

Opening an onconephrology clinic: recommendations and basic requirements

Laura Cosmai^{1,*}, Camillo Porta^{2,*}, Mark A. Perazella³, Vincent Launay-Vacher⁴, Mitchell H. Rosner⁵, Kenar D. Jhaveri⁶, Matteo Floris⁷, Antonello Pani⁷, Cécile Teuma⁸, Cèzary A. Szczylik⁹ and Maurizio Gallieni^{1,10}

¹Onco-Nephrology Clinic, Nephrology and Dialysis Unit, San Carlo Borromeo Hospital, ASST Santi Carlo e Paolo, Milan, Italy, ²Medical Oncology, IRCCS San Matteo University Hospital Foundation, Pavia, Italy, ³Section of Nephrology, Department of Medicine, Yale University School of Medicine, New Haven and Veterans Administration Medical Center, West Haven, CT, USA, ⁴Service ICAR, Pitié-Salpêtrière University Hospital, Paris, France, ⁵Department of Medicine, University of Virginia Health System, Charlottesville, VA, USA, ⁶Division of Kidney Diseases and Hypertension, Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, USA, ⁷Nephrology and Dialysis Unit, G. Brotzu Hospital, Cagliari, Italy, ⁸Nephrology Department, Centre Hospitalier Lyon Sud Pierre-Bénite, France, ⁹Department of Oncology, University of Warsaw School of Medicine, Warsaw, Poland and ¹⁰Department of Clinical and Biomedical Sciences "Luigi Sacco", University of Milan, Milan, Italy

Correspondence and offprint requests to: Laura Cosmai; E-mail: lacos@iol.it *These authors contributed equally to this work.

ABSTRACT

Onconephrology is a rapidly evolving subspeciality that covers all areas of renal involvement in cancer patients. The complexity of the field may benefit from well-defined multidisciplinary management administered by a dedicated team. Since there is an increasing need to address the needs of this population in dedicated outpatient clinics, it is critical to highlight basic characteristics and to suggest areas of development. In this brief perspective article, we analyse the requirements of an onconephrology clinic in terms of logistics, critical mass of patients and building a multidisciplinary team. We will further discuss which patients to refer and which conditions to treat. The last part of the article is dedicated to education and performance indicators and to analysis of the potential advantages of applying the hub-and-spoke model to this field. The ultimate aim of this experience-based article is to initiate debate about what an onconephrology outpatient clinic might look like in order to ensure the highest quality of care for this growing population of

Keywords: cancer, kidney, multidisciplinary team, onconephrology, outpatient clinic

INTRODUCTION: THE CANCER-KIDNEY CONNECTION

Onconephrology is a rapidly evolving subspeciality area that focuses on all aspects of kidney disease in cancer patients. Recently we proposed a 'decalogue of onconephrology' to highlight several of the areas where nephrologists and oncologists should collaborate to provide cutting-edge care for patients afflicted with cancer and kidney diseases [1]. In that article we highlighted the following 10 points of contact between the two specialties: (i) acute kidney injury (AKI) and chronic kidney disease (CKD) in cancer patients, (ii) nephrotoxic effects of anticancer therapy, (iii) paraneoplastic renal manifestations, (iv) management of patients nephrectomized for a kidney cancer, (v) renal replacement therapy and oncological treatments, (vi) kidney transplantation in cancer survivors and cancer risk in end-stage renal disease (ESRD) patients, (vii) oncological treatment in kidney transplant patients, (viii) pain management in cancer patients with concomitant kidney diseases, (ix) development of guidelines specific for onconephrology patients and (x) design of clinical trials with onconephrology endpoints [1].

Well-defined multidisciplinary management of cancer patients with kidney disease can help ensure the highest quality of care is administered by a dedicated speciality team with experience in these complex issues.

To aid implementation of this model, it is critical to identify recommendations and minimum requirements for the development of onconephrology outpatient clinics. There are examples of these types of multidisciplinary clinics in other fields of oncology where various specialists are brought together to improve outcomes and care pathways [2, 3]. The objective of our experience-based article is to initiate a dialogue on what such a clinic might look like to successfully serve this growing population of patients.

ONCONEPHROLOGY CLINICS—BASIC REQUIREMENTS

To develop and sustain a successful outpatient clinic for patients suffering from cancer and kidney disease, a number of basic requirements must be met. In our opinion, the following requirements are needed to create a successful and efficient onconephrology outpatient clinic.

