The evolving landscape of renal surgery for complex renal masses (CRM): implications for oncologic and functional outcomes

Savio Domenico Pandolfo[1,2] (ID), Achille Aveta[3], Sisto Perdonà[3], Gianluca Spena[3], Alessandro Izzo[3], Antonio Tufano[3], Zhenjie Wu[4], Clara Cerrato[5], Ferdinando Fusco[6], Celeste Manfredi[6], Davide Arcaniolo[6], Pierluigi Russo[7], Lorenzo Romano[6], Matteo Ferro[8], Rocco Bernardo[9], Giuseppe Lucarelli[10], Francesco Lasorsa[10], Salvatore Siracusano[1], Simone Cilio[11] (ID), Carlo Giulioni[12], Angelo Cafarelli[12], Fabio Crocerossa[13], Paolo Conforti[2]

[1]Department of Urology, University of L'Aquila, L'Aquila 67100, Italy.
[2]Department of Neurosciences and Reproductive Sciences and Odontostomatology, University of Naples "Federico II", Naples 80131, Italy.
[3]Department of Urology, Istituto Nazionale Tumori, IRCCS, "Fondazione G. Pascale", Naples 80131, Italy.
[4]Department of Urology, Changhai Hospital, Naval Medical University, Shanghai 200433, China.
[5]Urology Unit, University Hospital Southampton NHS Trust, Southampton SO16 6YD, UK.
[6]Unit of Urology, Department of Woman, Child and General and Specialized Surgery, University of Campania "Luigi Vanvitelli", Naples 80131, Italy.
[7]Department of Urology, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, Rome 00168, Italy.
[8]Unit of Urology, Department of Health Science, University of Milan, ASST Santi Paolo and Carlo, Milan 20142, Italy.
[9]Department of Urology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome 00168, Italy.
[10]Department of Precision and Regenerative Medicine and Ionian Area Urology, Andrology and Kidney Transplantation Unit, Aldo Moro University of Bari, Bari 70124, Italy.
[11]Department of Medicine and Surgery, Scuola Medica Salernitana, University of Salerno, Fisciano 84081, Italy.
[12]Urology Unit, Casa di Cura Villa Igea, Ancona 60127, Italy.
[13]Department of Urology, Magna Graecia University of Catanzaro, Catanzaro 88100, Italy.

Correspondence to: Dr. Savio Domenico Pandolfo, Department of Urology, University of L'Aquila, Palazzo Camponeschi, piazza Santa Margherita 2, L'Aquila 67100, Italy. E-mail: pandolfosavio@gmail.com

Abstract

Partial nephrectomy (PN) has become the standard of treatment for most T1 renal masses and is suitable for selected T2 renal cortical masses. In this setting, the management of complex renal masses (CRM) requires a

thorough understanding of the potential risks and benefits of both PN and radical nephrectomy (RN). Indeed, thanks to the advent of robotic surgery, indications of PN have expanded to include larger tumors and CRM, despite the associated surgical complexity and oncologic risks. The decision-making process for CRM treatment with PN or RN is complex. Thus, the current review aims to explore the decision-making essentials for patients with CRM, identify research gaps, and address the clinical challenge of determining the most suitable surgical approach. Current evidence suggests that while PN offers a clear advantage in renal tissue preservation, it may carry higher perioperative risks compared to RN. However, these risks should be balanced with the long-term benefits of renal function preservation. In conclusion, further high-quality, prospective studies are needed to better define the comparative effectiveness of PN *vs.* RN to guide clinical decision-making for CRM.

