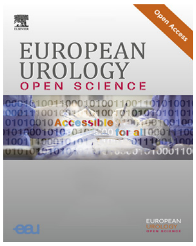
EUROPEAN UROLOGY OPEN SCIENCE 52 (2023) 7–21

available at www.sciencedirect.com
journal homepage: www.eu-openscience.europeanurology.com



European Association of Urology

Review

Resection Techniques During Robotic Partial Nephrectomy: A Systematic Review

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Article info

Article history:
Accepted March 21, 2023

Associate Editor:
Guillaume Ploussard

Keywords:
Enucleation
Enucleoresection
Outcomes
Partial Nephrectomy
Resection
Robot
Surgery
Technique

Abstract

Context: The resection technique used to excise tumor during robotic partial nephrectomy (RPN) is of paramount importance in achieving optimal clinical outcomes.
Objective: To provide an overview of the different resection techniques used during RPN, and a pooled analysis of comparative studies.
Evidence acquisition: The systematic review was conducted according to established principles (PROSPERO: CRD42022371640) on November 7, 2022. A population (P: adult patients undergoing RPN), intervention (I: enucleation), comparator (C: enucleoresection or wedge resection), outcome (O: outcome measurements of interest), and study design (S) framework was prespecified to assess study eligibility. Studies reporting a detailed description of resection techniques and/or evaluating the impact of resection technique on outcomes of surgery were included.
Evidence synthesis: Resection techniques used during RPN can be broadly classified as resection (non-anatomic) or enucleation (anatomic). A standardized definition for these is lacking. Out of 20 studies retrieved, nine compared "standard" resection

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https://doi.org/10.1016/j.euros.2023.03.008

versus enucleation. A pooled analysis did not reveal significant differences in terms of operative time, ischemia time, blood loss, transfusions, or positive margins. Significant differences favoring enucleation were found for clamping management (odds ratio [OR] for renal artery clamping 3.51, 95% confidence interval [CI] 1.13–10.88; $p = 0.03$), overall complications (OR for occurrence 0.55, 95% CI 0.34–0.87; $p = 0.01$) major complications (OR for occurrence 0.39, 95% CI 0.19–0.79; $p = 0.009$), length of stay (weighted mean difference [WMD] −0.72 d, 95% CI −0.99 to −0.45; $p < 0.001$), and decrease in estimated glomerular filtration rate (WMD −2.64 ml/min, 95% CI −5.15 to −0.12; $p = 0.04$).

Conclusions: There is heterogeneity in the reporting of resection techniques used during RPN. The urological community must improve the quality of reporting and research produced accordingly. Positive margins are not specifically related to the resection technique. Focusing on studies comparing standard resection versus enucleation, advantages with tumor enucleation in terms of avoidance of artery clamping, overall/major complications, length of stay, and renal function were found. These data should be considered when planning the RPN resection strategy.

Patient summary: We reviewed studies on robotic surgery for partial kidney removal using different techniques to cut away the kidney tumor. We found that a technique called "enucleation" was associated with similar cancer control outcomes in comparison to the standard technique and had fewer complications, better kidney function after surgery, and a shorter hospital stay.

1. Introduction

With the diffusion of technology, robotic surgery has become the preferred approach for partial nephrectomy (PN) [1]. The European Association of Urology guidelines recommend PN as the gold-standard treatment for patients with localized T1 renal tumors [2], and the technique used to resect the renal mass is of paramount importance in achieving perioperative safety, oncological efficacy, and maximum functional preservation. Debate regarding the merits and limitations of different resection techniques for robotic PN (RPN) is lively. Traditional PN included excision of a margin of peritumoral tissue to ensure negative margins [3]. This dogma has been revolutionized in the past number of decades. In particular, as the amount of functional parenchymal mass preserved during PN is one of the strongest modifiable predictors of functional recovery after surgery, some authors argued that without compromising oncological efficacy, tumor enucleation might have distinct benefits over "traditional" PN [4].

