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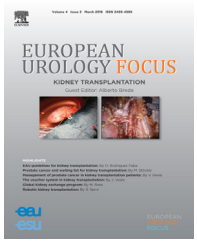

Review – Kidney Cancer

Near-infrared Fluorescence Imaging with Indocyanine Green in Robot-assisted Partial Nephrectomy: Pooled Analysis of Comparative Studies

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Abstract

Context: The use of near-infrared fluorescence (NIRF) imaging was described to facilitate selective clamping during robot-assisted partial nephrectomy (RAPN).
Objective: To perform a systematic review and cumulative analysis of available studies comparing the outcomes of RAPN with or without use of this technology (NIRF).
Evidence acquisition: A systematic review of the literature was performed to identify relevant studies up to December 2018 through PubMed and EMBASE databases. A meta-analysis was conducted with the RevMan 5.3 software.
Evidence synthesis: Six comparative studies were identified. Overall, 369 cases were included for the analysis (171 NIRF-RAPN and 198 standard RAPN). No significant difference was identified between groups in baseline characteristics, operating time, and estimated blood loss; however, a shorter clamping time was recorded for the NIRF-RAPN group. Functional outcomes revealed higher overall estimated glomerular filtration rate (eGFR) values in the NIRF-RAPN group at short-term (1–3 mo) postoperative follow-up (weighted mean difference [WMD]: 9.26 ml/min; 95% confidence interval [CI]: 6.46, 12.06; $p < 0.001$). In two studies, a renal scan-based assessment of split eGFR was available, and pooled analysis revealed higher split eGFR for NIRF-RAPN (WMD: 7.91 ml/min; 95% CI: 4.26, 11.56; $p < 0.001$), and lower Δ % between preoperative and 1-mo eGFR (WMD: −7.84%; 95% CI: −8.85, −6.83; $p < 0.00001$).
Conclusions: Current evidence regarding the use of NIRF-guided selective clamping during RAPN is based on a limited number of studies from high-volume institutions. Notwithstanding these limitations, NIRF-RAPN can be safely performed, and it might offer better short-term renal functional outcomes. It remains to be determined whether this can ultimately translate into a clinical benefit for patients undergoing RAPN, especially in the long term.
Patient summary: We assessed the outcomes of robot-assisted partial nephrectomy (RAPN) performed with or without the use of near-infrared fluorescence (NIRF) imaging. NIRF-RAPN appeared to be a safe procedure with potential better short-term functional outcomes.

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1. Introduction

Indocyanine green (ICG; IC-Green; Akorn, Lake Forest, IL, USA) is a safe Food and Drug Administration (FDA)-approved fluorescent dye, which is widely used in medical specialties to identify vascular structures and nodal drain [1,2]. Over the past 5 yr, near-infrared fluorescence (NIRF) using ICG has emerged as a safe technology to better visualize anatomical structures during surgery [3]. The integration of this tool into the da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) allowed robotic surgeons to explore its application for a wide range of robotic urologic procedures [4]. More specifically, the use of NIRF imaging was described to aid during minimally invasive partial nephrectomy (PN) [5,6]. In this setting, the technology was shown to differentiate normally perfused (healthy) renal parenchyma from the tumoral lesion, allowing easier scoring of the resection margin [7]. More recently, authors have reported the use of ICG-NIRF during robotic resection of totally endophytic renal masses [8].

The role and impact of warm ischemia on functional outcomes of PN are still debated. Our clinical practice has been driven by the long-standing dogma to limit ischemia time to under 30 min [9–11], which was then reduced to 25 min [12], eventually culminating in the principle of zero ischemia [13]. Several different surgical strategies have been explored to minimize ischemia-related damage, and techniques such as cold ischemia, selective clamping, early unclamping, and zero ischemia have been investigated to achieve this purpose [14].

Most studies on the use of NIRF during robotic urologic surgery focused on the use of this tool to facilitate selective artery clamping during robotic-assisted partial nephrectomy (RAPN). In this work, we performed a systematic review and pooled analysis of the available studies comparing the outcomes of RAPN with or without the use of ICG-NIRF.

