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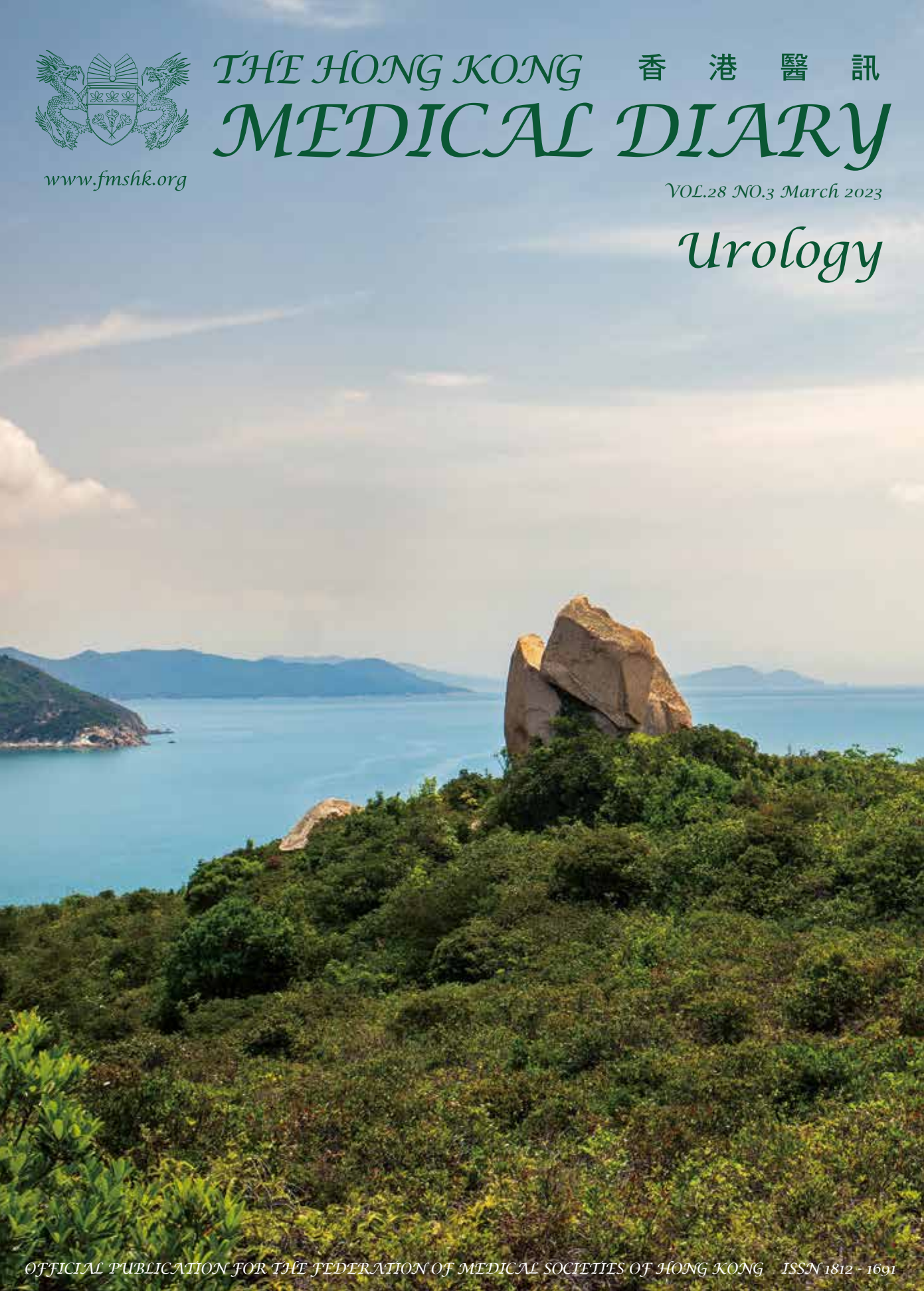

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Contents

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The Cover Shot

This photo was taken at Fan Lau (分流), which means "Spreading the water flows" in Chinese. It was at the southwest tip of Lantau Island and also the southwest part of the New Territories, dividing the current from the Pearl River and the water of the South China Sea. However, you may only see the phenomenal spreading of water flows at certain periods of time.

Dr LAM Kin-man

Specialist in Urology

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Editorial

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According to the Hong Kong Cancer Registry from 2011 to 2020, the incidence of Kidney cancer increased from 545 in 2011 to 843 in 2020. The age-standardised rate (ASR) was 5.3 per 100,000 persons in Hong Kong in 2020, approximately half of the ASR in North America and Europe. The epidemiology of kidney cancer at presentation has also changed considerably in the last decade. Most newly diagnosed cancers have shifted from large symptomatic tumours with haematuria and/or loin pain at presentation, to smaller asymptomatic tumours diagnosed incidentally on ultrasound or CT. Earlier diagnosis of smaller kidney cancers has enabled urologists to perform nephron-sparing partial nephrectomy to better preserve the renal function of cancer survivors. Partial nephrectomy is important to reduce the risk of chronic kidney disease and dialysis in the long run.

In this issue of the Medical Diary of Hong Kong, we focus on benign and malignant kidney tumours. Partial nephrectomy, laparoscopic, robotic-assisted or open, is currently the gold standard for treating small (< 4 cm, T1a) contrast-enhancing renal masses if technically feasible. The quest to minimise ischemic injury to the remaining renal parenchyma during a minimally invasive approach for partial nephrectomy remains a challenge to all urologists. In older patients or patients with higher operative risks, ablative therapy or 'active surveillance' can be used for managing these small renal masses. The role of renal mass biopsy is also discussed.

A separate chapter is dedicated to a short overview of hereditary renal cell carcinomas (RCCs). These hereditary RCCs, most commonly von-Hippel Lindau disease, are rare but these patients present with multiple or recurrent RCCs at a young age with multiple manifestations in other organs. The most common benign renal tumour, angiomyolipoma (AML), is also discussed in this issue with an update on the latest diagnosis and management options.

On behalf of the Hong Kong Urological Association (HKUA), the authors of this issue will bring to you state-of-the-art knowledge on the latest advances in the management of benign and malignant renal tumours.

基層醫療指南
Primary Care Directory

Primary Care Directory (PCD) is a web-based database set up to facilitate the public to search for suitable primary care service providers according to their practice information.

- **All registered doctors in Hong Kong are eligible** for enrolment.
- Shall accumulate the **required CME/CPD points for maintaining listing** in the directory.
- **Pre-requisite** for joining District Health Centre (DHC) Initiative, Vaccination Subsidy Scheme (VSS) and Residential Care Home Vaccination Programme (RVP).
- More than 2,600 doctors have enrolled and more than 70,000 public searches made in 2022.

The Primary Healthcare Blueprint redefines the role of the PCD into a Primary Care Register (PCR) which serves as a central register for all primary healthcare (PHC) professionals under one umbrella for better monitoring, co-ordination and quality assurance.

Key features of the Primary Care Register are,

Requiring all healthcare professionals to be enlisted in the PCD or PCR for all **Government-subsidised programmes**.

All PCD and PCR enrollees will be subject to **quality assurance**.

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Small Renal Mass - Who is Eligible for Active Surveillance?

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BACKGROUND

The incidence of renal malignancy has been on a rising trend in the recent decades. It is around 5 in 100,000 according to the latest Hong Kong Cancer Registry Report 2020[1]. This trend has been found to be associated with the increasing prevalence of metabolic syndromes, including obesity and hypertension. Introducing modern western dietary habits and a sedentary lifestyle may put the individual at risk of developing renal tumours. Other well known risk factors include smoking, acquired cystic kidney disease in patients with end-stage renal failure, and hereditary predisposition of renal cancers like von-Hippel Lindau syndrome.

Owing to the technological advancement and widespread availability of various imaging modalities in recent years, it is not uncommon for small renal masses to be incidentally picked up on routine imaging. Historical data showed a five-fold increment in renal mass detection, after the introduction of ultrasonography and computed tomography in daily clinical use[2]. And the finding often triggers a urological referral for further assessment of early disease.

A small renal mass is defined as a renal mass lesion measuring less than 4 cm in diameter[3]. (Fig. 1) Solid and cystic masses represent distinct entities and have different natural histories for disease progression.

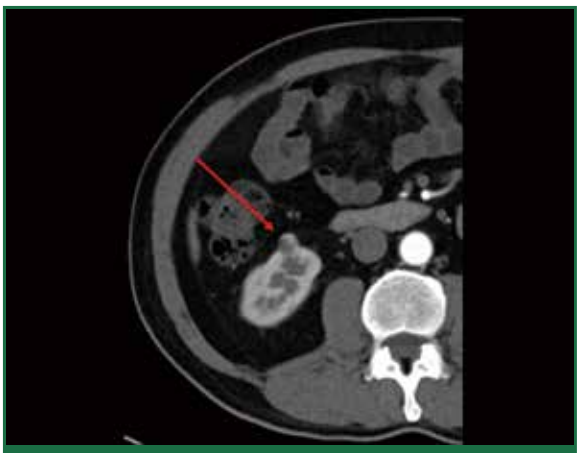

Fig. 1. An example of solid small renal mass. This is the contrast-enhanced CT image showing a right lower pole contrast-enhancing renal nodule, measuring 1 cm in diameter. (Personal collection)

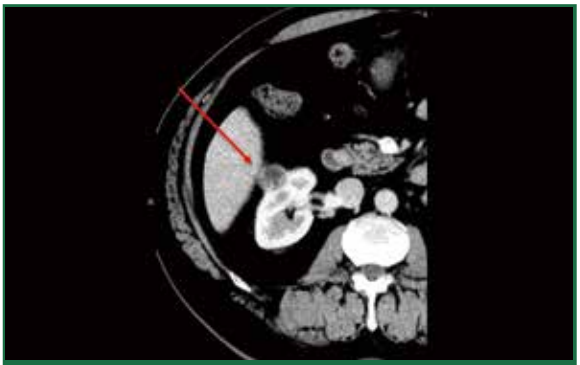

Fig. 2. An example of cystic renal neoplasm. This is the contrast-enhanced CT image showing a right mid-pole Bosniak 3 renal cyst, with thickened irregular wall, measuring 2.5 cm in diameter. (Personal collection)

CYSTIC RENAL MASSES

The risk of malignancy of cystic renal masses has been studied by Bosniak[4], who later published a classification system on cystic renal masses in 2005. (Table 1) The morphological description relies on a contrast-enhanced CT scan of the kidneys, and evaluates the presence of wall irregularity, septum, calcification, solid component, enhancement and size. Lesions of Bosniak 2F and above carry a risk of malignancy and, therefore, should be reviewed by a urologist for further action. (Fig. 2) The same author proposed a new Bosniak classification in 2019[5], further defining the numerical cutoff in thickness for septum/septa, rather than a pure morphological description. The new classification also incorporates the use of MRI in defining cystic renal masses; but the updated system still requires further validation.

Table 1. 2005 Bosniak classification of cystic renal masses (Excerpt from reference 6)

Bosniak Classification	Description	Chance of Malignancy
I	Simple cyst	Minimal
II	Septated cyst with hairline septum Hyperdense cyst < 3 cm Fine calcification	Minimal
IIF	Multiple hairline septa with minimal thickening Hyperdense cyst > 3 cm Nodular or thick calcification	5%
III	Thickened cyst wall or septa with enhancement	30 - 50%
IV	Obvious enhancing solid component	90%

Note: Adapted from Warren, K.S. and McFarlane, J. (2005), The Bosniak classification of renal cystic masses. BJU International, 95: 939-942

SOLID RENAL MASSES

On the contrary, the prognosis of solid renal masses mainly relies on the size of the lesion. The natural history of small renal mass has been studied by Mayo Clinic[7], where benign pathology may be found in 46% of those lesions < 1 cm, while malignant pathology may be found in 78 - 80% of those lesions measuring 1-4 cm. The case series by Chawla[8] also reported a low metastatic potential for small renal mass, which carries < 1% chance of metastasis in renal lesions less than 4 cm. From these studies, it is clear that the size of the lesion and the prognosis showed a good positive correlation.

MANAGEMENT OPTIONS

The management options for small renal mass include nephron-sparing surgery (partial nephrectomy), radical nephrectomy, ablative therapy and surveillance. Factors affecting a patient's wish for surveillance versus intervention have been reviewed by Campbell[9], and can be divided into patient factor, kidney factor and disease factor. (Table 2) Patient factor is determined by the baseline premorbid status of the patient and fitness to undergo a major operation, while the kidney factor involves evaluating the renal function and multifocality of the tumour. Factors affecting surgical planning would include tumour size and location, which are important before contemplating a surgical intervention or ablative therapy.

For good surgical candidates, partial nephrectomy has remained the gold standard in managing clinical T1a renal tumours. On the other hand, for frail patients with a higher surgical risk, ablative therapy could be an attractive option. Ablative therapy is also a good option in patients suffering from multi-focal or bilateral disease, with an aim to preserve renal function as much as possible.

Ablative therapy can be further divided into radiofrequency ablation (RFA) or cryoablation. Both techniques utilise image-guided access and thermal ablation of the renal tumour. Due to its minimally invasive nature, it is an attractive option for patients with higher anaesthetic risks. However, these patients should also be informed that it is considered oncologically inferior to a formal resection, be it partial or radical nephrectomy. The efficacy of ablative therapy has been evaluated by a meta-analysis by Kunkle & Uzzo, which showed a 5% local tumour progression rate in cryotherapy and 13% for RFA[10].

WHAT IS ACTIVE SURVEILLANCE?