INTRODUCTION

Renal cell carcinoma (RCC) accounted for 431,288 new cases globally in 2020, representing approximately 2.2% of all cancer diagnoses. RCC is the most common form of kidney cancer, comprising about 90% of all renal malignant masses. It ranks as the 16th most common malignancy worldwide and is the 6th most frequently diagnosed cancer in men[1]. Commonly recognized risk factors are several metabolic disorders such as diabetes, obesity, metabolic syndrome and chronic kidney disease (CKD)[2,3,4]. Moreover, in developed countries, the improvement and spreading of imaging techniques have promoted the incidental detection of renal masses. In this setting, current guidelines equally recommend surveillance, ablation therapies and surgery[5,6]. Among all the therapeutic options, nephron sparing surgery (NSS), when feasible, is widely recognized to be the preferred surgical method to manage T1a and T1b exophytic, favorably located, masses especially when using min-invasive approach[6,7,8,9,10]. When addressing complex renal masses (CRM), which include both larger and anatomically challenging cases, the historical preference often leaned towards radical nephrectomy (RN) due to the surgical complexity and potential oncologic risks[11,12]. Indeed, despite the lack of a standardized definition, CRM typically refers to renal tumors with a RENAL score of > 9, indicating high complexity due to their size, location, and closeness to critical structures[13,14,15,16,17]. However, with advancements in robotic surgical techniques, the scope for NSS has expanded, making partial nephrectomy (PN) a viable option for managing these CRM scenarios, especially in referral centers[6,18,19]. Yet, oncologic safety remains a paramount concern across all patient groups, especially in younger and healthier individuals. In this setting, the decision-making process for treating CRM with PN or RN is intricate, demanding a careful assessment of the risks and benefits associated with these surgical options.

Given the existence of a grey zone in the management of CRM, this review aims to delve into the decision-making essentials for patients presenting with this kind of malignancy, identify gaps in existing research, and address the clinical challenge of guiding physicians to choose the most suitable surgical approach for each patient by summarizing and organizing current evidence regarding PN *vs.* RN approaches.

METHODS

In August 2024, the most eminent scientific databases, including PubMed, Embase, and the Cochrane Library, were queried to collect scientific manuscripts related to CRM. Consequently, this research encompassed publications up to July 2024.

Search strategy and data extraction
The search strategy was formulated by combining essential terms pertinent to the objectives of this non-systematic review. These terms included: ("partial nephrectomy" OR "PN" OR "nephron-sparing surgery" OR "NSS") AND ("complex renal masses" OR "complex kidney tumors" OR "high-complexity renal tumors" OR "CRM") AND ("radical nephrectomy" OR "RN") AND ("oncologic outcomes" OR "cancer control" OR "tumor recurrence" OR "survival rates") AND ("surgical complications" OR "postoperative complications" OR "perioperative outcomes") AND ("renal function preservation" OR "kidney function preservation" OR "nephron preservation") AND ("RENAL nephrometry score" > 9 OR "PADUA score" > 9). These selected keywords were crucial for a comprehensive collection of literature addressing various aspects of nephrectomy procedures for CRM, such as procedural specifics, outcomes, and follow-up methods.

The review targeted studies offering in-depth descriptions of the procedures and outcomes related to PN and/or RN. To ensure a comprehensive and unbiased collection of studies, additional sources were located through manual searches of reference lists in relevant studies and review articles.

Data extraction was conducted independently by two authors (P.C. and A.A.), using a predetermined approach to address any discrepancies. In instances of disagreement, a consensus was achieved by consulting an Assistant Professor (S.D.P.). This methodical collaboration ensured the accuracy and dependability of the data compiled in our review.

Quantification of the anatomic complexity of renal masses
Structured, reproducible, and quantitative scoring systems to describe and classify the most surgically relevant anatomical features of solid renal neoplasms are mandatory. Several scoring systems, known as "nephrometry scores", have been developed to objectively characterize renal tumor complexity [Table 1]. The decision-making for CRM benefits from standardized reporting of renal tumor size, location, and depth[18,20,21]. Nephrometric scores were specifically developed to predict the risk of complications from NSS based on lesion complexity. In the literature, among various scores defining complexity of a renal mass, the most used one is that a CRM is defined as a cortical neoplasm with a RENAL Nephrometry Score > 9[6,13,15]. Similarly, the PADUA score, an alternative classification system categorizing the overall anatomic complexity into low, intermediate, or high categories (scores of 6-7, 8-9, and 10-14, respectively), also defines a CRM as a renal mass having a score greater than 9[22]. Additionally, for comprehensive assessments, calculators are available that allow for the conversion between RENAL and PADUA scores, facilitating comparisons across studies that may use different systems. To streamline and enhance the predictive capability of nephrometry scores, Ficarra *et al.* introduced the Simplified PADUA Renal (SPARE) scoring system[23]. This model simplifies the assessment by focusing on four key anatomical features: rim location, renal sinus involvement, exophytic rate, and maximal tumor size. The effectiveness of the SPARE system has been validated in several studies, comparing its predictive accuracy with that of the RENAL and PADUA scores[24].

