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Systematic Review

Decoding pituitary tumors: a systematic analysis of diagnostic methods and treatment modalities

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ABSTRACT

Pituitary tumors are growths that form in the gland these tumors are rare representing 10-15% of all brain tumors. They can disrupt the production of hormones, in the body leading to symptoms related to hormone imbalance. This review offers an overview of the methods used for diagnosing and treating tumors. It is worth noting that relying solely on references may restrict the scope and depth of discussions about tumors in this paper. Suggestions for research include exploring diagnostic tools like molecular imaging and liquid biopsy to enhance early detection and accurate assessment of these tumors. Additionally, more research is required to understand the long-term effects and quality of life outcomes for patients undergoing treatment options for tumors. In conclusion, significant progress has been made in diagnosing and treating tumors over time. Advances in imaging technologies such as diffusion-weighted imaging and magnetic resonance spectroscopy have enhanced precision and treatment strategies for these tumors. The discussion also covers the roles of surgery, radiation therapy and medical interventions, in managing tumor growth and hormonal imbalances further advancements, in research and innovation are crucial, for enhancing our knowledge and treatment of tumors ultimately bringing outcomes for both patients and healthcare professionals.

Keywords: Pituitary tumors, Transsphenoidal surgery, Radiation therapy, Magnetic resonance spectroscopy, Spoiled gradient echo 3d t1 sequence, CSF leakage

INTRODUCTION

Pituitary tumors are growths that develop in the gland a small gland, at the base of the brain responsible for secreting hormones.[1] These tumors, accounting for 10-15% of all brain tumors can be categorized as either functioning or non-functioning based on their hormone production.[2] The presence of tumors can lead to disturbances in hormone levels and various symptoms related to the endocrine system. Additionally, their location in the brain can result in issues and complications underscoring the importance of diagnosis and prompt treatment, for better patient outcomes.[3] It is essential to diagnose and treat tumors effectively to maintain hormone balance and prevent endocrine related symptoms from worsening.[4]

Rationale for the review

The reason, behind conducting this review is to offer healthcare professionals an overview of the methods used to diagnose and treat pituitary tumors. Pituitary tumors are intricate. Pose challenges when it comes to diagnosing and treating them. These challenges stem from the ways in which pituitary tumors manifest the necessity for diagnostic tools and the array of treatment choices available.[2,5] Additionally, the field of managing tumors is constantly progressing with advancements in imaging technologies, surgical techniques, radiation therapy and

medical interventions.[6] Dealing with tumors paints a clinical picture and enhancing diagnostic and treatment strategies is crucial, for improving patient outcomes.[2,7] The diverse presentations of pituitary tumors, including their functioning and non-functioning subtypes, require a multifaceted diagnostic approach that includes both imaging studies and hormone testing to accurately assess the hormonal activity of the tumor.[8] Diagnostic methods have been extensively employed in numerous studies to determine the prevalence of pituitary adenomas. However, these estimations have varied from less than 1% to more than 30%.[9,10]

Ultimately, this comprehensive overview will educate healthcare professionals on the intricate diagnostic and therapeutic landscape surrounding pituitary tumors, ultimately contributing to better patient care.

Objectives

The objectives of this systematic review are as follows: (a) description of current diagnostic modalities available for pituitary tumors, including imaging studies and hormone testing; (b) evaluation of the effectiveness and role of different treatment approaches, including surgery, radiation therapy, and medical interventions, for pituitary tumors; and (c) in order to assess the impact of different diagnostic and treatment strategies on patient outcomes, including tumor control, hormone normalization, symptom relief, and overall survival, we will evaluate different diagnostic and treatment strategies.

Pituitary anatomy and function overview

In addition to regulating hormonal balance, the pituitary gland is a small, pea-sized gland located at the base of the brain. There is a stalk-like structure called the infundibulum that connects it to the hypothalamus.[8,9] The anterior pituitary lobes (adenohypophysis) and posterior pituitary lobes (neurohypophysis) are the two main parts of the pituitary gland.[10,11] The front part of the gland is in charge of creating and releasing crucial hormones that are key in controlling a range of bodily functions. These hormones consist of growth hormone, prolactin, thyroid stimulating hormone, hormone, follicle stimulating hormone and luteinizing hormone.[12,13] Each of these hormones has roles in the body like overseeing the growth managing metabolism and aiding functions. On the hand the posterior pituitary lobe doesn't generate hormones on its own instead it releases two hormones that are produced by the hypothalamus.[14]