2. Evidence acquisition

2.1. Literature search

After establishing a study protocol, a research question was formulated according to the PICO model (P = patients with renal mass; I = NIRF-RAPN [with selective clamping]; C = standard RAPN [with main artery clamping]; O = surgical outcomes). A systematic review of the literature was performed using PubMed and EMBASE to identify relevant studies up to December 2018. The research was made adopting a free text protocol. The following search terms were used: “indocyanine green,” “near infrared fluorescence,” and “robotic partial nephrectomy.” Identification and selection of the studies were conducted according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) criteria (www.prisma-statement.org) [15,16]. Two of the authors performed the article selection, which was limited to English language only and those including adult patients. Only original studies comparing the outcomes of retroperitoneal and transperitoneal RAPN for renal tumors according to the PICO model were included. Title and abstracts were first reviewed to ascertain whether they would potentially follow the inclusion criteria. For those passing the first screening, a full-text analysis was performed to confirm inclusion. Studies without primary data (letters to the editor/authors, case reports, and commentaries) as well as conference abstracts were not considered. References of collected studies were manually reviewed to find additional studies of interest.

2.2. Assessment of study quality and publication bias

We classified each study according to the level of evidence [17]. The quality of the studies was determined using the Newcastle–Ottawa Scale for nonrandomized controlled trials [18]. A total score of 5 or less was considered low quality, 6–7 was considered intermediate quality, and 8–9 was considered high quality. Risk of publication bias was assessed using funnel plots.

2.3. Data extraction and analysis

Data were extracted from each selected study. Baseline demographics (age, sex, body mass index, Charlson Index, preoperative estimated glomerular filtration rate [eGFR], tumor size, R.E.N.A.L. score), intraoperative data (operative time [OT], estimated blood loss [EBL], warm ischemia time [WIT]), postoperative outcomes (complications, and positive surgical margin [PSM] rate), and short- and long-term functional outcomes (eGFR value and variation at discharge, and eGFR value at 1 and 3 mo after surgery) were assessed.

For continuous outcomes, the weighted mean difference (WMD) was used as a summary measure, whereas the odds ratio or risk ratio (RR) with 95% confidence interval (CI) was calculated for binary variables. RR was preferred in cases of a high number of events to avoid overestimation. As only means and standard deviations are permitted for the computational portion of meta-analyses, a validated mathematical model was used to convert median (range) to mean (standard deviation) for studies reporting medians and ranges [19]. Pooled estimates were calculated using the random-effect model to account for study heterogeneity. Potential publication bias was evaluated by funnel plots analysis for each outcome. All statistical analyses were performed using Review Manager (RevMan version 5.3; The Cochrane Collaboration/The Nordic Cochrane Centre, Copenhagen, Denmark).

3. Evidence synthesis

3.1. Description of included studies and quality assessment

Six comparative studies (all retrospective cohort studies, including four with match-paired analysis) published between 2012 and 2018 were identified [20–25] (Fig. 1). The characteristics of included studies are summarized in Table 1. Study quality was 3 for all studies. Owing to small number of studies, visual assessment was unlikely to be accurate, but no obvious publication bias was observed.

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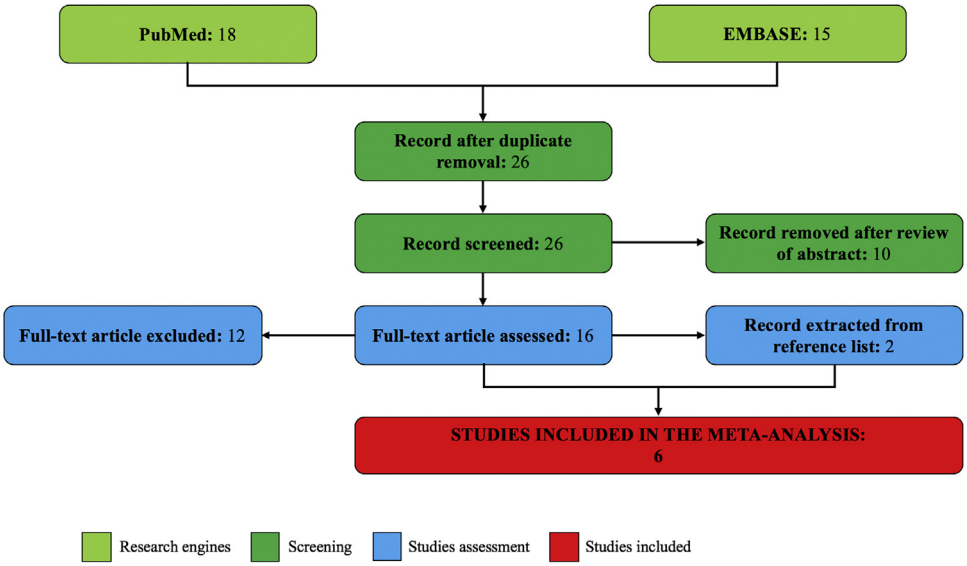

Fig. 1 – PRISMA flowchart. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses.

