Renal Tumor

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Abstract: Renal cell carcinoma, also known as hypernephroma or Grawitz tumor, is the most common kind of kidney cancer, accounting for almost 90% of adult cases. Renal cell carcinoma (RCC), which makes up more than 3% of all adult malignancies and includes a variety of histological subtypes. It is an older age group tumor with a roughly 2:1 male to female ratio that is most frequently observed between the ages of 50 and 70. Prognosis 90% - 2 year survival (with spread) and Poor prognosis with Loss of genetic material on Chr11q,16q and Gain of Chr1q. There are currently several different biomarkers available that could assist direct the tailored treatment of kidney cancer patients. Renal tumors, commonly referred to as kidney tumors, are abnormal growths that start in one or both kidneys' renal tissues. The many serum, imaging, and immunohistological biomarkers that are now used in clinical practice will be covered in this review, along with potential future paths for the creation of new RCC biomarkers.

Keywords: Biomarker, Kidney, Prognosis, Renal Tumor, RCC.

1. INTRODUCTION

Renal cell carcinoma, also known as hypernephroma or Grawitz tumor, is the most common kind of kidney cancer, accounting for almost 90% of adult cases. Additional varieties comprise transitional cell carcinomas with bladder-like characteristics in the renal pelvis. An additional uncommon kidney tumor is renal sarcoma. Renal cell carcinoma (RCC), which makes up more than 3% of all adult malignancies and includes a variety of histological subtypes. It is an older age group tumor with a roughly 2:1 male to female ratio that is most frequently observed between the ages of 50 and 70. Smoking is the biggest risk factor for renal cell carcinoma (RCC), and those who smoke cigars, pipes, and cigarettes also have an increased risk. Fatality is another significant risk factor, particularly in women. It is believed that giving up tobacco use and being overweight can cut the risk of kidney cancer in half. A number of other variables, such as high blood pressure, chronic renal failure, and occupational exposure to specific chemicals, such trichloroethylene, also enhances the risk.

A diet high in fruits and vegetables, moderate alcohol use (up to two drinks per day), and long-term consumption of fatty fish are linked to a lower risk of kidney cancer. Renal cell carcinoma (RCC) is one of the top 10 most prevalent cancers globally, encompassing a diverse range of tumors originating from renal tubular epithelial cells[1]–[5]. Over the past 20 years, significant developments in the histopathological and molecular characterisation of RCC have resulted in significant changes to its classification2–5. Clear cell RCC (ccRCC), papillary RCC (pRCC), and chromophobe RCC (chRCC) are the major subtypes6 with ≥5% incidence. The remaining subtypes have a combined incidence of less than 1%, making them extremely unusual. A tumor is classed as unclassified RCC (uRCC, ~4% total incidence) if it does not meet any of the

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subtype diagnostic criteria. The bulk of kidney cancer deaths are caused by the most prevalent subtype, ccRCC, which is the subject of this Primer.

In fact, tumors with non-clear cell histology have been classified as "nccRCC" for clinical trial viability due to the prevalence of clear cell histology in metastatic illness (83–88%)12,13. Additionally, the overt complexity of intra- and inter-tumour heterogeneity in ccRCC has been shown by current cancer genomic research, which may be a factor in the varied clinical outcomes seen. Renal cell carcinomas (RCCs) account for 75–80% of adult kidney cancers and 1-3 percent of human cancers. Renal carcinomas are classified pathologically in a variety of ways[6]–[8]. The nomenclature is based on factors such as architecture, cytoplasmic appearance, combination of morphologies, anatomic location, underlying disease, familial syndromes, and particular genetic abnormalities. In the 2016 World Health Organization classification, there are four emerging/provisional entities and fourteen subtypes. Future classifications will most likely include additional emergent entities that have lately been described in the literature [9], [10].

In biological research, classifications are natural and can play a major role in the development of knowledge for illness diagnosis and therapy. It can also be seen as a means of recording the evolutionary paths taken by complex genomes in cancer. Large cohorts have emerged in an era of globalization and big data collecting, revealing not only biological variety within known entities but also among hitherto unknown ones. However, in addition to diagnostic repeatability, official integration of new entities necessitates the presence of clinical, histopathologic, and/or molecular distinguishing criteria. Renal cell carcinomas are still primarily categorized at the world's major reference centers based on their appearance and immune histo chemical characteristics, despite significant advancements in molecular characterization.

