive overview of thyroid eye disease (TED), emphasizing its complexity as an autoimmune condition characterized by various ocular manifestations, including orbital inflammation, proptosis, strabismus, corneal ulceration, and optic neuropathy. The authors effectively highlight the significant impact of TED on patients' quality of life,

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underscoring the necessity for effective treatment strategies that not only alleviate symptoms but also modify the disease course.

One of the critical evaluations presented in the article is the current reliance on treatment modalities that primarily focus on immune suppression. While these approaches can relieve symptoms, they often fall short of addressing the underlying disease mechanisms, which can lead to persistent or worsening symptoms in patients. This gap in treatment efficacy is particularly concerning, as the authors note that inadequate management of TED can severely affect patients' daily functioning and mental well-being.

The article introduces teprotumumab, an insulin-like growth factor-1 receptor inhibitor antibody, as a promising emerging therapy. The authors provide a detailed discussion on how teprotumumab represents a novel approach that may offer disease-modifying benefits, contrasting it with traditional therapies that lack this capability. This focus on a targeted therapy is crucial, given the unmet need for interventions that provide a balanced safety-risk profile while effectively managing the disease.

Moreover, the article emphasizes the importance of ongoing research and clinical trials to further investigate the long-term effects and safety of teprotumumab and other emerging therapies. This is particularly relevant in the context of TED, where treatment responses can vary significantly among individuals, necessitating a personalized approach to management.

The article titled "Teprotumumab in Clinical Practice: Recommendations and Considerations From the OPTIC Trial Investigators" by (S. Douglas et al., 2021) provides a comprehensive overview of the evolving management strategies for Thyroid Eye Disease (TED), particularly in the context of the OPTIC trial findings. The authors highlight the historical reliance on achieving euthyroidism and nonspecific immunosuppression through corticosteroids, alongside surgical interventions when deemed necessary.

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One of the critical insights presented in the article is the consensus among the American Thyroid Association and the European Thyroid Association regarding the management of hyperthyroidism in TED patients. They advocate for the prompt control of hyperthyroidism with antithyroid medications, emphasizing the importance of maintaining a stable euthyroid state ((S. Douglas et al., 2021)). This approach underscores the need for a proactive management strategy that prioritizes the patient's overall thyroid health as a foundational element in treating TED.

The article also discusses the implications of radioactive iodine (RAI) treatment in patients with pre-existing mild active TED or those with increased risk factors for disease progression. The authors recommend the use of steroid prophylaxis in these scenarios, which is crucial for mitigating potential exacerbation of TED symptoms post-RAI treatment ((S. Douglas et al., 2021)). This recommendation reflects a nuanced understanding of the interplay between thyroid function treatments and the potential for TED exacerbation, which has historically been overlooked.

Moreover, the authors critique traditional therapies for TED, noting that they primarily focus on inflammation and symptomatic relief rather than effectively addressing the underlying issues of proptosis and strabismus. The article highlights the significant limitations of high-dose steroid treatments, which are associated with serious adverse events in a substantial proportion of patients, thus raising concerns about the safety and efficacy of long-standing treatment protocols ((S. Douglas et al., 2021)).

The article's emphasis on the variability of treatment recommendations based on disease activity and severity is particularly noteworthy. It indicates a shift towards a more individualized treatment approach, acknowledging that the management of TED is not one-size-fits-all. The lack of a standardized practice pattern from the American Academy of Ophthalmology further underscores the need for more research and consensus in the field ((S. Douglas et al., 2021)).

The article "Physician-Perceived Impact of Thyroid Eye Disease on Patient Quality of Life in the United States" by (S. Douglas et al., 2021) provides a critical

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examination of the implications of thyroid eye disease (TED) on the quality of life (QOL) for patients in the United States, highlighting a significant gap in the understanding of this condition's impact compared to previous European studies.

The authors elucidate that TED is characterized by autoimmune-mediated retro-orbital inflammation, leading to symptoms such as proptosis, corneal exposure, strabismus, and varying degrees of visual impairment. This multifaceted symptomatology not only affects the physical well-being of patients but also has profound psychological and social repercussions. The article emphasizes that the quality of life for individuals suffering from TED is markedly diminished, a notion that resonates with findings from European research but remains underexplored in the U.S. context.

A critical aspect of the study is its focus on physician perceptions of patient QOL, which is posited as a pivotal factor influencing the classification of TED severity and the consequent treatment approaches. The authors argue that understanding how physicians perceive the impact of TED on their patients' lives is essential for developing more effective management strategies. The article suggests that enhanced awareness among healthcare providers regarding the QOL implications of TED could lead to more comprehensive care plans that address both the physical and emotional needs of patients.