3.2. *Demographics and clinical characteristics*

Overall, 369 cases were included for the analysis (171 NIRF-RAPN and 198 standard RAPN). There was no significant difference between groups in baseline characteristics. Baseline features are summarized in Table 2.

3.3. *Outcomes*

Forest plots for relevant surgical outcomes are illustrated in Figure 2. No difference was found between groups in OT (WMD: 8.12 min; 95% CI: −22.46, 6.23; $p = 0.27$) [21–25] and EBL (WMD: 7.7 ml; 95% CI: −35.97, 20.50; $p = 0.59$) [20–25]; however, a shorter clamping time was recorded for the NIRF-RAPN group (WMD: −1.46 min; 95% CI −2.32, −0.60; $p < 0.001$) [20,22–25]. There was no significant difference in risk of postoperative complications ($p = 0.25$) [20–25] and PSMs ($p = 0.56$) [20,24,25].

3.4. *Functional outcomes*

Forest plots for functional outcomes are illustrated in Figure 3. Assessment of functional outcomes revealed no significant difference between the two groups in eGFR value at discharge (WMD: 4.62 ml/min; 95% CI: −3.49, 12.73; $p = 0.26$) [23,24] and eGFR % variation (WMD: 8.88%; 95% CI: −2.98, 20.73; $p = 0.14$) [20–23]. Higher overall eGFR values were found in the NIRF-RAPN group at short term (1–3 mo) postoperative follow-up (WMD: 9.26 ml/min; 95% CI: 6.46, 12.06; $p < 0.001$) [23–25]. In the two studies where a renal scan-based assessment of split eGFR was available, a pooled analysis revealed higher split GFR for NIRF-RAPN (WMD: 7.91 ml/min; 95% CI: 4.26, 11.56; $p < 0.001$) [24,25]. In addition, a lower Δ % was recorded between preoperative and 1-mo eGFR in the NIRF-RAPN group (WMD: −7.84%; 95% CI: −8.85, −6.83; $p < 0.00001$) [24,25].

4. Discussion

This is the first meta-analysis of studies comparing RAPN performed with or without the use of NIRF-ICG selective clamping. This analysis on a pooled sample of 369 patients (171 NIRF-RAPN and 198 standard-RAPN) can be cue for further studies and it gives a picture of the current evidence on this topic. Overall, our findings show that the use of NIRF can aid the surgeon in a selective clamping approach,

Table 1 – Study characteristics.

Authors	Year	Number of cases		Group allocation	ICG dose	LE	NOS score
		NIRF-RAPN	Standard RAPN				
Krane et al [20]	2012	47	47	Matched retrospectively	5–7.5 mg	3	✱✱✱✱✱✱
Borofsky et al [21]	2012	27	27	Matched retrospectively	7.5 mg	3	✱✱✱✱✱✱
Harke et al [22]	2014	15	15	Matched retrospectively	5 mg	3	✱✱✱✱✱✱
McClintock et al [23]	2014	42	42	Matched retrospectively	5–7.5 mg	3	✱✱✱✱✱✱✱
Lanchon et al [24]	2018	25	25	Matched retrospectively	0.5–2 cc	3	✱✱✱✱✱✱✱
Mattevi et al [25]	2018	15	42	Matched retrospectively	5 mg	3	✱✱✱✱✱✱✱

ICG = indocyanine green; LE = level of evidence; NIRF = near-infrared fluorescence; NOS = Newcastle–Ottawa Scale; RAPN = robot-assisted partial nephrectomy.

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Table 2 – Baseline features.

Variables	OR	95% CI	*p* value
Age (yr)	−1.29	−4.05, 1.45	0.36
Sex (male)	1.64	0.94, 2.87	0.08
BMI (kg/m^2)	0.21	−0.35, 0.76	0.46
Charlson index	0.12	−0.72, 0.96	0.78
Preoperative eGFR (ml/min/1.73 m^2)	0.58	−2.29, 3.44	0.69
Tumor size (cm)	−0.20	−0.70, 0.29	0.42
R.E.N.A.L. score	−0.34	−0.88, 0.20	0.22

BMI = body mass index; CI = confidence interval; eGFR = estimated glomerular filtration rate; OR = odd ratio.

possibly leading to a lower decline of renal function in the short term, compared with a standard technique, without compromising any of the other surgical outcomes.