An increasing number of essential molecular traits (such as the translocation of the MiT family, fumarate hydratase insufficiency, and succinate dehydrogenase deficiency) are being translated to immunohistochemistry, as explained below. Standardizing an efficient approach to classify renal cell carcinomas may be challenging for pathologists in places like several Brazilian regions that lack access to molecular resources and specialized immunohistochemistry markers. Financial constraints may prevent a thorough diagnostic workup or the availability of a broad range of genetic tests. In order to minimize the disparity utilizing simple instruments, it is crucial to regard morphology as the primary diagnostic driver. These guidelines are meant to offer a sensible method for the subtyping of renal cell cancers using auxiliary testing. Renal cancer ranks seventh among cancers in men and tenth among cancers in women, accounting for 5% and 3% of all adult malignancies in men and women, respectively[11]–[14].

Renal cell carcinoma (RCC) makes up around 80% of all kidney malignancies; however, figures that are currently accessible do not only include renal parenchymal tumors but include urothelial cancer of the renal pelvis. Global RCC incidence patterns appear to have peaked in recent years, following more than 20 years of rising rates. Moreover, the overall fatality rates from kidney

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cancer have stabilized. These patterns align with reports of incidental diagnosis and downward shift in tumor stage and size; in fact, the broad application of non-invasive radiological techniques, such as computed tomography (CT) and ultrasonography (US), makes early and small RCCs, which may be curable, more frequently detected. In addition to the well-known risk factors for RCC, like obesity, hypertension, and cigarette smoking, there is mounting evidence that some other variables, like trichloroethylene, may have an aetiological or even protective effect. Coffee consumption with caffeine was found to be associated with a lower risk of RCC in a recently published case-control study involving 699 RCC patients and 1001 frequency-matched controls; surprisingly, coffee with decaffeinated content was linked to a higher risk of aggressive clear cell RCC (ccRCC). Moreover, people with acquired renal cystic disease, end-stage renal failure, dialysis patients, kidney transplant recipients, and those with tuberous sclerosis syndrome all seem to have a higher incidence of RCC[15]–[17].

Renal tumors, commonly referred to as kidney tumors, are abnormal growths that start in one or both kidneys' renal tissues. The behavior of these tumors varies widely, from benign (noncancerous) growths to malignant (cancerous) growths. Renal tumors can present clinically in a variety of ways. Some individuals may show no symptoms at all, while others may exhibit hematuria (blood in the urine), lethargy, flank or lower back discomfort, and unexplained weight loss. The mainstay of treatment for kidney tumors is surgery, especially if the tumor is malignant or symptomatic[18]. Partial nephrectomies, in which the tumor plus a small margin of good tissue are removed, or a radical nephrectomy, in which the afflicted kidney is removed entirely, are two possible surgical techniques. Surgery is a useful treatment for renal tumors, although there are rising worries that tiny renal masses may be overtreated.

Research has shown that a sizable fraction of tiny renal masses are benign lesions that might not be dangerous to the patient's health, especially those with a diameter of 4 cm or less. When these benign tumors are surgically removed, patients may be subjected to needless risks and surgical consequences. In order to guide treatment decisions and avoid unneeded surgery or other interventions, it is imperative that kidney tumors be accurately classified utilizing non-invasive procedures. This will allow healthcare practitioners to treat patients appropriately and effectively. Magnetic resonance imaging (MRI) and computed tomography (CT) scans, which provide detailed images of the kidney, are frequently used to identify and classify renal malignancies. On the other hand, manually interpreting and annotating CT scans can be difficult and time-consuming. Renal tumor classification using CT imaging data has been more effective and accurate in recent years thanks to machine learning (ML) methods[19]–[21].

In order to increase diagnostic accuracy, studies have used a variety of texture predictors in their investigation of texture features in CT scans used to discriminate kidney cancers. Renal cell carcinoma (RCC) is the third most prevalent genitourinary cancer in the United Arab Emirates (UA), with 14,400 projected deaths and an estimated 63,990 new cases predicted in 2017 alone. The heterogeneity of RCC poses a unique challenge in treatment, since a renal mass can be

benign (e.g., oncocytoma), clinically indolent (e.g., papillary type I, chromophobe RCC (chRCC)), aggressive (e.g., papillary type II, high-grade clear cell renal cell carcinoma (ccRCC)), or both. Thus, urologists, interventional radiologists, and medical oncologists place a high value on the ability to correctly diagnose and treat a renal tumor. In general, biomarkers are measurable, objective aspects of biological processes that gauge a physiological state and can be substituted for endpoints in the prediction of outcomes. Biomarkers can be categorized according to their characteristics, such as illness prognosis biomarkers, predictive biomarkers, and diagnostic biomarkers (i.e., predicting a clinical response to a therapy) [22]–[24]. There are currently several different biomarkers available that could assist direct the tailored treatment of kidney cancer patients. The many serum, imaging, and immunohistological biomarkers that are now used in clinical practice will be covered in this review, along with potential future paths for the creation of new RCC biomarkers.