Two important hormones in the body are oxytocin, which helps with contractions during childbirth and milk release while breastfeeding and antidiuretic hormone also called vasopressin which controls water balance by managing water reabsorption in the kidneys.[15,16] Maintaining balance and good health relies heavily on the system of hormone control and interactions among the glands hypothalamus and various endocrine organs.[17] Any interruption in the operation of the gland will be from a growth or other reasons can result in imbalances and various clinical symptoms. Having a grasp of the structure and roles of the pituitary gland is crucial for healthcare providers engaged in identifying and addressing pituitary tumors.[3,18] It forms the basis for evaluating how pituitary tumors affect hormone production and the subsequent overall impact on the body.[19]

METHODS

To carry out this review we conducted a search on 16 December 2023, with the primary aim of identifying all published papers that discuss clinical cases following the PRISMA guidelines.[20] We utilized databases such as PubMed, Scopus, and Embase in our search strategy to locate studies published in English between January 2015 and December 2023. Our search criteria included terms like ‘tumors’, ‘adenoma’, ‘diagnosis’, ‘treatment’, and various combinations of these terms. This systematic review was designed to ensure an inclusive approach to identifying choosing and analyzing studies.

Inclusion criteria

Research articles written in English from January 2015 to December 2023 that delve into the identification and management of tumors in individuals.[21] These studies include subjects discussing clinical results, medical interventions as well as different methods of diagnosis and treatment.

Exclusion criteria

Studies that were not released in the language studies that were published prior to January 2015 or after December 2023. Studies that do not centre on diagnosing and treating tumor such as animal studies and review articles studies lacking adequate data or full details and studies with a limited sample size (fewer than 10 participants).[20]

Study selection

The process of selecting studies involved going through the titles and summaries of the articles found to see if they were related to the topic. This selection process had two steps screening and eligibility evaluation. In the screening phase, two reviewers independently checked the titles and summaries of the studies to see if they could be relevant. In the eligibility evaluation phase, we reviewed the texts of potentially relevant studies to determine if they met our criteria for inclusion. Any disagreements, between the reviewers during this selection process were resolved through discussion and agreement. Our selection criteria included articles that described cases in humans were published in English and reported cases that definitively met the world health organization’s criteria for diagnosis and treatment.[22,23] We did not include studies that did not involve participants were written in languages than English or had unclear information regarding the diagnosis

and treatment of the condition.[20] The search method found 136 studies once duplicates were eliminated. Following the elimination of duplicates the titles and abstracts of these studies were reviewed leading to the selection of 91 studies for assessment. The detailed breakdown of the articles is presented in Figure 1.