With the aim of limiting ischemic damage during PN, surgeons investigated new ways of managing the renal pedicle during kidney tumor resection. Selective clamping has emerged as a technique aiming at "regional" rather than "global" ischemia, thereby reducing potential damage to healthy renal parenchyma [26]. Current literature findings are not of enough quality to recommend the use of selective clamping over other techniques [27]. Moreover, an effective artery clamping is reliable only in understanding the unique patient's vascular anatomy. Currently available imaging techniques are not devoid of limitations, and traditional anatomical landmarks remain the main intraoperative guidance for the surgeon. Indeed, preoperative imaging cannot account for some anatomical nuances, and it does not give detailed information on intrarenal vascular distribution. The use of Doppler ultrasound has been shown to be feasible and to ease the tumor resection [28], but its use remains operator dependent, and it requires a specific set up of the robotic console. Modern three-dimensional and holographic technologies [29,30] provide a more comprehensible rendering of the vascular anatomy, allowing for a safer selective clamping, but neither of these tools can provide confirmation of ischemia of downstream kidney tissue. Recently, introduction of contrast-enhanced ultrasound to road-map renal blood flow has shown promising results to obtain selective clamping [31]. Nevertheless, this is a novel technique and requires further analysis to establish its feasibility and safety.

NIRF imaging with ICG overcomes each of the limitations of the aforementioned methods. In addition to its ability to delineate the tumor from the surrounding healthy parenchyma, NIRF imaging allows real-time visual confirmation of devascularization after the surgeon has clamped the arterial branch to achieve regional ischemia. If ischemia cannot be achieved after selective clamping, ICG can help identify other segmental arterial branches until the achievement of appropriate tumor devascularization.

Several findings from our systematic review and meta-analysis are worth mentioning. Notably, we did not find any difference in main surgical outcomes, such as OT and EBL. Only in one of the included studies, a longer OT was recorded for the NIRF-RAPN group, which can be explained by the "super-selective" dissection strategy adopted by the authors, ultimately translating into a more challenging and time-consuming procedure [21]. In general, the literature suggests a higher EBL during selective clamping RAPN procedures with no difference in transfusion rates [14–32]. A reasonable explanation might reside in the existing connections between several segmental arteries which cannot be assessed by NIRF because of its surface colorant characteristic. In this regard, recent evidence suggests a higher variability of renal vascular anatomy than previously thought [33].

By contrast, our cumulative analysis shows a shorter WIT for the NIRF-RAPN cohort. Shorter ischemia time for NIRF-RAPN was indeed recorded in all included studies, but was statistically significant in one of them [20]. Similarly, Komninos et al [34] retrospectively compared data of 180 patients with renal tumor who underwent PN with different clamping techniques and noticed shorter WIT in the selective clamp group. Several authors purposed to keep WIT under 20–25 min to preserve kidney function [35,36], suggesting that such limited ischemia duration is desirable. Notably, for all the studies included, the duration of ischemia time was under the 25-min threshold for both the NIRF-RAPN and s-RAPN groups. While shorter ischemia time contributes to better functional outcomes, ischemia time represents only one among several factors involved in impairment of kidney function during nephron-sparing surgery (NSS), including host features (age and baseline renal function) and surgical factors (parenchymal mass preservation, tumor resection technique, renorrhaphy technique) [37]. Notwithstanding a statistically significant difference between the two study groups, the cumulative difference was 1.4 min, which is unlikely to have a clinical significance.

Our analysis did not show a significant difference between the two study groups with regard to postoperative eGFR variation and eGFR value at discharge. Nevertheless, short-term (1–3 mo) functional outcomes were better in the NIRF group, potentially suggesting a higher functional recovery. Most of the literature on functional outcomes of PN is based on the assessment of eGFR, which however is a suboptimal tool, as it measures overall renal function without discerning the contribution of each kidney. Renal scan should be regarded as a better way to assess split-kidney function in patients with normal contralateral kidney, but it is not regularly used in clinical practice [38]. In two of the comparative studies we analyzed, the authors made an effort to report renal scan split-kidney function [24,25]. Both studies prospectively evaluated a cohort of 65 and 50 patients, respectively, and both found a lower decline of eGFR and higher split-kidney function in the operated kidney. Not surprisingly, the pooled analysis of these two studies reinforce the idea that NIRF-guided selective clamping might be of aid in preserving renal function.