According to the current literature, the "ideal" technique is enucleation, which virtually avoids removal of healthy tissue. However, some experts remain skeptical about its real advantages, arguing that it might lead to nonsignificant differences in postoperative renal function and complications in comparison to standard PN, at the cost of a higher risk of either tumor rupture or a positive surgical margin (PSM). Other experiences have underlined the pros of such an anatomic resection technique [5].

Here we provide an up-to-date overview of the different resection techniques for RPN and a pooled analysis of the literature data available on this issue.

2. Evidence acquisition

2.1. Review protocol and search strategy

The systematic review was conducted according to the principles highlighted by the European Association of Urology Guidelines Office [6] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement recommendations [7]. The review protocol was registered on November 10, 2022 (www.crd.york.ac.uk/prospero; CRD42022371640). An electronic search of the English-language literature was performed on November 7, 2022 by combining free-text and MeSH terms using the MEDLINE (via PubMed), Web of Science, and Embase databases without time limits. A detailed overview of the search strategy is provided in the Supplementary material.

2.2. Inclusion and exclusion criteria

A specific population (P), intervention (I), comparator (C), outcome (O), and study design (S) (PICOS) framework was prespecified to assess the study eligibility [6]. The PICOS framework for this review was as follows:

P: Adult patients (≥18 yr of age with a renal mass treated with RPN;
I: Enucleation;
C: Enucleoresection or wedge resection during RPN;
O: Operative time, clamping management, warm ischemia time, estimated blood loss, complication rates, length of stay, functional outcomes, and PSM status; and
S: Studies on patients undergoing RPN, reporting a detailed description of resection techniques or evaluating

the impact of the resection technique on the outcomes of surgery.

A manual search of the bibliographies of the studies included was also performed to identify any additional relevant studies. Review articles, letters, editorials, commentaries, case reports, and animal and preclinical studies were excluded.

In cases of multiple articles published by the same group with overlapping patient cohorts, only the study with the largest number of patients was included.

2.3. Study selection and data extraction

Two members of the review team (R.B. and A.P, assisted by collaborators) screened the titles and abstracts of the records retrieved. Disagreements were resolved by a third party (R.C.). The same authors confirmed study eligibility after full-text screening. Data from studies included in the review were extracted by three authors (U.C., P.D., and S. M.). The reliability and completeness of the data extraction were cross-checked by the whole review team.

The following information was extracted for each study: study identification (citation, authors, publication year, country, source of data); methods (study design, setting, enrolment period, number of centers involved); population characteristics (number of patients, age, sex, comorbidity, ethnicity); disease characteristics (stage, grading, complexity); intervention (surgical technique, intraoperative data); and postoperative outcomes (operative time, clamping management, warm ischemia time, estimated blood loss, complication rates, length of stay, functional outcomes, and PSM status).

2.4. Risk of bias and synthesis of results

Three reviewers (U.C., P.D., and S.M.) independently assessed the risk of bias for each study according to the Quality In Prognosis Studies (QUIPS) tool [8], with a fourth reviewer (A.P.) acting as an arbitrator. The quality of evidence was assessed according to Grading of Recommendations Assessment, Development, and Evaluation (GRADE) recommendations (https://www.gradeworkinggroup.org).

A narrative format was used for qualitative synthesis. A quantitative synthesis of the evidence was provided for a cluster of studies with similar characteristics.

For the computational part of the quantitative synthesis, various approaches were used to pool effect measures between studies. For continuous results, the mean and standard deviation (SD) were used if reported. For studies reporting only the median and interquartile range (IQR) or minimum/maximum range, two validated mathematical models were used to convert results to mean ± SD. For data with a likely normal distribution, the sample means estimator was used [9], while the Box-Cox and quantile estimation methods were used for time-based data or data suspected of being skewed [10]. As suggested by the Cochrane Collaboration, confidence intervals (CIs) were converted to SD by dividing by 3.92 and then multiplying by the square root of the sample size [11].

For continuous data measured on the same scale, the pooled weighted mean difference (WMD) and 95% CI were estimated using the inverse variance method. The pooled odds ratio (OR) and 95% CI were calculated using the Mantel-Haenszel method for binary data. Statistical heterogeneity between studies was assessed using the I^2 statistic. Results are presented as forest plots and summary tables showing average effect sizes, I^2, and 95% CIs. Statistical analyses were performed with RevMan version 5.3 (Nordic Cochrane Centre, Copenhagen, Denmark). Statistical significance was set to $p < 0.05$.