The term "active surveillance" has been widely adopted across different medical fields, from renal tumour to prostate cancer. By definition, active surveillance refers to the postponement of treatment and associated morbidities arising from treatment until a pre-defined endpoint for intervention, which usually signifies disease progression, with curative intent in patients enjoying a good life expectancy. The dynamic balance of treatment versus surveillance varies over time, especially taking into account the surgical fitness and the pathological progression. The trigger for intervention is often due to the rapid disease progression, which tilted the balance towards more aggressive approach.

A formal prospective study has been performed by the DISSRM group (Delayed intervention and Surveillance for Small Renal Mass)[11], where both arms of the surveillance group and intervention group enjoy a similar 5-year cancer-specific survival of 99% vs 100% (Intervention vs Surveillance). The subsequent update in 2021[12] also confirmed the safety profile of active surveillance in patients aged 60 or younger. This update has laid a strong foundation for patient counselling with the option of active surveillance for well-informed individuals who wish to delay the curative intervention till evidence of disease progression.

THE ROLE OF BIOPSY IN MANAGEMENT OF SMALL RENAL MASS

The role of renal biopsy has been widely investigated in the literature. The classical indications of the renal biopsy would be patients with an equivocal diagnosis on cross-sectional imaging, metastatic disease planning for systemic therapy, or patients undergoing active surveillance[13] or ablative therapies. Renal tumour biopsy can help us to confirm the diagnosis, risk stratify the tumour, and select the most suitable candidate for the surveillance group. It is especially helpful when the histopathological report comes back to be a more aggressive tumour, such as those with Type 2 papillary RCC or histological variants such as tumours with sarcomatoid features; for these patients, we can counsel the patient on more aggressive treatment based on the more adverse tumour behaviours. The current standard of renal biopsy will be done under ultrasound or CT guidance, using 18G co-axial needle and targeting the tumour peripheries in order to avoid sampling error in the central necrotic area. The complication profile of a

Table 2. Factors affecting patients' decision on management of small renal masses (Excerpt from reference 9)

Patient factors	Kidney factors	Tumour factors
• Age • Life-expectancy • Premorbids • Anaesthetic risk	• Baseline renal function • Medical conditions potentially affecting future renal function such as Diabetes / Hypertension • Bilateral renal tumour • Tumour in the solitary kidney (Anatomical or functional) • Hereditary renal tumour	• Size • Location in relationship to vital organs like the hilum or pelvicalyceal system • Growth rate • Nephrometry score to predict operative complexity

Note: Adapted from Campbell SC, Uzzo RG, Karam JA, Chang SS, Clark PE, Souter L. Renal Mass and Localized Renal Cancer: Evaluation, Management, and Follow-up: AUA Guideline: Part II. J Urol. 2021 Aug;206(2):209-218.

renal tumour biopsy is quoted to be low, with a 4% risk of bleeding and rare reports of tumour seeding in the literature[14,15].

HOW DO WE COUNSEL THE PATIENT FOR ACTIVE SURVEILLANCE?

The main purpose of active surveillance is to delay the intervention and its associated morbidities, without jeopardising the patient's survival. Therefore, it is essential to have a regular follow-up interval, and to actively look for any evidence of early progression, which should trigger intervention. We should always counsel the patient on the potential drawbacks of active surveillance, including the potential risk of missing the window of opportunity for curative nephron-sparing surgery in case of disease progression.

A structured framework of surveillance plays an important role in patient management. Despite the lack of a standardised protocol, we will monitor the patient clinically, biochemically and radiologically. A study by Smalden et al. in Nature[16] has proposed several triggers for active intervention, including the presence of symptoms, disease progression on radiological examination, or a high growth rate on interval imaging. In 2017, the American Urological Association (AUA) published a recommendation[17] on the surveillance protocol, which involves cross-sectional imaging every 3 to 6 months, and offers intervention when there is size or stage progression of the tumour.

CONCLUSION

The finding of a small renal mass does not always necessitate the initiation of surgical intervention. Careful patient selection and patient counselling on the potential options remain important in managing small renal tumours. Active surveillance plays an important role in managing small renal masses, and offers similar oncological outcome while delaying treatment-associated morbidities. In the modern era of personalised medicine, a holistic approach should be adopted when tailoring the management plan for these patients.

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OG = Obstetricians & Gynecologists.
*According to 2021 survey by Kantar HK. Respondents are doctors (Specialist in Obstetrics & Gynaecology). Sample size N=51.

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Partial Nephrectomy: Every Nephron Counts

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 March 2023.

HISTORICAL EVOLUTION OF PARTIAL NEPHRECTOMY

The traditional teaching of cancer management emphasised the prompt removal of malignant tumours by a wide margin. For renal cell carcinoma (RCC), the most reliable solution would be radical nephrectomy (RN) proposed by Robson in 1969[1]. However, this resulted in solitary kidney with long term implications. The idea of partial nephrectomy (PN) came from Spencer Wells and Vincenz Czerny. They performed the world's first partial nephrectomy (PN) on a perirenal lipoma and angiosarcoma in 1884 and 1887 respectively[2] and proved PN was a safe procedure. However, it took a whole century for PN to gain popularity in cancer surgery after Andrew Nowick coined the term "nephron-sparing surgery" (NSS)[3]. With the advancement in imaging such as ultrasound, CT or MRI scans, most renal tumours are found incidentally. These tumours are often small and asymptomatic, yet still pose a significant malignant threat. PN is more acceptable to patients as only part of the kidney is removed; yet is it oncologically justified? When is PN the best surgical option?

INDICATION OF PARTIAL NEPHRECTOMY

Historically, PN was considered for patients who would immediately be rendered anephric following radical nephrectomy. Examples would be patients with anatomically or functionally solitary kidney and bilateral synchronous tumours. Nowadays, patients at risk of renal impairment following nephrectomy are considered a relative indication as well. This group includes patients with diabetes mellitus, renovascular disease, polycystic kidney disease or familial syndrome with an increased risk of recurrence. In the modern era, PN is even considered the standard of care for all localised cortical tumours with feasible anatomy.

KEY STEPS OF PARTIAL NEPHRECTOMY

Prior to the operation, a contrast-enhanced CT-angiogram is performed to assess the tumour complexity and vascular anatomy (Fig. 1). The surgery could be performed in an open, laparoscopic or robotic-assisted manner via a transperitoneal or retroperitoneal approach. The patient is usually put in a lateral position breaking the table at the flank. The renal hilum is isolated (Fig. 2), with the border of the index tumour marked (Fig. 3). During tumour excision, the renal artery, and sometimes the renal vein, is clamped to minimise haemorrhage (Fig. 4). Cold ischaemia with ice sludge could be applied as surface cooling in an open approach. Any breach of the collecting system should be closed with absorbable sutures. The defect would then be closed in dual layers with parenchymal and capsular compression sutures (Fig. 5). After surgery, contrast-enhanced CT is performed regularly to monitor for recurrence (Fig. 6).

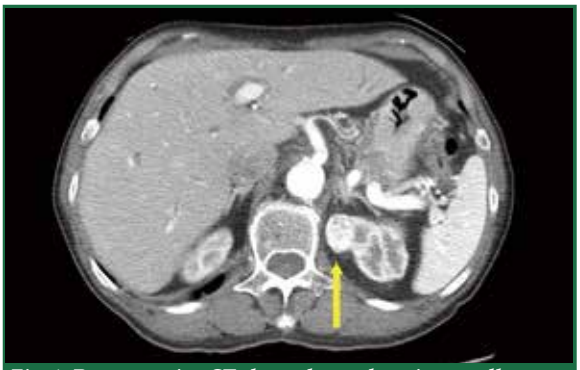

Fig. 1. Pre-operative CT showed an enhancing small renal mass over the upper pole of left kidney (Personal collection)

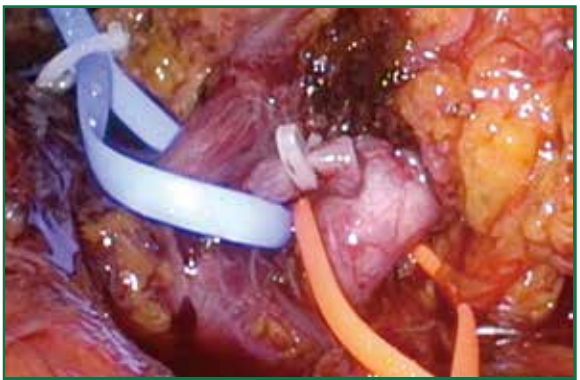

Fig. 2. Hilar control of left renal artery (red) and renal vein (blue) prior to tumour excision (Personal collection)

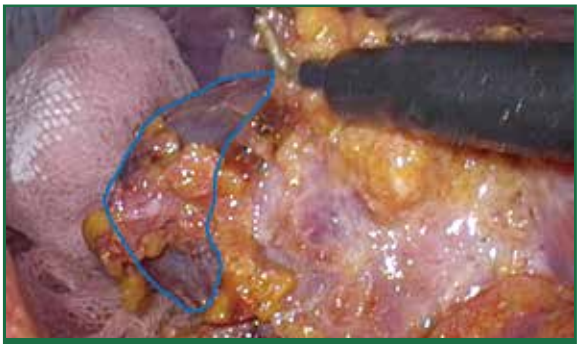

Fig. 3. Laparoscopy photo showed left kidney with tumour located at upper pole circled in blue (Personal collection)

Fig. 4. Tumour excision during laparoscopic PN (Personal collection)

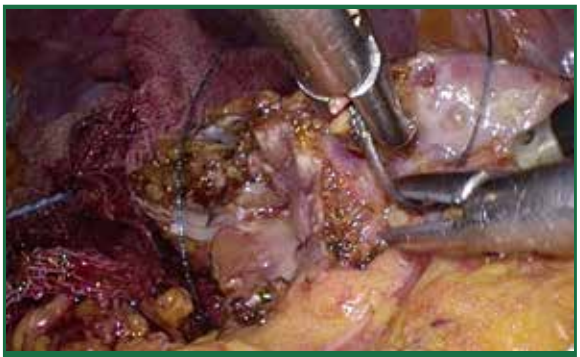

Fig. 5. Renorrhaphy after PN (Personal collection)

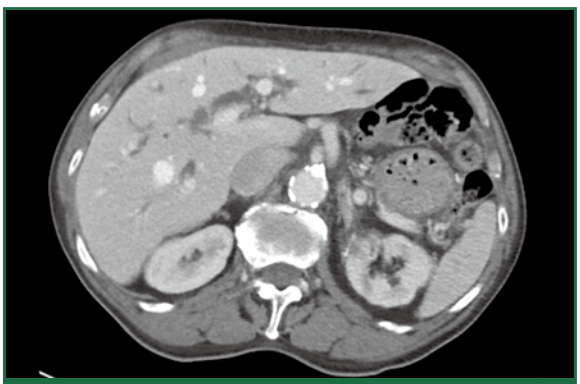

Fig. 6. Post-PN CT showed complete excision of renal mass with no recurrence 1 year later (Personal collection)

ONCOLOGICAL OUTCOME OF PARTIAL NEPHRECTOMY

The concept of PN is appealing. It is more acceptable for patients to have only part of the kidney removed as 20% of enhancing small renal mass could be benign in nature . Even if the patient later develops recurrence in the contralateral kidney, PN provides more flexibility towards future management plans. However, would it jeopardise the oncological outcome?

There are numerous retrospective studies[5,6,7,8,9], including a large meta-analysis[10] showing comparable survival statistics with PN and RN. As of now, only one prospective randomised controlled trial (EORTC 30904) compared PN vs RN in renal tumours up to 5cm in diameter. In this cohort of RCC patients, PN showed non-inferiority to RN in terms of 10-year overall, cancer-specific and progression-free survival (75%, 97% and 95% respectively). However, we must note that it was an underpowered study without meeting its target accrual of 1,300 participants (N=541). If such limitation is put aside, this study serves as the only level 1 evidence confirming PN is oncologically safe.

RENAL FUNCTION PRESERVATION IN PARTIAL NEPHRECTOMY

31% of patients diagnosed with RCC have chronic kidney disease (CKD) III or above. A follow-up study of EORTC 30904 in 2014[11] showed PN successfully reduced the development of postoperative moderate renal impairment (GFR < 60 ml/min) by 20% as compared to RN (65% vs 85%). It was also found that chronic kidney disease as a result of nephrectomy (CKD-S) had a lower risk of progression compared to renal impairment resulting from a medical cause (CKD-M)[12]. Yet, it was important to note that there was no evidence showing PN could reduce the development of end-stage renal failure or improve overall survival.

SURGICAL MARGIN FOR PARTIAL NEPHRECTOMY

The concept of nephron-sparing surgery (NSS) has further evolved in the past decade. In order to preserve nephron mass, urologists have moved towards tumour enucleation rather than the classically described "wedge resection". Literature previously showed that achieving a zero resection margin was sufficient to avoid local recurrence[13]. Even if the final pathology shows a positive surgical margin after PN (2 - 5%[14]), it does not seem to negatively influence cancer-specific survival[15]. A completion nephrectomy (removal of the entire remaining kidney) is often unnecessary and may result in overtreatment in the majority of cases[16]. Regular radiological surveillance to look for recurrence would be sufficient in the setting of a positive surgical margin.