Furthermore, the article raises important questions about the methodologies used to assess QOL in TED patients, indicating a need for standardized measures that could facilitate better comparisons across studies and regions. The authors call for further research to quantify the QOL impact of TED more robustly and to explore the potential benefits of various treatment modalities, including orbital radiotherapy, in improving patient outcomes.

The article "Thyroid eye disease: From pathogenesis to targeted therapies" by (Sook Yoon & O. Kikkawa, 2022) provides a comprehensive overview of thyroid eye disease (TED), particularly in the context of its association with Graves' disease (GD) and other thyroid conditions. TED stands out as the most common

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extrathyroidal manifestation of GD, with a notable incidence rate that underscores its clinical significance. The authors highlight that TED can also occur in patients with euthyroidism and Hashimoto's thyroiditis, broadening the understanding of its pathogenesis and clinical presentation.

The article effectively outlines the clinical characteristics of TED, noting that approximately 40% to 50% of patients with GD will develop this orbital inflammatory autoimmune disorder. The symptoms, which include eyelid retraction, exophthalmos, and diplopia, reflect the complex nature of the disease and its impact on patients' quality of life. The authors' identification of the diverse clinical phenotypes associated with TED is particularly valuable, as it emphasizes the need for tailored therapeutic approaches.

In discussing treatment modalities, the article notes that high-dose glucocorticoids and orbital radiation therapy have historically been the cornerstones of management aimed at alleviating orbital inflammation. This is significant, as it establishes a foundation for understanding how orbital radiotherapy fits into the broader treatment landscape for TED. The authors also acknowledge that for chronic inactive TED, surgical interventions may be necessary, particularly for correcting exophthalmos and strabismus.

Moreover, the article highlights recent advancements in targeted therapies, including the introduction of biologic inhibitors such as teprotumumab, which specifically target the insulin-like growth factor-1 receptor (IGF-1R). The approval of teprotumumab by the FDA in 2020 represents a significant milestone in TED management, providing new hope for patients with this challenging condition.

While the article provides a thorough overview of TED and its treatments, it could benefit from a more detailed discussion on the specific role and efficacy of orbital radiotherapy compared to other treatment modalities. A critical evaluation of the current evidence supporting the use of radiotherapy, including potential benefits and risks, would enhance the understanding of its place in the therapeutic hierarchy for TED.

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The article "Future Projections in Thyroid Eye Disease" by (Barbesino et al., 2022) provides a comprehensive review of recent translational studies and clinical trials focused on the treatment of thyroid eye disease (TED). The authors conducted a thorough search of peer-reviewed literature using specific keywords related to TED, including “thyroid eye disease,” “Graves’ ophthalmopathy,” “thyroid orbitopathy,” and “Graves’ orbitopathy,” which demonstrates a systematic approach to gathering relevant data.

One of the key insights from the article is the emphasis on the evolving landscape of treatment options for TED, particularly the role of orbital radiotherapy. The authors highlight that while traditional therapies have included corticosteroids and surgical interventions, there is an increasing interest in the application of radiotherapy as a viable treatment modality. This reflects a shift towards more targeted therapies that aim to mitigate the inflammatory processes associated with TED.

The review critically evaluates the effectiveness of orbital radiotherapy, noting that clinical trials have shown promising results in reducing proptosis and improving ocular symptoms. However, the authors also acknowledge the need for further research to establish optimal treatment protocols and to better understand the long-term outcomes associated with radiotherapy. They point out that while some studies have reported favorable responses, there is variability in patient outcomes, which underscores the necessity for personalized treatment approaches.

Moreover, (Barbesino et al., 2022) discuss the safety profile of orbital radiotherapy, suggesting that it is generally well-tolerated by patients. However, they caution about potential side effects, such as radiation-induced complications, which must be carefully weighed against the benefits of treatment. This critical analysis of the risks and benefits is essential for clinicians considering radiotherapy as a treatment option for TED.

The article "Teprotumumab and the Evolving Therapeutic Landscape in Thyroid Eye Disease" by (Lora Kossler et al., 2022) provides a comprehensive review of

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the advancements in the management of thyroid eye disease (TED), particularly emphasizing the emergence of teprotumumab as a targeted therapy. The authors conducted a thorough literature review spanning from 1979 to 2021, utilizing a variety of search terms that reflect the complexity and multifaceted nature of TED, including its association with Graves' disease and the mechanisms underlying dysthyroid optic neuropathy.

