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Commentary Open Access

Composite Outcome Measures in Nephron-Sparing Surgery

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Commentary

Nephron-sparing surgery (NSS) has become the standard of surgical management in small renal masses (SRM) due to its ability to achieve similar outcomes as compared to radical nephrectomy, with the additional preservation of renal function. The concept of ‚trifecta' and 'MIC' (margin, ischaemia and complications) in the setting of NSS, were introduced as measures of quality of surgical management and serve as standardised tools for comparing outcomes in NSS. Although the definitions of ‚trifecta' show slight variation across published literature, they encompass the desire to avoid complications, achieve optimum oncological outcomes and maximise functional renal preservation peri-operatively.

A review of the published literature reveals a gamut of definitions of complications ranging from zero complication to no major or urological complications. Despite the differences in defining complications, the general consensus is to achieve negative surgical margins intra-operatively as an indirect measure of oncological safety outcomes. However, consensus on appropriate treatment in patients with positive histological surgical margins has yet to be established to date.

With regard to functional outcomes, warm ischaemia time (WIT) has been largely used as a predictor in renal functional outcomes. Research has shown a negative correlation between the prolongation of the duration of WIT and renal function outcomes in the long term [1,2]. However, WIT may not be the strongest predictor of the final renal function — the volume of preserved functional parenchyma and baseline renal function are independent predictors of functional outcomes [3,4]. In most available literature, serum creatinine and estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) have been the cornerstone of assessing post-operative preserved renal function. However, such methods are largely limited in their ability to assess the level of preserved renal function in the operated kidney as the contralateral kidney often compensates for lost function post-operatively. Sophisticated mathematical formulas to estimate resected and ischaemic volume (RAIV) [5], computed tomography (CT) volumetric analysis [3] and tumour contact surface area [6] have also been enlisted in an attempt to circumvent this limitation, but unfortunately require labour-intensive renal volume measurement and advanced imaging technology. Where MAG3 renal scan available, it enables the assessment of split renal function at baseline and post-operatively, allowing reliable evaluation of the functional outcomes of NSS [7]. Table 1 provides a summary of some of the published methods for assessing functional outcomes after NSS.

A recent study confirmed the utility of trifecta and MIC for assessment of functional outcomes after NSS [7]. Achievement of each of this composite outcomes correlated with better functional outcomes post-operatively assess by MAG3 renal scan validating their utility as surrogates for functional renal preservation post-partial nephrectomy.

In the era of minimally invasive surgeries, there has been a gradual transition towards adopting a robotic approach in kidney surgery. A recent meta-analysis by Zhang et al. [11] reported similar peri-operative outcomes in robot-assisted partial nephrectomy (RAPN) as compared to laparoscopic partial nephrectomy (LPN), with significantly shorter WIT in the robotic approach. Composite outcomes can prove to be useful tools in comparing outcomes between different surgical approaches (Table 2). The favourable results of RAPN reported by Zhang et al were replicated and surpassed LPN in a recent published study [20], where RAPN achieved a trifecta rate in 27.1% more cases than in LPN.

With increased comfort in performing RAPN, the number of NSS is on the rise. As such, standardisation of reporting of results and more reliable tools for measurement of outcomes are essential in establishing robust data to serve as a benchmark for gauging surgical quality and assess for attainability of 'nephron-sparing' in NSS.