3. Evidence synthesis

The initial search identified 1926 papers. Of these, 24 were identified for detailed review. Finally, 20 studies met the inclusion criteria and were included in the analysis. Of these, five were single-arm studies [12–16] and 15 were comparative studies [5,17–30]. Review of the quality assessment and level of evidence revealed a moderate to high risk of bias overall, and a moderate to very low level of evidence (Supplementary Fig. 1, Table 1). A flowchart showing the review process is reported in Figure 1. Table 1 summarizes the studies retrieved.

3.1. Resection techniques during RPN

Resection techniques used during RPN can be broadly classified as resection, enucleoresection, or enucleation. Resection is removal of the renal tumor plus a “consistent” rim of healthy peritumoral tissue (historically, a safety margin thickness of ≥1 cm was recommended); enucleoresection is removal of the tumor plus a “thin” rim of healthy peritumoral parenchyma; and enucleation is removal of the tumor with “virtually” no surrounding healthy parenchyma (the tumor pseudocapsule is followed during excision and drives the resection technique). In real clinical practice, a wider range of alternatives is experienced when excising a renal mass, as outlined in Figure 2. For example, “resection” is a single word but covers both polar resection (which is likely to include a very consistent amount of healthy parenchyma) and wedge resection (for which a lower quantity of healthy parenchyma will be removed). Moreover, the thickness of the safety-margin can vary, ranging from 1 to 0.5 cm, depending on the surgeon’s preference. Enucleoresection can include both “traditional” enucleoresection (including a couple of millimeters of healthy peritumoral tissue) and “mini-enucleoresection” (for which the rim of healthy peritumoral parenchyma will be minimal; surgeons know that the intrinsic features of the parenchyma/pseudocapsule interface mean that some attempted enucleations end up being mini-enucleoresection). For instance, mini-enucleoresection involves a 1-mm margin before the subsequent cut to find the tumor pseudocapsule plane and pursue a pure enucleation technique.

Table 1 – Summary of studies investigating the impact of the PN resection technique on surgical outcomes