With regard of complications, the main concerns about off-clamp RAPN and NIRF selective clamping derive from the necessity to dissect artery branches with a higher risk of vascular injury, complications, and PSM [39]. However, the literature seems not to bear this out. Indeed, our cumulative analysis confirms no significant difference between the

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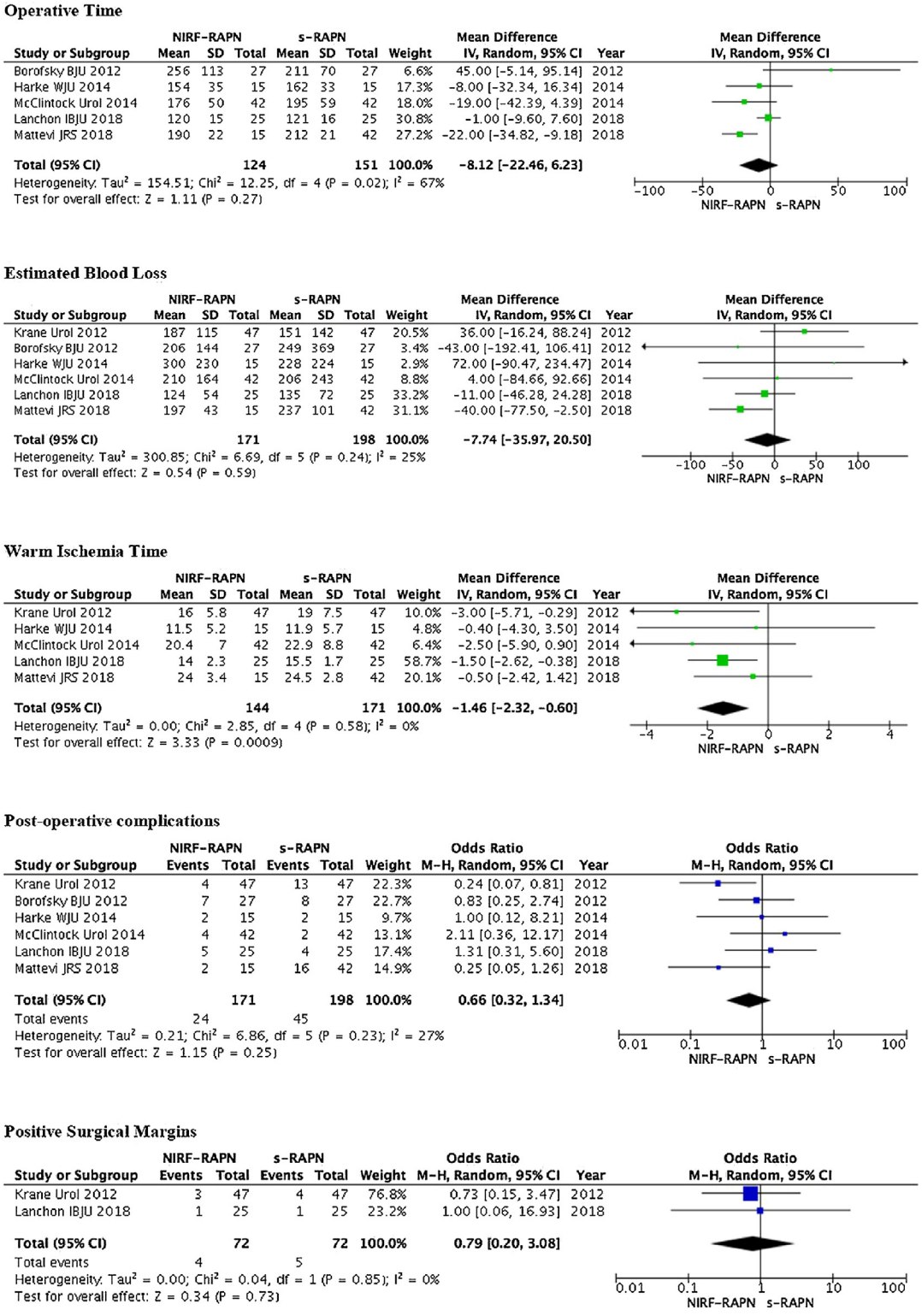

Fig. 2 – Forest plots of surgical outcomes. See also [20–25]. CI = confidence interval; NIRF = near-infrared fluorescence; RAPN = robot-assisted partial nephrectomy; SD = standard deviation; IV = inverse variance; M-H = Mantel-Haenszel test.

NIRF-RAPN and s-RAPN groups in terms of complications and PSM. Moreover, a recent review pointed out that intraoperative NIRF allows to discern healthy tissue from pathological one during NSS only for exophytic tumors [40].