Critical mass of patients

For many reasons, there should be a sufficient number of patients enrolled in the clinic. This is to ensure operational efficiency and financial viability and to develop expertise in the unique overlap of kidney problems seen in patients with cancer. Recent studies have demonstrated that the prevalence of estimated glomerular filtration rate (eGFR) <60 mL/min in patients affected by solid tumours overall exceeds 12% [4] and a 1-year risk of AKI of any stage may be as high as 17% for incident cancer patients [5]. Since the cancer incidence in Europe and the USA approaches 300 cases per 100 000 inhabitants/year [6], the clinic should be affiliated with a large- or medium-size hospital (serving at least 500 000 inhabitants). At least 150 new patients per year would thus be considered a sufficient size to maintain a robust clinic. In certain major cancer centres, it is ideal that the onconephrology clinic is physically housed in the cancer hospital. The choice of 150 new patients, as a minimum number of cases justifying the development of an onconephrology clinic, is empiric, though justified on the basis of the experience of three of the co-authors of this article, who have already created such clinics across Europe; of course, this should be considered just as a starting number, which is expected to increase over time.

In most academic centres, this critical mass will be needed to enhance the experience and expertise of the onconephrologist.

Proximity to the haematology and oncology ward

In addition to an adequate patient number, the clinic should be located within a reasonable distance from the primary site of oncology care. This is particularly important when a patient develops significant AKI or progressive CKD that might impede active cancer therapy. Rapid nephrology evaluation and treatment would be greatly facilitated by a nearby onconephrology clinic. Furthermore, an active, local and bidirectional relationship between nephrologists and oncologists would promote shared decision making and development of collaborative care models. This would engender a comprehensive evaluation of patients that would hopefully result in improved outcomes [7]. For example, the onconephrology team could provide critical information about life expectancy and quality of life for patients facing decisions regarding dialysis initiation. This integrative, patient-centred medical approach is key to ensuring appropriate and optimized care for patients and their diseases, including cancer and comorbidities.

An ideal model is to allow the onconephrologist to see the cancer patient in the haematology/oncology office. This might be logistically possible in some centres and not others. Thus a reasonable physical proximity would be a key requirement to

provide a structured and multidisciplinary environment for effective management of patients referred to the clinic.

Of course, not every patient has to be physically seen by the multidisciplinary group; furthermore, a telemedicine approach could be very useful in the hub-and-spoke model described later within this article.

Availability of medical records across clinics

The history of patients with cancer is complicated, with multiple visits to various specialists and complex medical regimens that can change rapidly depending upon side effects and tumour response. This is particularly true for patients with extended therapeutic courses. These patients have often undergone a large number of diagnostic studies and treatment regimens. The availability of original source documents (which, once again, is facilitated by proximity) would thus be key to having a complete understanding of the patient's past and present medical (and oncologic) history. The easy availability of this information would facilitate a rapid, comprehensive evaluation by the consulting nephrologist.

Shared (electronic) database

Since the subspeciality of onconephrology is still in its infancy, both cancer specialists and nephrologists may benefit immensely from knowledge of previous cases, their treatments and outcomes. A comprehensive database containing electronic medical records (EMRs) would represent a source of precious information (both prospective and retrospective) for clinical and research purposes. Such databases can be 'mined' to look for outcomes of specific subgroups of patients and can be used to develop hypotheses for future studies.

Referral to the onconephrologist

Although an onconephrology outpatient clinic may operate once or twice a week (or more frequently as needed), a dedicated onconephrologist should always be available to provide expertise.

Since a sizeable number of patients falling within the competence of an onconephrological evaluation are often hospitalized, an onconephrology consultation should be available, on demand, for inpatients; specific protocols should thus be implemented within the hospital in order to clearly define when this kind of consultation is needed within the inpatient ward (e.g. in the case of those conditions reported in Table 1) and how to ask for it.

The onconephrology consultant must be versed and knowledgeable in the complex relationships between cancer and the kidney, the pharmacological properties of all antineoplastic drugs and the harm:benefit ratio of antineoplastic treatment strategies in patients with underlying kidney disease.

Considering the need for evaluating some of these patients on short notice, as well as obvious organization issues such as vacations, illnesses, etc., more than one dedicated specialist is needed in order to fulfil all the above requirements.

Overall, a curriculum in onconephrology, such as the one developed by the American Society of Nephrology [8], would be useful to facilitate competency in this complicated area.

