International Journal of Surgery 36 (2016) 560–567

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

The future of partial nephrectomy

Theo Malthouse [a, *], Veeru Kasivisvanathan [b], Nicholas Raison [c], Wayne Lam [a], Ben Challacombe [a]

[a] Guy's and St Thomas' NHS Foundation Trust, Great Maze Pond, London SE1 9RT, United Kingdom
[b] University College London Hospital, 235 Euston Rd, Fitzrovia, London NW1 2BU, United Kingdom
[c] King's College Hospital NHS Foundation Trust, Denmark Hill, London SE5 9RS, United Kingdom

HIGHLIGHTS

- Innovation in the last century has been rapid, with no predictions of current technologies proving correct.
- New robots, and new adjuncts to the robots will become more accessible, and more widespread.
- Once WIT, parenchymal loss & pre-op renal function are optimized, new targets of preventative measures may become priority.

ARTICLE INFO

Article history:
Received 8 March 2016
Accepted 10 March 2016
Available online 11 March 2016

Keywords:
Partial nephrectomy
Robotic partial nephrectomy
Future

ABSTRACT

Innovation in recent times has accelerated due to factors such as the globalization of communication; but there are also more barriers/safeguards in place than ever before as we strive to streamline this process.

From the first planned partial nephrectomy completed in 1887, it took over a century to become recommended practice for small renal tumours. At present, identified areas for improvement/innovation are 1) to preserve renal parenchyma, 2) to optimise pre-operative eGFR and 3) to reduce global warm ischaemia time. All 3 of these, are statistically significant predictors of post-operative renal function.

Urologists, have a proud history of embracing innovation & have experimented with different clamping techniques of the renal vasculature, image guidance in robotics, renal hypothermia, lasers and new robots under development. The DaVinci model may soon no longer have a monopoly on this market, as it loses its stranglehold with novel technology emerging including added features, such as haptic feedback with reduced costs.

As ever, our predictions of the future may well fall wide of the mark, but in order to progress, one must open the mind to the possibilities that already exist, as evolution of existing technology often appears to be a revolution in hindsight.

1. Introduction

The central objectives of future study and development are to 1) preserve renal parenchyma, 2) optimise pre-operative eGFR and 3) to reduce global warm ischaemia time (WIT). All 3 have shown to be important predictors of post-operative renal function.

1.1. Clamping: variations of a theme

Although clamping controls operative blood loss, facilitates tumour excision and renal reconstruction, it does cause temporary renal ischaemia and the potential for renal injury [1]. Therefore various techniques have been proposed to reduce WIT and improve renal outcomes.

1.1.1. Off-clamp partial nephrectomy

PN without clamping the renal pedicle has been performed. Renal ischaemia is abolished at the expense of increased blood loss and more difficult renorrhaphy. Techniques for controlling bleeding during 'off-clamp' PN have been explored, for example manual compression of the peri-tumoural parenchyma, or using Kauffman clamps but with mixed success [2].

A recent meta-analysis [3] compared the results of 'off' and 'on' clamp techniques. No significant differences were found in

* Corresponding author. Permanent Address: 29 Audley Park Road, Bath, BA1 2XJ, United Kingdom.
E-mail address: theo.malthouse@doctors.org.uk (T. Malthouse).

http://dx.doi.org/10.1016/j.ijsu.2016.03.024
1743-9191/

operative times, complications rates or length of stay. A trend was seen towards increased positive margins, blood loss and transfusion rates (Fig. 1) in the off-clamp group, which could be explained by impaired visualization, though this difference did not reach statistical significance.

There was a significantly lower reduction in eGFR at mean 8.36 months associated with off-clamp than on-clamp PN (Standard weighted mean difference 0.27, 95% CI 0.14, 0.40, p < 0.0001) (Fig. 2) [3]. It is not clear whether this corresponds to a reduced risk of CKD; some studies show a disappearance of this advantage at 3 months (as long as the WIT is kept to below 30 min) [3], whereas others show a reduced risk of new onset CKD when followed up [1,4] (Fig. 3).

To conclude, it seems that the bulk of the evidence suggests that the off-clamp technique for PN when compared to on-clamp PN, leads to a reduced risk of acute kidney injury after surgery, but it is unclear whether it protects from long-term renal impairment. The off-clamp cohort may have a trend towards slightly higher estimated blood loss and transfusion rates (although no statistically significant difference), but with similar numbers of positive margins and complication rates [5] highlighting potential for this technique.