Fig. 7. Image under white light (left) and fluorescence mode (right) during robotic assisted laparoscopic partial nephrectomy. During selective arterial clamping, the use of ICG confirms the renal tumour is not perfused while blood supply to the adjacent kidney parenchyma remains uninterrupted. This technique further reduces ischemic injury to the remaining normal renal parenchyma. (Reproduced with permission from Prof Peter Chiu with special acknowledgment)

LATEST ADVANCEMENT IN PARTIAL NEPHRECTOMY

Another aspect that urologists strive to achieve is the minimisation of ischaemic time. Some studies suggested that 25 minutes was the optimal cut-off. Using cold ischaemia, the total ischaemic time could be stretched to 35 minutes without jeopardising outcome[17]. Various techniques have been proposed to minimise ischaemia, including selective clamping[18] to the supplying vessels alone, early unclamping[19] after completion of the first layer of renorrhaphy, or even avoiding clamping[20] altogether at the expense of haemorrhage and poor surgical view during incision. In recent years, the emergence of indocyanine green (ICG)[21] allows easier identification of tumour-feeding vessels for selective arterial clamping and reduces ischemic time to the normal renal parenchyma (Fig. 7). With the use of ICG, it is also easier to identify RCC which will appear hypofluorescent from a lack of bilitranslocase enzyme. The development of robotic surgery[22, 23], non-knot tying barbed sutures[24] and sliding hemo-lok technique has certainly also minimised the renorrhaphy and ischaemic clamp time.

LIMITATION

Nonetheless, we must accept that PN is not the best option for all renal tumours. The major limitation lies in the technical difficulty and associated morbidity. Contraindications would include those with insufficient remaining parenchyma volume to maintain proper organ function or locally advanced tumours with venous thrombus. Over the years, various scoring systems have been developed to predict the tumour complexity and operative complications, such as the centrality index, and R.E.N.A.L. and PADUA scores[25].

COMPLICATION OF PARTIAL NEPHRECTOMY

Given the increased application of PN, it is crucial to recognise common complications and their associated management. Important complications include severe bleeding (3%), pseudoaneurysm and urinary fistula (4%). The risk of adjacent visceral injuries, including the liver, spleen, duodenum, great vessels, and diaphragm should be well counselled prior to surgery. The quoted reoperation and perioperative mortality rates were 4% and less than 1%, respectively[26].

CONCLUSION

PN in RCC has been proven to be an oncologically and surgically safe procedure while allowing for the preservation of renal function. As of date, PN is considered the treatment of choice for all T1 RCC, or selected T2 tumours[27], whenever technically feasible according to the European Association of Urology (EAU)[28] and American Urological Association (AUA) guidelines[29].

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Dermatology Quiz

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Specialist in Dermatology & Venereology

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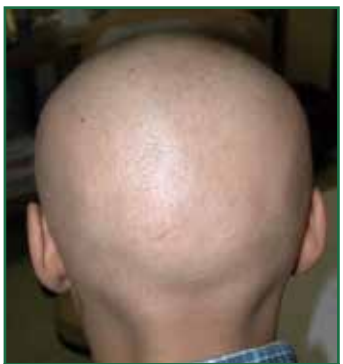

Fig. 1: Total loss of scalp hair

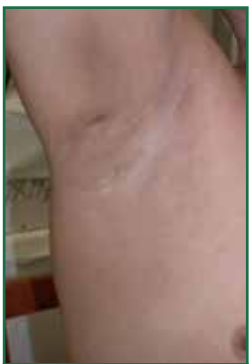

Fig. 2: Total loss of axillary hair

This 20-year-old man had rapidly progressive hair loss in the past six months. There was a complete loss of hair at his scalp (Fig. 1), eyebrows, axillae (Fig. 2) and pubic hair. He had a history of atopy in his childhood. Physical examination also revealed he had nail pitting.

Questions

1. What is your diagnosis?
2. What is the pathogenesis of this disease?
3. What are the useful clinical prognostic factors in this disease?
4. How do you treat this patient?

(See P.32 for answers)

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  - *Delivers significantly improved overall survival during the 1st year of treatment[4‡, 5††]*
  - *Significantly improves QoL and reduces prostate size compared with LHRH agonist + antiandrogen treatment[6‡‡]*
- PATIENTS ARE ASSOCIATED WITH 48% LESS RISKS OF CARDIOVASCULAR EVENTS WHEN RECEIVING FIRMAGON® COMPARED TO LHRH AGONISTS[5††]
- EAU RECOMMENDS LHRH ANTAGONISTS FOR PROSTATE CANCER PATIENTS WITH AN IMPENDING SPINAL CORD COMPRESSION OR BLADDER OUTLET OBSTRUCTION[7]

EAU: European Association of Urology; LHRH: luteinising hormone-releasing hormone; MOA: mechanism of action; PSA: prostate-specific antigen; QoL: quality of life

† A phase III, randomized, open-label trial that evaluated the efficacy of FIRMAGON vs leuprolide in achieving testosterone suppression in patients with prostate cancer (N=610). The primary endpoint was suppression of testosterone to ≤0.5 ng/mL at all monthly measurements from day 28 to day 364 (treatment response).

‡ Pooled analysis of 5 phase III/IIIb trials (N=1925) comparing prostate cancer disease control outcomes in patients received FIRMAGON vs LHRH agonists. Efficacy and safety outcomes were assessed.

†† Meta-analysis of 8 randomized controlled trials (N=2632) on clinical safety and oncologic outcomes in metastatic prostate cancer, in patients receiving FIRMAGON vs LHRH agonist±anti-androgen.

‡‡ A randomized, open-label trial comparing 3-month neoadjuvant FIRMAGON vs goserelin + bicalutamide in men with intermediate- to high-risk prostate cancer (N=244). Primary endpoint was total prostate volume reduction. Secondary objectives included the effect on lower urinary tract symptom relief and changes of quality of life related to urinary symptoms.

FOR PATIENTS WITH ADVANCED HORMONE-DEPENDENT PROSTATE CANCER[1,2]

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REFERENCES: 1) Hong Kong Product Package Insert of FIRMAGON 80mg (Date of revision: May 2015); 2). Hong Kong Product Package Insert of FIRMAGON 120mg (Date of revision: May 2015); 3) Klotz L, *et al. BJU Int.* 2008;102:1531–8; 4) Klotz L, *et al. Eur Urol.* 2014;66:1101–8; 5) Abufaraj M. *et al. Eur Urol.* 2021 Jan;79(1):44-53; 6) Mason M *et al. Clin Oncol.* 2013 Mar;25(3):190-6; 7) EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2020.

Abbreviated Prescribing Information of FIRMAGON

Active Ingredient: Degarelix. **Indications:** Treatment of advanced hormone-dependent prostate cancer in adult males. **Dosage and Administration:** Initially: 240 mg administered as 2 SC inj of 120 mg each. Maintenance: 80 mg administered as 1 SC inj mthly. The first maintenance dose should be given one mth after the starting dose. Administered as SC inj in abdominal region. **Contraindications:** Hypersensitivity. **Special Warnings and Precautions:** The vials should not be shaken. Administration of other conc is not recommended. Long-term androgen deprivation therapy may prolong QT interval. Use w/ caution in patients with Hx of QTc interval >450 msec. Hx or risk factors of torsades de pointes or CVD. Hx of severe untreated asthma, anaphylactic reactions, severe urticaria or angioedema. May decrease bone density. May reduce glucose tolerance, diabetic patients may require more frequent monitoring of blood glucose. Use w/ caution in patients w/ severe renal & hepatic impairment. ADR of fatigue & dizziness might influence ability to drive or operate machinery. May inhibit male fertility as long as the testosterone is suppressed. No relevant indication for use in women, children and adolescents. Must not be mixed with other medicinal products. **Side Effects:** Hot flush, inj site reactions, anaemia, increased wt, insomnia, dizziness, headache, diarrhoea, nausea, increased liver transaminases, hyperhidrosis (incl, night sweats), rash, musculoskeletal pain & discomfort, gynaecomastia, testicular atrophy, erectile dysfunction, chills, pyrexia, fatigue, flu-like illness. **Interactions:** Medicinal products known to prolong the QTc interval or able to induce torsades de pointes such as Class IA (e.g. quinidine, disopyramide) or Class III (amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmics, methadone, cisapride, moxifloxacin, antipsychotics.

Reference:
Hong Kong Product Package Insert of FIRMAGON 80mg (Date of revision: MAY 2015)
Hong Kong Product Package Insert of FIRMAGON 120mg (Date of revision: MAY 2015)

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Partial Nephrectomy: Every Nephron Counts" by Dr Adrian CH TAM and Dr Wayne KW CHAN and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 March 2023. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. Partial nephrectomy is contraindicated in a patient with RCC in a solitary kidney.
2. Partial nephrectomy could reduce the risk of developing moderate renal impairment compared to radical nephrectomy.
3. Chronic kidney disease due to nephrectomy has a lower risk of progression compared to renal impairment resulting from a medical cause.
4. The use of non-knot tying sutures could potentially reduce the ischaemic time during partial nephrectomy.
5. Urinary fistula is a common complication after partial nephrectomy and could occur in more than 80% of patients.
6. The patient with positive surgical margins from partial nephrectomy must undergo complete radical nephrectomy.
7. Partial nephrectomy can be performed using a robotic surgical system.
8. RCC will appear hypofluorescent after ICG injection due to the presence of bilitranslocase enzyme.
9. The centrality index could be used to predict tumour complexity.
10. A partial nephrectomy could be performed from a retroperitoneal approach.

ANSWER SHEET FOR MARCH 2023

Please return the completed answer sheet to the Federation Secretariat on or before 31 March 2023 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Partial Nephrectomy: Every Nephron Counts

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1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Name (block letters):_____ HKMA No.: _____ CDSHK No.: _____

HKID No.: __ __ - __ __ __ __ X X (X) HKDU No.: _____ HKAM No.: _____

Contact Tel No.:_____ MCHK No. / DCHK No.: _____(must fill in)

Answers to February 2023 Issue

Hybrid Functional Positron Emission Tomography and Computed Tomography Imaging: Now and the Future

1. F **2.** F **3.** T **4.** F **5.** F **6.** F **7.** T **8.** T **9.** T **10.** F

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An Introduction to Hereditary Renal Cell Carcinoma

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Dr LAW Man-chung
MBBS (HK), FRCSEd (Uro), FHKAM (Surgery)
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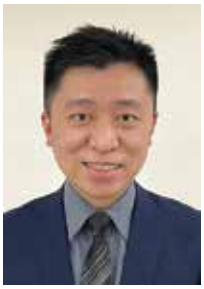

Dr Clara YC CHAN Dr LAW Man-chung

Renal cell carcinoma (RCC) is one of the most lethal genitourinary cancers. The risk factors include smoking, hypertension, end-stage renal disease, obesity and family history. It comprises a number of different diseases with different clinical courses and prognoses, each linked with a distinct histological subtype and separate genetic mutation. Familial RCC, inherited through generations in families, comprises approximately 4% of all RCCs.

Germline mutations in 12 genes have been found to be linked with hereditary renal cancer syndrome Table 1.

Table 1. Germline mutations associated with hereditary renal cancer syndrome (Excerpted from Reference 1)

Gene	Chromosome	Syndrome
Von Hippel-Lindau tumour suppressor gene	3p25	Von Hippel-Lindau disease
MET oncogene	7q31	Hereditary papillary renal carcinoma
Fumarate hydratase gene	1q42	Hereditary leiomyomatosis and RCC
Folliculin gene	17p11.2	Birt-Hogg-Dubé syndrome
Succinate dehydrogenase (subunit B/C/D) gene	5p15	Succinate dehydrogenase-deficient kidney cancer
BRCA1-associated protein 1 gene	3p21	BAP1- tumour predisposition syndrome
Microphthalmia-associated transcription factor gene (MITF)	3p13	MITF-associated cancer syndrome
Tuberous sclerosis genes 1 and 2 (TSC 1 and 2)	9q34 (TSC1) 16p13 (TSC2)	Tuberous sclerosis complex
Phosphatase and tensin homolog gene	10q23	Cowden syndrome

This article will guide you through the clinical features of these syndromes. Let's go!

VON HIPPEL-LINDAU DISEASE (VHL)

The name is derived from two medical doctors, German ophthalmologist Eugene von Hippel, who described angiomas of the retina back in 1904 and Swedish pathologist Arvid Lindau, who recognised an association between angiomas of retina and hemangiomas of the cerebellum as well as the central nervous system. It is an autosomal dominant disorder involving multiple organs.

Clinical features are listed in Table 2.

Table 2. Clinical features of Von Hippel-Landau disease (Summarised by author)

Central nervous system (CNS)	Hemangioblastoma
Retina	Hemangioblastoma
Ear	Endolymphatic sac tumour
Liver	Cyst Cystadenoma
Pancreas	Cyst Cystadenoma Islet cell tumours
Adrenal gland	Pheochromocytoma
Kidney	Cyst Renal cell carcinoma
Epididymis	Cyst Cystadenoma

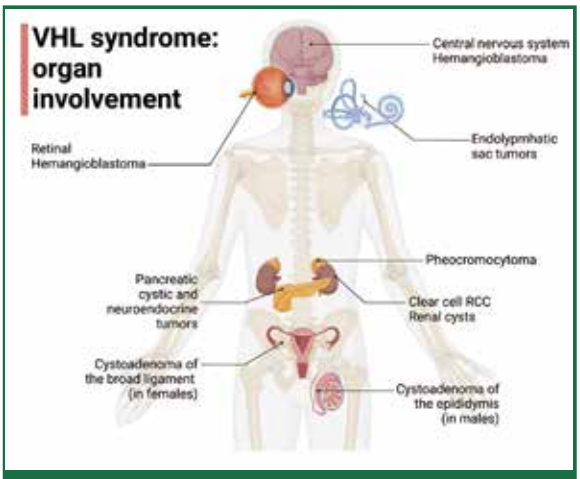

Fig. 1. Organ involvement in VHL disease (Excerpted from "Human Internal organs", by BioRender.com (2022) and https://app.biorender.com/biorender-templates.)

The incidence of Von Hippel-Lindau disease is 1 in 36,000[2]. Both sexes are equally affected. Up to 50% of the affected patients may develop clear cell renal cell carcinomas. Most of them tend to develop bilateral tumours in their 30s.

