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CORRESPONDENCE

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Do hilar clamping and renorrhaphy influence postoperative renal function after partial nephrectomy?

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Abstract: Preservation of renal function is an important goal of partial nephrectomy (PN) for renal tumors. Several attempts to preserve postoperative renal function, including hilar control surgery and omission of renal cortical renorrhaphy, have been reported, but the influence of each procedure remains controversial. We conducted a literature review based on PubMed to summarize the current situation and clarify the influence of each procedure on postoperative renal function. Effects of hilar control, omitting renorrhaphy, and a combination of both on post-PN renal function were reviewed. While hilar clamping does not influence postoperative renal function, cortical renorrhaphy tends to deteriorate. Parenchymal ischemia/reperfusion by hilar clamping leads to acute kidney injury through production of radical oxygen species. Recent randomized controlled studies, however, showed no differences in the postoperative renal function between on- and off-clamp laparoscopic PN. Finally, the effects of soft coagulation on renal parenchymal denaturation and postoperative renal function were reviewed. Although soft coagulation can lead to denaturation and necrosis of the renal parenchyma, the shortened warm ischemic time might positively affect postoperative renal function. In conclusion, off-clamp, non-renorrhaphy PN is feasible and safe for small renal tumors. Renorrhaphy, but not hilar clamping, tends to worsen postoperative renal function.

***Keywords*:** estimated glomerular filtration rate, kidney failure, nephrectomy, organ preservation

Introduction

Radical nephrectomy was the standard treatment for renal tumors until Novick *et al*. pioneered partial nephrectomy (PN) in the early 1980s (*1-3*). In the beginning, PN was applied under absolute indication for tumors in solitary kidneys, bilateral renal tumors, and patients with impaired renal function. Subsequently, the surgical technique was refined, and the surgical indication continued to expand gradually to selective patients.

The preservation of renal function is an important goal in the treatment of renal tumors and PN. A negative surgical margin, warm ischemia time less than 25 min, and no urological complications are the trifecta of PN (*4*). Furthermore, pentafecta is defined as the achievement of a trifecta with the addition of preserving over 90% estimated glomerular filtration rate (eGFR) and no chronic kidney disease stage upgrading after 1 year (*5,6*). Several methods have been introduced to preserve renal function, including omitting renal hilum clamping, renal cortical renorrhaphy, or a combination of both. The influence of each technique on postoperative renal function remains unclear. Herein, we review the current evidence regarding the influence of renal pedicle clamping and renorrhaphy on postoperative renal function. PubMed was searched to identify relevant articles published up to January 15, 2023. Detailed information is provided in Table 1.

Renal hilum clamping

Hilar control techniques, including off-clamp, selective/super-selective clamp, or early unclamp surgeries, may contribute to reduced renal parenchymal ischemia and better preservation of postoperative renal function. There are multiple reports on the pros and cons of the effect of hilar control on postoperative renal function (*7-18*). Regarding surgical complications, one multicenter propensity score-matched case-control study concluded that off-clamp robot-assisted PN (RAPN) is feasible for a small subgroup of renal tumors without postoperative complications, although off-clamp surgeries are at an increased cost of higher estimated blood loss and conversion to radical nephrectomy (*18*).

As for postoperative renal function, parenchymal ischemia/reperfusion by hilar clamping lead to acute kidney injury through production of radical oxygen species (*19*). A meta-analysis reported that short- and long-term renal function are superior in the hilar

Table 1. Search strategy summary

Items	Specification
Date of search	January 10, 2023
Databases and other sources searched	PubMed
Search terms used	Hilar clamping, kidney function, off-clamp, partial nephrectomy, and renorrhaphy
Timeframe	Not applicable
Inclusion and exclusion criteria	Inclusion criteria: *i*) The type of literature should be either a prospective study, a retrospective study, or a meta-analysis; *ii*) The literature focus on the maintenance of perioperative renal function; *iii*) The research subjects must meet the criteria for undergoing partial nephrectomy as outlined in the guidelines; *iv*) Only documents published in English were considered. Any studies that do not meet one or more of these inclusion criteria were excluded.
Selection process	A systematic search was conducted on 10/1/2023 using PubMed with the keywords listed above. The relevant search results were selected for this narrative review.
Any additional consideration	Not applicable