1.1.2. Early unclamping

Early unclamping has been used successfully to reduce the WIT. Clamps are released immediately after placement of the initial central running suture and prior to the placement of subsequent mattress or bolster sutures. When used in LPN, the technique reduces WIT by >50% with improved post-operative renal function up to 90 days post-operatively ($p < 0.001$) [6]. However, RPN is normally associated with shorter WIT, and therefore the physiological significance of shortening the WIT further is difficult to establish. Although the method comes at a risk of higher blood loss, it has been demonstrated to have no effect on transfusion rates or haemorrhagic complications even for complex renal tumours, or for tumours being operated on by less experienced surgeons [7]. It has also been hypothesised that early unclamping may lead to reduced rates of post-operative haemorrhage, as arterial bleeds will be easier to identify in perfused kidney [6].

1.2. Fluorescence image-guided robotic surgery

Fluorescence image-guidance in robotic surgery can potentially improve outcomes for partial nephrectomy in two ways. More accurate dissection of the renal tumour will allow greater preservation of renal parenchyma and more selective arterial clamping will reduce unnecessary ischaemia within healthy renal parenchyma.

The technology uses near-infrared fluorescence (NIRF). A fluorescent contrast agent is administered intravenously, which emits light in the near-infrared wavelength (700–850 nm) after activation by a light emitting diode [8]. The light, not visible to the human eye, is recorded using a charge-coupled device camera. The Da Vinci Si Surgical System has integrated this into its robotic systems, where the surgeon can then switch between standard (white) light and fluorescence-enhanced views in real-time [9]. This is named the Firefly© imaging system.

1.2.1. Preventing ischaemia by selective arterial clamping by NIRF, & the Firefly© imaging system

The action of selective arterial clamping to minimise unnecessary ischaemia and reperfusion injury has been shown to help aid the preservation of renal function [10]. The selection process is aided by NIRF, to identify renal vasculature, assess renal perfusion and dictate the arteries that are to be clamped. The technique allows the surgeon to only clamp off arteries supplying areas of the renal parenchyma that supply the tumour and its immediate margin, while maintaining perfusion of unclamped segments [8].

A dye, commonly indocyanine green (ICG), is injected intravenously and can be identified throughout the vascular system in less than 1 min [11]. It has 4 properties that make it ideal for this purpose; it stays within the vascular compartment after administration, a plasma half-life of 3–5 min, is cleared by hepatic metabolism (and therefore not nephrotoxic), and can be detected by the NIRF camera [12]. This dye is also used for the identification of tumour margins since the fluorescence varies between normal tissue, tumour as well as cysts and necrotic fat. Before administering the dye, the major arterial branches should be clamped with micro bulldog clips. Once the dye has been given, each clamp is released individually to identify the areas of perfusion.

This technique shows great promise. Compared to standard arterial clamping, early results showing significantly superior post-operative kidney function at discharge, and a trend towards significance at 3 months [8].

Other methods of selective arterial clamping have been trialed, for example Colour Doppler ultrasonography. However, due to a complex learning curve and the technology being very operator dependent, uptake has been very limited.

The main limitations to NIRF are the high costs of the Firefly system together with limited evidence of longer-term benefit. Given the good long term renal function and very low dialysis rates already achieved following RAPN, Firefly will need to demonstrate a significant clinical benefit to justify the additional cost.

In conclusion, available evidence suggests that RPN with NIRF provides an improvement of the preservation of renal function at discharge, however this effect may diminish with time.

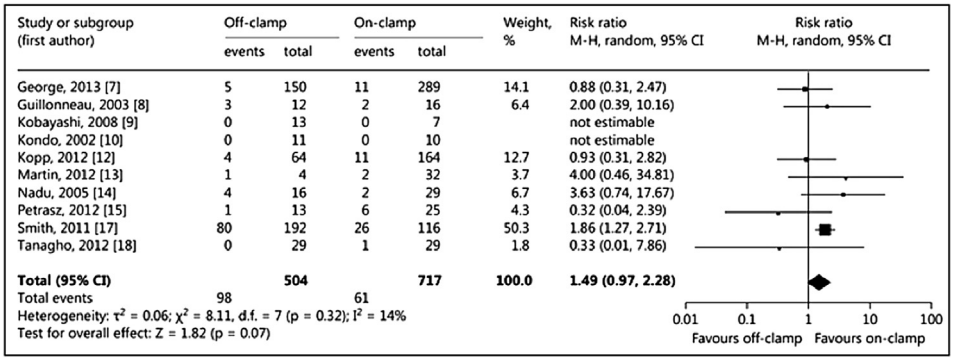

Fig. 1. Meta-analysis of blood transfusion rates [3].