Study	Study design and country	GRADE	Study period and patients	Resection techniques	Preoperative characteristics	Tumor characteristics
Noncomparative studies						
Mottrie 2009 [12]	RSC, Belgium	Very low	2006–2007 *N* = 17	ENR	Males, median age, median eGFR, median CCI: NR	Complexity and location: NR Mean diameter: 3.8 ± 1.6 cm
Minervini 2018 [13]	RSC; Italy	Low	2011–2013 *N* = 140	TE	Male: 75 (62%) Median age: 62 yr Median eGFR: 84 Median CCI: NR	Complexity (RENAL score): low 83 (69%); intermediate 23 (19%); high 15 (12%) Location: 77 (63%) polar; 44 (37%) midrenal Diameter: 3.0 cm (IQR 2.0–3.7)
Mari 2019 [14]	RSC; Italy	Low	2012–2018 *N* = 259	TE	Male: 159 (61.4%) Median age: 62 yr Median eGFR: 89.3 Median CCI: NR	Complexity (PADUA score) low 160 (61.7%); intermediate 69 (26.6%); high 30 (11.7%) Location: NR Diameter: 2.72 ± 1.9 cm
Dong 2021 [15]	RSC; China	Low	2008–2017 *N* = 146	TE	Male: 98 (67.1%) Median age: 53 yr Median eGFR: 95 Median CCI: NR	Complexity: median RENAL score 7 Location: NR Diameter: 3.4 cm (IQR 2.6–4.6)
Bertolo 2022 [16]	PSC; Italy	Low	2022 *N* = 11	TE, ENR, resection	Male: 6 (54.5%) Median age: 64 yr Median eGFR: 87 Median CCI: NR	Complexity: median RENAL score 7 Location: NR Diameter: 2.8 cm (IQR 1.9–4.0)
Comparative studies						
Satkunasivam 2015 [17]	RSC; USA	Very low	2009–2013 *N* = 179 Group 1: 70 Group 2: 60 Group 3: 49	Unclamped MM RPN: Group 1: SSC, LC experience Group 2: SSC, mature experience Group 3: MM clampless	Male: 46 (66%) vs 39 (65%) vs 36 (73%) Median age: 59 vs 62 vs 62 yr Median eGFR: 71 vs 74 vs 78	Complexity: median RENAL score 7 vs 8 vs 9 Hilar location: 19 (27%) vs 10 (17%) vs 11 (22%) Diameter: 3.0 (IQR 0.9–13.6) vs 3.4 (1.3–7.9) vs 3.4 (1.5–1.4) cm
Minervini 2015 [18]	RSC; Italy	Low	2010–2013 *N* = 197 ERASE: 130 LAPSE: 67	ERASE vs LAPSE	Male: 76 (59%) overall Mean age: 61.8 ± 11.3 yr overall Median creatinine: 0.86 mg/dl overall Median CCI: overall 1 (IQR 0–1).	Complexity: median PADUA score 8 (IQR 7–9) Location: NR Diameter: 3.2 ± 1.5 cm overall Clinical stage: cT1a 101 (78%), cT1b 28 (21%), cT2a 1 (1%) overall
Oh 2016 [20]	RSC; Korea	Moderate	2003–2015 *N* = 702 OPN: 385 RPN: 317	OPN vs RPN	Male: 268 (70%) vs 230 (73%) Mean age: 54.9 vs 52.1 yr Mean eGFR: 77.5 vs 91.4	Complexity: NR Hilar location: 11 (3%) vs 5 (2%) Diameter: 2.3 ± 0.8 vs 2.2 ± 0.8 cm Clinical stage: all cT1a
Zhao 2018 [19]	RSC; China	Moderate	2012–2016 *N* = 383 RTE: 278 LTE: 105	RTE vs LTE	Male: 166 (59.7%) vs 62 (59%) Median age: 53.6 vs 55.4 yr Median eGFR: 102.2 vs 97.5	Complexity (PADUA score): low, 110 (39.5%) vs 50 (47.6%); intermediate, 107 (38.5%) vs 42 (40%); high, 61 (21.9%) vs 13 (12.4%) Location: NR Diameter: 3.8 ± 1.6 vs 3.9 ± 1.5 cm
Lu 2021 [21]	RSC; China	Low	2014–2017 *N* = 58 [a] RACP-RASE: 29 RASE:29	RACP-RASE vs ERASE	Male: 19 (66%) vs 20 (69%) Mean age: 52.5 ± 13.2 vs 54.45 ± 14.3 yr Mean eGFR: 98 (IQR 79–109) vs 91 (76–110)	Complexity: median RENAL score 10 (IQR 10–11) vs 10 (10–11) Hilar location: 12 (41%) vs 4 (14%) Mean diameter: 4.9 vs 5.0 cm
Campi 2022 [22]	RSC; Italy	Low	2014–2015 *N* = 113 OPN: 47 RPN: 66	TE, ENR, resection	Male: 34 (72.3%) vs 39 (59.1%) Median age: 62 vs 57 yr Median eGFR: 83.9 vs 90.3 Median CCI: NR	Complexity (PADUA score): 10, 27 (57.4%) vs 35 (53%); 11, 12 (25.5%) vs 22 (33.3%); 12, 6 (12.8%) vs 9 (13.6%) Location: NR Diameter: 4.6 vs 4.1 cm
Comparison of TE versus “standard” PN						
Blackwell 2016 [23]	RSC; USA	Low	2008–2015 *N* = 110 TE: 57 RPN: 53	TE vs standard RPN	Male: 34 (60%) vs 31 (58.5%) Median age: 60.1 vs 57.6 yr Median eGFR: 73.1 vs 78.3	Complexity (RENAL score): low, 17 (30%) vs 23 (43%); intermediate, 17 (30%) vs 20 (38%); high, 23 (40%) vs 10 (19%) Location: NR Diameter: 3.0 (IQR 2.1–3.6) vs 2.5 (2.2–3.5) cm