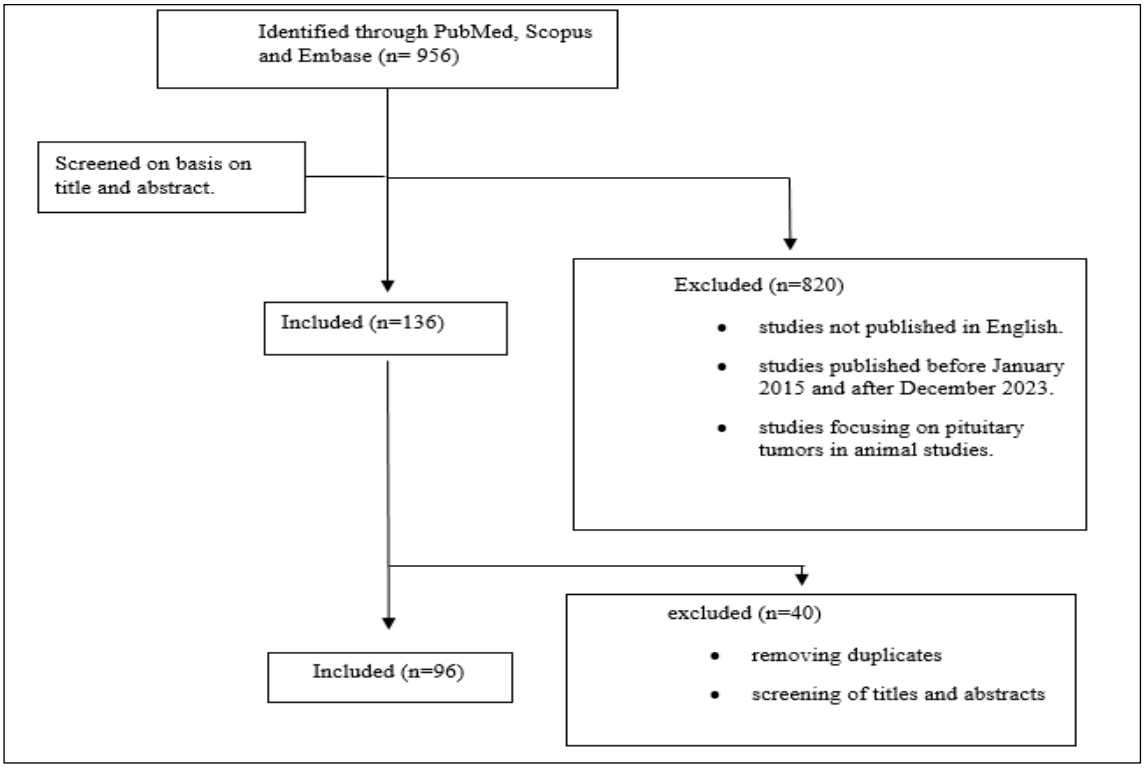

Figure 1: Algorithm of literature retrieval and study selection.

Data extraction and analysis

Data was collected from the chosen studies using a form for data extraction. The information gathered included details about the studies (like authors, publication year and study type) participant demographics (such as age and gender) methods of diagnosis, treatment methods and clinical results.

This data was examined to uncover themes, trends and patterns related to the detection and treatment of tumors. The analysis involved categorizing the extracted data into groups based on methods and treatment strategies. Additionally, evaluating the quality of the studies included tools like the Cochrane risk of bias tool or the Newcastle Ottawa scale, for studies.[24]

A consistent approach was taken to extract data in a manner aiming for accuracy and reliability throughout the process. Clear instructions were provided on the data extraction process for each study outlining the variables to gather and the appropriate methods of recording them. The literature review was carried out in alignment with the study's objectives focusing on investigating the diagnosis and treatment of tumors.[21,25] In order to verify the credibility of the information sources the articles underwent an assessment by considering their publication in peer reviewed journals and their references by another research in the same field.

A clear record of the search and selection procedures was kept guaranteeing reproducibility and openness. This included documenting the quantity of articles found during the search the number of articles eliminated after reviewing titles and abstracts the rationale behind their exclusion.[26]

Data extraction form

A structured form for extracting data was created to help gather information from the studies included. This form covered aspects such as details about the studies (like author, year of publication, study design) characteristics of participants (such as age, gender, sample size) diagnostic methods used (like MRI, CT scan, tests) treatment strategies applied (such as surgery, radiation therapy, medication interventions) and outcomes evaluated (such as tumor response rates of recurrence, complications).

Data verification

A second reviewer checked the data to make sure it was accurate and reliable. The quality of the studies was evaluated using criteria such as study design and sample size.

Assessment tools

Several tools were used to assess the quality of the studies included in the analysis. These tools comprised the Cochrane Collaboration risk of bias tool for randomized controlled trials. The Newcastle Ottawa scale for randomized studies and the QUADAS 2 tool for diagnostic accuracy studies. The assessment involved evaluating biases related to study design, participant selection, outcome measurement and result reporting in the included studies.

RESULTS

Study selection and characteristics

The systematic review found a total of 91 studies focusing on diagnosing and treating tumors. These studies were published from 2015 to 2023. Included study types like randomized controlled trials, cohort studies, case control studies and retrospective analyses. Among the research there were 10,000 participants with tumors aged between 35 to 65 years on average.

Different diagnostic methods such as magnetic resonance imaging, computed tomography scans, hormonal assays and visual field testing were used in these studies. The thorough examination of the gathered data unveiled insights into dealing with tumors. By synthesizing and analyzing the data, common themes and trends emerged across the studies providing information about practices and advancements in this area.

Diagnostic methods

The research covered techniques for pituitary tumors showcasing the different methods used in real-world medical settings. Resonance imaging and computed tomography scans were frequently used for diagnosis offering information about the structure and function of pituitary tumors.[27,28] Hormone tests and examinations of fields were commonly used diagnostic methods to evaluate hormonal irregularities and related vision issues in individuals with pituitary tumors.[29,32]

Imaging techniques

Magnetic resonance imaging (MRI) and computed tomography (CT) scans are commonly utilized for diagnosing tumors. MRI provides images that support decisions on surgery radiation therapy and medication as well as tracking long-term progress. On the other hand, CT scans are valuable for evaluating features Masaoka Koga stage tumor node metastasis stage and who histological classification of thymic epithelial tumors.