2. LITERATURE REVIEW

James J. Hsieh et al. [1] proposed that more than 90% of kidney cancers are classified as renal cell carcinomas (RCCs), which are malignancies that started in the renal epithelium. There are over ten histological and molecular subtypes of the disease, the most common of which is clear cell RCC (ccRCC), which also causes the majority of cancer-related deaths. While somatic VHL mutations have been known for a while, more recent genomic studies on cancer have shown significant intratumor heterogeneity and discovered mutations in regulatory genes related to epigenetics, which may have implications for prognosis, prediction, and treatment. Metastatic RCC is resistant to traditional chemotherapy, however localized RCC can be effectively treated with surgery. The treatment of metastatic RCC has, however, significantly improved over the last ten years thanks to the approval of targeted drugs such as everolimus and temsirolimus, which inhibit mTOR complex 1, and sorafenib, sunitinib, bevacizumab, pazopanib, and axitini, which block vascular endothelial growth factor (VEGF) and its receptor (VEGFR). Since 2015, drugs like cabozantinib and lenvatinib that target targets other than VEGFR have been licensed; immunotherapies like nivolumab have also been introduced to the arsenal of treatments for metastatic RCC. Here, we offer a summary of the molecular biology of RCC, emphasizing ccRCC, together with updates to support the most recent clinical recommendations and a roadmap for possible future developments in RCC therapy and research.

Daniel Abensur Athanazio et al. [2] said that renal cell carcinoma classification has grown increasingly difficult. In addition to the four emerging/provisional entities and fourteen distinct subtypes, the 2016 WHO classification also contained new entities, according to recent literature. The architecture, morphological combinations, anatomical locations, underlying diseases, familial disorders, and particular genetic mutations are all taken into consideration when naming organisms. While immunohistochemistry can be helpful in some situations, it may not be enough for an entity that needs molecular confirmation of a particular gene mutation. In situations where

resources are scarce, these guidelines are intended to offer a rational and optimal method for the subtyping of renal malignancies using ancillary testing.

Jie Xu et al.[3] said that When kidney tumors measuring 4 cm or less are surgically excised, up to 20% of them turn out to be benign, which raises concerns about overtreating. But at this point, imaging alone cannot reliably predict the likelihood of malignancy before surgery. Using easily accessible clinical and CT imaging data, this study aims to present a machine learning (ML) framework for pre-operative kidney tumor categorization. To create the classification model, we experimented with both deep learning (DL) techniques—such as multilayer perceptron (MLP) and 3D convolutional neural network (3DCNN)—and classic machine learning (ML) techniques, such as XGBoost and random forest (RF). The optimal findings, as indicated by the AUC [95% CI] of 0.719 [0.712–0.726], precision [95% CI] of 0.976 [0.975–0.978], recall [95% CI] of 0.683 [0.675–0.691], and specificity [95% CI] of 0.827 [0.817–0.837], were found to be obtained when clinical and radiomics features were combined. According to our investigation, using ML models with clinical data and CT scans shows potential for risk classification of kidney cancer. In order to better assist clinical decision-making in the diagnosis of kidney cancer, future study should concentrate on externally validating the suggested model and features.

Nicholas J. Farber et al.[4] said that a unique problem in the management of kidney tumors is the variety of tumor phenotypes and histologies that a renal mass can represent. From benign tumors like oncocytomas to clinically indolent malignancies like papillary type I and chromophobe to aggressive diseases like papillary type II or high-grade clear cell renal cell carcinoma (ccRCC), kidney tumors can take many different forms. Kidney tumors are genetically heterogeneous, with varying prognoses and treatment response rates even among different subtypes. Therefore, distinguishing between these subgroups is essential for appropriate treatment. There are currently a large number of diagnostic, prognostic, and predictive biomarkers available that could assist direct the tailored treatment of individuals with kidney cancer. The many serum, urine, imaging, and immunohistological biomarkers that are now used in practice will all be covered in this review.