Unfortunately, these nephrometry scores do not account for all the necessary elements that define a CRM. Although numerous nephrometry scores exist, there is a pressing need to include key elements from these scores in radiological assessments, as this would provide a richer data set for comparison and enhance their utility in clinical decision-making. Future considerations should include parameters such as adjacent organ involvement, patient's body mass index, and characteristics such as the density and distribution of perirenal fat, including the tricky 'toxic fat' that complicates surgical procedures by affecting visibility and dissection difficulty. These additional aspects are essential for a comprehensive assessment of CRM and should be integrated into the next nephrometry scoring systems to enhance the precision of surgical planning and

Table 1. Summary of the similarities and differences of the most used nephrometry scoring systems

| Scores	Size (diameter)	Growth	Distance to renal sinus	Anatomical location of the tumor	Location with respect to polar line	Complexity
RENAL	< 4 cm: 1pt 4-7 cm: 2pt > 7 cm: 3pt	> 50% exophytic: 1pt < 50% exophytic: 2pt Entirely endophytic: 3pt	> 7 mm: 1pt 4-7 mm: 2pt < 4 mm: 3pt	Anterior or posterior: 1pt On the lateral border: 2pt	Upper polar line: 1pt Below polar line: 2pt	Low: 4-6pt Moderate: 7-9pt High: 10-12pt
PADUA	< 4 cm: 1pt 4-7 cm: 2pt > 7 cm: 3pt	> 50% exophytic: 1pt < 50% exophytic: 2pt Entirely endophytic: 3pt	Not involving the renal rim: 1pt Involving the renal rim: 2pt	Anterior or posterior: 1 pt On the lateral border: 2 pt	Not available	Low: 6-7pt Intermediate: 8-9pt High: 10-14pt
SPARE	≤ 4 cm: 1pt > 4 cm: 2pt	> 50% exophytic: 1pt < 50% exophytic: 2pt	> 7mm: 1pt ≤ 7 mm: 2pt	Not available	Not available	Low: 4pt Moderate: 5-6pt High: 7-8pt

outcome prediction.

Advancing surgical planning with 3D reconstructions

The scientific community is currently navigating the age of precision medicine, which is progressively being implemented in surgical practices, including oncological conditions. During the last decade, the integration of 3D vascular model (3DVM) reconstructions significantly enhances the application of these models in preoperative evaluation and surgical planning[25,26,27]. In this context, 3DVMs exceed the traditional 2D computed tomography (CT) scans, which were previously insufficient for comprehensive preoperative evaluation of CRM [Figure 1A and B][28,29]. Indeed, this detailed view facilitates the assessment of the tumor's complexity and assists in strategizing the optimal approach for resection, minimizing potential surgical complications.

In a recent study by Grosso *et al.*, a detailed analysis using a propensity-score matched approach was performed comparing patients undergoing robot-assisted PN (RAPN) for renal neoplasms[30]. This analysis distinctively focused on the application of 3DVMs. Notably, the use of these models facilitated a more targeted approach in vascular clamping - selective clamping was preferred significantly more in the 3DVM group than in the non-3DVM group (21% *vs.* 9%, *P* = 0.03). This choice is attributed to the enhanced and detailed understanding of renal vasculature provided by the models. Moreover, the integration of "rainbow technology" in 3D rendering marks a significant advancement [Figure 1]. This technology color-codes the vascular regions, allowing surgeons to visualize and navigate the complex arterial network of the kidney.