Table 1 Patients for whom referral to the onconephrology clinic is suggested

Type of patient(s)	Main issue(s)
Cancer patients with kidney impairment before, during or af-	To guarantee the best cancer treatment possible, without unnecessary dose reduction
ter active cancer treatment	and/or treatment interruptions, which could hamper the possibility of success of the oncological treatment
Cancer patients at risk of kidney impairment	To prevent the development of kidney impairment, possibly leading to dose reduction
• due to concomitant illnesses (e.g. hypertension, diabetes,	or treatment interruption
etc.)	Education of oncologists and patients about classic kidney failure risks
• due to the potential nephrotoxicity of the planned treatment	
Cancer patients developing adverse renal events from antineo-	AKI
lastic treatment	Worsening of CKD
	Hypertension
	Proteinuria
	Electrolyte disturbances
	TMA
Cancer patients at significant risk of CIN	Prevention of AKI or worsening of CKD through implementation of prophylactic
	measures
Kidney cancer patients at risk for postsurgical (or postablative)	Prevention of AKI or worsening of CKD
AKI or progressive CKD	Management of treatment-related AEs
Patients with urothelial cancer (all)	Prevention of AKI or worsening of CKD
	Prevention/management of obstructions
	Prevention/management of chronic infections
	Management of treatment-related AEs
Patients with suspected or <i>de facto</i> paraneoplastic	Screening for an occult cancer (if any)
glomerulopathies	Diagnosis
	Management strategies (e.g. use of immunosuppressive agents in the cancer patient)
Transplantation patients:	When to allow transplantation or donation in a patient with previous or active cancer
• donors	Management strategies (e.g. use of immunosuppressive agents in the cancer patient)
• recipients	
 transplanted patient who develops cancer 	
Cancer patients on dialysis	Management of drug dosing, toxicity
	Use of erythropoietin-stimulating agents
	Shared decision making
Haematological cancer patients	Management of renal involvement in myeloma and lymphomas
	Management of secondary amyloidosis
Bone metastases in cancer patients with CKD	Management of bone-targeted therapies (bisphosphonates or denosumab)
	Management of bone-targeted therapies-induced hypocalcaemia

Multidisciplinary team

A multidisciplinary approach is critical for the success of this model [9]. Multidisciplinary care requires a proactive and bidirectional relationship between the various specialists (see section 'Core team' below) involved in the patient's care. Furthermore, performance indicators and regular assessment of outcomes are essential to monitor the effectiveness of the outpatient clinic and to allow changes and improvements over time. It is important to recognize that multidisciplinary care does not mandate the participation of onconephrologists on all tumour boards. We do believe that a significant number of those patients brought for multidisciplinary discussion into the Genitourinary (GU) Tumour Board could benefit from the presence of a nephrologist. In addition, the onconephrologist's opinion can be sought when needed for complex cases where kidney disease is integral to diagnostic or therapeutic plans. Where clear renal issues exist or may develop, protocols for early nephrology involvement are important. In complex drug toxicities such as immune checkpoint inhibitor-induced acute nephritis [10] or venetoclax-induced tumour lysis syndrome [11], an onconephrologist's expertise can help standardize care in the inpatient and outpatient settings.

Core team

A core team of various specialists dealing with cancer patients with kidney disease and related issues is mandatory. The core team would consist of nephrologists, haematologists and oncologists along with a dedicated data manager, nursing and care coordinator team members. The team members should ideally have specialized training in onconephrology and should spend an agreed amount of weekly time with these patients to maintain proficiency [8]. Participating nephrologists should also partake of continuing professional medical education. All core team members must attend multidisciplinary meetings for case management and audit purposes. Other specialists, including urologists, radiation therapists, pathologists, radiologists, palliative care providers and others, would be invited to attend multidisciplinary rounds, as needed. This model currently exists in many U.S. cancer centers and is emerging in many European countries. Notably, within the onco-nephrological web community of the American Society of Nephrology (ASN), this is a topic that has recently been the object of a dedicated forum (http://community.asn-online.org/communities/communityhome?communitykey=0ca61c6c-1f2f-4f15-9ae5-86fc6ef4c260 &tab=groupdetails; accessed on 8 May 2018).

In addition, case discussions, which should be held at least weekly, must be attended by all involved professionals.

Furthermore, the role of a dedicated pharmacologist, who may or may not be in the core team, is critical in order to provide advice on possible pharmacologic interactions (in a population of patients highly comorbid and thus taking many different drugs) and to explore the pharmacokinetic properties of each oncological drug in CKD patients, as well as in those on dialysis.