control surgery groups to hilar clamping surgery groups (*20*). After that report, however, results of two prospective randomized control trials, the EMERALD (NCT03679572), and the CLOCK (NCT022/7987) have been published with contrary results (*21,22*). First, the EMERALD study compared the six postoperative month eGFR changes in the operated kidney after RAPN with super-selective clamping and early artery unclamping. The relative eGFR reduction in the operated kidney were not significantly different (-21.4% *vs.* -23.4%, $p = 0.7$) (*21*). Considering the absence of trend in favor of super-selective surgery, the study was interrupted before the entry reached the originally designed number. The CLOCK II prospective randomized study compared effects of on-clamp and off-clamp surgery on postoperative renal function. In this study, 69 of 164 patients (42%) assigned in off-clamp group underwent on-clamp surgery, while 23 of 160 patients (14%) in on-clamp group underwent off-clamp surgery due to tumor complexity and surgeons' preference. They showed no differences in the eGFR between on- and off-clamp laparoscopic PN within 24 months of operation both in intention-to-treat analysis and per-protocol analysis (*22*). Absolute variation in eGFR at 6 months was -6.8 mL/min and -4.2 mL/min for on- and off-clamp RAPN, respectively (*22*). Complication rates were similar between groups (*23*). Taken together, hilar control surgery is feasible and safe for small renal tumors, while its contribution to postoperative renal function is practically small.

Renorrhaphy

Renorrhaphy was first introduced in partial nephrectomy to minimize postoperative complications by hemostasis and closure of the collecting system. In association with preserving parenchyma, necessity of renorrhaphy has been an issue to be discussed. Considering the risk of damaging renal vessels and increasing warm ischemic time that result in reducing renal parenchyma, growing application of non-renorrhaphy technique have been observed (*24-29*).

A meta-analysis registered in the PROSPERO study (CRD42022293977) analyzed 634 patients from 5 retrospective studies. The results showed a significant benefit of the non-renorrhaphy technique in terms of operating and warm ischemic time and, thus, preservation of renal function, compared with that by the renorrhaphy technique. The weighted mean difference for eGFR decline was -4.19 mL/min with a 95% confidence interval of -7.64 to -0.73 ($p < 0.001$). However, they found no difference in postoperative complications between the groups (*30*).

Renorrhaphy is divided into two parts: medullary and cortical layers, also known as inner and outer layers, respectively. Hence, some comparative studies compare single- and double-layer renorrhaphy (both medullary and cortical layer renorrhaphy) (*29,31,32*). Another meta-analysis analyzing single- versus double-layer renorrhaphy showed a benefit of the single-layer technique in the preservation of postoperative renal function (-3.19 mL/min *vs.* -6.07 mL/min, $p = 0.01$) (*33*). The difference could partly be explained by damage to parenchymal vessels, shortening of the warm ischemic time, and reduction in renal parenchyma. In this regard, the results of an ongoing randomized prospective study (NCT02131376) whose endpoint includes the impact of cortical renorrhaphy on renal volume loss and postoperative renal function are awaited.

Therefore, non-renorrhaphy surgery might contribute to the preservation of postoperative renal function by avoiding damage to renal vessels, shortening the warm ischemic time, and preserving renal parenchymal volume.

Off-clamp, non-renorrhaphy PN with a new hemostasis technology

Considering the effects of hilar clamping and renorrhaphy described above, the omission of both is an inevitable attempt. However, owing to the difficulty in controlling bleeding during tumor resection, the surgical indication should be strictly limited. For instance, predominantly exophytic tumors less than 4 cm in diameter are good candidates for off-clamp, non-renorrhaphy surgery. Although the safety and feasibility of this technique have been reported, comparative studies on off-clamp, non-renorrhaphy PN in laparoscopic settings are lacking *(34-36*).

We recently reported the surgical results of off-clamp, non-renorrhaphy open PN performed in a single institution (*37,38*). In our study, hemostasis was performed using a monopolar SOFT COAG system (VIO300D, ERBE, Germany). Medullary renorrhaphies were performed using 4-0 VICRYL® only when the collecting system was opened. The mean eGFR preservation at 5 days, 1 month, and 3 months after surgery was 95.3%, 91.0%, and 90.7%, respectively, and age was a predictor of eGFR decline at 3 months after surgery. Our results suggest that off-clamp non-renorrhaphy open PN can be safely adopted in patients with impaired renal function. We have also performed off-clamp, non-renorrhaphy open PN for cT1b tumor (*37*). Appropriate hemostasis during and after tumor resection using SOFT COAG and hemostatic agents is mandatory to perform the surgery safely.