Further insights were gained from a sensitivity analysis across different PADUA risk categories (low-risk PADUA 6-7, intermediate-risk PADUA 8-9, high-risk PADUA ≥ 10). This analysis highlighted that the functional benefits of using 3DVMs were predominantly seen in high-risk category masses. The study concluded that both cohorts demonstrated similar perioperative risk profiles and oncological outcomes. This similarity underscores the potential of 3DVMs to enhance surgical precision without compromising safety or efficacy in managing renal neoplasms[30]. Moreover, the utilization of 3DVMs in preoperative planning not only assists in the visualization but also in the simulation of surgical steps, offering a clear roadmap for the surgery. This advanced preparation is vital for improving the accuracy of tumor resection and preserving as much of the healthy kidney tissue as possible, thereby enhancing postoperative outcomes[31]. Ultimately, the adoption of the single port robotic system has introduced significant advantages, including shorter hospitalization times and optimized postoperative outcomes, further
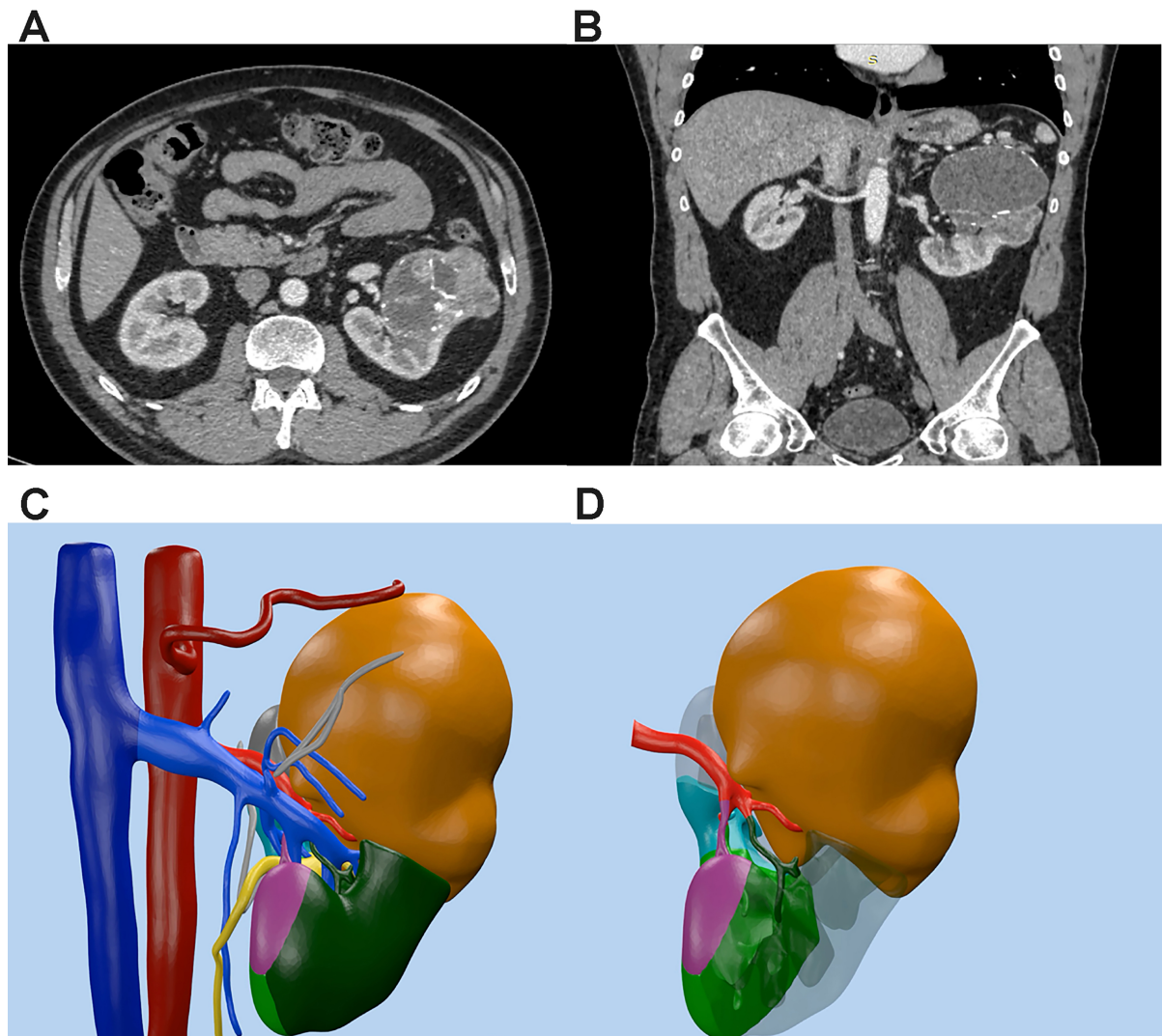
Figure 1. CT findings of patients with CRM and 3DVM preoperative reconstruction - rainbow technology. (A and B) Axial and coronal CT scan of high complexity renal cell carcinoma (RENAL = 12); (C and D) 3DVM reconstruction (red represents artery, blue incicates vein, and yellow stands for collective system. Brown denotes tumor). CRM: Complex renal masses; 3DVM: 3D vascular model.

advancing the role of precision medicine in minimally invasive surgery[32].