Zheng Gong et al.[5] said that the second most common urological tumor is a kidney tumor. There are numerous varieties, the majority of which are malignant tumors. This research suggests developing a model of simultaneous segmentation and classification of kidney cancers based on convolutional neural networks to aid medical professionals in diagnosis in order to increase the accuracy of kidney tumor segmentation and classification. Kidney tumor segmentation and classification are combined to create a two-task neural network, or 2D SCNet. According to our suggested methodology, segmentation can help the network concentrate on local features and regions of interest (ROI), while classification can provide feedback on the network's overall contextual knowledge. Each job increases the prior information of the other and works together to boost network feature learning. When segmentation and classification of 2D SCNet are combined, the accuracy rate for both benign and malignant classification can

reach 99.5%. After segmenting the data using "2D SCNet + three-label," the Dice coefficients obtained were 0.946 and 0.846, respectively. Our network's kidney and tumor segmentation outcomes are better than PSPNet by 4.9% and 5.0%, respectively. This indicates that the segmentation network's learning process benefits from the addition of a classification module. The cross-validation findings demonstrate that kidney tumor segmentation and classification tasks can be more successfully completed by 2D SCNet and the two-step segmentation technique. Any feature can have its network extracted by the 2D SCNet base network. In this research, the outcomes of the base network's segmentation and classification are compared between Res Net50+ PPM and Dense Net. Res Net50+ PPM produces superior outcomes. Kidney tumors can be more properly and efficiently segmented and examined with the aid of 2D SCNet.
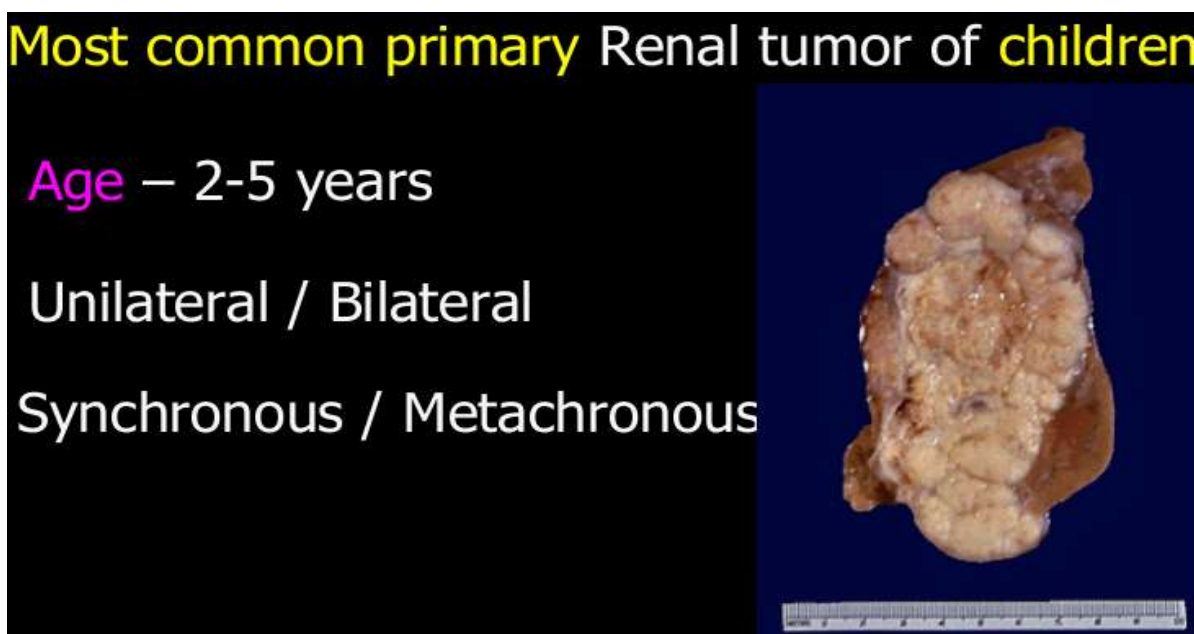
3. METHODOLOGY

Fig 1 shows Wilm's Tumor

Risk with congenital malformation:

WAGR syndrome

- Loss of Ch 11p13 (WT1) & PAX6
- Aniridia, genetic abnormalities, mental retardation