Involvement of other health professionals

Depending on different organization systems, which can greatly vary from country to country, different health professionals, including physician extenders, nurses and postgraduate students, could be involved in the activities of the clinic, especially when patients need to be seen on short notice or for frequent follow-ups.

Availability of certain diagnostic tests

Ideally, a histological evaluation of both nonneoplastic and neoplastic tissue within the pathologic specimens of resected kidney cancer patients would be mandatory, as stated by the 2012 International Society of Urologic Pathology (ISUP) consensus conference [12]. This evaluation would indeed provide important details for the future management of these patients. However, since the implementation of this evaluation could be troublesome on a wide scale, we believe that optical microscopy analysis of the normal tissue should be reported in almost all patients' pathological reports, while immunofluorescence and/ or electron microscopy should be performed in more specialized centres (i.e. the hubs, as reported below) whenever needed and tissue preserved for possible future analyses.

Furthermore, a comprehensive and efficient workup for a patient attending the onconephrology clinic often requires the prompt execution of diagnostic tests. Those providing important information for many patients include renal ultrasound (including Doppler interrogation), venous blood gas (VBG) analysis and ambulatory blood pressure monitoring (ABPM), although the importance of the availability of the latter two has not been agreed upon. Indeed, although hypertension is by far the most common treatment-related renal adverse event observed in cancer patients on antiangiogenic treatment, it is clear that ABPM is not strictly necessary in many other cancer patients. As far as VBG, although it provides important information, such as pH, bicarbonates, ionized calcium and potassium levels, this information can also be obtained without the need of a blood gas and in a timely manner by a stat lab. Thus, since in some countries (e.g. the USA) institution-specific regulations do not allow the presence of lab equipment in outpatient clinical space, stat labs should be regarded as a realistic substitute for VBG.

These tests, in particular renal ultrasound, maintain the potential to provide critical information about the cause of AKI or CKD in the cancer patient and can be used to monitor for acid-base disturbances and blood pressure changes due to anticancer drugs (both hypotension and hypertension). The ability to promptly perform these tests would allow rapid, efficient care

in the spirit of the state-of-the-art onconephrology clinic care plan.

WHICH PATIENTS ARE APPROPRIATE FOR THE ONCONEPHROLOGY CLINIC?

In some countries, chemotherapy is only validated after regular multidisciplinary meetings. At that stage, it might be interesting to obtain a minimal renal checkup before any treatment to identify 'at-risk patients' and further educate oncologists and patients about a number of classic kidney failure risks.

In previous publications, we and others have identified the main areas of interest and intervention of onconephrology [1, 13–15]. In our opinion, there are categories of cancer patients who must always be referred to the onconephrology outpatient clinic for a comprehensive evaluation. Table 1 notes the types of patients and reasons for referral to the outpatient clinic.

MINIMUM WORKUP FOR THE ONCONEPHROLOGY PATIENT

The minimum workup needed by a cancer patient with some form of kidney disease is summarized in Table 2. In general, the workup should include routine generic examinations and tests, as well as tests specific for the kidney or oncological aspects of the patient's care.

It is critical that patients have an accurate estimate of GFR in order to optimize medications' dosing and avoid side effects. The best estimating equation for GFR to gauge kidney function has not been well studied in patients with cancer and kidney disease. These equations have their strengths and limitations in the general population and likely have other issues in the patients being evaluated in the onconephrology clinic [16-19]. Although some authors have suggested that the Modification of Diet in Renal Disease (MDRD) equation could underestimate kidney function in cancer patients [20, 21], the MDRD and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations are still the two equations recommended in this setting [22–24]. It is likely that they will provide similar estimates of kidney function in patients with stable CKD and they are not appropriate to use in patients with AKI where the patient's GFR is not in a steady state [25]. A recent publication evaluating GFR estimating equations in cancer patients noted that the body surface area (BSA)-adjusted CKD-EPI method appears to be the most accurate published model to estimate GFR in patients with cancer. BSA-adjusted CKD-EPI eGFR, based on the analysis of data from 2582 cancer patients using 51 Chromium Ethylenediamine tetra-acetic acid (51Cr-EDTA) GFR measurement as the gold standard, was found to be the most accurate and least biased published model to estimate GFR [17]. The authors also developed a new model that further improves the estimation of GFR and allows calculation of predictive confidence intervals for this estimation. The new model has been implemented as an online tool found at the following link: http://tavarelab.cruk.cam.ac.uk/ JanowitzWilliamsGFR/. This new model to estimate GFR may represent a new standard of care and should be further examined along with the BSA-adjusted CKD-EPI equation in clinical onconephrology practice.