Some limitations of our study need to be acknowledged. The major limitation is related to the design of included studies. All the studies suffered from a high risk of selection bias due to the absence of randomization, and treatment

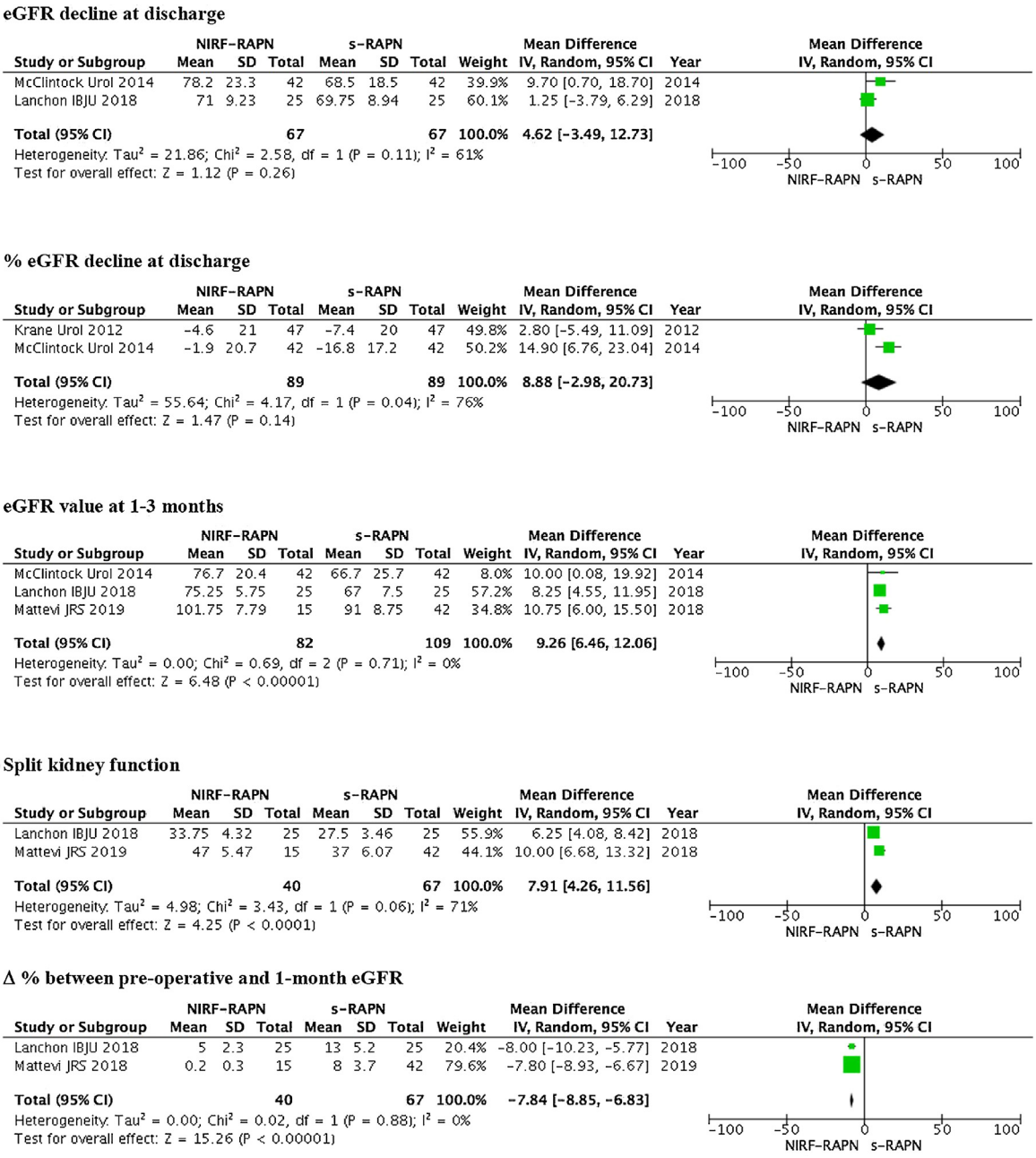

Fig. 3 – Forest plots of functional outcomes. See also [20,23–25]. CI = confidence interval; eGFR = estimated glomerular filtration rate; NIRF = near-infrared fluorescence; RAPN = robot-assisted partial nephrectomy; SD = standard deviation; IV = inverse variance; M-H = Mantel-Haenszel test.

choice based on surgeon preference. Moreover, none of the reports gave a picture of the blinding of participants and of the outcomes' assessment, so this risk of bias was uncertain. Despite representing a robust statistical tool, meta-analyses certainly carry intrinsic biases, and randomized controlled trials should ideally be included. In our analysis, all studies were either retrospective or prospective nonrandomized, and study samples were limited. Moreover, our cumulative analysis was necessarily limited to certain parameters that were extractable and available. Besides, more robust oncological outcomes, other than the PSM rate, were not available for analysis. To note, it was not possible to account for existing differences among institutions and surgeons in terms of surgical technique and expertise, as well as protocols of perioperative management and follow-up. In addition, all the studies assessed came from high-volume institutions and the results achieved might not be applicable for other centers, especially for OT and complication rate. Consequently, our meta-analysis might not be indicative of different clinical settings. When looking at functional outcomes, one must keep in mind that most studies had short term (1–3 mo) follow-up except one which reported a slightly longer one (6 mo) [24]. Despite these limitations, our findings can be used as reference for further clinical

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investigation. In the future, comparative prospective, ideally randomized, multicenter studies are needed to better define the role of ICG-NIRF imaging during RAPN.