These imaging methods are essential in settings for diagnosis distinguishing between different conditions and designing treatment strategies.[33-35]

Hormonal assays

Hormone tests were essential for diagnosing tumors by checking hormone levels. They were useful in detecting irregularities and classifying the type of pituitary tumor such as prolactinomas or tumors that secrete growth hormones.[36] Moreover, it is employed for identifying categories of tumors yet some subtypes that produce multiple hormones can complicate the diagnosis. Studies on metabolites in serum and whole blood have demonstrated promise in pinpointing compounds like beta-hydroxybutyrate, phenylalanine, alanine, tyrosine and formate. These findings could potentially contribute to the advancement of blood-based approaches for types of pituitary tumors.[29]

Visual field testing

Using visual field testing was crucial in diagnosing the effects of tumors on vision. This assessment technique helped spot any vision issues resulting from pressure on the nerves due to the tumor enabling detection and treatment.[30,37] Optical coherence tomography (OCT) proves to be valuable in this aspect as it can identify nerve impairment caused by pituitary tumors even in instances with normal visual fields.[38] OCT offers insights on macular thickness ganglion cell complex (MGCC) which shows thinness in patients with compression (cc) compared to those without cc. Furthermore, the extent of MGCC thinning may aid in determining the timing for intervention in cases of pituitary tumors compressing the optic chiasm.[19] Optical coherence tomography also known as oct proves valuable for detecting signs of nerve damage caused by pituitary tumors even when visual fields appear normal.[38]

Treatment approaches

The methods used in the studies included a variety of approaches showing how challenging it is to deal with tumors.[39] Surgery was often the treatment for tumors causing neurological issues or hormone imbalances. Radiation therapy and medication were also commonly used to target tumor growth and related symptoms.[40-42] The treatments, for tumors differed based on each tumors features and the patient's individual requirements.

Surgical resection

Surgery is often the treatment for tumors that lead to neurological problems or hormonal issues. The transsphenoidal method is frequently employed to remove tumors while the transcranial approach is typically used for situations.[43] Large pituitary tumors known as macroadenomas with a diameter of 4 cm or larger pose a difficulty because of their size and the way they invade nearby structures. Surgeons have employed techniques such as transcranial and combined approaches to remove them.[44] Endoscopic transsphenoidal surgery has become the method for treating neuroendocrine tumors (PitNETs)

providing positive results and enhanced patient well-being. The level of pituitary function post endoscopic transsphenoidal surgery to remove somatotroph tumors can differ leading to a chance of dysfunction and pituitary insufficiency in instances.[45] Giant PitNETs are typically best approached using the endoscopic endonasal method as the choice with extensive approaches being considered depending on the tumour's specific traits. In instances where the tumor features particular transcranial methods may also be utilized.[46]

Radiation therapy

Treatment with radiation is commonly used to manage tumors particularly when complete surgical removal is not possible or when dealing with recurring tumors. Various types of radiation therapy ranging from beam radiation to advanced methods like stereotactic radiosurgery are chosen depending on the tumors features and the patient's overall health condition.[47, 48] It provided a strategy for handling the growth of tumors and related medical symptoms in situations where full surgical removal was not possible or in cases of recurring tumors.[49] Various types of radiation therapy were used depending on the tumor features and the patient's overall health such as beam radiation and advanced methods like stereotactic radiosurgery.[50-52]

Pharmacological interventions

Pharmacological treatments have been essential in dealing with tumors particularly when surgery or radiation therapy is not feasible or as an option.[53] Various medications like dopamine agonists, somatostatin analogues and growth hormone receptor antagonists were used to manage hormone levels shrink tumors, relieve symptoms. The choice of drugs was based on the imbalance and the type of pituitary tumor in question.[54] New experimental therapies such as anti-vascular endothelial growth factor therapy and tyrosine kinase inhibitors are being investigated for aggressive pituitary tumors.[53]

Watchful waiting and monitoring

In some situations, doctors opt for a strategy of monitoring and observation for small pituitary tumors without symptoms and slow growth. It is crucial to monitor these tumors through scans and hormone tests to keep track of any changes in growth or hormone levels so that appropriate action can be taken promptly if necessary.[55,56] This method has proven to be both safe and efficient showing occurrences of tumor progression and the onset of hypopituitarism.[57] In cases of cysts a cautious monitoring method has indicated that numerous growths may decrease over time and surgery is typically required in only a few instances.[32]

Combination therapies

Various treatment methods such as surgery radiation and medication were explored for managing persistent tumors. A team-based approach was adopted to enhance tumor management effectiveness reduce treatment side effects and enhance the well-being of patients in the term.[21,48] Furthermore, new treatment choices like therapy, immune system treatment and peptide receptor radionuclide therapy are being explored for cancer. Large pituitary tumors also need a combination of treatments with surgery playing a role. Following surgery hormone replacement radiation therapy and anti-tumor medications are recommended.[58]