Table 2. Clinical evaluation of the patient with cancer and kidney disease

Physical examination

Evaluation of comorbidities and preexisting kidney impairment (clinical and subclinical)

Evaluation of ongoing (and previous) therapies, both oncological and not oncological

Renal function tests

eGFR with a CKD-EPI formula

When needed, directly measure eGFR (creatinine clearance, nuclear medicine GFR evaluation, etc.)

Basic haematology, including differential white blood cell count

Urinalysis and examination of urinary sediment examination; quantification of proteinuria

Electrolytes and serum enzymes (including serum calcium, phosphorus, uric acid and magnesium, LDH and uric acid).

Obtain trends of all pertinent labs including SCr, LDH, CBC and urine protein:creatinine ratio

Acid-base balance and abnormalities

Blood pressure (including ABPM whenever necessary)

Basic imaging: renal/abdominal US

Basic imaging: oncological disease status evaluation, as appropriate (CT, MRI, etc.)

CBC, complete blood count; SCr, serum creatinine; LDH, lactate dehydrogenase; US, ultrasound; CT, computed tomography; MRI, magnetic resonance imaging.

Table 3. Disease management in the onconephrology clinic

Management of renal AEs from anticancer therapy and dose modification for

cytotoxic chemotherapy

targeted agents

immune checkpoint inhibitors

bone targeting agents

in patients with conserved or altered renal function (including ESRD and dialysis patients)

Management of renal complications from

surgery

radiation therapy

other diagnostic and therapeutic procedures (e.g. renal stenting, etc.)

Management of CIN

Management of transplantation patients' issues:

management of kidney transplant patient that develops a cancer

clearance (or not) of a cancer patient to donate for kidney transplantation

clearance (or not) of a cancer patient to receive a kidney transplantation

administration of targeted therapy and or immunotherapy in a kidney transplant patient

Management of paraneoplastic nephrological syndromes, including screening or not these patients

Choice of antipain therapy and dose adaptation in cancer patients with renal impairment

Discussion of ethical issues (to treat or not to treat cancer patients in dialysis or with ESRD)

AEs, adverse events; CIN, contrast-induced nephropathy.

DISEASES MANAGED IN THE ONCONEPHROLOGY OUTPATIENT CLINIC

Based on our experience, the areas where a joint onconephrology approach (consultation) is mandatory are those reported in Table 3 [14]. The involvement of specialists other than nephrologists and oncologists should be considered in many of the case discussions, diagnostic approaches and treatment plans.

DEVELOPMENT OF PROTOCOLS FOR THE ONCONEPHROLOGY CLINIC

The development of specific protocols for the screening, management and follow-up of cancer patients with various kidney problems is one of the major goals of onconephrology clinic. Different protocols should be proposed and discussed within the core team, brought to the attention of multidisciplinary teams (MDTs) and then disseminated to all onconephrology clinics (Table 4). These protocols should be shared across centres in order to support the development of best practices.

In addition to developing various clinical protocols, it should be part of the onconephrology core team's mission to participate in the proposal, design and conducting of clinical trials addressing specific issues related to cancer and kidney disease. Finally, lobbying to introduce well-defined and clinically relevant nephrology endpoints into oncological clinical trials (from Phase I to postmarketing Phase IV studies) would be of the utmost importance [26].

AUDITS AND (PROPOSED) INDICATORS OF PERFORMANCE

The onconephrology clinic must hold regular internal audit meetings in order to review indicators of performance, establish or change procedures and amend protocols as necessary [2, 27]. Written protocols should be developed and agreed upon by the multidisciplinary members and then discussed and reevaluated at any audit. Revising many of the proposed indicators of performance over time in order to dismiss those not relevant and implement novel ones (e.g. those emerging from

Table 4. Onconephrology protocols

Screening and follow-up protocols to prevent kidney damage for each given antineoplastic agent

Screening and follow-up protocols to prevent kidney damage from radiology contrast media

Developing indications for kidney biopsy and implementing their use in cancer patients

Screening and follow-up protocols for cancer patients in dialysis and with ESRD

Screening and follow-up protocols for transplantation patients (evaluation and possibly prevention of the risk of malignancy)