Table 1 (*continued*)

Study	Study design and country	GRADE	Study period and patients	Resection techniques	Preoperative characteristics	Tumor characteristics
Takagi 2017 [24]	RSC; Japan	Moderate	2014–2016 *N* = 282 TE: 48 SPN: 234	TE vs standard RPN	Male: 30 (63%) vs 172 (74%) Mean age: 57 ± 13 vs 58 ± 14 yr Mean eGFR: 71 ± 16 vs 66 ± 18	Complexity (RENAL score): low, 6 (13%) vs 97 (41%); intermediate, 28 (58%) vs 117 (50%); high, 14 (29%) vs 20 (9%) Location: NR Diameter: 3.4 ± 1.0 vs 2.8 ± 1.0 cm Clinical stage: NR
Lu 2019 [25]	RSC; China	Very low	2014–2017 *N* = 166 RPN: 72 TE: 94	Standard RPN vs TE	Male: 43 (59.7%) vs 62 (65.9%) Median age: 52.4 vs 51.4 yr Median eGFR: 99.4 vs 107.7	Complexity (PADUA score): 10, 53 (73.7%) vs 67 (71.3%); 11, 8 (11.1%) vs 14 (14.9%); 12, 6 (8.3%) vs 7 (7.4%); 13, 5 (6.9%) vs 6 (6.4%) Location: NR Diameter: 4.77 ± 1.03 vs 4.66 ± 1.14 cm
Guo 2019 [26]	RSC; China	Low	2015–2018 *N* = 130 2-mm ENR: 64 5-mm ENR: 67	2 vs 5 mm ENR	Male: 40 (62%) vs 41 (61%) Mean age: 54.79 ± 7.64 vs 55.21 ± 8.36 yr Mean eGFR: 42.47 ± 3.61 vs 43.92 ± 4.08 Mean ASA score: 1.9 ± 0.4 vs 1.8 ± 0.6	Complexity: RENAL score 8.6 ± 1.9 vs 8.4 ± 1.4 Location: NR Mean diameter: 3.9 vs 3.8 cm
Minervini 2020 [5]	PMC; Italy	Moderate	2014–2015 *N* = 507 AR: 207 Non-AR: 230	AR vs non-AR	Male: NR Age: 52 yr (IQR 53–70) overall Median eGFR: 86.5 overall Median CCI: 0 overall	Complexity (RENAL score): low, 41% vs 37%; intermediate, 35% vs 41%; high, 24% vs 22% Location: NR Diameter: 3.0 cm (IQR 2.5–4.3) overall Clinical stage: all cT1a
Culpan 2021 [27]	RMC; Turkey	Low	2011–2018 *N* = 1070 TE: 848 RPN: 222	TE vs standard RPN	Male: 548 (67%) vs 145 (65%) Mean age: 55.85 ± 11.85 vs 57.5 ± 11.84 yr Mean eGFR: 92.06 ± 25.21 vs 90.71 ± 22.96	Complexity (RENAL score): low, 551 (65%) vs 169 (76.5%); intermediate, 275 (32%) vs 52 (23%); high, 22 (3%) vs 1 (0.5%) Hilar location: 7 (0.8%) vs 4 (1.8%) Mean diameter: 3.4 vs 3.5 cm
Minoda 2021 [28]	RSC; Japan	Moderate	2013–2022 *N* = 90 [b] TE: 45 RPN: 45	TE vs standard RPN	Male: 31 (69%) vs 32 (67%) Mean age: 54 ± 14 vs 53 ± 13 yr Mean eGFR: 67 ± 17 vs 67 ± 19 ASA 1: 18% vs 24% ASA 2: 71% vs 67% ASA 3: 11% vs 9%	Complexity: RENAL score: 9.0 ± 1.8 vs 9.1 ± 1.5 Location: NR Mean diameter: 2.6 vs 2.7 cm
Zhao 2021 [29]	RSC; China	Low	2014–2018 *N* = 203 ERASE: 139 RPN: 64	Modified ERASE vs standard RPN	Male: 87 (63%) vs 42 (66%) Mean age: 56 ± 13 vs 54 ± 14 yr Mean eGFR: NR	Complexity: RENAL score 8.7 ± 1.2 vs 8.8 ± 1.2 Location: NR Mean diameter: 4.5 ± 1.0 vs 4.8 ± 1.1 cm Clinical stage: all cT1b
Patel 2022 [30]	RSC; USA	Low	2008–2020 *N* = 467 TE: 176 RPN: 291	TE vs standard RPN	Male: 112 (63.6%) vs 165 (56.7%) Median age: 59.3 vs 60.1 yr Median eGFR: 76.1 vs 78.2	Complexity: [RENAL score] TE vs RPN: low – 71 (40.4%) vs 125 (43.0%); intermediate – 81 (46.0%) vs 132 (45.3%); high – 8 (4.5%) vs 16 (5.5%); missing – 16 (9.1%) vs 18 (6.2%); Location: NR Diameter: 2.7 (2.0–3.5) vs 2.9 (1.9–3.9) cm