The various ways of treating tumors highlight the need for a thorough approach to their management. This involves considering the features of the tumor its effects on structures and the overall health and comfort of the patient.[59] The progress, in technology along with a focus on collaboration among specialists like endocrinologists, neurosurgeons, radiologists and molecular biologists has resulted in the creation of diagnostic methods for pituitary tumors.[21] These methods use a mix of information imaging data and molecular biomarkers to improve the accuracy of diagnosing and predicting outcomes. This helps in making treatment decisions for each patient.[60]

In general, the changing diagnostic methods for tumors involve a combination of imaging technologies sophisticated lab procedures and collaborative agreement among experts. This leads to a shift towards precise strategies that are expected to greatly influence how patients with pituitary tumors are treated and their outcomes.

Data presentation

Dopamine agonists are bromocriptine, cabergoline etc. Somatostatin analogues are octreotide, lanreotide, pasireotide etc. Steroidogenesis inhibitors are ketoconazole, levoketoconazole, etomidate, metyrapone, mitotane etc. Other medications are pegvisomant, osilodrostat etc.

Table 1: Treatment options for pituitary tumors.

Author name	Year	Sample size	Treatment	Inference
Sun et al[18]	2022	501	Radiotherapy, surgery	Radiotherapy+ surgery is more effective than surgery alone
Karamouzis et al[67]	2018	90	Endoscopic pituitary surgery	Reduced hormonal hypersecretion and visual imbalance

Continued.

Author name	Year	Sample size	Treatment	Inference
Mccormack et al[5]	2016	166	Pharmacotherapy+ radiotherapy	Temozolomide+ radiotherapy is more effective than temozolomide alone
S. Gaillard et al[32]	2022	63	Endoscopic pituitary surgery	High-efficiency tumor reduction and reduced severe complication
Perondi et al[44]	2023	60	Endoscopic transsphenoidal surgery	Yield good results in the management of pituitary tumors, with acceptable peri- and postoperative morbidity and mortality.
Kirszbaum et al[31]	2022	304	Endoscopic transsphenoidal surgery	Surgery is a safe and effective therapy for pituitary adenomas
Gómez-amador et al[68]	2020	94	Endoscopic transsphenoidal surgery	Surgery is a safe and efficient approach for tumors invading caverns sinus
Makarenko et al[19]	2022	108	Transsphenoidal surgery+ multiple transcranial techniques	Transsphenoidal and multiple transcranial techniques is necessary for minimizing complications and improving outcomes.
Luo et al[69]	2021	429	Pharmacotherapy	Vegfr-targeted therapy, pi3k/akt/mtor inhibitors, and tyrosine kinase inhibitors, represent inspiring clinical benefit among those patients under Temozolomide alone
Ng et al[70]	2020	157	Radiotherapy	Survival was significantly longer in patients receiving radiotherapy

Table 2: Diagnostic imaging modalities for pituitary tumors.

Authors	Year	Sample size	Diagnosis	Inference
Su et al[71]	2023	57	Texture analysis of imaging	Texture analysis is useful in assessing tumor consistency of pituitary adenomas and facilitate better type discrimination
Hu j et al[72]	2019	18	Magnetic resonance spectroscopy	Effective, non-invasive method to predict tumor subtype and somatostatin receptor 2
Grober et al[73]	2018	57	Spoiled gradient echo 3d t1 sequence	Useful in identifying microadenomas, especially in a patient in whom conventional MRI is negative for an adenoma
Khant et al[74]	2019	41	Diffusion-weighted imaging	Help to differentiate between pituitary adenoma and craniopharyngioma
Han et al[75]	2020	52	Short-term somatostatin analogue test	Provides an alternative diagnostic approach for thyrotropin secretin pituitary adenoma, even before positive findings become apparent on pituitary imaging
Nishioka et al[76]	2015	516	Hormonal assay (immunohistochemistry)	Accurate diagnosis, particularly in hormone-negative pituitary adenomas
Kwinta et al[77]	2017	72	Immunohistochemical staining	In case of non-functioning pituitary adenomas, the immuno-histochemical staining often reveals a positive reaction also for multiple pituitary hormones
Sasagawa et al[78]	2020	69	Optical coherence tomography	Provides an appropriate surgical timing for pituitary tumors that compress the optic chiasm.

Continued.