Screening and follow-up protocols for transplantation candidates

if and when to transplant a patient who previously had cancer

if and when to allow donation from a patient who previously had a cancer

Table 5. Performance indicators for an onconephrology clinic

Indicator of performance	Reason(s)	Value to be achieved (in Year 1)
Percentage of patients discussed by the core team	To ensure that (ideally) all patients presenting with onconephrology issues are adequately evaluated at least by the core team	100%
Percentage of patients brought to the attention of the MDT	To ensure that all complex patients presenting are brought to the attention of and discussed within each given MDT	100%
Number of episodes of AKI from anticancer	AKI episodes lead to worsening of cancer patients' prognosis	Reduction of at least 25% as com-
treatment	(especially in terms of reduced overall survival); also increase CKD	pared to the previous year
Number of episodes of CIN	CIN episodes lead to both AKI and worsening of CKD	Reduction of at least 25% as compared to the previous year
Number of visits to emergency ward due to kid- ney toxicity from oncological treatments	Increase of costs and hospitalization rates	Reduction of at least 25% as compared to the previous year
Number of hospital admissions due to kidney toxicity	Increase of costs	Reduction of at least 25% as compared to the previous year
Number of treatment interruptions due to kidney toxicity	Potentially hampers treatment efficacy	Reduction of at least 25% as compared to the previous year
Number of treatment withdrawals due to kidney toxicity	Hampers treatment efficacy precluding the continuation of potentially life-extending treatments	Reduction of at least 25% as compared to the previous year
Number of drug-related adverse reactions due to	Increases morbidity and (potentially) also mortality, as well as	Reduction of at least 25% as com-
kidney disease	hospitalization rates; increases treatment interruptions and withdrawals	pared to the previous year
Patients' satisfaction	Linked to improved QoL	100%
Health care workers' satisfaction	Linked to improved medical service quality and patients' satisfaction	100%

CIN, contrast-induced nephropathy; QoL, quality of life.

the use of novel anticancer agents/strategies) is an integral part of the indicators/audits system we propose.

Ideally, among possible initial indicators of performance, we propose those described in Table 5.

THE 'HUB-AND-SPOKE' MODEL FOR ONCONEPHROLOGY

While one of the requirements for an onconephrology outpatient clinic is the presence of a critical mass of patients, the need for an onconephrology consultation can also occur in a small, peripheral hospital. We believe that the concept of the huband-spoke model [28, 29] could optimally be applied to onconephrology. Indeed, the goal of the hub-and-spoke model is to position a specialized care delivery facility as a central hub and build a network of feeders or spoke facilities. This system creates value by generating learning curve benefits at the hub, as well as by operating all assets within the network at maximum utilization. One of the goals of this model is to bring complex cases to the central hub, where they can be managed at the

highest level of competence, and this can be achieved either at the central hub or virtually. Web-based consultations or even MDT rounds could potentially replace physical visits in the case of logistical issues, bringing the competence of the hub directly to the spoke.

EDUCATION AND TRAINING TO CREATE THE ONCONEPHROLOGIST

In the introduction to the American Society of Nephrology (ASN) core curriculum in onconephrology [8], Perazella and Rosner clearly stated that one of the goals of such a tool was to 'provide the ASN membership, including veteran nephrologists, newly minted nephro-clinicians, and fellowship trainees, with the building blocks on which further information can be added as technology advances'. This would be a potential model to follow on an international level. Nephrologists must be prepared to care for patients with cancer and renal complications. Indeed, as already evidenced, the renal manifestations of cancer have many unique features, and these conditions often require

Table 6. Foreseen obstacles in establishing an outpatient onconephrology clinic

Obstacle(s)	
· ·	
Presence of a small oncology/haematology service	
Nihilistic approach to patients with both kidney diseases and cancer	
Structural difficulties (especially in hospitals not built to favor multidisciplinarity)	
Not an issue	
Not an issue	
Clear-cut identification of the onconephrology referral specialist within the hospital	
Clear-cut definition of the patients to refer for consultation	
Information/education of physicians who should know when an onconephrological referral is needed	
Time	
Bringing together and motivating different specialists towards a real multidisciplinary consultation	
Nihilistic approach to patients with both kidney diseases and cancer	
Need for specific training and for maintaining proficiency in onconephrology	
Bringing together and motivating different health professionals and caregivers	
Not an issue	
Clear-cut definition of the patients to refer for consultation	
Nihilistic approach to patients with both kidney diseases and cancer	
Sharing minimal requirements among different specialists	
Sharing a common language	
Clear-cut evaluation of kidney function	
Nihilistic approach to patients with both kidney diseases and cancer	
Identification of topics and objectives	
Time and personnel	
Variability of indicators over time	
Costs	
Bringing together and motivating different structures and health professionals	
Identification of educational needs	
Standardization of trainees' curriculum	

specialized approaches to manage all of them. Furthermore, the rapidly evolving field of cancer treatments requires a comprehensive approach from the different and varied expertise of nephrologists, oncologists and many other specialists. As such, it is essential for all who are interested in onconephrology to develop expertise in the practice of this intriguing and complex subspeciality. Specific courses in post-graduate training in nephrology and oncology could be employed to increase the awareness of onconephrology issues and to prepare the next generation of specialists in this subspeciality.