EVIDENCE SYNTHESIS

Current factors guiding the decision-making process between PN *vs.* RN

Currently, PN is preferred for treating localized renal masses due to its effective cancer control and superior preservation of renal function post-surgery compared to RN. Consequently, PN has surpassed its initial narrow scope of indications, which included conditions such as a solitary kidney, bilateral renal masses, or pre-existing CKD[33,34,35,36,37,38]. This expansion is driven by the potential decline in quality of life and increased mortality risks associated with deteriorating renal function and the subsequent necessity of dialysis[39,40]. Indeed, the use of PN has progressively broadened to include patients with a normal contralateral kidney and normal renal functional indexes, thus reducing the likelihood of post-surgical CKD and maintaining oncological results comparable to those of RN[6,41]. To date, international Guidelines have not included the preoperative nephrological assessment and the significant role of the multidisciplinary team in their

recommendations[42]. Indeed, the management of CRM currently depends on two main factors: the specific center experience, influenced by institutional logistics, and the availability of multidisciplinary technologies and specialists, and the surgeon's perspective, which includes preference, skill, and confidence in performing PN over RN[43,44].

Functional outcomes
A preserved renal function following PN is the most widely acknowledged advantage of these procedures over radical ones. Although evidence suggests that survival outcomes and life expectancy of patients who underwent PN are not inferior to patients treated with RN[4,45,46,47], the overall prognosis and overall survival (OS) may benefit from NSS by also lowering the risk of cardiovascular and metabolic sequelae[48,49]. Indeed, OS has been correlated with an estimated glomerular filtration rate (eGFR) decline below 45 ml/min/1.73 m^2[50].

Initial studies highlighting these benefits were based on retrospective single-institution reports, showing that patients who underwent PN for a renal mass experienced better renal functional outcomes than those who underwent RN[51]. Indeed, Lau *et al.* reported early suggestive evidence that both NSS and RN are equally safe. However, NSS achieved better functional preservation supported by a reduction in proteinuria and chronic renal insufficiency, compared to RN[51].

To investigate the effectiveness of PN in preserving renal function, Simmons *et al.* assessed postoperative renal outcomes by using the RENAL scoring system. They observed a positive correlation between the comprehensive RENAL score and the preservation of long-term eGFR. Additionally, they found that alterations in tumor diameter and RENAL Score corresponded to fluctuations of 0.5% and 1.6% in postoperative eGFR, respectively[52]. Similarly, research findings have shown that for each 1-point increase in the RENAL score or for each 1-cm increase in tumor size, there is a consequent decline in eGFR of 2.5% (P = 0.002) and 1.8% (P = 0.013), respectively[53].

Overall, it has been shown that a higher RENAL score can predict functional outcomes following PN. Therefore, there has been concern regarding whether PN for CRM offers substantial functional advantages over RN to warrant the potentially heightened risks.

In this scenario, Cerrato *et al.* reported findings from a multicenter analysis of the ROSULA (RObotic SUrgery for LArge) study, which is the first to compare functional outcomes of minimally invasive RN (MIS-RN) and RAPN in the setting of CRM (defined as cortical neoplasm with a RENAL score of 10-12 points). The authors concluded that RAPN provides functional benefit, with decreased difference in postoperative eGFR (ΔeGFR) and risk of developing a *de-novo* eGFR < 60 and < 45 mL/min/1.73 m^2, without a significantly higher rate of major complications[15]. Despite well-founded theoretical concerns, these findings indicate that retaining the remaining parenchyma in CRM could still represent a noteworthy increase in functional nephron mass compared to the total loss of functional parenchyma in the affected kidney during RN.

Taken together, literature data suggest an average less clinically apparent renal morbidity for patients who underwent elective PN *vs.* RN.

Prediction of renal failure
Even with the development of advanced models aimed at estimating renal function after surgery[54,55,56], forecasting postoperative kidney performance in patients undergoing PN or RN for localized renal tumors

with initially preserved renal function, continues to be a highly intricate process in the clinical settings[57].