Soft coagulation for hemostasis

Soft coagulation or hemostatic agents are used for hemostasis after PN when cortical renorrhaphy is omitted. Although soft coagulation can lead to denaturation and necrosis of the renal parenchyma, shrinkage of the kidney volume after PN using soft coagulation is not well known. In the on-clamp setting, a favorable result in 1 postoperative month renal function is reported for the soft coagulation group compared with that in the double-layer renorrhaphy group (-3.5 mL/min *vs.* -13 mL/min, $p = 0.009$) (*39*). In this study, the shortened warm ischemic time (11.4 min *vs.* 20.3 min) might have also positively affected postoperative renal function. Intriguingly, an *in vivo* study in pigs revealed that renal parenchymal denaturation after soft coagulation reached a depth of 4 mm, and the temperature increased by 15.6 °C at a depth of 5 mm and 8.8 °C at 10 mm (*40*). Presumably, the effect of soft coagulation on ipsilateral renal function is not negligible. Further studies are necessary to clarify the effect of soft coagulation on renal volume.

In conclusion, off-clamp, non-renorrhaphy PN is safe for small renal tumors. Hilar control PN is reported to be feasible without an increased risk of severe complications; however, whether it deteriorates postoperative renal function remains controversial. Conversely, cortical renorrhaphy negatively affects renal function by damaging renal vessels and increasing the warm ischemic time. A prospective comparative study is required to verify these findings. Nevertheless, with the accumulation of clinical experience with off-clamp, non-renorrhaphy PN with a new hemostasis technology in robot-assisted settings, we may be one step closer to realizing the ideal PN.

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References

1. Novick AC, Stewart BH, Straffon RA, Banowsky LH. Partial nephrectomy in the treatment of renal adenocarcinoma. J Urol. 1977; 118:932-936.
2. Topley M, Novick AC, Montie JE. Long-term results following partial nephrectomy for localized renal adenocarcinoma. J Urol. 1984; 131:1050-1052.
3. Novick AC. Partial nephrectomy for renal cell carcinoma. Urol Clin North Am. 1987; 14:419-433.
4. Buffi N, Lista G, Larcher A, Lughezzani G, Ficarra V, Cestari A, Lazzeri M, Guazzoni G. Margin, ischemia, and complications (MIC) score in partial nephrectomy: A new system for evaluating achievement of optimal outcomes in nephron-sparing surgery. Eur Urol. 2012; 62:617-618.
5. Gu L, Liu K, Du S, *et al.* Prediction of pentafecta achievement following laparoscopic partial nephrectomy: Implications for robot-assisted surgery candidates. Surg Oncol. 2020; 33:32-37.
6. Kobayashi S, Cho B, Mutaguchi J, Inokuchi J, Tatsugami K, Hashizume M, Eto M. Surgical navigation improves renal parenchyma volume preservation in robot-assisted partial nephrectomy: A propensityscore matched comparative analysis. J Urol. 2020; 204:149-156.
7. White WM, Goel RK, Haber GP, Kaouk JH. Robotic partial nephrectomy without renal hilar occlusion. BJU Int. 2010; 105:1580-1584.
8. Tanagho YS, Bhayani SB, Sandhu GS, Vaughn NP, Nepple KG, Figenshau RS. Renal functional and perioperative outcomes of off-clamp versus clamped robot-assisted partial nephrectomy: Matched cohort study. Urology. 2012; 80:838-843.
9. Novak R, Mulligan D, Abaza R. Robotic partial nephrectomy without renal ischemia. Urology. 2012; 79:1296-1301.
10. Krane LS, Mufarrij PW, Manny TB, Hemal AK. Comparison of clamping technique in robotic partial nephrectomy: Does unclamped partial nephrectomy improve perioperative outcomes and renal function? Can J Urol. 2013; 20:6662-6667.
11. Borofsky MS, Gill IS, Hemal AK, Marien TP, Jayaratna I, Krane LS, Stifelman MD. Near-infrared fluorescence imaging to facilitate super-selective arterial clamping during zero-ischaemia robotic partial nephrectomy. BJU Int. 2013; 111:604-610.
12. Kaczmarek BF, Tanagho YS, Hillyer SP, Mullins JK,