OBSTACLES IN THE DEVELOPMENT OF AN ONCONEPHROLOGY OUTPATIENT CLINIC

The development and implementation of every novel activity is almost always coupled with difficulties, obstacles and barriers; this is certainly the case with our proposal.

Recognizing these pitfalls is the first step to overcoming them. Through our experience, we have summarized these obstacles in Table 6, coupling each requirement we have highlighted with relative obstacles. Notably enough, in our opinion, the first and most important obstacle to overcome is the typical nihilistic approach surrounding patients with both kidney diseases and cancer.

CONCLUSIONS

Due to the dramatic improvements in cancer treatment, a growing number of patients affected by cancer now survive longer, often with an adequate quality of life. However, the presence of

concomitant chronic illnesses, including kidney disease, may greatly complicate their care and alter their quality and quantity of life. The relationship between kidney disease and cancer could be regarded as 'circular' [30]. For example, the presence of a tumour or its treatment may directly or indirectly damage renal function and the presence of kidney disease in cancer patients may worsen their prognosis, increase mortality and disturb the bioavailability and/or safety profile of antineoplastic drugs in patients with underlying kidney disease.

Onconephrology is presently more experience-based than evidence-based. Indeed, onconephrology has developed in recent years with the main intent of managing those orphan patients (e.g. those with CKD, ESRD, on dialysis, transplanted, etc.) who are not enroled in clinical trials (the cornerstones of evidence-based medicine), who cannot benefit from the availability of guidelines (which indeed do not exist) or even of sound supporting literature (mainly limited to single case reports or small retrospective series). Only with a thorough knowledge of the issues of onconephrology and of the drugs and their pharmacokinetic properties in patients with cancer and kidney diseases, together with a tight interspeciality collaboration, can we provide these patients better treatment and management.

Thus a multidisciplinary onconephrology team led not only by cancer specialists and nephrologists, but also including other health professionals, is critical to providing the best possible care for this group of cancer patients. Here we have proposed minimum requirements and recommendations to develop an onconephrology outpatient clinic, with the overall aim of providing experience-based considerations that will initiate further discussion on this important and growing speciality area.

Finally, as far as multidisciplinarity is concerned, we cannot but agree with the following strong statement by Champiat *et al.* [31]: 'Organ specialist . . . referral is needed for mainly two reasons: for oncologists to learn proper management of specific . . . toxicities, but also for organ specialists to increase their knowledge about these new drug-mediated toxicities and therefore creating a virtuous circle for patients management'.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

- Cosmai L, Porta C, Gallieni M et al. Onco-nephrology: a decalogue. Nephrol Dial Transplant 2016; 31: 515–519
- Valdagni R, Albers P, Bangma C et al. The requirements of a specialist prostate cancer unit: a discussion paper from the European School of Oncology. Eur J Cancer 2011; 47: 1–7
- EUSOMA. The requirements of a specialist breast unit. Eur J Cancer 2000; 36: 2288–2293
- Launay-Vacher V, Oudard S, Janus N et al. Prevalence of renal insufficiency in cancer patients and implications for anticancer drug management: the renal insufficiency and anticancer medications (IRMA) study. Cancer 2007; 110: 1376–1384
- Christiansen CF, Johansen MB, Langeberg WJ et al. Incidence of acute kidney injury in cancer patients: a Danish population-based cohort study. Eur J Intern Med 2011; 22: 399–406
- Ferlay J, Soerjomataram I, Dikshit R et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136: E359–E386
- Ko C, Chaudhry S. The need for a multidisciplinary approach to cancer care. J Surg Res 2002; 105: 53–57
- American Society of Nephrogy. Onco-Nephrology Curriculum. https:// www.asn-online.org/api/download/? file=/education/distancelearning/cur ricula/onco/OncoNephrologyCurriculum.pdf (24 March 2018, date last accessed).
- 9. Abdulrahman GO Jr. The effect of multidisciplinary team care on cancer management. *Pan Afr Med J* 2011; 9: 20
- Wanchoo R, Riella LV, Uppal NN et al. Immune checkpoint inhibitors in the cancer patient with an organ transplant. J Onco-Nephrol 2017; 1: 42–48
- Howard SC, Trifilio S, Gregory TK et al. Tumor lysis syndrome in the era of novel and targeted agents in patients with hematologic malignancies: a systematic review. Ann Hematol 2016; 95: 563–573
- Rioux-Leclercq N, Ferran A, Mahul A et al. [Renal tumors: the International Society of Urologic Pathology (ISUP) 2012 consensus conference recommendations]. Ann Pathol 2014; 34: 448–461
- 13. Finkel KW, Howard SC. Onco-nephrology: an invitation to a new field. *J Clin Oncol* 2014; 32: 2389–2390