Interesting findings come from Pecoraro *et al.*, who declared that the risk of post-PN acute kidney impairment (AKI) was mainly related to tumor complexity and surgery-related factors, including warm ischemia time (WIT) and surgical approach. Moreover, the authors reported predictors of new-onset CKD during the follow-up including nonmodifiable patient-related characteristics, namely: the preoperative "functional nephrological reserve" (i.e., higher baseline eGFR), age-adjusted Charlson Comorbidity Index, and tumor complexity. Overall, these findings suggest that the likelihood of postoperative CKD is conditioned by both the baseline kidney characteristics and the volume of renal parenchyma spared[58,59,60].

Interestingly, Off-clamp robotic PN (Off C-RPN) has emerged as a viable option, even in the hands of training surgeons. A propensity score-matched analysis conducted at a single institution demonstrated that, after appropriate training, perioperative outcomes of Off C-RPN performed by training surgeons were comparable to those achieved by expert surgeons, including hospital stay, complication rates, and functional outcomes such as hemoglobin and eGFR at discharge. These findings suggest that with proper training, the learning curve has a negligible impact on outcomes, further supporting the feasibility of PN in complex settings[61].

A recent study by Saitta introduces the RENSAFE model, which predicts postoperative AKI and CKD in patients undergoing renal surgery. The model considers key variables such as male sex, the American Society of Anesthesiologists (ASA) score, hypertension, RENAL score, preoperative eGFR, and surgical type (RN *vs.* PN), showing an area under the curve (AUC) of 0.80 for AKI prediction and 0.76 for CKD ≥ 3b prediction. The authors describe the model as an easily implementable tool that reliably predicts postoperative AKI and CKD, thus facilitating point-of-care decision-making for both urologists and patients[57]. Additionally, a study by Flammia *et al.* investigated the risk of CKD upstaging at 3-year follow-up in patients who underwent RAPN. The study utilized a multi-institutional database to identify patients treated with RAPN for localized renal tumors and defined significant CKD (sCKD) upstaging as the development of newly onset CKD stages 3a, 3b, and 4/5. The model accurately predicted a 3-year sCKD-upstaging of 84% and highlighted risk categories with varying sCKD-upstaging rates[62].

These predictive tools may add valuable insights to the ongoing debate between the use of RN and PN, enhancing patient counseling and management by accurately forecasting postoperative outcomes.

How does renal score or complexity affect the survival outcomes?
Although widely accepted indications for PN for large polar or mostly exophytic masses, debate persists regarding its application for CRM. Concerns have been raised regarding the oncological effectiveness and safety of PN in this context[63]. This comes from different historical evidence where increasing RENAL scores showed an association with worsened oncological outcomes[64]. Indeed, Bradshaw *et al.* reported results from a retrospective multicenter propensity score-matched analysis with overall 648 patients (216 RAPN *vs.* 432 MIS-RN). The authors showed that increasing RENAL scores (HR = 1.3, *P* = 0.037), high tumor grade (HR = 2.5, *P* = 0.043), and histology findings of sarcomatoid tumor (HR = 2.8, *P* = 0.02) were associated with higher risk of recurrence[63]. However, more recent and promising evidence has reported more encouraging results and a progressive shift in favor of NSS for CRM management. Indeed, an interesting head-to-head comparison of RN and PN for the treatment of CRM using the multi-institutional database ROSULA was reported by Cerrato *et al.* The authors found no association between PN and survival outcomes for renal masses with a RENAL score of 10-12, even in cases of higher-stage disease. Additionally, results from the Kaplan-Meier Analysis show no statistically significant differences in 5-year

cancer-specific survival (CSS) between RN and PN for pT1 (P = 0.473), pT2 (P = 0.735), and pT3 (P = 0.581) malignancies. Additionally, there were no significant differences in 5-year non-CSS between RN and PN for pT1 (P = 0.107), pT2 (P = 0.485), and pT3 (P = 0.403) tumors. Similarly, no significant differences were found in OS for patients diagnosed with pT1 (P = 0.078), pT2 (P = 0.442), and pT3 (P = 0.863) masses[13].