Von Hippel-Lindau disease is diagnosed when one of the following clinical criteria is met:

1. Family History of VHL and one major feature (retinal, brain, or spinal hemangioblastoma; pheochromocytoma; renal cell carcinoma or pancreatic endocrine tumour)

2. Two major features without family history of VHL

In addition, the diagnosis can be supported by genetic testing.

Affected individuals should receive multidisciplinary care with early initiation of lifelong surveillance and treatment of disease manifestation[3]. Patients with small renal tumours receive active surveillance until the tumour diameter reaches 3 cm. Nephron-sparing surgery is recommended for tumours greater than 3 cm to preserve renal function.

HEREDITARY PAPILLARY RENAL CARCINOMA (HPRC)

HPRC is an autosomal dominant inherited syndrome. It is a rare disorder with no more than 30 families reported worldwide up to now. Affected patients are prone to develop bilateral, multifocal type 1 papillary RCCs. No extra-renal manifestation has been found.

Type 1 papillary RCCs are relatively slow growing. Magnetic resonance imaging (MRI) or computed tomography (CT) are preferred due to the isoechoic nature of the tumours on ultrasound. Affected patients with small renal tumours less than 3 cm are managed by active surveillance. Nephron-sparing surgery is recommended for tumours greater than 3 cm to preserve renal function.

HEREDITARY LEIOMYOMATOSIS AND RCC (HLRCC)

Patients with this autosomal dominant inherited syndrome are more prone to develop cutaneous and uterine leiomyomas (fibroids) as well as type 2 papillary RCCs.

Cutaneous leiomyomas are benign smooth muscle tumours more commonly found over the trunk and extremities. They can cause pain and discomfort to the patients. Type 2 papillary RCCs are aggressive in nature and can metastasise even if the tumour size is small[4]. Hence excision with nephron-sparing approach and wide margin is preferred over active surveillance.

Affected individuals should receive care from the dermatologist and gynaecologist to screen for disease manifestation. Annual abdominal MRI and CT are recommended to screen for renal tumours, which can be found in up to 20% of HLRCC patients.

BIRT-HOGG-DUBE SYNDROME (BHD)

Birt-Hogg-Dubé (pronounced as Birt-Hog-DooBAY) syndrome is named after Arthur Birt, Georgina Hogg and William Dubé, the three Canadian doctors who first described it in 1977[5]. It is again an autosomal dominant inherited disease which is prone to develop fibrofolliculomas, lung cysts, spontaneous pneumothorax and renal tumours. Clinical manifestation varies between different members of a BHD-affected family. Fibrofolliculomas which are benign painless tumours of hair follicles and lung cysts, can be seen in 80% of the BHD patients. They are 50 times more likely to develop spontaneous pneumothorax and seven times more likely to develop renal tumours. BHD patients can present with renal tumours of various histologies, such as hybrid tumours with chromophobe and oncocytic features, chromophobe RCC, clear cell RCC and oncocytomas. The tumours should be monitored and only be removed with nephron-sparing surgery if they have grown to 3 cm in diameter.

Fig. 2. (A) Axial CT slice through the lung bases demonstrated multiple cystic changes within the lung parenchyma. (B) Photograph of the face demonstrating multiple pale papules on the cheeks and nose, consistent with fibrofolliculomas
Reproduced from Facial papules and lung cysts: a case of Birt-Hogg-Dubé syndrome, Griffiths P, Bull A, 12:e232083, 2019 with permission from BMJ Publishing Group Ltd

SUCCINATE DEHYDROGENASE-DEFICIENT KIDNEY CANCER

Succinate dehydrogenase (SDH) is a mitochondrial enzyme with four subunits (SDHA, SDHB, SDHC and SDHD). While SDHB gene mutation is known to cause tumourigenesis, families with SDHC and SDHD mutations were also reported to have early-onset RCCs. Succinate dehydrogenase-deficient kidney cancer is a very rare autosomal dominant disorder. Affected individuals are at risk of developing bilateral, multiple renal tumours at a young age. They are also prone to develop paragangliomas, pheochromocytomas and gastrointestinal stromal tumours.

BAP1-TUMOUR PREDISPOSITION SYNDROME

The tumour suppressor gene BRCA1 associated protein one mutations were found to have an increased risk of uveal melanomas, malignant mesothelioma, cutaneous melanoma, clear cell renal cell carcinoma and basal cell carcinoma. Due to the limited number of families reported, the natural history, penetrance and

frequencies of these BAP1-mutated tumours remain unclear. Affected individuals should undergo screening for renal tumours with yearly MRI or CT.

MICROPHTHALMIA-ASSOCIATED TRANSCRIPTION FACTOR (MITF)-ASSOCIATED CANCER SYNDROME

MITF is an important transcription factor for melanocyte development and differentiation. The MITF p.E318K variant is found to confer risk for not only melanoma but also renal cell carcinoma and pancreatic tumours[6].

TUBEROUS SCLEROSIS COMPLEX (TSC)

Tuberous sclerosis complex is seen in 1 in 6,000 to 1 in 10,000 people. It is a rare multisystem autosomal dominant disorder. In one-third of cases, patients inherit mutated TSC1 or TSC2 gene from a parent with the disorder. The remaining two-thirds of patients are born with new variants of TSC1 or TSC2 in the absence of family history. 20% of patients have TSC1 Hamartin mutation, and 80% have TSC2 Tuberin mutation.

Affected patients are prone to develop cortical tubers, cutaneous angiofibromas (Fig. 3), cardiac rhabdomyomas, pulmonary lymphangioleiomyomatosis and kidney neoplasia. Angiomyolipomas, benign tumours which consist of blood vessels, smooth muscle cells and fat cells, are the commonest renal manifestation. Other renal tumours such as oncocytomas, clear cell, papillary and chromophobe RCCs can occasionally be found in patients with TSC. Regular renal imaging should be done in affected patients.

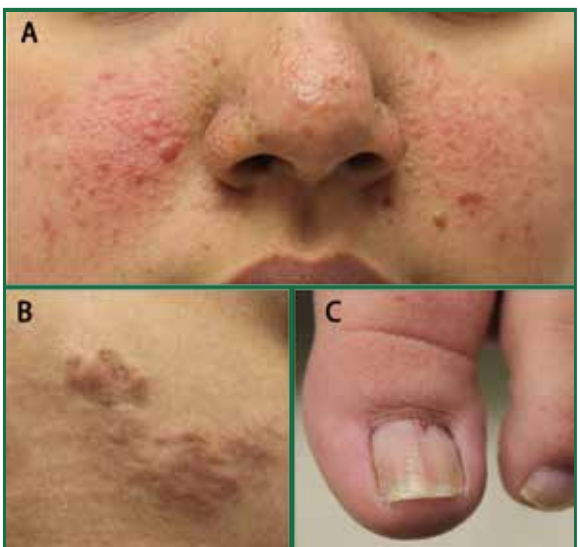

Fig. 3. Representative skin lesion subtypes in tuberous sclerosis. (A) Facial angiofibromas, (B) shagreen patch and (C) periungual or subungual fibromas
Reproduced from Cutaneous manifestations of tuberous sclerosis complex and the paediatrician's role, Cardis MA, DeKlotz CMC, 102:858-863, 2017 with permission from BMJ Publishing Group Ltd

COWDEN SYNDROME

Cowden syndrome was named after the Cowden family and was discovered and reported in 1963 by Lloyd and Dennis. It is an autosomal dominant multisystem disorder characterised by the development of hamartomas. Benign mucocutaneous lesions are most seen, followed by benign and malignant tumours of the thyroid, breasts and endometrium. Papillary RCC is associated with Cowden syndrome.

In summary, renal cancers can be associated with several hereditary conditions. Understanding the clinical features and genetic basis of these conditions can help us make a more accurate diagnosis with better treatment.

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for injection

ZERBAXA® is now indicated for
Hospital-acquired Pneumonia (HAP) / Ventilator-associated Pneumonia (VAP)[1]

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Consider ZERBAXA® for ventilated patients

ZERBAXA® was studied in critically ill patients with vHAP/VAP, including[2]

- Patients in the ICU **(92%)**
- Mechanically ventilated **(100%)**
- Failing current antibiotic therapy **(13%)**

ZERBAXA® in vHAP/VAP[2]

PRIMARY ENDPOINT
Non-inferior to meropenem in 28-day all-cause mortality in ITT population

FAVOURABLE SUBGROUPS
Favourable 28-day all-cause mortality for the subgroups of vHAP and previous failure of antibiotics for current nosocomial pneumonia episode

MICROBIOLOGICAL RESPONSE RATE
Higher microbiologic eradication rates in ME population with *P. aeruginosa*

Study Design: A randomized, controlled, double-blind, non-inferiority trial conducted between Jan 16, 2015 and April 27, 2018 at 263 hospitals in 34 countries. Patients were randomly assigned (1:1), and stratified by type of nosocomial pneumonia (either VAP or vHAP) and age (<65 years vs ≥65 years), to receive either 3 g ZERBAXA® or 1 g meropenem intravenously every 8 h for 8–14 days. The primary endpoint was 28-Day all-cause mortality (at a 10% non-inferiority margin). ME population: patients with key gram-negative lower respiratory tract pathogens at baseline

Reference: 1. ZERBAXA® Hong Kong Product Circular. 2. Kollef N *et al.* Ceftolozane-tazobactam versus meropenem for treatment of nosocomial pneumonia (ASPECT-NP): a randomised, controlled, double-blind, phase 3, non-inferiority trial. *The Lancet, Infectious Diseases.* 2019;19(12):1299-1311.

ICU = Intensive Care Unit, ITT = Intent-to-treat, vHAP = ventilated Hospital-acquired Pneumonia, HAP = Hospital-acquired pneumonia, ME population = Microbiologically evaluable, VAP = ventilator-associated Pneumonia

Clinical Cure Rates in a Phase 3 Trial of cIAI by Baseline Renal Function (MITT Population)

Baseline Renal Function	ZERBAXA® plus Metronidazole n/N (%)	Meropenem n/N (%)
CrCl greater than 50 mL/min	312/366 (85.2)	355/404 (87.9)
CrCl 30 to 50 mL/min	11/23 (47.8)	9/13 (69.2)

Zerbaxa® Selected Safety Information

Indications:
Zerbaxa® is indicated for the treatment of the following infections in adults:
- Complicated intra-abdominal infections;
- Complicated urinary tract infections, including pyelonephritis;
- Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP)

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Contraindications:
ZERBAXA® is contraindicated in patients with known serious hypersensitivity to the components of ZERBAXA® (ceftolozane and tazobactam), piperacillin/tazobactam, or other members of the beta-lactam class.

Precautions:
- Decreased Efficacy in Patients with Baseline Creatinine Clearance of 30 to 50 mL/min
  In a subgroup analysis of a Phase 3 cIAI trial, clinical cure rates were lower in patients with baseline CrCl of 30 to 50 mL/min compared to those with CrCl greater than 50 mL/min (below Table). The reduction in clinical cure rates was more marked in the ZERBAXA® plus metronidazole arm compared to the meropenem arm. A similar trend was also seen in the cUTI trial. Monitor CrCl at least daily in patients with changing renal function and adjust the dosage of ZERBAXA® accordingly (see Dosage).
- Hypersensitivity reactions
  Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam antibacterial drugs.
  Before initiating therapy with ZERBAXA®, make careful inquiry about previous hypersensitivity reactions to other cephalosporins, penicillins, or other beta-lactams. If this product is to be given to a patient with a cephalosporin, penicillin, or other beta-lactam allergy, exercise caution because cross sensitivity has been established. If an anaphylactic reaction to ZERBAXA® occurs, discontinue the drug and institute appropriate therapy.
- *Clostridium difficile*-associated diarrhea
  Clostridium difficile-associated diarrhea (CDAD) has been reported for nearly all systemic antibacterial agents, including ZERBAXA®, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of *C. difficile*. *C. difficile* produces toxins A and B which contribute to the development of CDAD. CDAD must be considered in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary because CDAD has been reported to occur more than 2 months after the administration of antibacterial agents.
  If CDAD is confirmed, discontinue antibacterials not directed against *C. difficile*, if possible. Manage fluid and electrolyte levels as appropriate, supplement protein intake monitor antibacterial treatment of *C. difficile*, and institute surgical evaluation as clinically indicated.
- Development of Drug-Resistant Bacteria
  Prescribing ZERBAXA® in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

Adverse Events:
- Complicated Intra-abdominal Infections and Complicated Urinary Tract Infections, Including Pyelonephritis
  The most common adverse reactions (5% or greater in either indication) occurring in patients receiving ZERBAXA® were nausea, diarrhea, headache, and pyrexia.
- Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP)
  The most common adverse reactions (2% or greater) occurring in patients receiving ZERBAXA® were hepatic transaminase increased[1], renal impairment/renal failure[2], diarrhea, intracranial hemorrhage[3], vomiting, clostridium difficile colitis[4].

1 Includes alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, hypertransaminasaemia, liver function test abnormal.
2 Includes acute renal failure, anuria, azotemia, oliguria, prerenal failure, renal failure, renal impairment.
3 Includes cerebellar hemorrhage, cerebral hematoma, cerebral hemorrhage, hemorrhage intracranial, hemorrhagic stroke, hemorrhagic transformation stroke, intraventricular hemorrhage, subarachnoid hemorrhage, subdural hematoma.
4 Includes Clostridium difficile colitis, Clostridium difficile infection, Clostridium test positive.

- Laboratory Values
  In clinical trials, there was no evidence of hemolysis in patients who developed a positive direct Coombs test in any treatment group.