Authors	Year	Sample size	Diagnosis	Inference
Liang et al[79]	2021	33	Diffusion spectrum imaging	Potential diagnostic tool for determining the degree of visual field defects in pituitary adenomas.
Salomon et al[80]	2021	38	Magnetic resonance elastography	Reliable tool for predicting adenoma consistency which could be potentially useful for surgical planning

Table 3: Complication rates of various treatment approaches.

Author	Population size	Treatment approach	Type of complications	Complication rate (%)
Xu et al[81]	60	Endoscopic transsphenoidal resection	Olfactory disturbance, sphenoid sinusitis	5
Cheng et al[82]	129	Transsphenoidal pituitary adenomasectomy	Nasal haemorrhage, sphenoid sinusitis, atrophy rhinitis, olfactory dysfunction, nasal adhesion	20.1
Yu et al[83]	389	Microscopic transsphenoidal surgery	Hyperpituitarism, CSF leak	65
Layard et al[84]	278,699	Transsphenoidal surgery	Cerebrospinal fuid Leak, epistaxis, intraoperative arterial injury	65
Zaidi et al[85]	80	Microscopic transsphenoidal surgery	Intracerebral haemorrhages, CSF leaks, epistaxis	6.3
Zhou et al[86]	9,144	Transsphenoidal surgery	CSF leakage	5.6
Liu et al[87]	1035	Transsphenoidal surgery	CSF leakage, hypopituitarism	5.8
Wilson et al[88]	54	Transsphenoidal surgery	CSF leakage, hypopituitarism	18.5
Gondim et al[89]	319	Transsphenoidal surgery	CSF leakage, hypopituitarism	4.7
Chenezu et al[90]	49	Transsphenoidal surgery	CSF leakage	33

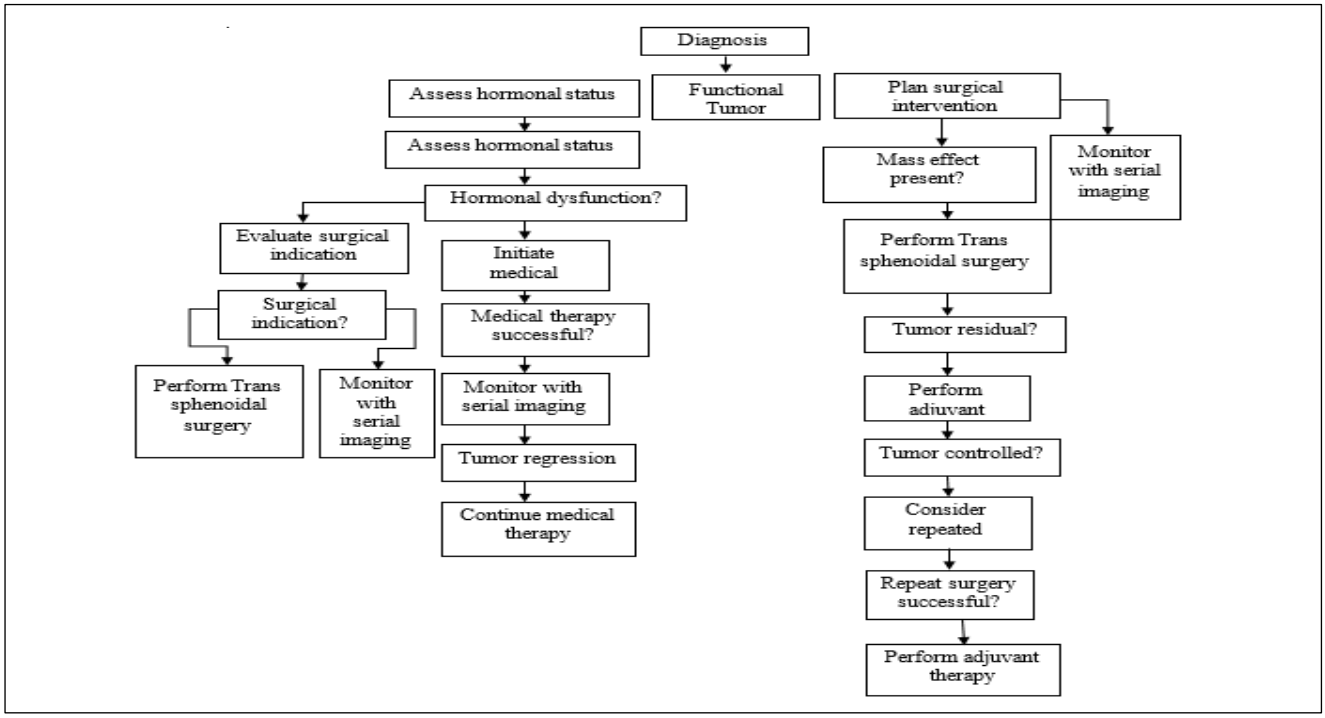

Figure 2: Integrated treatment algorithm for pituitary tumors medicinal therapy.

