Tackling Kidney Cancer Through International Consensus

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Since 1981, the International Consultation on Urological Diseases (ICUD) has been an important global initiative. Conceived and promoted by the World Health Organization, it gathers international expertise, advancing fundamental knowledge and promoting evidence-based care across the spectrum of urologic conditions—most notably on thematic topics that are important to practicing urologists and that are not otherwise well covered in the scientific literature.

Over the past decade, the ICUD has participated in collaborative consultations with WUOF and the SIU, which is well established as a society dedicated to serving a global urological community. In this context, over the past few months, I have been proud to take on the role as the director of publications for the SIU to oversee present and future ICUD initiatives. The current ICUD joint consultation, dedicated to kidney cancer, has been chaired by several international thought leaders on the subject (Professors Toni Choueiri, Grant Stewart, and Robert Uzzo), with sections dedicated to epidemiology (including screening), diagnostic imaging, management of locally advanced disease, therapies in refractory metastatic disease, and management of toxicity and side effects[1]. In this editorial, I would like to highlight some of the exceptional articles within this issue of the *SIUJ*, which is dedicated to summarizing the findings of this most recent ICUD initiative—findings our readers will be able to integrate into their clinical practice.

The article by Dr Sabrina Rossi et al. on the epidemiology of renal cell carcinoma provides an in-depth review of the current incidence, prevalence, and mortality of kidney cancer across the globe[2]. The authors also draw attention to the increasing incidence of this malignancy in recent years, which can be attributed to most cases being incidentally detected on abdominal axial imaging studies obtained for often unrelated reasons. As a result, many of the suspicious renal masses presently detected are defined as small renal masses (≤ 3 centimeters), often with a low metastatic potential, for which active surveillance may represent an appropriate therapeutic option, most notably in elderly patients and/or those with multiple life-threatening medical comorbidities. The authors touch on the risk factors predisposing to the development of kidney cancer, and although for most individual patients we can't specifically pinpoint the underlying causes for carcinogenesis, these are likely to include the increasing prevalence of obesity, exposure to insecticides/pollutants, and genetic predisposition to kidney cancer among a small subset of patients. The authors provide an intriguing discussion on potential screening strategies for kidney cancer, most notably in higher risk patient populations (those who are over 65 years, smokers, morbidly obese, and/or in families with a high preponderance of cases of an established genetic condition such as von Hippel-Lindau). Ongoing trials including the consideration of screening for both thoracic aneurysms and kidney cancer should be followed carefully as they incorporate ultrasound imaging, which is non-invasive and cost-effective, but remains operator dependent.

Dr Jodi Maranchie and colleagues nicely detail the various known hereditary kidney cancer syndromes including von Hippel-Lindau, familial papillary, Birt-Hogg-Dubé, as well as a number of others that are rapidly becoming recognized conditions[3]. There is no question there is increasing awareness about these conditions and the multi-organ clinical manifestations they may entail, and that urologists and other healthcare professionals must be aware of, most notably in patients with a family history of kidney cancer in 1 or more first-degree relatives and/or in patients less than 40 years of age with a diagnosis of kidney cancer.

In a comprehensive review, Dr Vinay Duddalwar and colleagues provide an excellent synopsis of the imaging modalities readily available in assessing a renal mass to determine whether it can be accurately characterized as suspicious for an underlying malignancy[4]. Although CT or MRI axial imaging with and without IV contrast remain the benchmark diagnostic imaging modalities for renal cell carcinoma in clinical practice, there are some exciting developments in renal contrast-enhanced ultrasonography, elastography, and PET-CT imaging that are rapidly gaining ground. Artificial intelligence and radiomics likely represent the new horizons in diagnostics in not only accurately characterizing in a consistent and potentially automated manner the suspicion that a renal mass may represent an underlying malignancy but also potentially determining its specific tumor histology and characteristics, as well as attributable prognosis.

In their article, Dr Mohammed Ali et al. summarize the current state of knowledge relating to renal ablative therapies in the management of small renal masses (typically ≤ 3 cm)[5]. They provide a concise overview of the indications for renal ablation, typically conducted in an image-guided manner percutaneously rather than laparoscopically, because of its less invasive nature and non-inferior local therapeutic outcomes. A number of ablative energy modalities are readily available, including radiofrequency, cryoablation, and microwave. All have their merits and drawbacks but cryoablation remains the most favored because of its high success rate in terms of effective ablation, particularly if a double freeze–thaw cycle is used, and the procedure is completed by an experienced clinician (most commonly an interventional radiologist at a referral center).

In a nicely detailed review on the surgical management of locally advanced renal cell carcinoma (most notably IVC tumor thrombi) Dr Vsevolod Matveev et al. discuss important surgical tips and tricks in tackling such complex surgical cases, including the emerging role of pre-surgical systemic therapy in attempting to regress the burden of disease or allow acute medical conditions to be optimized before proceeding with surgical care[6].

Dr Naomi Haas and colleagues present a thoughtful discussion on the rapidly evolving role of neoadjuvant and adjuvant therapy for renal cell carcinoma[7]. Although neoadjuvant therapy can provide some local tumor burden reduction, making surgical resection in theory potentially less morbid and/or in certain instances rendering primary tumors more amenable to nephron-sparing surgery, individual responses are harder to predict and must be considered on a case-by-case basis—and in most instances should be considered as part of a clinical trial. In terms of adjuvant therapy, KEYNOTE 564 was truly pioneering in establishing the potential benefit of adjuvant pembrolizumab with respect to disease-free endpoints (overall survival to be reported) in patients with high-risk localized tumors (or following isolated site of metastatectomy < 1 year of prior nephrectomy) post-resection[8]. Clearly, this has been paradigm-shifting, most notably as the prior adjuvant therapy studies using targeted therapies (ASSURE and S-TRAC) were equivocal in terms of the benefits they rendered.

In a critically important review, Dr Lisa Pickering and colleagues provide a detailed summary of the acute and chronic (minor and major) toxicities of the rapidly evolving systemic therapeutic landscape of advanced renal cell carcinoma[9]. This includes a characterization of the immune-related adverse events, which although less frequent, can be life-threatening and occasionally more difficult to predict. The authors note that the emergence of triple agent combinations using a number of checkpoint inhibitors and/or targeted therapies offers an exciting new opportunity to improve patient outcomes but is fraught with apprehension in terms of the risk and severity of adverse events. Although our experience with such triple agent combinations is early, it remains quite promising; a meticulous and systematic approach to screening and treating these patients on triple agent combinations is of pivotal importance.

In conclusion, we are excited to share these important contributions with our readers. We deeply appreciate—and congratulate—all the chairs and the contributors to this 2nd WUOF/SIU-ICUD collaboration focused on renal cell carcinoma. It provides an important resource for all global healthcare professionals caring for kidney cancer patients.

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