5. Conclusions

Current evidence regarding the use of NIRF-guided selective clamping during RAPN is based on a limited number of studies from high-volume institutions. These studies are mostly retrospective, of medium quality, with a limited sample size and short follow-up. Notwithstanding these limitations, NIRF-RAPN can be safely performed, and it might offer better short-term renal functional outcomes. It remains to be determined whether this can ultimately translate into a clinical benefit for patients undergoing RAPN, especially in the long term.

Author contributions: Riccardo Autorino has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Autorino, Veccia.
Acquisition of data: Veccia.
Article selection: Veccia, Autorino.
Drafting of the manuscript: Veccia, Autorino.
Critical revision of the manuscript for important intellectual content: Antonelli, Hampton, Greco, Perdonà, Lima, Hemal, Derweesh, Porpiglia.
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Other: None.

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References

[1] United States Food and Drug Administration. Approval of "ICGreen". https://www.accessdata.fda.gov/scripts/cder/daf.
[2] Reinhart MB, Huntington CR, Blair LJ, Heniford BT, Augenstein VA. Indocyanine green: historical context, current applications, and future considerations. Surg Innov 2016;23:166–75.
[3] Polom K, Murawa D, Rho Y, Nowaczyk P, Hünerbein M, Murawa P. Current trends and emerging future of indocyanine green usage in surgery and oncology: a literature review. Cancer 2011;117:4812–22.
[4] Autorino R, Zargar H, White WM, et al. Current applications of near-infrared fluorescence imaging in robotic urologic surgery: a systematic review and critical analysis of the literature. Urology 2014;84:751–9.
[5] Porpiglia F, Fiori C, Checcucci E, Pecoraro A, Di Dio M, Bertolo R. Selective clamping during laparoscopic partial nefrectomy: the use of near infrared fluorescence guidance. Minerva Urol Nefrol 2018;70:326–32.
[6] Ferroni MC, Sentell K, Abaza R. Current role and indications for the use of indocyanine green in robot-assisted urologic surgery. Eur Urol Focus 2018;4:648–51.
[7] Golijanin DJ, Marshall J, Cardin A, et al. Bilitranslocase (BTL) is immunolocalised in proximal and distal renal tubules and absent in renal cortical tumors accurately corresponding to intraoperative near infrared fluorescence (NIRF) expression of renal cortical tumors using intravenous indocyanine green (ICG). J Urol 2008;179:137.
[8] Simone G, Tuderti G, Anceschi U, et al. "Ride the green light": indocyanine green–marked off-clamp robotic partial nephrectomy for totally endophytic renal masses. Eur Urol. In press. https://doi.org/10.1016/j.eururo.2018.09.015.
[9] Porpiglia F, Renard J, Billia M, et al. Is renal warm ischemia over 30 minutes during laparoscopic partial nephrectomy possible? One-year results of a prospective study. Eur Urol 2007;52:1170–8.
[10] Simone G, Gill IS, Mottrie A, et al. Indications, techniques, outcomes, and limitations for minimally ischemic and off-clamp partial nephrectomy: a systematic review of the literature. Eur Urol 2015;68:632–40.
[11] Rod X, Peyronnet B, Seisen T, et al. Impact of ischaemia time on renal function after partial nephrectomy: a systematic review. BJU Int 2016;118:692–705.
[12] Cacciamani G, Gill TS, Medina L, et al. Impact of host factors on robotic partial nephrectomy outcomes: comprehensive systematic review and meta-analysis. J Urol 2018;200:716–30.
[13] Gill IS, Patil MB, Abreu AL, et al. Zero ischemia anatomical partial nephrectomy: a novel approach. J Urol 2012;187:807–14.
[14] Cacciamani G, Medina L, Gill TS, et al. Impact of renal hilar control on outcomes of robotic partial nephrectomy: systematic review and cumulative meta-analysis. Eur Urol Focus. In press. https://doi.org/10.1016/j.juro.2017.12.086.
[15] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg 2010;8:336–41.
[16] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic reviews and meta-analyses protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;349:g7647.
[17] Howick J, Chalmers I, Glasziou P, et al. Explanation of the 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence (Background Document). Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653.
[18] Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomized Studies in Meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
[19] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 2005;5:13.
[20] Krane LS, Manny TB, Hemal AK. Is near infrared fluorescence imaging using indocyanine green dye useful in robotic partial nephrectomy: a prospective comparative study of 94 patients. Urology 2012;80:110–6.
[21] Borofsky MS, Gill IS, Hemal AK, et al. Near-infrared fluorescence imaging to facilitate super-selective arterial clamping during zero-ischaemia robotic partial nephrectomy: near-infrared fluorescence imaging in zero ischaemia RPN. BJU Int 2013;111:604–10.
[22] Harke N, Schoen G, Schiefelbein F, Heinrich E. Selective clamping under the usage of near-infrared fluorescence imaging with indocyanine green in robot-assisted partial nephrectomy: a single-surgeon matched-pair study. World J Urol 2014;32:1259–65.
[23] McClintock TR, Bjurlin MA, Wysock JS, et al. Can selective arterial clamping with fluorescence imaging preserve kidney function during robotic partial nephrectomy? Urology 2014;84:327–32.
[24] Lanchon C, Arnoux V, Fiard G, et al. Super-selective robot-assisted partial nephrectomy using near-infrared fluorescence versus early-unclamping of the renal artery: results of a prospective matched-pair analysis. Int Braz J Urol 2018;44:53–62.