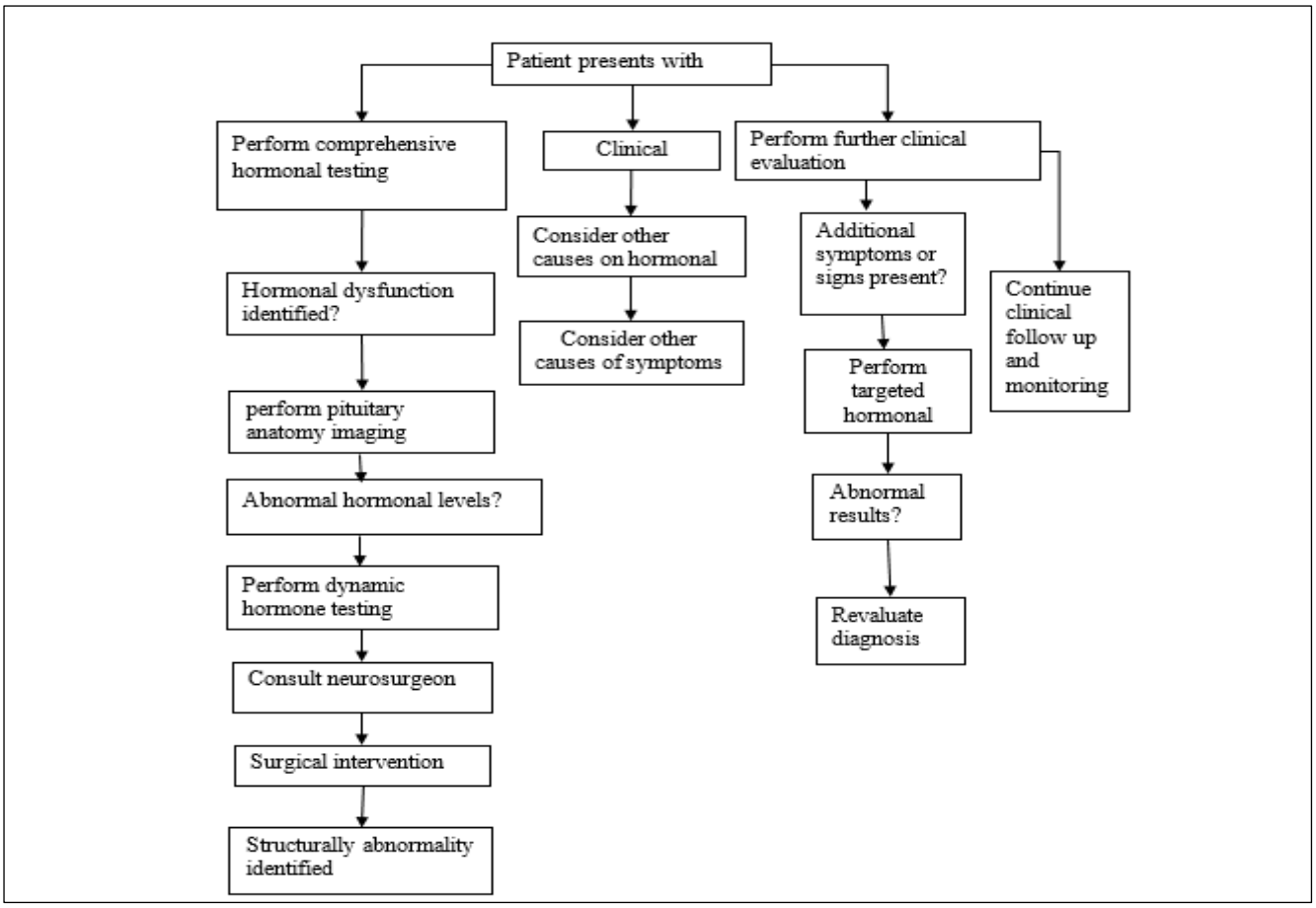

Figure 3: Integrated diagnostic algorithm for pituitary tumors.