- Perazella MA, Berns JS, Rosner MH. Cancer and the kidney: the growth of onco-nephrology. Adv Chronic Kidney Dis 2014; 21: 4–6
- Launay-Vacher V, Porta C, Cosmai L. Introduction to the *Journal of Onco-Nephrology*. J Onco-Nephrol 2017; 1: 1–4
- Marx GM, Blake GM, Galani E et al. Evaluation of the Cockroft-Gault, Jelliffe and Wright formulae in estimating renal function in elderly cancer patients. Ann Oncol 2004; 15: 291–295
- Janowitz T, Williams EH, Marshall A et al. New model for estimating glomerular filtration rate in patients with cancer. J Clin Oncol 2017; 35: 2798–2805
- Hingorani S, Pao E, Schoch G et al. Estimating GFR in adult patients with hematopoietic cell transplant: comparison of estimating equations with an iohexol reference standard. Clin J Am Soc Nephrol 2015; 10: 601–610
- Funakoshi Y, Fujiwara Y, Kiyota N et al. Validity of new methods to evaluate renal function in cancer patients treated with cisplatin. Cancer Chemother Pharmacol 2016; 77: 281–288
- Lauritsen J, Gundgaard MG, Mortensen MS et al. Reliability of estimated glomerular filtration rate in patients treated with platinum containing therapy. Int J Cancer 2014; 135: 1733–1739
- Hahn T, Yao S, Dunford LM et al. A comparison of measured creatinine clearance versus calculated glomerular filtration rate for assessment of renal function before autologous and allogeneic BMT. Biol Blood Marrow Transplant 2009; 15: 574–579
- Kleber M, Cybulla M, Bauchmuller K et al. Monitoring of renal function in cancer patients: an ongoing challenge for clinical practice. Ann Oncol 2007; 18: 950–958
- Launay-Vacher V, Chatelut E, Lichtman SM et al. Renal insufficiency in elderly cancer patients: International Society of Geriatric Oncology clinical practice recommendations. Ann Oncol 2007; 18: 1314–1321
- Giglio D. A new equation for estimating glomerular filtration rate in cancer patients. Chemotherapy 2014; 60: 63–72
- Bragadottir G, Redfors B, Ricksten SE. Assessing glomerular filtration rate (GFR) in critically ill patients with acute kidney injury-true GFR versus urinary creatinine clearance and estimating equations. Crit Care 2013; 17: R108
- Porta C, Cosmai L, Gallieni M et al. Harmonization of renal function assessment Is needed throughout the whole process of anticancer drug development. J Clin Oncol 2016; 34: 2429–2430
- van Dam PA, Tomatis M, Marotti L et al. Time trends (2006–2015) of quality indicators in EUSOMA-certified breast centres. Eur J Cancer 2017; 85: 15–22
- Zucchetti G, Bertorello N, Angelastro A et al. Improving healthcare in pediatric oncology: development and testing of multiple indicators to evaluate a hub-and-spoke model. Tumori 2017. doi: 10.5301/tj.5000645
- Khakwani A, Rich AL, Powell HA et al. The impact of the 'hub and spoke' model of care for lung cancer and equitable access to surgery. Thorax 2015; 70: 146–151
- Porta C, Cosmai L, Gallieni M et al. Renal effects of targeted anticancer therapies. Nat Rev Nephrol 2015; 11: 354–370
- Champiat S, Lambotte O, Barreau E et al. Management of immune checkpoint blockade dysimmune toxicities: a collaborative position paper. Ann Oncol 2016; 27: 559–574

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