Diaz M, Trinh QD, Bhayani SB, Allaf ME, Stifelman MD, Kaouk JH, Rogers CG. Off-clamp robot-assisted partial nephrectomy preserves renal function: A multi-institutional propensity score analysis. Eur Urol. 2013; 64:988-993.
13. Desai MM, de Castro Abreu AL, Leslie S, Cai J, Huang EY, Lewandowski PM, Lee D, Dharmaraja A, Berger AK, Goh A, Ukimura O, Aron M, Gill IS. Robotic partial nephrectomy with superselective versus main artery clamping: A retrospective comparison. Eur Urol. 2014; 66:713-719.
14. Peyronnet B, Baumert H, Mathieu R, *et al*. Early unclamping technique during robot-assisted laparoscopic partial nephrectomy can minimise warm ischaemia without increasing morbidity. BJU Int. 2014; 114:741-747.
15. Komninos C, Shin TY, Tuliao P, Han WK, Chung BH, Choi YD, Rha KH. Renal function is the same 6 months after robot-assisted partial nephrectomy regardless of clamp technique: analysis of outcomes for off-clamp, selective arterial clamp and main artery clamp techniques, with a minimum follow-up of 1 year. BJU Int. 2015; 115:921-928.
16. Satkunasivam R, Tsai S, Syan S, Bernhard JC, de Castro Abreu AL, Chopra S, Berger AK, Lee D, Hung AJ, Cai J, Desai MM, Gill IS. Robotic unclamped "minimal-margin" partial nephrectomy: Ongoing refinement of the anatomic zero-ischemia concept. Eur Urol. 2015; 68:705-712.
17. Furukawa J, Miyake H, Hinata N, Muramaki M, Tanaka K, Fujisawa M. Renal functional and perioperative outcomes of selective versus complete renal arterial clamping during robot-assisted partial nephrectomy: Early single-center experience with 39 cases. Surg Innov. 2016; 23:242-248.
18. Peyronnet B, Khene ZE, Pradère B, *et al*. Off-clamp versus on-clamp robotic partial nephrectomy: A multicenter match-paired case-control study. Urol Int. 2017; 99:272-276.
19. Johnson KJ, Weinberg JM. Postischemic renal injury due to oxygen radicals. Curr Opin Nephrol Hypertens. 1993; 2:625-635.
20. Cacciamani GE, Medina LG, Gill TS, Mendelsohn A, Husain F, Bhardwaj L, Artibani W, Sotelo R, Gill IS. Impact of renal hilar control onoutcomes of robotic partial nephrectomy: Systematic review and cumulative meta-analysis. Eur Urol Focus. 2019; 5:619-635.
21. Long JA, Fiard G, Giai J, Teyssier Y, Fontanell A, Overs C, Poncet D, Descotes JL, Rambeaud JJ, Moreau-Gaudry A, Ittobane T, Bouzit A, Bosson JL, Lanchon C. Superselective ischemia in robotic partial nephrectomy does not provide better long-term renal function than renal artery clamping in a randomized controlled trial (EMERALD): should we take the risk? Eur Urol Focus. 2022; 8:769-776.
22. Antonelli A, Cindolo L, Sandri M, *et al*. Is off-clamp robot-assisted partial nephrectomy beneficial for renal function? Data from the CLOCK trial. BJU Int. 2022; 129:217-224.
23. Antonelli A, Cindolo L, Sandri M, *et al*. Safety of on- vs off-clamp robotic partial nephrectomy: Per-protocol analysis from the data of the CLOCK randomized trial. World J Urol. 2020; 38:1101-1108.
24. Farinha R, Rosiello G, Paludo AO, Mazzone E, Puliatti S, Amato M, De Groote R, Piazza P, Berquin C, Montorsi F, Schatteman P, De Naeyer G, D'Hondt F, Mottrie A. Selective suturing or sutureless technique in robot-assisted partial nephrectomy: Results from a propensity-score matched analysis. Eur Urol Focus. 2022; 8:506-513.
25. Ye J, Zhang S, Tian X, Wang G, Zhao L, Ma L. Knotless retroperitoneoscopic nephron-sparing surgery for small renal masses: comparison of bipolar sutureless technique and barbed suture technique. J Int Med Res. 2018; 46:1649-1656.