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[25] Mattevi D, Luciani LG, Mantovani W, et al. Fluorescence-guided selective arterial clamping during RAPN provides better early functional outcomes based on renal scan compared to standard clamping. J Robotic Surg. In press. https://doi.org/10.1007/s11701-018-0862-x.
[26] Benway BM, Baca G, Bhayani SB, et al. Selective versus nonselective arterial clamping during laparoscopic partial nephrectomy: impact upon renal function in the setting of a solitary kidney in a porcine model. J Endourol 2009;23:1127–33.
[27] Greco F, Autorino R, Altieri V, et al. Ischemia techniques in nephron-sparing surgery: a systematic review and meta-analysis of surgical, oncological, and functional outcomes. Eur Urol 2019;75:477–91.
[28] Kaczmarek BF, Sukumar S, Petros F, et al. Robotic ultrasound probe for tumor identification in robotic partial nephrectomy: initial series and outcomes. Int J Urol 2013;20:172–6.
[29] Porpiglia F, Fiori C, Checcucci E, Amparore D, Bertolo R. Hyperaccuracy three-dimensional reconstruction is able to maximize the efficacy of selective clamping during robot-assisted partial nephrectomy for complex renal masses. Eur Urol 2018;74:651–60.
[30] Antonelli A, Veccia A, Palumbo C, et al. Holographic reconstructions for preoperative planning before partial nephrectomy: a head-to-head comparison with standard CT scan. Urol Int. In press. https://doi.org/10.1159/000495618.
[31] Alenezi A, Motiwala A, Eves S, et al. Robotic assisted laparoscopic partial nephrectomy using contrast-enhanced ultrasound scan to map renal blood flow. Int J Med Robot 2017;13.
[32] Zhou L, Wei X, Sun WJ, et al. Selective versus hilar clamping during minimally invasive partial nephrectomy: a systematic review and meta-analysis. J Endourol 2015;29:855–63.
[33] Macchi V, Crestani A, Porzionato A, et al. Anatomical study of renal arterial vasculature and its potential impact on partial nephrectomy. BJU Int 2017;120:83–91.
[34] Komninos C, Shin TY, Tuliao P, et al. 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;115:921–8.
[35] Becker F, Van Poppel H, Hakenberg OW, et al. Assessing the impact of ischaemia time during partial nephrectomy. Eur Urol 2009;56:625–34.
[36] Thompson RH, Lane BR, Lohse CM, et al. Every minute counts when the renal hilum is clamped during partial nephrectomy. Eur Urol 2010;58:340–5.
[37] Mir MC, Autorino R, Porpiglia F. Ischemia time and beyond: the concept of global renal damage. Minerva Urol Nefrol 2018;70:447–9.
[38] Bertolo RG, Zargar H, Autorino R, et al. Estimated glomerular filtration rate, renal scan and volumetric assessment of the kidney before and after partial nephrectomy: a review of the current literature. Minerva Urol Nefrol 2017;69:539–47.
[39] Klatte T, Ficarra V, Gratzke C, et al. A literature review of renal surgical anatomy and surgical strategies for partial nephrectomy. Eur Urol 2015;68:980–92.
[40] Hekman MCH, Rijpkema M, Langenhuijsen JF, Boerman OC, Oosterwijk E, Mulders PFA. Intraoperative imaging techniques to support complete tumor resection in partial nephrectomy. Eur Urol Focus 2018;4:960–8.

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