NEW BASELINE GLOMERULAR FILTRATION RATE ESTIMATION AS A GUIDANCE FOR NEPHRECTOMY STRATEGY IN LOCALIZED RENAL CELL CARCINOMA

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ABSTRACT

Objective: *This literature review aims to explain the role of nephrectomy in the treatment of localized RCC and its effects on postoperative renal function, as well as the role of the new baseline glomerular filtration rate (NBGFR) estimation method in the determination of the RCC method.* ***Material & Methods:*** *Articles were obtained through online searches using Pubmed, ScienceDirect, Web of Science, and Wiley Online Library using keywords NBGFR, renal function, nephrectomy, or localized renal cell carcinoma.* ***Results:*** *The development of several diagnostic factors as well as operative factors has made partial nephrectomy (PN) replace radical nephrectomy (RN) which for decades has been the main therapy in localized RCC. Postoperative determination of renal function is a crucial factor in the selection of therapies and several methods of determining NBGFR have been proposed in several previous studies.* ***Conclusion:*** *The NBGFR measurement method can be an accurate guide in the determination of nephrectomy methods in the treatment of localized RCC while use of computer software can help improve accuracy in the implementation of radical nephrectomy in RCC.*

Keywords: *Kidney cancer, new baseline GFR, nephrectomy.*

ABSTRAK

Tujuan: *Tinjauan literatur ini bertujuan untuk menjelaskan peran nefrektomi dalam penanganan localized RCC dan efeknya pada fungsi ginjal paska operasi, serta peran metode estimasi new baseline glomerular filtration rate (NBGFR) dalam penentuan metode RCC.* ***Bahan & Cara:*** *Artikel didapatkan melalui penelusuran secara online menggunakan Pubmed, ScienceDirect, Web of Science, dan Wiley Online Library menggunakan kata kunci keywords NBGFR, renal function, nephrectomy, atau localized renal cell carcinoma.* ***Hasil:*** *Perkembangan dari beberapa faktor diagnostik maupun factor operatif membuat nefrektomi parsial (PN) menggeser nefrektomi radikal (RN) yang selama beberapa dekade menjadi terapi utama pada localized RCC. Penentuan fungsi ginjal pasca operasi menjadi factor krusial dalam pemilihan terapi dan beberapa metode penentuan NBGFR telah diusulkan dalam beberapa penelitian sebelumnya.* ***Simpulan:*** *Metode pengukuran NBGFR dapat menjadi panduan yang akurat dalam penentuan metode nefrektomi dalam pengobatan localized RCC, sedangkan penggunaan perangkat lunak komputer dapat membantu meningkatkan akurasi dalam pelaksanaan RN pada RCC.*

Kata kunci: *Kanker ginjal, new baseline GFR, nefrektomi.*

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INTRODUCTION

Renal cancer occurs in 3% of all adult malignancies with 338.000 new cases in 2012 and 100.000 deaths annually. Renal cell carcinoma (RCC) occurs in 80-85% cases of renal cancer.[1] RCC is an insidious neoplasm that compasses a heterogenous group of renal tubular epithelial neoplasm.[2-3] This cancer more commonly affects men than women.[2,4,5] Between 1975 and 2009, the prevalence of localized RCC increased by +4.55%. Additionally, the mortality rates for localized RCC are still rising by 3.92% annually.[6]

The treatment of choices for localized RCC remains surgical such as partial nephrectomy (PN) and radical nephrectomy (RN).[7] In the past, RN was considered to be the best treatment option for localized renal cancer. To avoid the morbidity related to severe chronic kidney disease (CKD) and dialysis, PN was initially suggested for localized renal cancer. Meanwhile, PN for localized RCC is recommended because of its capability to improve functional outcomes and overall survival.[8] However, RN is still a viable choice for disease with a significant oncologic risk, especially in cases where the tumor is more complicated, no history of CKD, healthy contralateral kidney and estimated new-baseline glomerular filtration rate (NBGFR) >45 ml/min/1.73 m^2.[9]

Substantial reduction in GFR may result from the sudden loss of renal mass following nephrectomy. From this post-nephrectomy GFR baseline, CKD progression rates might vary. The early decline in renal function depends on the amount of renal mass lost. So, PN shows a considerably less decline in GFR after nephrectomy.[10] In order to choose the best surgical therapy for the patient, accurate prediction of the NBGFR, therefore, becomes important because RN is the viable choice if NBGFR >45 ml/min/1.73 m^2.[9]

OBJECTIVE

This literature review aims to explain the role of nephrectomy in the treatment of localized RCC and its effects on postoperative renal function, as well as the role of the new baseline glomerular filtration rate (NBGFR) estimation method in the determination of the RCC method.

MATERIAL & METHODS

Electronic literature searches were conducted from databases such as Pubmed, ScienceDirect, Web of Science, and Wiley Online Library using keywords. NBGFR, renal function, nephrectomy, or localized renal cell carcinoma. Following these criteria, we evaluated each study's title and abstract to see whether it met our inclusion: studies (1) involving localized RCC treated with radical or partial nephrectomy; (2) involving studies with new-baseline GFR data; (3) showing statistical performance of new-baseline GFR estimation methods. There were a total of 7 articles retrieved and we include all of them because the inclusion criteria had been met.