Before prescribing, please consult the full prescribing information

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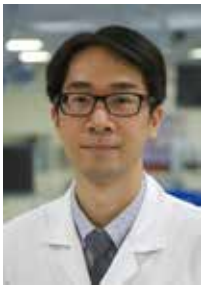
HK-ZER-200005 Oct/2020

Renal Angiomyolipoma

Dr Chloe HT YU
Tseung Kwan O Hospital

Dr CHAN Ning-hong
Tseung Kwan O Hospital



Dr Chloe HT YU Dr CHAN Ning-hong

INTRODUCTION

Angiomyolipomas (AMLs) are mesenchymal tumours derived from perivascular cells composed of thick-walled blood vessels, smooth muscles and adipose tissues[1]. The majority of AMLs are benign, but the rare epithelioid variant is considered potentially malignant.

EPIDEMIOLOGY

The incidence of renal AMLs is 0.13%[2]. Most AMLs occur sporadically (80%), while the rest occur in association with tuberous sclerosis. In sporadic cases, AML occurs predominantly in females, and commonly presents in middle age as an incidental finding of a single slow growing asymptomatic lesion.

Patients with tuberous sclerosis also have female predominance; they frequently present with multiple and bilateral AML with a higher growth rate of 20%, and are more likely to result in spontaneous haemorrhage and malignant transformation[3]. Up to 70% of patients with tuberous sclerosis will be diagnosed with AML. Nephron loss is more likely in these patients due to the higher likelihood of requiring treatment.

CLINICAL PRESENTATION

AMLs usually present as an incidental finding on imaging performed for other indications, or for those with tuberous sclerosis who undergo screening. Symptomatic patients present with symptoms of haemorrhage, such as ipsilateral loin pain or mass, haematuria, and haemorrhagic shock. Wunderlich syndrome is defined as spontaneous, non-traumatic renal haemorrhage into the subcapsular or perirenal spaces, with AMLs being one of the most common causes.

Risk factors for bleeding include those with AMLs greater than 4 cm, tuberous sclerosis patients, pregnant females, exophytic growth pattern, intralesional aneurysms greater than 5 mm and high grade of angiogenic component[4,5,6]. For AMLs greater than 4 cm, 80% present symptomatically, while 9% will present with haemorrhagic shock[7].

DIAGNOSIS

Asymptomatic patients are usually diagnosed by imaging such as computed tomography (CT) or magnetic resonance imaging (MRI) with contrast. Confirmation of diagnosis by the above imaging is preferred in those who have ultrasound findings suggestive of AML. The characteristic finding is the presence of fat components within the renal mass. (Fig. 1 and 2) CT scans typically show low attenuation lesions of less than -15 Hounsfield units, with homogeneous enhancement and delayed washout upon contrast administration. AMLs appear hyperintense on T1 sequences and hypointense on T2 sequences on MRI, with the addition of gadolinium contrast establishing the presence of intralesional aneurysms and angiogenic components. After confirmation with CT or MRI, ultrasonography can be used in the surveillance of lesion size.

Differentiating AML from other renal lesions on imaging may be difficult in those with fat-poor AML. These patients with indeterminate findings should be managed as potential renal malignancies.

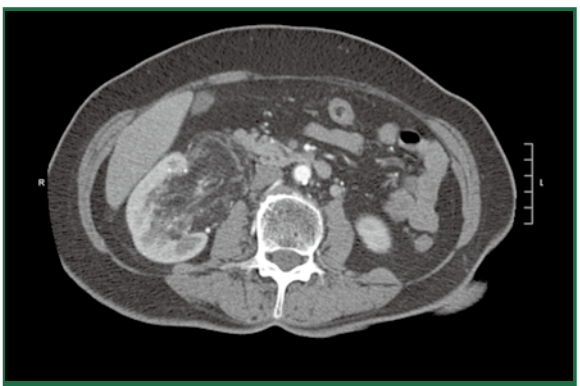


Fig. 1. Axial cut computed tomography scan of right renal AML, with fat component seen. (Personal collection)

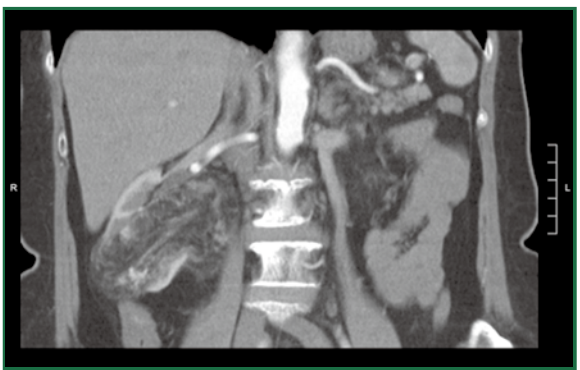


Fig. 2. Coronal cut computed tomography scan of right renal AML. (Personal collection)

SUBTYPES

Histologically there are the classic and epithelioid variants. The classic variant is far more common, consisting of a variable proportion of blood vessels, smooth muscle and adipose tissue. They are considered benign but may also invade locally, involving the perirenal fat, collecting system, renal vein and inferior vena cava. The prognosis is not affected. The epithelioid variant is made up of more than 80% epithelioid cells[8], and may undergo malignant transformation[9]. They are commonly fat-poor on imaging due to the high proportion of epithelioid cells. Variants are only distinguishable by biopsy.

EMERGENCY MANAGEMENT OF ACTIVE BLEEDING FROM AML

The treatment goals are active resuscitation, early recognition of the pathology, control of the bleeding site and preservation of renal function.

In patients who present with haemorrhagic shock, active resuscitation with intravenous fluids or blood products should be performed via large bore intravenous cannulas. Vitals signs should be monitored closely, and intensive care unit colleagues should be consulted for assessment.

Clinicians should maintain a high level of suspicion for bleeding AML in patients who present with symptoms or signs of retroperitoneal haemorrhage, especially in those with known AML or with a history of tuberous sclerosis. Urgent imaging with CT should be arranged to assess for any active bleeding.

The mainstay of emergency treatment is selective artery embolisation (SAE) by interventional radiologists. (Fig. 3) Embolic agents injected intra-arterially, occluding the blood supply can stop the bleeding, as well as induce coagulative necrosis of the AML. (Fig. 4) Embolisation is a minimally invasive procedure which is well tolerated by patients, and reduces the need for nephrectomy by 85% among patients with bleeding AMLs[10]. Complications include those associated with vascular access (e.g. pseudoaneurysm, hematoma, vessel thrombosis), use of intravenous contrast (e.g. contrast allergy, contrast induced nephropathy), and post-embolisation syndrome. Post-embolisation syndrome typically presents with severe flank pain, fever and vomiting after embolisation of large AMLs, and is managed conservatively.

In those for whom SAE is not technically feasible or has failed at controlling the bleeding, emergency partial or total nephrectomy should be performed.

Patients should be closely monitored post-procedure for any rebleeding and need for re-intervention.

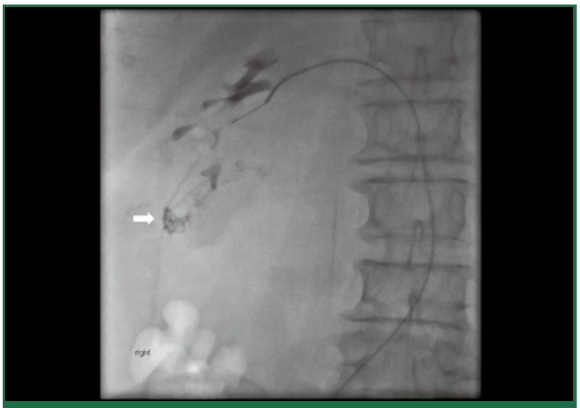


Fig. 3. Angiogram of the right renal artery showing increased vascularity over the lower pole of right kidney, supplying the AML. (Personal collection)

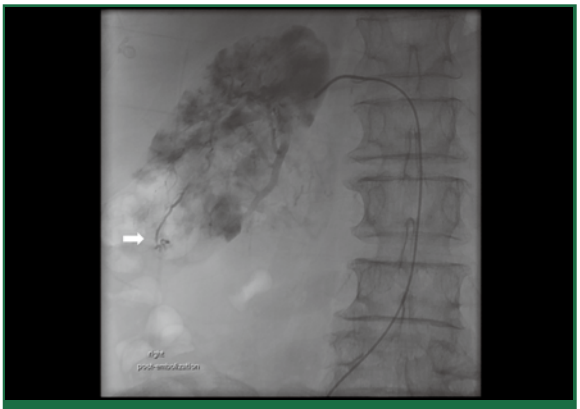


Fig. 4. Angiogram of the patient shown in Figure 3 of the right renal artery post-selective arterial embolisation with microsphere and glue: no more vascularity seen within the right AML. (Personal collection)

ELECTIVE MANAGEMENT OF AML

Small, asymptomatic AMLs should be put on active surveillance with regular imaging.

Active intervention in the form of SAE or surgery should be considered in those with high risk of future bleeding, which includes those with AMLs greater than 4 cm, tuberous sclerosis patients, pregnant females, exophytic growth patterns, intralesional aneurysms greater than 5 mm and high grade of angiogenic component. There are currently no randomised controlled trials nor guidelines comparing SAE and surgery in the management of AMLs[11].

SAE is less invasive and can reduce the size of AMLs by 25-80%[12]; however, technical difficulty, higher recurrence rates, and the need for secondary treatment (31% for SAE vs 0.85% for surgery)[13] may play a role in influencing the choice of treatment.

Surgery, preferably partial nephrectomy, is recommended for those with equivocal imaging findings and prefer pathological confirmation. It is, however, more invasive than SAE, and total nephrectomy may be required for centrally located AML or in those with

difficult dissection intra-operatively. Risks of partial nephrectomy include urinary fistula, severe bleeding, pseudoaneurysm formation, infectious complications, damage to viscera and conversion to total nephrectomy with increased risk of renal impairment.

Patients with tuberous sclerosis present with multiple, bilateral AMLs with high growth rates. Everolimus, an mTOR pathway inhibitor, was found to be successful in reducing the size of AMLs in this population. A randomised controlled trial showed that 42% of patients with tuberous sclerosis or sporadic lymphangioleiomyomatosis associated AMLs more than 3 cm responded with at least 50% volume reduction of angiomyolipoma relative to baseline at a median medication exposure of 28.9 months[14], and the effect was found to persist up to 4 years follow up with a response rate of 58%[15]. Extended follow up of the study showed efficacy in both AMLs related to tuberous sclerosis and in sporadic cases[16]. Common treatment related side effects include stomatitis, hypercholesterolemia, acne and nasopharyngitis.

FOLLOW UP

Patients on active surveillance with increasing AML size on serial ultrasound should undergo contrast CT or MRI scans for better documentation and identification of vascular anatomy for possible treatment planning.

Post-SAE patients should also undergo follow-up imaging to confirm embolisation of all involved vasculature and to review the success of tumour downsizing.

CONCLUSION

Renal AMLs are mostly benign tumours composed of blood vessels, smooth muscles and adipose tissues. They are common referrals to a urologist. The majority of AMLs are sporadic in nature and are incidentally found on imaging for other indications. Tuberous sclerosis-associated AMLs are frequently multiple and bilateral, with faster growth and a higher risk of bleeding. Diagnosis is by CT or MRI scans with visualisation of fat components. SAE is the mainstay of emergency treatment of bleeding AML. Elective treatments include active surveillance, SAE, partial nephrectomy and the mTOR inhibitor Everolimus, with treatments tailored to each individual.

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References: 1. ERLEADA® Hong Kong Prescribing Information P03. **2.** Chi KN, et al. N Engl J Med. 2019;381(1):13–24. **3.** Chi KN, et al. N Engl J Med. 2019;381(1):13–24. Supplementary information.

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Black Belt and Judo Coach, 2007 - present

Dr LO Ka-lun

WHAT IS JUDO ABOUT?

History of Judo

Judo was created in 1882 by Kanō Jigorō (KJ, 嘉納 治五郎) as an eclectic martial art, distinguishing itself from its predecessors[1]. Judo's philosophy revolves around two primary principles: " 精力善用 , maximum efficiency with minimum effort", and " 自 他 共 榮 , mutual welfare and benefit". KJ set up the rules and regulations for referees of competitions. Moreover, he travelled to Europe and spread Judo outside Japan in the 1930s. It was officially announced as an Olympic event in the 1964 Tokyo Olympic.

Rank System (Belt Colour) in Judo

The kyu and dan of Judo are distinguished by different coloured belts, with the colour representing the rank. The sixth kyu is the lowest grade and the tenth dan is the highest, and athletes who successfully attain a dan ranking can apply to become coaches.

Fig. 1. Belt Colour in Judo (The sixth kyu is from white to brown colour and the tenth dan is from black to red colour) (Personal collection)

Judo and Rei - Etiquette

Judo etiquette can be divided into standing (for throwing practice) and sitting Rei (for grappling practice). We need to perform Rei to our partner before and after throwing or grappling practice. The spirit and protocols of Rei are two of the fundamental aspects when learning Judo. It shows great respect and thanks our partner for giving us the opportunity to improve our judo technique[2].

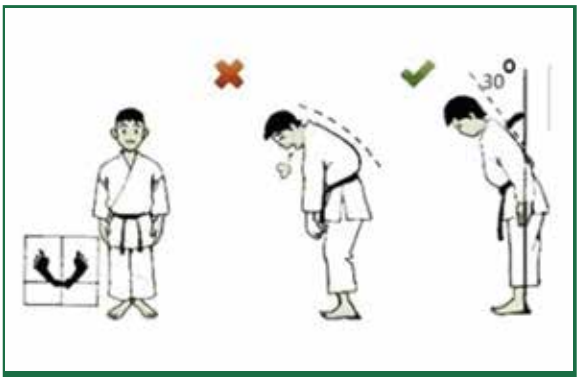

Fig. 2. Standing Rei (Personal collection)

Fig. 3. Sitting Rei (Adapted from reference 3)

Judo Falling Techniques - Ukemi (護身倒法)

The principle of "自他共榮, mutual welfare and benefit" requires that we learn to fall as well as throw[4]. Fall breaking is employed to prevent injury and minimise the pain when a contestant falls or is thrown by an

Fig. 4. Ukemi (Adapted from reference 5)

opponent. Fall breaking includes front, back, right, and left break falls, and a forward roll break fall. In addition to being a basic component of throwing techniques, fall breaking is also a fundamental part of all judo techniques, and is, therefore, of the highest importance. Break fall drills begin gently and from low postures, and are gradually performed faster and from higher postures. Finally, they are performed during actual movement.