PN = partial nephrectomy; AR = anatomic resection (enucleation and enucleoresection); ASA = American Society of Anesthesiologists score; PMC = prospective multicenter study; PSC = prospective single-center study RMC = retrospective multicenter study; RSC = retrospective single-center study; NR = not reported; eGFR = estimated glomerular filtration rate (reported in ml/min/1.73 m^2); CCI = Charlson comorbidity index; ERASE = endoscopic robot-assisted simple enucleation; GRADE = Grading of Recommendations Assessment, Development and Evaluation; LAPSE = pure laparoscopic simple enucleation; OPN = open PN; RPN = robotic PN; RACP-RASE = robot-assisted simple enucleation with renal arterial cold perfusion; ENR = enucleoresection; TE = tumor enucleation; MM = minimal margin; SSC = superselective clamping; LC = learning curve; RTE = robotic TE; LTE = laparoscopic TE.

[a] After propensity score matching in an overall cohort of 351 patients.

[b] After propensity score matching in an overall cohort of 144 patients.

Readers should note that the descriptions provided are based on experts' opinions. In 2014, Minervini et al. [31,32] published and validated the surface-intermediate-base (SIB) margin scoring system in an attempt to standardize reporting of nephron-sparing resection techniques. The SIB score was externally validated by Antonelli et al. [33]. In this system, the surface of each area of the tumor (surface, intermediate, and base) is circumferentially analyzed, and