RESULTS

Despite the fact that renal tubular epithelial cell cancers may take many different forms, we refer to all of them under the umbrella term renal cell carcinoma (RCC).[3] Clear cell renal cell carcinoma is the most prevalent subtype of RCC (ccRCC). Seventy-five percent of all cases of primary kidney cancer are found in this category. Chromophobe and papillary RCC are two rarer forms of the disease.[1] In 2020, around 180,000 people died from RCC, accounting for 1.8% of total cancer patient mortality.[4] Furthermore, incidence rates and mortality rates of localized RCC are still rising annually.[6] The term "localized renal cancer" refers to a stage I or stage II tumor that is still contained within the kidney capsule.[11]

Surgical treatment including (PN) and RN remain to be the gold standard for localized RCC.[7] PN treatment for localized RCC is more recommended due to its ability to improve functional outcomes and overall survival.[8] Furthermore, GFR decreases less in PN than in RN.[12] The minimally invasive techniques such as renal ablations by radio-frequency and cryotherapy give new perspectives to the treatment of localized RCC.[13]

Many urological surgeons regarded radical surgery for locally advanced renal cancer as the gold standard of therapy for big renal mass, particularly when there was a healthy contralateral kidney present. For the treatment of renal cancers, radical nephrectomy entails complete kidney replacement from exterior of Gerota fascia combined with total regional lymphadenectomy from the ipsilateral adrenal and diaphragmatic crus to the aortic bifurcation.[14] Since the adrenal gland excision, when it is not affected by a tumor, has not been demonstrated to enhance kidney cancer patients survival, the adrenal gland is now routinely avoided when medically possible.[15]

RN should be considered for tumors with features suggesting increased oncologic potential (e.g., large tumor size, aggressive histology on RMB, or concerning imaging characteristics, such as an infiltrative appearance), and RN is generally preferred in this setting only if all of the following criteria are met: High tumor complexity makes PN difficult for even the most skilled surgeons to perform; there is no history of chronic kidney disease or proteinuria; the opposite kidney is healthy; and the new baseline GFR is expected to be more than 45 mL/min/1.73 m^2. When these conditions are not met, it may be advisable to consider PN.[16-18]

Renal imaging improvements, expertise with renal vascular surgery for other diseases, better ways to minimize ischemia damage, an increase in incidentally discovered renal tumors, a greater understanding of the possibly dangerous consequences of CKD, and the encouragement of long-term survival in patients undertaking this type of procedure have all contributed to the rise in interest in PN for RCC.[19] Nephron-sparing surgery required complete local tumor removal while conserving as much of the kidney's normal functional parenchyma as possible.

When a RN would leave a patient physiologically or structurally anephric and require dialysis, a partial nephrectomy is suggested.[20-21] Candidates for essential partial nephrectomy may also include patients who have significant calculus disease, congenital anomalies, nephropathy, impaired renal function from co-occurring conditions like diabetes, nephritis, and hypertension, as well as patients who have congenital anomalies, nephropathy, or other nephropathy.[22] For a patient who is not receiving dialysis, there must be at least 20% functioning renal residual.[10]

The overall strategy has been to conduct bilateral PNs on patients with bilateral synchronous RCC whenever possible, often as phased operations, especially if the tumors are rather big. An RN is carried out on the side with higher involvement together with a contralateral PN when a restricted significant unilateral malignancy prevents nephron-sparing.[23-24] Forasmuch as the final margins remain negative, it seems that the margin width does not matter. This is especially the case when the tumor is in the hilum and maintaining renal function is crucial.[25-27]

RCC patients that involve a single functionally or physically isolated kidney need to be informed that either temporary or long-term dialysis may be necessary. It was shown in the previous study that a small fraction of patients with a single kidney treated with PN needed interim dialysis before progressing to end-stage renal failure. CKD was already present in several of these patients, and it was generally impossible to save more than a small portion of the kidney due to anatomical restrictions.[28] A functional renal residual of at least 20 to 30 percent of one kidney is required to prevent end-stage renal disease, assuming that the remaining parenchyma is in excellent functional condition.[19]

The etiology of a decline in kidney function after PN remains uncertain, but recent research indicates that nephron mass preservation is the significant variable affecting new baseline GFR following PN, with ischemia playing a secondary role.29 The only significant exception is PN which causes a urinary leak or ureteral blockage which is often only transient and recoverable with the help of urologic therapy. Renal function may also be impaired by medical illnesses that arise during the perioperative period, such as antibiotic-induced interstitial nephritis. However, they are unusual and, in most cases, reversible.