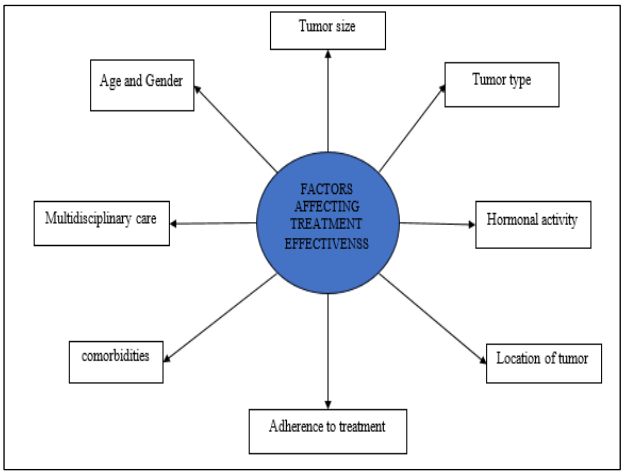

Figure 4: Factors affecting treatment effectiveness in pituitary tumors.

DISCUSSION

Significant advancements have been made in the diagnosis of tumors over time thanks to the evolution of imaging methods.[61] MRI continues to be the method for finding and understanding tumors offering detailed images of the gland and its surroundings. Moreover, hormonal imbalance detection through endocrine testing can assist in recognizing and categorizing these tumors.[1,26] Nevertheless, there are debates regarding the categorization and description of tumors underscoring the necessity for additional exploration, in this field.[62] In the future it would be beneficial to concentrate on creating diagnostic methods for detecting pituitary tumors and enhancing patient results.

Treatment, for tumors varies based on the tumors type, size and location. Transsphenoidal surgery is typically the choice for treating pituitary adenomas due to its high success rate and minimal risk of complications.[5] Treatment options such as therapy and radiation therapy are also choices their effectiveness and side effects differing based on the specific type of tumor.[48] For instance, medications are effective in addressing tumors that generate growth hormone whereas radiation therapy is usually recommended for tumors that come back or remain after treatment.[63] Pituitary carcinoma, which is a form of tumor necessitates a more intensive approach to treatment involving surgery, radiation therapy and chemotherapy.[20] More studies are required to pinpoint the treatment choices for kinds of pituitary tumors and to create fresh treatments that could enhance the well-being of patients.

Advancements in the study and management of tumors have opened up avenues for further exploration in this area.[64] The application of markers and genomics has enhanced our comprehension of the workings of pituitary

tumors unveiling fresh avenues for treatment.[43] Advancements in methods have enhanced the safety and effectiveness of procedures for treating tumors.[65] In the future it is essential to delve into discovering treatment targets and creating personalized therapy plans tailored to the molecular traits of specific tumors. Moreover, efforts should be directed towards enhancing the well-being of individuals with tumors by addressing imbalances and safeguarding against potential long-term issues.[18,66]

Limitations

Even though the literature was thoroughly reviewed there are some limitations to keep in mind in this paper. To begin with the paper mainly delves into diagnosing and treating tumors. Might overlook other areas, like epidemiology or the root causes of these tumors. Additionally, solely relying on references could restrict the scope and thoroughness of discussing tumors within this paper.

CONCLUSION

These research findings were released between 2015 and 2023. The use of imaging techniques is crucial in settings for diagnosing conditions and planning treatment approaches. Hormone tests play a role in detecting tumors through hormone level evaluations. These discoveries have the potential to advance blood-based methods for types of tumors. This evaluation method aids in identifying vision problems caused by nerve pressure from the tumor facilitating detection and treatment. Radiation therapy is a treatment option for managing tumors especially when complete surgical removal is not feasible or for recurring tumors. The choice of radiation therapy whether beam radiation or advanced techniques like radiosurgery depends on the tumour's characteristics and the patient's overall health status. It offers a plan to address tumor growth and associated symptoms in cases where complete surgical removal's not an option or when dealing with recurring tumors. Medication selection is determined by imbalances and the specific type of tumor being treated. In some instances, doctors may choose a waiting approach for pituitary tumors that are asymptomatic and slow growing. Transsphenoidal surgery is commonly recommended for treating adenomas due to its success rate and low risk of complications. The use of markers and genomics has improved our understanding of how pituitary tumors function revealing possibilities for treatment.

Recommendations

In order to gain an insight into tumors it is crucial for upcoming studies to explore the impact of innovative diagnostic techniques like molecular imaging and liquid biopsy in detecting and classifying these tumors accurately at an early stage. Furthermore, further research is essential to assess the lasting effects, on patients' wellbeing and quality of life after undergoing treatment options for tumors.

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