Denys-Drash syndrome

- Inactivation of Ch 11p13 (WT1)

- Gonadal dysgenesis & gonadoblastoma
- Renal abnormalities (Mesangial sclerosis)

Beckwith-Weidmann syndrome

- Enlarged body organs (tongue, kideny, liver), adrenal enlargement, hemihypertrophy (body segment enlargement)
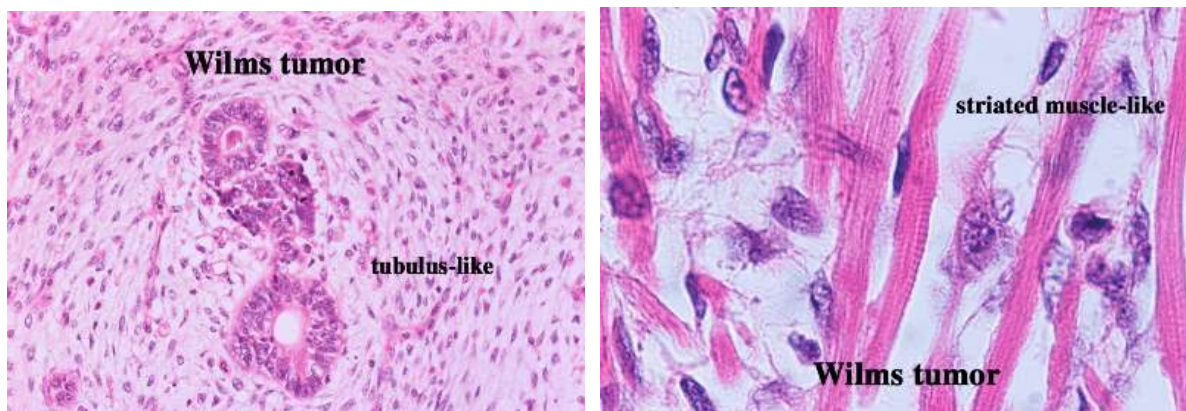- Ch 11p15.5 (WT2)

Fig 2 shows Microscopic Examination of Wilm's Tumor

Microscopic Examination

- Primitive tissue attempting to form glomeruli
- Stroma – fibrocytic/ myxoid
- Other tissue – squamous, adipose smooth muscle, cartilage bone

Treatment

- Chemotherapy, Radiotherapy + Surgery

Prognosis 90% - 2 year survival (with spread)

Poor prognosis-

1) Loss of genetic material on Chr11q,16q
2) Gain of Chr1q

UROTHELIAL CARCINOMA

(Transitional cell)