Judo Techniques

There are three basic categories of waza (techniques) in Judo: nage-waza (throwing techniques), katame-waza (grappling techniques) and atemi-waza (striking techniques)[6]. Judo is mostly known for nage-waza and katame-waza.

Fig. 5. Nage-waza (Throwing techniques) (Personal collection)

Fig. 6. Katame-waza (Grappling techniques) (Personal collection)

Basic rules of Judo

In judo competitions, both contestants will use judo techniques at will, and there are no fixed moves. The contestant who scores an "ippon (一本)" wins the contest.

However, Judo itself has a set of strictly prescribed practice methods called "Kata", which are like martial arts routines. Kata illustrates the theory of Judo and is practised in pairs. Kata is mandatorily assessed in rank examinations. During practice, the two parties are divided into the tori (taker) and the uke (receiver), namely the person who performs the technique and the person to whom the technique is performed. Judo attaches great importance to the cultivation of Kata, and a different assessment range of Kata is expected each day. The athletes must be familiar with both roles as the taker and the receiver when using various techniques.

WHAT CAN WE BENEFIT FROM JUDO?

Judo is a sport that trains strength, speed, physical fitness and body coordination. The various movements of Judo involve multiple sets of muscles of the body, which not only increase muscle strength but also improve the elasticity of bones, ligaments and joints; all these movements offer certain benefits for maintaining bone health. Ukemi is about receiving the fall gracefully[4]. It protects us and prevents our injury from falling.

Fig. 7. A forward roll break fall to protect us from injury (Personal collection)

On the other hand, Judo focuses on etiquette and decent character, which can cultivate good behaviour, such as athletes' willpower, endurance and respect for others in the long run. The progressive learning method of Judo has resulted in a clear advancement model and has transformed traditional Japanese Jujutsu into a modern sport with a fair referee system. Because of the above advantages of Judo, some family members of a few Urologists started to learn Judo when they were young. They also won the championship and represented Hong Kong, competing in 2022 Jeju Cup International Judo Tournament.

Fig. 8. Hong Kong Representatives in 2022 Jeju Cup International Judo Tournament (Personal collection)

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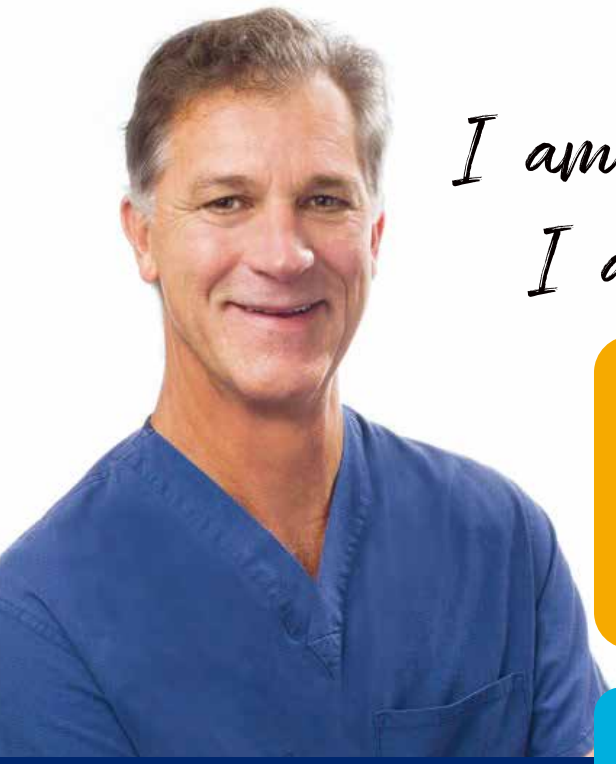
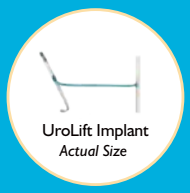
UROLIFT

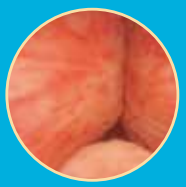


I am a urologist.
I am a patient.

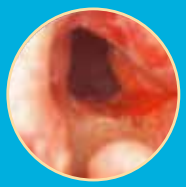
> "I went from getting up 3 times a night to sleeping through 6-8 hours! What a difference it has made at work as well. I can now complete longer surgeries without urgency to void."
>
> **Philip Butler, M.D., F.A.C.S.*** *Genesis Healthcare Partners* and UROLIFT SYSTEM PATIENT



UroLift Implant
Actual Size



PRE-PROCEDURE



POST-PROCEDURE

FDA cleared to treat patients with prostate volumes up to 100cc

MAIN REASONS I CHOSE THE UROLIFT SYSTEM AND RECOMMEND IT TO MY PATIENTS

Patients have a better recovery experience than TURP, with durable results and no new and lasting sexual dysfunction**[1,7,9]

Rapid relief and recovery in days, not months[1,6]

Lowest catheter rate of the leading BPH procedures[2,5-7,9,10]

The only leading BPH procedure that does not destroy tissue

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Real world outcomes consistent with randomised controlled data[8]

Check out the data at **UroLift.com**
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Indicated for the treatment of symptoms of an enlarged prostate up to 100cc in men 50 years or older. As with any medical procedure, individual results may vary. Most common side effects are temporary and include haematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence.[1] Rare side effects, including bleeding and infection, may lead to a serious outcome and may require intervention. Consult the Instructions for Use (IFU) for more information.

*Dr. Butler is a paid consultant of NeoTract | Teleflex. Results may vary.
**No instances of new, sustained erectile or ejaculatory dysfunction in the L.I.F.T. pivotal study.

1. Roehrborn, J Urol 2013 2. Bachmann, Eur Urol 2013; 3. AUA BPH Guidelines 2003, 2010, 2018 4. Naspro, *Eur Urol* 2009 5. Montorsi, *J Urol* 2008; McVary, *J Sex Med* 2016 6. Shore Can J Urol 2014 7. Roehrborn et al. *Can J Urol* 2017 8. Eure et al J Endourol 2019 9. Mollengarden, Prostate Cancer Prostatic Dis 2018; 10. Gilling, J Urol 2017

Teleflex

INTERVENTIONAL UROLOGY

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
			★Zoom Live Update on the Management of Osteoarthritis - Online **1**	★Certificate Course in Ophthalmology 2023 - Module I (Video Lectures) **2**	**3**	★In-person / Zoom Live CME Hybrid Symposium - COVID-19: Towards Endemicity 1: COVID-19: Looking back and Challenges Forward 2: COVID-19: Emerging variants and Boosting Strategies **4**
5	★Zoom Live Doctor, Why Can't I Get Pregnant? - Online **6**	★In-person / Zoom HKMA - HKSH CME Programme 2022-2023 (Physical Lecture + Online) Topic: Complication of Pregnancy - Preeclampsia ★Certificate Course on Complaint Management 2023 (Video Lectures) **7**	★The Hong Kong Neurosurgical Society Monthly Academic Meeting - Giant Pituitary Adenoma: Treatment Strategies & Outcome ★Zoom Live Management of DM and Microalbuminuria - Online **8**	★Zoom Live Management of Dyslipidemia in 2023: What Should We Know? - Online ★Certificate Course in Ophthalmology 2023 - Module I (Video Lectures) **9**	★Zoom Live HCC Surveillance and Use of PIVKA II as a New HCC Biomarker - Online **10**	**11**
12	★Zoom Live Update & Management in Severe Mental Illness - Online **13**	★Zoom Live Updates in Management of Allergic Rhinitis - Online ★Certificate Course on Complaint Management 2023 (Video Lectures) **14**	★Zoom Live Management of Hip Pain - More than Osteoarthritis - Online **15**	★Zoom Live Understanding Children with Autism Spectrum Disorder (ASD) & Providing Counseling to Their Families ★Certificate Course in Ophthalmology 2023 - Module I (Video Lectures) **16**	★Zoom Live Recent Advances in Diagnosis and Management of Benign Breast Conditions and Breast Cancer - Online **17**	**18**
19	**20**	★In-person / Zoom HKMA-GHK CME Programme 2023 - Cataract/ Glucoma ★Certificate Course on Complaint Management 2023 (Video Lectures) **21**	★In-person / Zoom HKMA-CUHK Medical Centre CME Programme 2023 (Physical Lecture + Online) Common health problems amongst middle age - Topic: Stroke - Is it preventable? Management and Rehabilitation **22**	★Certificate Course in Ophthalmology 2023 - Module I (Video Lectures) ★FMSHK Executive Committee Meeting ★FMSHK Council Meeting **23**	**24**	**25**
26	**27**	**28**	**29**	★Zoom Live Enlarged Lymph Nodes - A Practical Approach and the Red Flags - Online ★Certificate Course in Ophthalmology 2023 - Module I (Video Lectures) ★Symposium on pneumococcal diseases and vaccines in pediatric and adult patients (In-person/ Zoom) **30**	**31**	

Certificate Course for Doctors, Radiographers, and Nurses who are working in the Emergency Department, Family Medicine, Obstetric or women's clinic • Course No. C392 • CME/CNE Course

Certificate Course on
Medical Ultrasound 2023

Jointly organised by

The Federation of Medical Societies of Hong Kong

HKSUM Hong Kong Society for Ultrasound in Medicine

Hong Kong Society for Ultrasound in Medicine

Objectives:

To provide up-to-date knowledge on point-of-care (POC) ultrasound to diagnose common and important medical problems seen in the acute, ward, and clinic settings. This program will include ultrasonography of abdomen, point-of-care ultrasound (POCUS) for emergency and general. Ultrasonography in women's health including breast, gynaecology, and obstetrics will be covered. The course will be suitable for doctors, radiographers, and nurses who are working in the emergency department, family medicine, obstetric or women's clinic.

Date	Topics	Speakers
4 April 2023	Ultrasonography of abdomen	Dr. WONG Ho-ting, Christie Dr. MOK Kar-yan, Natalie Residents Radiology, Queen Mary Hospital
11 April 2023	Point-of-care ultrasound for emergency (for Accident & Emergency)	Dr. TSUI Chi-leung Associate Consultant Accident & Emergency, Prince of Wales Hospital
18 April 2023	Point-of-care ultrasound for general (for Family Medicine)	Dr TANG Hok-him, Wisely Resident Radiology, Queen Mary Hospital
25 April 2023	Mammogram + breast ultrasound	Dr. LAM Poy-wing, Tina Chief of Service, Radiology Queen Mary Hospital
2 May 2023	Gynaecological ultrasound	Dr. Grace HO Consultant, Radiology Queen Mary Hospital
9 May 2023	Obstetric ultrasound: from the first to the third trimester	Dr. LEUNG Kwok-yin President Hong Kong Society for Ultrasound in Medicine

Date : 4, 11, 18, 25 April and 2, 9 May 2023 (Tuesday)
Duration of session: 1.5 hours (6 sessions)
Time : 7:00 pm – 8:30 pm
Course Feature: Video lectures (with Q&A platform for participants to post the questions)
Quiz for doctors: DOCTORS are required to complete a quiz after the completion of each lecture
Language Media : Cantonese (Supplemented with English)
Course Fee : HK$1,000
Certificate : Awarded to participants with a minimum attendance of 70% (4 out of 6 sessions)
Deadline : 28 March 2023
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax : 2865 0345 Email : vienna.lam@fmshk.org

CME / CNE/ CPD (Radiographers) Accreditation in application
Online Application from website: http://www.fmshk.org