One of the critical insights from the article is the shift from traditional steroid regimens to novel biologic therapies, which marks a significant evolution in the therapeutic landscape for TED. The authors highlight how recent research has elucidated the pathophysiology of TED, particularly the involvement of the insulin-like growth factor 1 receptor (IGF-1R). This receptor's role in the disease process has been pivotal in the development of teprotumumab, an IGF-1R-inhibiting monoclonal antibody. This targeted approach not only addresses the underlying mechanisms of TED but also offers an alternative for patients who may experience adverse effects from conventional steroid treatments.

The review effectively summarizes the clinical implications of teprotumumab, detailing its efficacy and safety profile as demonstrated in clinical trials. The authors provide a critical evaluation of the data, discussing the positive outcomes associated with teprotumumab, including improvements in proptosis and quality of life for patients suffering from TED. However, they also acknowledge the need for further research to fully understand the long-term effects and potential limitations of this treatment.

CONCLUSION

The literature on orbital radiotherapy for thyroid eye disease (TED) reflects a significant evolution in the understanding and management of this complex autoimmune condition. Early foundational work highlighted the necessity of a multidisciplinary approach and the implications of uncontrolled thyroid function on ocular manifestations (D Bothun et al., 2009). As research progressed, it became evident that traditional therapies often failed to adequately modify the disease

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trajectory, leading to a call for innovative treatments that could address both the physical and psychosocial burdens of TED [ref: 9c6f64d6-7f7b-4fa2-bf71-1c648dea8b4e; ref: c09ded44-e51d-4309-95d0-6772ea287f5b].

A notable advancement in the therapeutic landscape is the introduction of teprotumumab, a monoclonal antibody targeting the insulin-like growth factor 1 receptor, which has shown promise in modifying disease activity and improving patient outcomes [ref: b86ce04c-838d-4659-9853-4f46137ce1c7; ref: 9490db16-9cf1-482f-94ad-b0ce8637f064]. However, the role of orbital radiotherapy remains critical, particularly in addressing the inflammatory processes associated with TED. Recent studies indicate that radiotherapy can effectively reduce proptosis and improve ocular symptoms, although the variability in patient responses necessitates further investigation to optimize treatment protocols (Barbesino et al., 2022).

The literature emphasizes the importance of individualized treatment strategies, taking into account the severity of the disease and the patient's quality of life. The need for comprehensive care that addresses both physical symptoms and psychosocial impacts is a recurrent theme [ref: c09ded44-e51d-4309-95d0-6772ea287f5b; ref: 6e31a688-4819-48f7-9c41-7840d75117d4]. Smoking cessation and careful management of thyroid function are also highlighted as essential components of effective TED management (D Bothun et al., 2009).

In conclusion, the body of literature on TED illustrates a shift towards more targeted and personalized treatment approaches, with orbital radiotherapy playing a vital role in the management of ocular symptoms. The integration of novel therapies such as teprotumumab alongside traditional modalities signifies a promising direction for improving patient outcomes in TED.

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REFERENCES

1. D Bothun, E., A Scheurer, R., R Harrison, A., & S Lee, M., 2009. Update on thyroid eye disease and management. ncbi.nlm.nih.gov
2. Wang, Y., Patel, A., & S Douglas, R., 2019. Thyroid Eye Disease: How A Novel Therapy May Change The Treatment Paradigm. ncbi.nlm.nih.gov
3. S. Douglas, R., Wang, Y., A. Dailey, R., J. Harris, G., T. Wester, S., S. Schiffman, J., A. Tang, R., Fowler, B., Fleming, J., & J. Smith, T., 2021. Teprotumumab in Clinical Practice: Recommendations and Considerations From the OPTIC Trial Investigators. ncbi.nlm.nih.gov
4. Wang, Y., Sharma, A., Padnick-Silver, L., Francis-Sedlak, M., J. Holt, R., Foley, C., Massry, G., & S. Douglas, R., 2021. Physician-Perceived Impact of Thyroid Eye Disease on Patient Quality of Life in the United States. ncbi.nlm.nih.gov
5. Sook Yoon, J. & O. Kikkawa, D., 2022. Thyroid eye disease: From pathogenesis to targeted therapies. ncbi.nlm.nih.gov
6. Barbesino, G., Salvi, M., & K Freitag, S., 2022. Future Projections in Thyroid Eye Disease. ncbi.nlm.nih.gov
7. Lora Kossler, A., Douglas, R., & Dosiou, C., 2022. Teprotumumab and the Evolving Therapeutic Landscape in Thyroid Eye Disease. ncbi.nlm.nih.gov

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