Age – 80% between 50-80 years

M: F – 3: 1

Site – Renal / Ureter/Bladder

-Lateral & Posterior wall

- may be multicentric

Etiological Factors:-

- Cigarette smoking

- Industrial exposure to arylamines

- Schistosoma haematobium infections

- Drugs / Caffeine / Alcohol / Artificial Sweeteners

4. RESULTS

MICROSCOPY-

Papilloma- benign, can be inverted or exophytic

Papillary neoplasm of low malignant potential- no invasion ,mild cytological

atypia, rare mitosis

Low grade papillary carcinoma-

moderate atypia ,invasion ,occ. Mitosis,papillary structures complex & branched
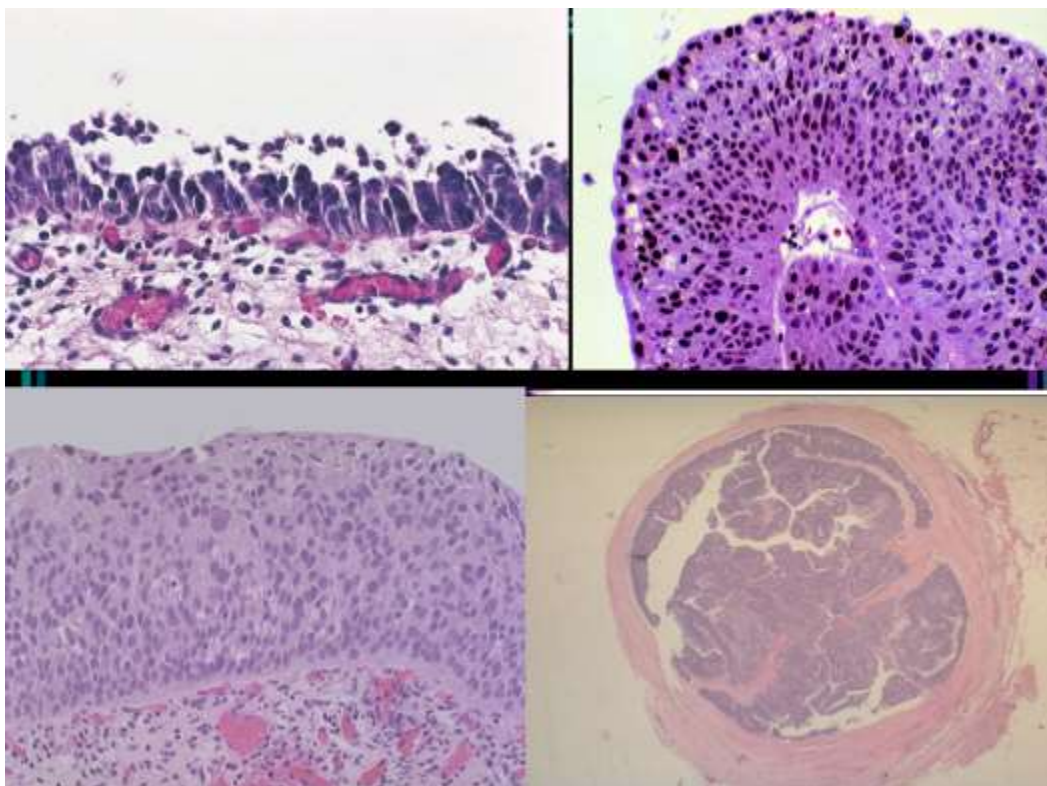
High grade papillary carcinoma

Fig 3 shows frond like Papillary projections

Clinical Features:-

- Painless hematuria
- Frequency, Urgency & dysuria
- Recurrence common

Metastasis:-

- Direct to surrounding organ
- Metastasis – Regional lymph nodes
- Via blood – Lung / Liver / B.M

5. CONCLUSION

INVESTIGATIONS-

-Cytologic examination of urine – malignant cells shed from the surface of the neoplasm in figure 4.

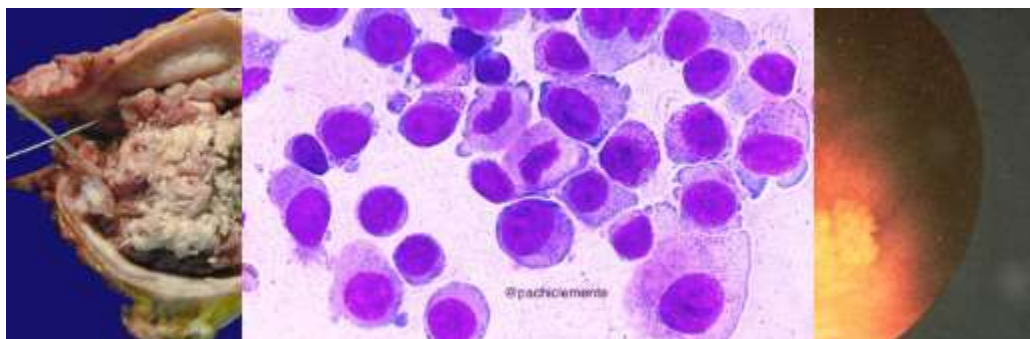-Cystoscopy can be performed and biopsies taken in figure 5.
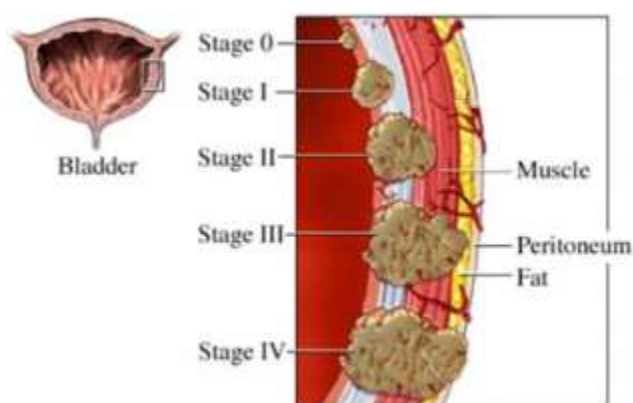
Fig 4 shows the Investigations

Fig 5 shows the staging process

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