Date / Time	Function	Enquiry / Remarks
1 WED 2:00 PM	**Zoom Live** **Update on the Management of Osteoarthritis - Online** Organiser: The Hong Kong Medical Association Speaker: Dr Adrian Hon-bong LEUNG	HKMA CME Dept. Tel: 3108 2507 1 CME Point
2 THU 7:00 PM	**Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Kelvin Hon-nam WAN, Prof Clement THAM	Ms Vienna LAM Tel: 2527 8898
4 SAT 2:00 PM	**In-person / Zoom Live** **CME Hybrid Symposium - COVID-19: Towards Endemicity** **1: COVID-19: Looking back and Challenges Forward** **2: COVID-19: Emerging variants and Boosting Strategies** Organiser: The Hong Kong Medical Association and the HK Society of Infectious Diseases Speaker: Prof David HEYMANN; Dr TSANG Kay-yan Venue: Hotel in Yau Tsim Mong District	HKMA CME Dept. Tel: 3108 2507 2 CME Point
6 MON 2:00 PM	**Zoom Live** **Doctor, Why Can't I Get Pregnant? - Online** Organiser: The Hong Kong Medical Association Speaker: Dr Jennifer Sze-man MAK	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7 TUE 1:00 PM	**In-person / Zoom** **HKMA - HKSH CME Programme 2022-2023 (Physical Lecture + Online)** **Topic: Complication of Pregnancy - Preeclampsia** Organiser: The Hong Kong Medical Association and the Hong Kong Sanatorium & Hospital Speaker: Dr Chan Wan-pang Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7:00 PM	**Certificate Course on Complaint Management 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Ms LEUNG Suk-chong, Ms Asha SHARMA	Ms Vienna LAM Tel: 2527 8898
8 WED 7:30 AM	**The Hong Kong Neurosurgical Society Monthly Academic Meeting - Giant Pituitary Adenoma: Treatment Strategies & Outcome** Organiser: Hong Kong Neurosurgical Society Speaker(s): Dr WONG Mei-ting Chairman: Dr Faith Lok-yan HO Venue: Conference Room, F2, Department of Neurosurgery, Queen Elizabeth Hospital; or via Zoom meeting	Dr Calvin MAK Tel: 2595 6456 Fax. No.: 2965 4061 1.5 Points College of Surgeons of Hong Kong
2:00 PM	**Zoom Live** **Management of DM and Microalbuminuria - Online** Organiser: The Hong Kong Medical Association Speaker: Dr WONG Wai-sheung	HKMA CME Dept. Tel: 3108 2507 1 CME Point
9 THU 2:00 PM	**Zoom Live** **Management of Dyslipidemia in 2023: What Should We Know? - Online** Organiser: HKMA-KLN East Community Network Speaker: Dr Andy Wai-kwong CHAN	Mr. Peter Ho Tel: 3108 2514 1 CME Point
7:00 PM	**Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr HO Wing-lau	Ms Vienna LAM Tel: 2527 8898
10 FRI 2:00 PM	**Zoom Live** **HCC Surveillance and Use of PIVKA II as a New HCC Biomarker - Online** Organiser: HKMA-KLN City Community Network Speaker: Dr Henry Lik-yuen CHAN	Ms Candice TONG Tel: 3108 2513 1 CME Point
13 MON 2:00 PM	**Zoom Live** **Update & Management in Severe Mental Illness - Online** Organiser: The Hong Kong Medical Association Speaker: Dr LAM Chun	HKMA CME Dept. Tel: 3108 2507 1 CME Point
14 TUE 2:00 PM	**Zoom Live** **Updates in Management of Allergic Rhinitis - Online** Organiser: The Hong Kong Medical Association Speaker: Dr Julian Kay-chung YAU	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7:00 PM	**Certificate Course on Complaint Management 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr CHOW Kai-ming	Ms Vienna LAM Tel: 2527 8898
15 WED 2:00 PM	**Zoom Live** **Management of Hip Pain - More than Osteoarthritis - Online** Organiser: HKMA-Shatin Community Network Speaker: Dr CHENG Hang-cheong	Ms Candice TONG Tel: 3108 2513 1 CME Point
16 THU 2:00 PM	**Zoom Live** **Understanding Children with Autism Spectrum Disorder (ASD) & Providing Counseling to Their Families** Organiser: HKMA-NT West Community Network Speaker: Dr HUNG Chi-hong	M. Peter HO Tel: 3108 2514 1 CME Point
7:00 PM	**Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Alvin Ka-hong AU, Dr Candice Chi-han LIU	Ms Vienna LAM Tel: 2527 8898
17 FRI 2:00 PM	**Zoom Live** **Recent Advances in Diagnosis and Management of Benign Breast Conditions and Breast Cancer - Online** Organiser: HKMA-YTM Community Network Speaker: Dr Bonita Hor-kee MARK	Ms Candice TONG Tel: 3108 2513 1 CME Point

Lynparza™ is indicated as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and BRCA1/2-mutations (germline and/or somatic) who have progressed following prior therapy that included a new hormonal agent[1].

Lynparza™ more than tripled median imaging-based PFS vs. physician's choice	Lynparza™ increased median OS by 5.7 months vs. physician's choice	Majority of patients stayed on Lynparza™
Lynparza™ 9.8 months; Physician's choice 3.0 months	Lynparza™ 20.1 months; Physician's choice 14.4 months	80% of patients in the PROfound trial remained on Lynparza™ without discontinuing due to adverse events

Test your prostate cancer patients for BRCA mutations

References

1. Lynparza™ Hong Kong Prescribing Information. 2. De Bono J, et al. N Engl J Med 2020; 382:2091-2102. 3. Hussain M, et al. N Engl J Med 2020;383:2345-2357.

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Website: www.astrazeneca.com.hk

Lynparza™ olaparib tablets 100 mg 150 mg

Date / Time	Function	Enquiry / Remarks
21 TUE 2:00 PM	**In-person / Zoom** **HKMA-GHK CME Programme 2023 - Cataract/ Glucoma** Organiser: The Hong Kong Medical Association and the Gleneagles Hong Kong Hospital Speaker: Dr Jonathan Cheuk-hung CHAN Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept Tel: 3108 2507 1 CME Point
7:00 PM	**Certificate Course on Complaint Management 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr ONG Kim-lian	Ms Vienna LAM Tel: 2527 8898
22 WED 1:00 PM	**In-person / Zoom** **HKMA-CUHK Medical Centre CME Programme 2023 (Physical Lecture + Online)** **Common health problems amongst middle age - Topic: Stroke - Is it preventable? Management and Rehabilitation** Organiser: The Hong Kong Medical Association and the CUHK-Medical Centre Speaker: Dr Alexander Yuk-lun LAU Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 3108 2507 1 CME Point
23 THU 7:00 PM	**Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Frank Hiu-ping LAI, Dr Danny NG	Ms Vienna LAM Tel: 2527 8898
7:00 PM	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Nancy CHAN Tel: 2527 8898
8:00 PM	**FMSHK Council Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Nancy CHAN Tel: 2527 8898
30 THU 2:00 PM	**Zoom Live** **Enlarged Lymph Nodes - A Practical Approach and the Red Flags - Online** Organiser: HKMA-HK East Community Network Speaker: Dr Kitty Wai-yan LO	Ms Candice TONG Tel: 3108 2513 1 CME Point
7:00 PM	**Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr MOHAMED Shaheeda, Dr Nancy Shi-yin YUEN	Ms Vienna LAM Tel: 2527 8898
7:30 PM	**Symposium on Pneumococcal Diseases and Vaccines in Pediatric and Adult Patients (In-person/Zoom)** Organizer: Hong Kong Chinese Medical Association Ltd Speakers: Prof Ivan HUNG, Dr Mike KWAN, Prof David GREENBERG Moderator: Dr Jane CHAN	Mr Kenneth Tel: 3952 5345 CME points in progress

Certificate Course for Allied Health Professionals ● **Course No. C393** ● **CME/CNE Course**

Certificate Course on
Communication and Swallowing Problems in the Elderly Population 2023 *(Video Lectures)*

Jointly organised by

The Federation of Medical Societies of Hong Kong

The Hong Kong Association of Speech Therapists

Date	Topics	Speakers
13 April 2023	Communication Problems in the Elderly Population	Dr. Cymie Wing Yee NG Clinical Associate, The Hong Kong Polytechnic University
20 April 2023	Communication Disorders in Patients with Parkinson's Disease	Dr. Lorinda Li Ying KWAN-CHEN Senior Lecturer, Department of Special Education & Counseling, The Education University of Hong Kong
27 April 2023	Dysphagia and Feeding Problems in the Elderly Population	Mr. Joshua LAI Senior Speech Therapy Practitioner, Tung Wah Group of Hospitals Lok Ying Outreaching Allied Health Service
4 May 2023	Neurogenic Communication Disorders – Aphasia and Related Cognitive Communication Disorders	Prof. Anthony Pak Hin KONG Associate Professor, Academic Unit of Human Communication, Development, and Information Sciences, The University of Hong Kong, Hong Kong
11 May 2023	Motor Speech Disorders – Dysarthria and Apraxia of Speech	Dr. Raymond FONG Senior Lecturer, Department of Otorhinolaryngology, Head and Neck Surgery, The Chinese University of Hong Kong
18 May 2023	Hearing Ability and Problems in the Geriatric Population	Dr. Iris Hoi Yee NG Assistant Professor, Department of Otorhinolaryngology, Head and Neck Surgery, The Chinese University of Hong Kong Chairperson of Professional Council, Hong Kong Institute of Audiologists (the healthcare professional body responsible for administering a register for the audiologist profession accredited by the Department of Health)

Date : 13, 20, 27 April & 4, 11, 18 May 2023 (Thursday)
Time : 7:00 pm – 8:30 pm
Course Feature: Video lectures (with Q&A platform for participants to post the questions)
Language Media : Cantonese (Supplemented with English)
Course Fee : HK$1,000
Certificate : Awarded to participants with a minimum attendance of 70%
Deadline : 4 April 2023
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax : 2865 0345 Email : vienna.lam@fmshk.org

Online Application from website: http://www.fmshk.org

Answers to Dermatology Quiz

Answers:

1. The diagnosis is alopecia universalis.

   Alopecia areata (AA) is a recurrent, patchy, nonscarring and non-inflammatory type of alopecia. It can manifest in many different clinical patterns. Alopecia totalis is an extensive subtype of AA characterised by complete loss of scalp hair, while alopecia universalis is the most severe subtype involving total loss of scalp and body hair.

2. Alopecia areata is a Th1-mediated autoimmune disease. The immuno-pathogenesis of AA involves IL-15 and interferon-gamma, which signal through the JAK-STAT pathway. AA has shared pathogenesis with vitiligo involving Th1-mediated CD8+ cytotoxic T cells, which are assisted by CD4+ T helper cells to produce interferon-gamma.

3. The bad prognostic factors in AA include prepubertal onset, extensive lesions, ophiasic pattern, and associated atopy and nail pitting. Patients with alopecia universalis are more likely to have pitted fingernails, atopy, associated autoimmune diseases, and younger age of onset. Less than 10% of patients with alopecia universalis would have a full recovery, in contrast to 80% spontaneous remission rate in AA with limited patchy lesions.

4. In alopecia universalis, conventional treatments for AA, such as topical steroids, topical minoxidil, and intralesional steroid are practically infeasible and useless. Oral steroids, cyclosporine, methotrexate, azathioprine, and topical immunotherapy with DNCB (dinitrochlorobenzene), SADE (squaric acid dibutyl ester) or DPCP (diphenylcyclopropenone) have been used in desperate patients. The use of these drugs, however, are greatly limited by their potential serious side-effects. Along with the advancement in the understanding of immune-pathogenesis of alopecia universalis, JAK-inhibitors are potentially promising agents in treating this autoimmune disease. One such JAK-inhibitor was approved for treating severe AA by Food and Drug Administration of the US in 2022 .

Dr CHONG Lai-yin
MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Specialist in Dermatology and Venereology

TAKE ON THE CHALLENGES OF COVID-19[1]

TEST. TREAT. TAKE CHARGE. molnupiravir

You can NOW PURCHASE Molnupiravir from us!

For more information,
please contact MSD Professional sales representatives.

Reference: 1. molnupiravir US EUA Product Insert.

MOLNUPIRAVIR Selected Safety Information

Authorized Use

1. Molnupiravir is authorized for use under an Emergency Use Authorization (EUA) for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults:
   - with positive results of direct SARS-CoV-2 viral testing, and
   - who are at high risk for progression to severe COVID-19, including hospitalization or death, and
   - for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate
2. Molnupiravir is not approved for any use, including the treatment of COVID-19, but is authorized for emergency use by the FDA under an Emergency Use Authorization (EUA).
3. The emergency use of molnupiravir is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1) unless the declaration is terminated or authorization revoked sooner.

Limitations of Authorized Use

4. Molnupiravir is not authorized:
   - for use in patients who are less than 18 years of age
   - for initiation of treatment in patients hospitalized due to COVID-19. Benefit of treatment with molnupiravir has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19
   - for use for longer than 5 consecutive days
   - or pre-exposure or post-exposure prophylaxis for prevention of COVID-19
5. Molnupiravir may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which molnupiravir belongs (i.e., anti-infectives).

Contraindications

6. No contraindications have been identified based on the limited available data on the emergency use of molnupiravir authorized under this EUA.

Warnings and Precautions

7. There are limited clinical data available for molnupiravir. Serious and unexpected adverse events may occur that have not been previously reported with molnupiravir use.
8. Molnupiravir is not recommended for use during pregnancy. Based on findings from animal reproduction studies, molnupiravir may cause fetal harm when administered to pregnant individuals. There are no available human data on the use of molnupiravir in pregnant individuals to evaluate the risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.
9. Molnupiravir is authorized to be prescribed to a pregnant individual only after the healthcare provider has determined that the benefits would outweigh the risks for that individual patient. If the decision is made to use molnupiravir during pregnancy, the prescribing healthcare provider must document that the known and potential benefits and the potential risks of using molnupiravir during pregnancy were communicated to the pregnant individual.
10. Advise individuals of childbearing potential of the potential risk to a fetus and to use an effective method of contraception correctly and consistently during treatment with molnupiravir and for 4 days after the final dose.
11. Prior to initiating treatment with molnupiravir, assess whether an individual of childbearing potential is pregnant or not, if clinically indicated.
12. Hypersensitivity reactions, including anaphylaxis, have been reported with molnupiravir. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue molnupiravir and initiate appropriate medications and/or supportive care.
13. Molnupiravir is not authorized for use in patients less than 18 years of age because it may affect bone and cartilage growth. The safety and efficacy of molnupiravir have not been established in pediatric patients.

Adverse Reactions

14. The most common adverse reactions occurring in ≥1% of subjects in the molnupiravir treatment group in the Phase 3 double-blind MOVe-OUT study were diarrhea (2% versus placebo at 2%),nausea (1% versus placebo at 1%), and dizziness (1% versus placebo at 1%) all of which were Grade 1 (mild) or Grade 2 (moderate).
    Serious adverse events occurred in 7% of subjects receiving molnupiravir and 10% receiving placebo; most serious adverse events were COVID-19 related. Adverse events leading to death occurred in 2 (<1%) of the subjects receiving molnupiravir and 12 (2%) of subjects receiving placebo.

Drug Interactions

15. No drug interactions have been identified based on the limited available data on the emergency use of molnupiravir. No clinical drug-drug interaction trials of molnupiravir with concomitant medications, including other treatments for mild to moderate COVID-19, have been conducted.