From a pathological standpoint, nuclear high-grade is commonly reported to be associated with more aggressive pathology and worsened survival outcomes[65,63,66]. Moreover, greater tumor complexity has been linked to an increased risk of high-grade disease. A systematic review and meta-analysis by Veccia *et al.* revealed that patients with the diagnosis of clinical T1 malignancies, who were upstaged to pT3a, had a higher risk of having a nuclear grade of 3 or higher (OR = 2.57, P < 0.00001). This suggests that high-grade disease may independently correlate with a greater risk of upstaging to pT3a[65]. In this scenario, RCC recurrence showed to be independently associated with higher-grade disease (HR = 2.38, P < 0.001) by van der Mijn *et al.*[67]. On the other hand, low-grade disease has been linked to better OS (HR = 1.18, P = 0.018) and CSS (HR = 1.18, P = 0.017)[13]. Overall, all those data suggest high-grade disease occurs more frequently in tumors of high complexity. Consequently, even in the management of CRM, high-grade disease is associated with poorer survival outcomes and the type of surgery did not result in differing outcomes.

In recent literature, the survival benefit observed for PN over RN is primarily attributed to the subsequent metabolic effects resulting from the preservation of renal function[68,69]. However, those data come from retrospective and observational reports which may be influenced by selection bias. Indeed, due to the relationship between tumor's biology and complexity, patients with tumors in advantageous locations are more frequently chosen for PN over RN at many medical centers[70]. This provocative finding implies that the OS benefit might partially result from the selection of patients with more favorable renal tumors, in terms of size and location, for PN. Therefore, numerous inherent imbalances related to unmeasured confounders in cohorts comparing the effectiveness of PN and RN likely exaggerate the observed treatment effect of PN.

Assessing the risk: complications associated with PN in CRM management
Historically, PN has been linked to a higher incidence of complications compared to RN. Indeed, in 2010, the EORTC 30904 trial showed higher perioperative bleeding rates in patients who underwent PN with respect to patients who underwent RN, regardless of tumor complexity[71]. PN has been demonstrated to be a safe management option for renal masses, with infrequent and manageable complications mostly connected to the anatomical complexity of the tumor and the individual patient's characteristics. However, increasing RENAL score has been associated with increasing risk of complications in PN[53,72]. Various radiographic scoring systems are designed to assess the risk of postoperative complications using preoperative imaging. Anatomic characteristics of renal masses, including size and depth, are typically viewed as predictors of major complications following PN, including hemorrhage and urinary fistula[73]. For instance, Wheat *et al.* recently identified that for each 1-cm increase in tumor size, the odds of encountering a major complication rose by 33%[74]. For this reason, a thorough assessment of the risks of perioperative morbidity and complications is essential in the decision-making process for any PN, and even more critical when dealing with CRM.

Liu *et al.* analyzed tumors classified by the RENAL score as low, moderate, and high complexity and treated with laparoscopic PN. They observed a significantly higher rate of overall complications in tumors of moderate to high complexity compared to those with low (P = 0.01)[75]. In a retrospective study involving 128 patients who had either open or laparoscopic PN, Reddy *et al.* found that a higher RENAL score

significantly raised the likelihood of complications (OR = 1.29, P = 0.043)[76]. A recent retrospective cohort study, involving five institutions, revealed increased rates of perioperative and postoperative complications after PN for CRM, although the majority of these complications were minor (grade I or II)[77]. Furthermore, evidence from high-volume centers indicates that complication rates for elective PN and certain historically reported complications, such as fistulas, are becoming increasingly rare due to advancements in modern surgical techniques[78]. A recent analysis from a multi-institutional database, comparing outcomes from CRM managed with PN *vs.* RN, showed that neither the type of surgery (P = 0.094) nor tumor size (P = 0.515) was linked to major complications. Thus, literature indicates that management of CRM with PN is an effective oncological option and does not increase the risk of complications[13].

Finally, in a single-center report, Malkoc *et al.* reported the outcome of robotic NSS for management of renal tumors > 7 cm in size. The major complication rate stood at 3.7%, with 52.8% of patients undergoing RAPN presenting RENAL scores of 10-12[79]. These complication rates were similar to those reported for PN in T1a tumors[80]. Similarly, Yim *et al.* reported in a multicenter retrospective analysis for cT3aN0M0 RCC 12.1% of overall complication rate with 4.5% of major complication[81].