In order to eliminate the possibility of positive margins, tumor resections are usually planned to include a border of healthy parenchyma. Devascularization of neighboring tissue also results through the use of sutures to occlude transected arteries inside the parenchymal bed and to re-approximate the capsule.[30] Parenchyma around the tumor's periphery may also lose blood supply in cases of PN that are more complicated. For this reason, in the context of conventional PN, there will inevitably be some degree of dysfunctional loss associated with these procedures. The majority of research indicates that this is the leading cause of functional impairment after PN, hence it is imperative that efforts be focused there.

Multiple studies have shown that preoperative GFR is a significant predictor of long-term renal function after nephrectomy. Nevertheless, this factor just establishes the floor for functional recovery.[31] A patient having a baseline glomerular filtration rate (GFR) of 40 ml/min/1.73 m^2 would, at most, stabilize with a GFR approaching 40 ml/min/1.73 m^2 provided little nephron mass has been resected and permanent ischemia damage has been averted.[32] This factor is rarely emphasized because, in practice, it is rarely modifiable and it does not play a role to functional deterioration after PN.

NBGFR cutoff of about 45 ml/min/1.73 m^2 has been linked to excellent overall survival and renal preservation, on par with individuals without CKD.[18,29] Therefore, the surgical therapy of localized RCC might be significantly impacted by an accurate prediction of NBGFR following RN. Age, sex, body mass index, eGFR, pertinent comorbidities, and preoperative parenchymal volumes are among of the characteristics that have been used as predictors of NBGFR in various models. However, there has been a large deal of variation across these models, suggesting that heterogeneity in research populations and the prevalence of subjectivity may have further contributed to their limited clinical value.

The subjective assessment method has several limitations due to the possibility of observer

Table 1. Summary of the studies.

Author	Variables	R^2
Sorbellini et al.[35]	Age, gender, A.S.A score, PreOp creatinine, Kidney Volume Change	0.697
Kim et al.[36]	Age, weight, PreOp CrCl, tumor size	RN: 0.573 PN: 0.719
Yokoyama et al.[37]	Age, DM, eGFR,	RN: 0.396
Liss et al.[38]	Preoperative eGFR, surgery, contralateral volume, ipsilateral volume, tumor volume, age, gender, race, hypertension, diabetes	0.68
Bhindi et al.[39]	Age, presence of a solitary kidney, diabetes, hypertension, surgical approach, time from surgery, preoperative eGFR, and preoperative proteinuria	RN: 0.41 PN: 0.62
McIntosh et al.[40]	Age, sex, creatinine	AUC: 0.79
Palacios et al.[41]	PreOp GFR, surgical approach, age, tumor size, DM	0.82

bias in determining the relative significance of each of these criteria. For instance, even when evaluating clearly observable anatomic characteristics, physician generated nephrometry scoring systems have always been regarded as being limited by high interobserver variability.[33] Previous study found that when readers with varying degrees of medical experience or no training at all were responsible for assigning scores, the accuracy, interpretability, and repeatability of the various nephrometry scoring systems were compromised.[34]

Predicting the NBGFR after RN has historically been shown to be a more difficult task than predicting it after PN. This is because the preoperative global GFR acts as a very strong anchor, and PN generally only decreases the global GFR by a little amount, about 10-11%.[30] The predictive effectiveness of a multivariate model including age, global-GFR, diabetes, proteinuria, and tumor size presented by Bhindi, for instance, was low (marginal $R2 = 0.41$ for RN vs 0.62 for PN), despite the inclusion of these factors (Table 1).[39]

Some of the more objective measurement methods are measurements using variables from the results of Split Renal Function (SRF) and Renal Functional Compensation (RFC). Computer-assisted parenchymal-volume analysis (PVA) has made it possible to get SRF without resorting to invasive procedures like nuclear-renal scans (NRS). The SRF-based model established SRF and RFC as essentially significant predictors of kidney function following RN, with a higher predictive power for NBGFR than previously published non-SRF-based model that integrate various comorbidities (e.g. hypertension, diabetes, or obesity) or the presence of proteinuria.[9,42]

DISCUSSION

RCC is one of the most prevalent malignant tumors, while incidence rates and mortality rates of localized RCC are still rising annually. Historically, radical nephrectomy is a gold standard procedure for localized RCC, although some recent developments in both diagnostic and operative factors have increased the use of PN over RN. Consequently, the selection of PN may put the patient at increased risk for oncologic and perioperative complications. These circumstances emphasize the significance of precise NBGFR determination and encourage a number of research initiatives aimed at developing the most reliable calculation methodology.

Several methods that incorporate clinical gestalt showed promising results, especially for PN. Estimation methods for RN showed better results with the assistance of software variables, suggesting that future medical imaging analysis may make increased use of deep learning-based computer vision algorithms. Despite providing comprehensive explanation of NBGFR and its utilization in localized RCC, this review also has its limitation. There are limited number of references available discussing NBGFR estimation using computer-assisted method, especially for RN.

CONCLUSION

The NBGFR measurement method can be an accurate guide in the determination of nephrectomy methods in the treatment of localized RCC, and the use of computer software can help improve accuracy in the implementation of radical RCC.

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