26. Jin D, Ren D, Zhang J, Xu G, Ge C, Jiang Q, Wang D, Zhang W, Zhang Y. A propensity score-matched comparison between sutureless and suture techniques in laparoscopic nephron-sparing surgery: A retrospective non-randomized observational study. J Laparoendosc Adv Surg Tech A. 2020; 30:1314-1319.
27. Takagi T, Kondo T, Omae K, Iizuka J, Kobayashi H, Yoshida K, Hashimoto Y, Tanabe K. Assessment of surgical outcomes of the non-renorrhaphy technique in open partial nephrectomy for ≥ T1b renal tumors. Urology. 2015; 86:529-533.
28. Tohi Y, Murata S, Makita N, Suzuki I, Kubota M, Sugino Y, Inoue K, Kawakita M. Comparison of perioperative outcomes of robot-assisted partial nephrectomy without renorrhaphy: Comparative outcomes of cT1a versus cT1b renal tumors. Int J Urol. 2019; 26:885-889.
29. Bahler CD, Cary KC, Garg S, DeRoo EM, Tabib CH, Kansal JK, Monn MF, Flack CK, Masterson TA, Sandrasegaran MK, Foster RS, Sundaram CP. Differentiating reconstructive techniques in partial nephrectomy: A propensity score analysis. Can J Urol. 2015; 22:7788-7796.
30. Liu P, Li Y, Shi B, Zhang Q, Guo H. The outcome of sutureless in partial nephrectomy: A systematic review and meta-analysis. Biomed Res Int. 2022; 2022:5260131.
31. Lu SY, Chung HJ, Huang EY, Lin TP, Lin ATL. The perioperative outcomes between renal hilar and non-hilar tumors following robotic-assisted partial nephrectomy (RAPN). J Chin Med Assoc. 2018; 81:676-681.
32. Williams RD, Snowden C, Frank R, Thiel DD. Has sliding-clip renorrhaphy eliminated the need for collecting system repair during robot-assisted partial nephrectomy? J Endourol. 2017; 31:289-294.
33. Bertolo R, Campi R, Mir MC, Klatte T, Kriegmair MC, Salagierski M, Ouzaid I, Capitanio U. Systematic review and pooled analysis of the impact of renorrhaphy techniques on renal functional outcome after partial nephrectomy. Eur Urol Oncol. 2019; 2:572-575.
34. Dell'Atti L, Scarcella S, Manno S, Polito M, Galosi AB. Approach for renal tumors with low nephrometry score through unclamped sutureless laparoscopic enucleation technique: functional and oncologic outcomes. Clin Genitourin Cancer. 2018; 16:1251-1256.
35. Simone G, Papalia R, Guaglianone S, Gallucci M. 'Zero ischaemia', sutureless laparoscopic partial nephrectomy for renal tumours with a low nephrometry score. BJU Int. 2012; 110:124-130.
36. Zhang F, Gao S, Chen XN, Wu B. Clampless and sutureless laparoscopic partial nephrectomy using monopolar coagulation with or without N-butyl-2-cyanoacrylate. World J Surg Oncol. 2019; 17:72.
37. Nakamura M, Ambe Y, Teshima T, Shirakawa N, Inatsu H, Amakawa R, Inoue Y, Yoshimatsu T, Imai S, Kusakabe M, Morikawa T, Kameyama S, Shiga Y. Assessment of surgical outcomes of off-clamp open partial nephrectomy without renorrhaphy for ≥ T1b renal tumours. Int J Clin

Oncol. 2021; 26;1955-1960.
38. Nakamura M, Kameyama S, Ambe Y, Teshima T, Izumi T, Tsuru I, Inoue Y, Yoshimatsu T, Inatsu H, Amakawa R, Kusakabe M, Morikawa T, Shiga Y. Predictive factors for postoperative renal function after off-clamp, non-renorrhaphy partial nephrectomy. Transl Androl Urol. 2022; 11:1226-1233.
39. Nakamura K, Imamura Y, Yamamoto S, Sazuka T, Sakamoto S, Ichikawa T. Soft coagulation in robot-assisted partial nephrectomy without renorrhaphy: Comparison with standard suture. Int J Urol. 2020; 27:352-354.
40. Fujisaki A, Takayama T, Teratani T, Kubo T, Kamei J, Sugihara T, Ando S, Morita T, Fujimura T. Histological and radiological evaluation of thermal denaturation depth using soft coagulation during partial nephrectomy in living pigs. Int J Urol. 2021; 28:1274-1280.

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