Overall, although larger and more complex tumors may be associated with a higher morbidity profile, these reports confirm that the overall and major complication rates remain acceptable and manageable in reference centers.

Generally, over the anatomical complexity of the tumor, the decision-making process should take into account both patient and surgeon-related clinical factors. Indeed, the selection for patients with CRM suitable for PN should also consider ability to handle potential complications. In this process, surgeons should consider that older patients may face a higher risk of both surgical and medical complications following PN compared to RN, and their recovery ability may be reduced[82]. In this regard, the impact of comorbidities must be included in the decision-making process for surgical treatment[83].

Composite outcome

The concept of "Trifecta", as defined as negative surgical margin, no major urological complications, and no AKI on postoperative period, has been progressively adopted as a standard measure to systematically report successful outcomes for NSS[84]. This composite outcome has been traditionally described for surgical NSS approaches, focusing on oncologic efficacy, safety, and preservation of renal function. However, even for non-surgical NSS, such as ablations, recent reports have employed the same aggregated outcome linking oncological safety with surgical and renal preservation[85,86].

Focusing on Trifecta for CRM, Campi *et al.* reported Trifecta achievement of robotic *vs.* open PN for highly complex (PADUA > 10) tumors in high-volume referral centers. The authors collected a significantly lower morbidity for RAPN compared to open PN in achieving Trifecta criteria (69.7% *vs.* 42.6%, P < 0.004). Indeed, their multivariable analyses indicate that the surgical approach independently influenced the risk of "sub-optimal" PN. This observation could be attributed to the varying levels of experience and expertise among robotic and open surgeons. However, the impact of these factors was likely reduced, given that the cohort included patients treated by high-volume surgeons at tertiary referral centers. Considering the complexity of cases handled, as well as those for CRM in general, tertiary referral centers are especially crucial for managing complex conditions, underscoring their importance in ensuring optimal surgical outcomes[22].

However, various definitions of the Trifecta have been developed over time by different groups. Insights derived from the Surface-Intermediate-Base Margin Score International Consortium, as reported by Campi *et al.*, highlight substantial variability in the rates of unsuccessful partial nephrectomies, ranging from 66.4% to 85.9%, contingent upon the Trifecta definition employed. This variability is largely attributed to the diverse thresholds set by various Trifecta scores for defining "clinically meaningful" surgical complications, such as the severity of complications (Clavien-Dindo II *vs.* Clavien-Dindo III) and the metrics used to measure post-surgical renal functional damage - namely WIT *vs.* percentage changes in postoperative eGFR[87]. Overall, evaluating the influence of Trifecta definitions on the success rate of PN still represents a significant gap in the existing research and it is an unmet need. To fill this gap, evaluating Trifecta scores that are adjusted for standardized outcomes, individual patient characteristics and tumor features may enhance the reliability and applicability of these metrics in clinical practice.

CONCLUSION

Our findings suggest that CRM requires an intricate decision-making process that should take into consideration all the potential benefits and risks of PN over RN. Despite literature suggesting similar oncological outcomes, it is essential to examine the limitations and potential complications of each treatment approach. In addition to tumor complexity, surgeons should consider clinical factors such as contralateral renal function, patient age, and comorbidity profile.

Current evidence does not allow for a conclusive resolution of the open question on the superiority of PN over RN and vice versa. Indeed, most data are based on retrospective results and more high-quality, better-designed prospective studies are needed to definitively answer the open question of effectiveness of PN over RN in CRM. In the meantime, patients with CRM requiring a NSS approach should be referred to tertiary centers specializing in advanced PN surgery to optimize outcomes.

DECLARATIONS

Authors' contributions
Conceptualization: Pandolfo SD, Conforti P
Methodology: Pandolfo SD, Conforti P, Manfredi C
Formal analysis: Wu Z
Investigation: Giulioni C, Lucarelli G
Resources: Pandolfo SD, Conforti P
Data curation: Siracusano S, Lucarelli G
Writing - original draft preparation: Pandolfo SD, Conforti P
Writing - review and editing: Manfredi C, Lasorsa F, Perdonà S, Tufano A, Izzo A
Visualization: Manfredi C, Siracusano S, Ferro M
Project administration: Pandolfo SD

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Ethical approval and consent to participate

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