Breastfeeding

16. There are no data on the presence of molnupiravir or its metabolites in human milk. It is unknown whether molnupiravir has an effect on the breastfed infant or effects on milk production. Based on the potential for adverse reactions in the infant from molnupiravir, breastfeeding is not recommended during treatment with molnupiravir and for 4 days after the final dose. A lactating individual may consider interrupting breastfeeding and may consider pumping and discarding breast milk during treatment and for 4 days after the last dose of molnupiravir.

Males of Reproductive Potential

17. Nonclinical studies to fully assess the potential for molnupiravir to affect offspring of treated males have not been completed. Advise sexually active individuals with partners of childbearing potential to use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose of molnupiravir. The risk beyond three months after the last dose of molnupiravir is unknown.

Before prescribing, please consult the full prescribing information.

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HK-ANV-00809 May/2022

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(dutasteride/tamsulosin HCl) Capsules

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*The **ONLY** fixed-dose combination in relieving BPH symptoms and reduce risk of AUR or BPH-related surgery*

DUAL ACTION:

- **Superior symptoms improvement**[1]
  (adjusted mean change in IPSS from baseline to year 4 was **-6.3** points for combination therapy versus **-3.8** points for tamsulosin)
- **Reduce prostate size up to 27%**[1#]

DUAL PROTECTION:

Reduce relative risk of

- **AUR by 68%**
- **BPH related surgery by 71%**

vs tamsulosin monotherapy[1]

BPH: Benign Prostatic Hyperplasia
AUR: Acute Urinary Retention

DUODART Safety Information: Renal impairment: Patients with creatinine clearance of less than 10 mL/min should be approached with caution as these patients have not been studied. **Hypotension:** Patients beginning treatment with Duodart should be cautioned to sit or lie down at the first signs of orthostatic hypotension until the symptoms have resolved. Concomitant use of α-blockers and PDE5 inhibitors can lower blood pressure and cause symptomatic hypotension. **Fertility and sexual function in men:** Dutasteride has been reported to affect semen characteristics (reduction in sperm count, semen volume and sperm motility) in healthy men. The possibility of reduced male fertility cannot be excluded. Effects of tamsulosin hydrochloride on sperm counts or sperm function have not been evaluated.

DUODART (Dutasteride-tamsulosin) abbreviated prescribing information[2]: Indications Treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH), Reduction in the risk of acute urinary retention (AUR) and surgery in patients with moderate to severe symptoms of BPH, Limitations of use: Dutasteride-containing products, including DUODART, are not approved for the prevention of prostate cancer, **Dosage and Administration** The recommended dose of DUODART (Dutasteride-tamsulosin) is one capsule (0,5 mg/ 0,4 mg) taken once daily, The capsules should be swallowed whole and not chewed or opened, Contact with the contents of the dutasteride capsule contained within the hard-shell capsule may result in irritation of the oropharyngeal mucosa, **Contraindications** Patients with known hypersensitivity to dutasteride, other 5 alphareductase inhibitors, tamsulosin (including tamsulosin- induced angio-edema), soya, peanut or any of the excipients; history of orthostatic hypotension; with severe hepatic impairment; women and children and adolescents, **Warnings and Precautions** *Cardiac Failure* In two 4-year clinical study, the incidence of cardiac failure (a composite term of reported events, primarily cardiac failure and congestive cardiac failure) was higher among subjects taking the combination of dutasteride and an alpha1- adrenoceptor antagonist, primarily tamsulosin, than it was among subjects not taking the combination, In these two trials, the incidence of cardiac failure was low (≤1%) and variable between the studies, *Effect on prostate-specific antigen (PSA) and prostate cancer detection* Serum prostate-specific antigen (PSA) concentration is an important component in the detection of prostate cancer, DUODART causes a decrease in mean serum PSA levels by approximately 50%, after 6 months of treatment, Patients receiving DUODART should have a new PSA baseline established after 6 months of treatment with DUODART, It is recommended to monitor PSA values regularly thereafter, Any confirmed increase from lowest PSA level while on DUODART may signal the presence of prostate cancer or noncompliance to therapy with DUODART and should be carefully evaluated, even if those values are still within the normal range for men not taking a 5-alpha reductase inhibitor, In the interpretation of a PSA value for a patient taking dutasteride, previous PSA values should be sought for comparison, Treatment with DUODART does not interfere with the use of PSA as a tool to assist in the diagnosis of prostate cancer after a new baseline has been established, Total serum PSA levels return to baseline within 6 months of discontinuing treatment, The ratio of free to total PSA remains constant even under the influence of DUODART, If clinicians elect to use percent free PSA as an aid in the detection of prostate cancer in men undergoing DUODART therapy, no adjustment to its value appears necessary, Digital rectal examination, as well as other evaluations for prostate cancer or other conditions which can cause the same symptoms as BPH, must be performed on patients prior to initiating therapy with DUODART and periodically thereafter, *Prostate cancer and high grade tumours* The REDUCE study, a 4-year, multicentre, randomised, double-blind, placebo controlled study investigated the effect of dutasteride 0,5 mg daily on patients with a high risk for prostate cancer (including men 50 to 75 years of age with PSA levels of 2,5 to 10 ng/ml and a negative prostate biopsy 6 months before study enrolment) compared to placebo, Results of this study revealed a higher incidence of Gleason 8 – 10 prostate cancers in dutasteride treated men (n=29, 0,9%) compared to placebo (n=19, 0,6%), The relationship between dutasteride and Gleason 8 - 10 prostate cancers is not clear, Thus, men taking Avodart should be regularly evaluated for prostate cancer, *Renal impairment* The treatment of patients with severe renal impairment (creatinine clearance of less than 10 ml/min) should be approached with caution as these patients have not been studied, *Hypotension* Orthostatic: As with other alpha1-adrenoceptor antagonists, a reduction in blood pressure can occur during treatment with tamsulosin, as a result of which, rarely, syncope can occur, Patients beginning treatment with DUODART should be cautioned to sit or lie down at the first signs of orthostatic hypotension (dizziness, weakness) until the symptoms have resolved, Symptomatic: Caution is advised when alpha adrenergic blocking agents including tamsulosin are co-administered with PDE5 inhibitors, Alpha1-adrenoceptor antagonists and PDE5 inhibitors are both vasodilators that can lower blood pressure, Concomitant use of these two drug classes can potentially cause symptomatic hypotension, *Intraoperative Floppy Iris Syndrome* IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin, IFIS may increase the risk of eye complications during and after the operation, The initiation of therapy with DUODART in patients for whom cataract surgery is scheduled is therefore not recommended, During pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being or have been treated with DUODART in order to ensure that appropriate measures will be in place to manage the IFIS during surgery, Discontinuing tamsulosin 1 – 2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of stopping therapy prior to cataract surgery has not yet been established, *Leaking Capsule* Dutasteride is absorbed through the skin, therefore women and children and adolescents must avoid contact with leaking capsules, If contact is made with leaking capsules, the contact area should be washed immediately with soap and water, *Inhibitors of CYP3A4 and CYP2D6* Concomitant administration of tamsulosin hydrochloride with strong inhibitors of CYP3A4, or to a lesser extent, with strong inhibitors of CYP2D6 can increase tamsulosin exposure, Tamsulosin hydrochloride is therefore not recommended in patients taking a strong CYP3A4 inhibitor and should be used with caution in patients taking a moderate CYP3A4 inhibitor, a strong or moderate CYP2D6 inhibitor, a combination of both CYP3A4 and CYP2D6 inhibitors, or in patients known to be poor metabolisers of CYP2D6, *Hepatic Impairment* DUODART has not been studied in patients with liver disease Caution should be used in the administration of DUODART to patients with mild to moderate hepatic impairment, *Excipients* This medicinal product contains the colouring agent Sunset Yellow (E110), which may cause allergic reactions, *Breast neoplasia* There have been rare reports of male breast cancer reported in men taking dutasteride in clinical trials and during the post-marketing period, However, epidemiological studies showed no increase in the risk of developing male breast cancer with the use of 5-alpha reductase inhibitors, Physicians should instruct their patients to promptly report any changes in their breast tissue such as lumps or nipple discharge, **Interactions** *Tamsulosin* Concomitant administration of tamsulosin hydrochloride with drugs which can reduce blood pressure, including anaesthetic agents, PDE5 inhibitors and other alpha1- adrenoceptor antagonists could lead to enhanced hypotensive effects, Dutasteride-tamsulosin should not be used in combination with other alpha1- adrenoceptor antagonists, Concomitant administration of tamsulosin hydrochloride and ketoconazole (a strong CYP3A4 inhibitor) resulted in an increase of the Cmax and AUC of tamsulosin hydrochloride by a factor of 2,2 and 2,8 respectively, Concomitant administration of tamsulosin hydrochloride and paroxetine (a strong CYP2D6 inhibitor) resulted in an increase of the Cmax and AUC of tamsulosin hydrochloride by a factor of 1,3 and 1,6 respectively, A similar increase in exposure is expected in CYP2D6 poor metabolisers as compared to extensive metabolisers when co-administered with a strong CYP3A4 inhibitor, The effects of co-administration of both CYP3A4 and CYP2D6 inhibitors with tamsulosin hydrochloride have not been evaluated clinically, however there is a potential for significant increase in tamsulosin exposure, Concomitant administration of tamsulosin hydrochloride (0,4 mg) and cimetidine (400 mg every six hours for six days) resulted in a decrease in the clearance (26%) and an increase in the AUC (44%) of tamsulosin hydrochloride, Caution should be used when dutasteride-tamsulosin is used in combination with cimetidine, A definitive drug-drug interaction study between tamsulosin hydrochloride and warfarin has not been conducted, Results from limited in vitro and in vivo studies are inconclusive, Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin, Caution should be exercised with concomitant administration of warfarin and tamsulosin hydrochloride, **Fertility, pregnancy and lactation** DUODART is contraindicated for use by women, There have been no studies to investigate the effect of DUODART on pregnancy, lactation and fertility, As with all 5 alpha reductase inhibitors, when the patient's partner is or may potentially be pregnant it is recommended that the patient avoids exposure of his partner to semen by use of a condom, As with other 5 alpha reductase inhibitors, dutasteride inhibits the conversion of testosterone to dihydrotestosterone and may, if administered to a woman carrying a male foetus, inhibit the development of the external genitalia of the foetus, Dutasteride has been reported to affect semen characteristics (reduction in sperm count, semen volume, and sperm motility) in healthy men, The possibility of reduced male fertility cannot be excluded, Effects of tamsulosin hydrochloride on sperm counts or sperm function have not been evaluated, The effects of dutasteride 0,5 mg/day on semen characteristics were evaluated in healthy volunteers aged 18 to 52 (n=27 dutasteride, n=23 placebo) throughout 52 weeks of treatment and 24 weeks of post-treatment follow-up, At 52 weeks, the mean percent reduction from baseline in total sperm count, semen volume and sperm motility were 23%, 26% and 18%, respectively, in the dutasteride group when adjusted for changes from baseline in the placebo group, Sperm concentration and sperm morphology were unaffected, After 24 weeks of follow-up, the mean percent change in total sperm count in the dutasteride group remained 23% lower than baseline, While mean values for all parameters at all time points remained within the normal ranges and did not meet the predefined criteria for a clinically significant change (30%), two subjects in the dutasteride group had decreases in sperm count of greater than 90% from baseline at 52 weeks, with partial recovery at the 24 week follow-up, The possibility of reduced male fertility cannot be excluded, It is not known whether dutasteride or tamsulosin are excreted in human milk, **Adverse Reactions** *Clinical Trial Data* ((Dutasteride and tamsulosin co-administration): Impotence, altered (decreased) libido, ejaculation disorders, breast disorders (includes breast tenderness and breast enlargement), dizziness and cardiac failure, (Dutasteride monotherapy): Impotence, altered (decreased) libido, ejaculation disorders, breast disorders (includes breast tenderness and breast enlargement), alopecia (primarily body hair loss), hypertrichosis, (Tamsulosin Monotherapy): Dizziness, abnormal ejaculation, palpitations, constipation, diarrhoea, vomiting, asthenia, rhinitis, rash, pruritis, urticaria, orthostatic hypotension, syncope, headache, nausea, angioedema, priapism, Stevens-Johnson syndrome, During postmarketing surveillance, reports of Intraoperative Floppy Iris Syndrome (IFIS), a variant of small pupil syndrome, during cataract surgery have been associated with alpha1- adrenoceptor antagonists, including tamsulosin, In addition atrial fibrillation, arrhythmia, tachycardia, dyspnoea, epistaxis, vision blurred, visual impairment, erythema multiforme, dermatitis exfoliative, ejaculation disorder, retrograde ejaculation, ejaculation failure and dry mouth have been reported in association with tamsulosin use, The frequency of events and the role of tamsulosin in their causation cannot be reliably determined, Abbreviated PI based on HK072017(GDS15v1/eMC20170628), Please refer to the full prescribing information before prescribing, Full prescribing information is available upon request.

At month 48, the adjusted mean percentage change from baseline in total prostate volume was -27.3% for combination therapy, +4.6% (p<0.001) for tamsulosin, and -28.0% (p=0.42) for dutasteride.

References: 1. Roehrborn CG, *et al. Eur Urol* 2010;57(1):123–31 **2.** DUODART Hong Kong Full Prescribing Information. Version number: HK072017(GDS15v1/eMC20170628).

For adverse events report, please call GlaxoSmithKline Limited at (HK) 852 9046 2498 Full prescribing information is available on request from GlaxoSmithKline Ltd. 23/F, Tower 6, The Gateway, 9 Canton Road, Tsimshatsui, Kowloon, Hong Kong.
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