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Fergany et al. [8]	117 PN	Cr	Increased dialysis-free period with NSS
Lucas et al. [9]	27 RAPN, 15 LPN, 54 OPN	WIT, eGFR (MDRD) & Cr	WIT longer in RAPN vs. OPN but similar post-op renal function. eGFR lower in post-op LPN vs. OPN but similar in long term
Froghi et al. [10]	92 RAPN, 140 LPN	WIT	Decrease in WIT with RAPN but similar functional outcomes
Zhang et al. [11]	425 RAPN, 341 LPN	WIT	Similar outcomes peri-operatively but shorter WIT for RAPN approach
Park et al. [4]	98 OPN	WIT, Cr	No significant difference baseline eGFR and Cr at pre-op, discharge and 6-month.
			Baseline function more accurate in predicting poor renal functional outcomes
Yossepowitch et al. [12]	662 NSS with cold ischaemia time	eGFR (MDRD)	Early changes in GFR after NSS significantly influenced by duration of cold renal ischaemia but does not appear to influence long-term renal functional outcomes
Springer et al. [13]	190 LESS-PN	eGFR (MDRD), CKD staging	Cr increased significantly post-op immediately and at 6/12. Significant increase in percentage of patients with CKD III-IV. WIT <20 min in 45/120 robot-assisted LESS-PN with no decreased renal function.
Lau et al. [14]	1492 RN vs 1189 NSS	Cr, Proteinuria, CKD staging	RN proves to have worse renal functional outcomes
Leslie et al. [6]	200 PN	CSA of tumour	CSA is an independent predictor of peri-operative complications and renal functional outcomes
Porpiglia et al. [15]	18 LPN with WIT >30 mins	WIT, AAP/GGT/ lysozyme proteinuria	Worse renal outcomes if WIT between 32-42 mins as confirmed on MAG3 scan
Simmons et al. [16]	138 OPN + LPN	CT, eGFR (MDRD)	96% correlation between predicted and observed change in eGFR - pre-op GFR and PFVP are primary determinants of long-term functional outcomes
Shin TY et al. [5]	217 RAPN	RAIV vs. Cr & eGFR (MDRD)	Superior correlation with absolute and % percentage change in eGFR compared to Cr and MDRD formula

Zargar et al. [17]	1185 RPN, 646 LPN	WIT, MAG3, CKD staging	Median WIT significantly longer in LPN vs. RPN (26 min vs. 18 min) . No significant difference between RPN & LPN in GFR preservation or proportion of patients with CKD upstaging
Mir et al. [3]	92 NSS	eGFR, CT	WIT did not correlate with %GFR preserved but lower R.E.N.A.L. scores & use of hypothermia& volume of preserved parenchyma are predictive factors of %GFR preserved
NSS: Nephron-Sparing Surgery; RN: Radical Nephrectomy; OPN: Open Partial Nephrectomy; RAPN: Robot-Assisted Partial Nephrectomy; LPN: Laparoscopic Partial Nephrectomy; LESS-PN: Laparoendoscopic Single-Site Partial Nephrectomy; WIT: Warm Ischaemia Time; Egfr: Estimated Glomerular Filtration Rate; MDRD: Modification Of Diet In Renal Disease; CSA: Contact Surface Area; CT: Computed Tomography; RAIV: Resected And Ischaemic Volume; CKD: Chronic Kidney Disease; MAG3: Mercaptoacetyltriglycine; AAP: Aminopeptidase A Protein; GGT: Gamma-Glutamyl Transpeptidase			

Table 1: Renal function measurements and outcomes in partial nephrectomy series.

	Surgical Technique	Study Type	Definition	Trifecta Rate %	Tumour size
Zargar et al. [17]	646 LPN vs. 1185 RAPN	Comparative case series	Trifecta WIT ≤ 25 min, NSM, no major complications	70% RAPN, 33% LPN	T1a, T1b
Komninos et al. [18]	89 RAPN vs. 78 R-LESS PN	Comparative case series	Trifecta WIT <20 mins, NSM, no surgical complications	42.7% in multiport RAPN, 25.6% R-LESS PN	T1a
Minervini et al. [19]	301 OPN vs. 149 LPN	Matched comparative case series	Trifecta NSM, WIT <25 min, no complications	78.6% OPN, 74.3% LPN	T1a
Khalifeh et al. [20]	261 RAPN vs. 231 LPN	Case comparative series	Trifecta WIT <25 min, NSM, peri-operative complication	58.7% RAPN vs. 31.6% LPN	T1a
Hung et al. [2]	RAPN / LPN	Case series	Trifecta NSM, renal function loss <10%, no urological complications	45-68%	Mostly T1a
Buffi et al. [21]	RAPN	Case series	MIC NSM, WIT<20 mins, no major complications	75.80%	T1a/T1b
Porpiglia et al. [22]	LPN	Case series	MIC NSM, WIT <20 mins, no major complications	63.10%	Mostly T1a
PN: partial nephrectomy; OPN: open partial nephrectomy; RAPN: robot-assisted partial nephrectomy; LPN: laparoscopic partial nephrectomy; NSM: negative surgical margins; WIT: warm ischaemia time; MIC: margin, ischaemia, complications.					

Table 2: Composite outcomes in partial nephrectomy series: an overview.

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