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UPPER TRACT SURGERY
MINI-REVIEW

Robot-assisted partial nephrectomy: How to minimise renal ischaemia

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KEYWORDS

Partial nephrectomy;
Ischaemia;
Renal cell carcinoma;
Renal function;
Renorrhaphy

ABBREVIATIONS

AKI, acute kidney injury;
AO, artery only;
CKD, chronic kidney disease;
NSS, nephron-sparing surgery

Abstract Renal ischaemia research has shown an increase in renal damage proportional to ischaemic time. Therefore, we assessed the importance of renal ischaemic times for warm and cold ischaemia approaches, and explored the different surgical techniques that can help to minimise renal ischaemia in robot-assisted partial nephrectomy (RAPN). Minimising renal ischaemia during nephron-sparing surgery (NSS) is a key factor in preserving postoperative renal function. Current data support a safe warm ischaemia time (WIT) of ≤25 min and cold ischaemic time of ≤35 min, resulting in no significant deterioration in renal function. In general, patients undergoing NSS have increased comorbidities, including chronic kidney disease, and in these patients it is difficult to predict their postoperative renal function recovery. With RAPN, efforts should be made to keep the WIT to < 25 min, as minimising the ischaemic time is vital for preservation of overall renal function and remains a modifiable risk factor. Parenchymal or segmental artery clamping, early unclamping or off-clamp techniques can be adopted when ischaemic times are likely to be > 25 min, but may not lead to superior functional outcome. Careful preoperative planning, tumour factors, and meticulous surgical technique are critical for optimum patient outcome.

Introduction

The 'gold standard' for treatment of T1a renal lesions is partial nephrectomy (PN) where technically feasible [1]. With advances in techniques, larger lesions including T1b renal masses are also being treated with PN. Minimally invasive techniques including laparoscopic PN (LPN) and robotic-assisted laparoscopic PN (RAPN)

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have become established procedures for PN over the traditional open PN (OPN). Cancer control, whilst preserving renal function, is the basis of successful surgery, with a complex interaction between three elements: preoperative parenchymal quality, postoperative parenchymal quantity preserved, and the recovery of the preserved nephrons to the ischaemic insult [2].

The technical difficulty of LPN and morbidity associated with OPN has led to a rapid rise in the utilisation of RAPN due to several advantages. Zhang et al. [3] in a recent meta-analysis showed that although parameters such as operative time, estimated blood loss, and hospital stay were similar for LPN and RAPN, the later had significantly shorter ischaemic times. Along with the known advantages of RAPN such as a three-dimensional view, reduction in tremor, and precise fine EndoWrist movements using the robotic platform, the key advantage with performing RAPN is the shorter learning curve to achieve ischaemic times of <20 min [4].

Pathophysiology of renal-reperfusion injury

Renal-reperfusion injury is caused by a sudden temporary impairment of blood flow to the kidney. This leads to an inflammatory response and oxidative stress to the kidney from the reduction in oxygen to the tissues, which ultimately leads to an alteration in organ function. The complete pathophysiology of renal-reperfusion injury is not fully understood, with several important mechanisms thought to be involved that can result in subsequent renal failure.

Activation of an inflammatory cascade leading to chemokine release, including pro-inflammatory cytokines such as interleukin 6 and TNFα, play a major role in renal dysfunction that causes renal damage [5].

During renal-reperfusion injury, the damaged tissue produces excessive amount of reactive oxygen species causing oxidative stress, which changes mitochondrial oxidative phosphorylation, ATP depletion, increases intracellular calcium and active membrane proteases, causing cell injury [6].

Types of ischaemia

Animal studies on dogs that were conducted to test the safe limit of renal ischaemia concluded that 30 min is a safe limit, as it allowed full recovery of renal function [7]. Laven et al. [8] demonstrated in a porcine model with a solitary kidney that this warm ischaemia time (WIT) can be extended with full recovery of renal function up to 90 min, although it was noted that decreased renal function occurred in the initial 72 h.

Studies have shown that cold ischaemia can provide superior postoperative renal function recovery when used concordantly with warm ischaemia [9]. When performing OPN the most common method of achieving cold ischaemia is by making an ice slush to go around the kidney. Using this method of initial cooling for 10 min, cold ischaemic times of up to 35 min have been shown to be safe for renal preservation [10].

A study of 660 patients who underwent OPN with half having warm ischaemia and the other half having cold ischaemia, showed that the group with cold ischaemia, despite longer ischaemic times, had no significant difference in postoperative renal function. The authors concluded from their study that although postoperative renal function is primarily achieved by the quality and quantity of parenchymal preservation, the type and duration of ischaemia were the most important modifiable factors [11].

Postoperative renal function in the presence of a normal contralateral kidney can sometimes be masked based on measurement of postoperative serum creatinine or estimated GFR (eGFR) values. One study incorporated technetium 99 m mercaptoacetyltriglycine (^{99m}Tc-MAG3) renal scintigraphy to assess renal function in patients undergoing LPN in the presence of a normal contralateral kidney. The findings showed that split renal function can be altered significantly from 48% down to 36.9% at 5 days and only recover to 42.8% after 1 year. The study concluded that parenchymal preservation and having a WIT of >32 min were most significant for predicting renal outcome [12].

Patient and tumour factors

Preoperative optimisation

Optimising patients' preoperatively is important for maximising renal function after PN. Minimising renal ischaemia is important, as up to 24% of patients with T1 tumours have a GFR <60 mL/min/1.73 m^2 (Stage 2 chronic kidney disease [CKD]). Those patients with a GFR <45 mL/min/1.73 m^2 (Stage 3 CKD) undergoing PN were associated with a higher risk of a 50% reduction in GFR. Another interesting finding is that patients with a normal GFR (Stage 1 CKD) or moderately reduced (Stage 3 CKD) did not get any benefit in renal function despite undergoing nephron-sparing surgery (NSS) compared to the patients with Stage 2 CKD [13].

Furthermore, there is a high incidence of comorbid disease in patients with RCC including diabetes mellitus (9–30%), hypertension (40–69%), smoking history (40–70%), obesity (40%), as well as advanced age [14].

Malcolm et al. [15] compared groups with diabetes, hypertension, high body mass index (BMI) >30 kg/m^2, age >60 years, and smoking, as risk factors in patients undergoing radical nephrectomy (RN) or PN against patients with none of these comorbidities and found that all these factors were associated with an increase in postoperative creatinine, decrease in eGFR, and metabolic acidosis.