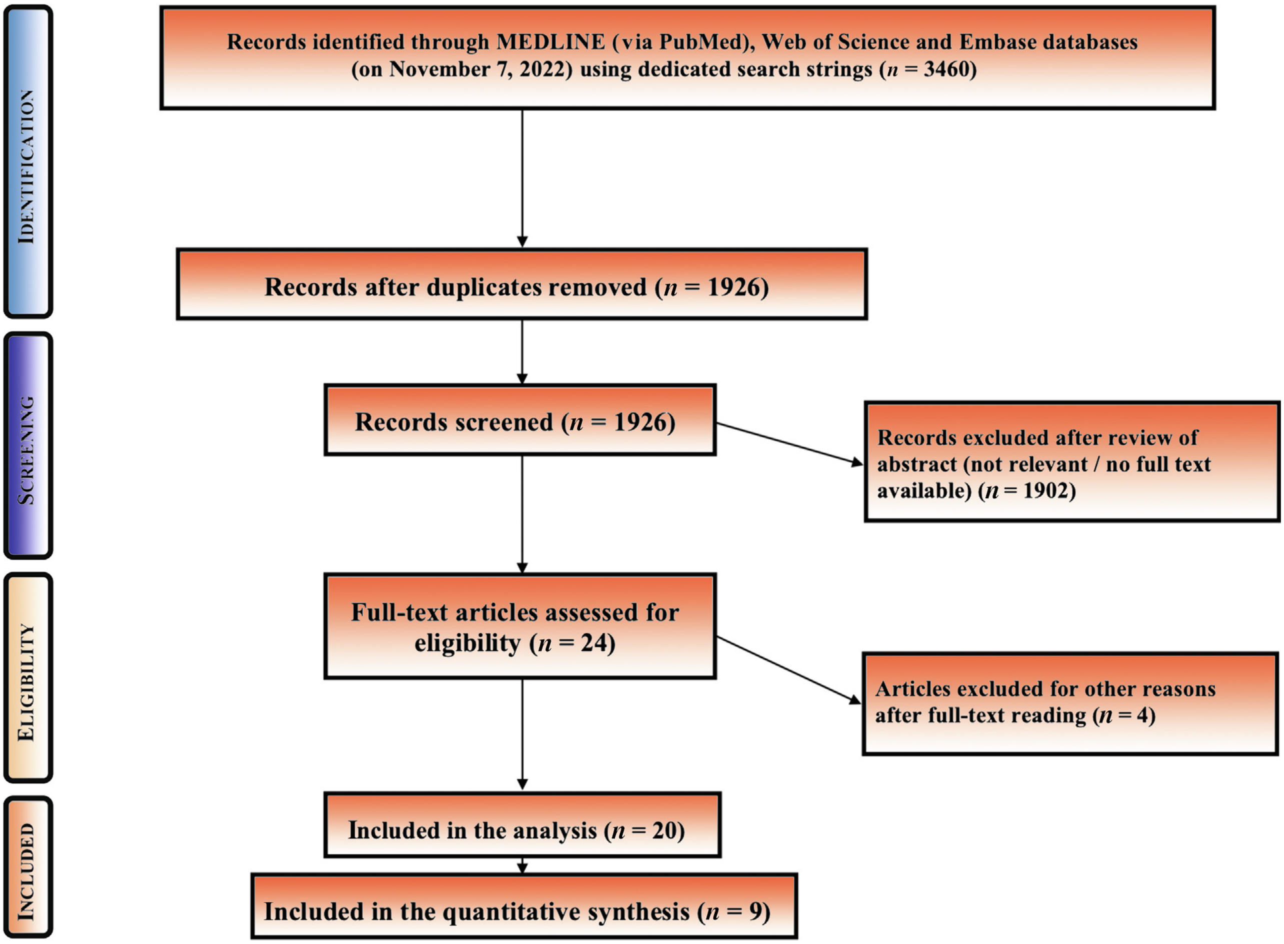


Fig. 1 – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

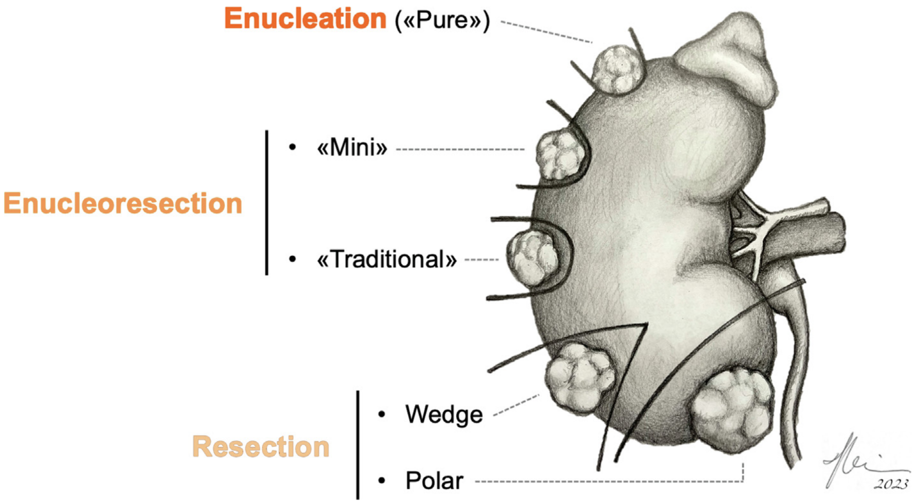


Fig. 2 – Sketch of resection techniques during robotic partial nephrectomy.

the minimal margin for each area is recorded and assigned a score of 0–2 points according to the thickness of the healthy peritumoral parenchyma. The score sum defines different resection techniques. On adopting the SIB score in clinical practice, Minervini et al. [5] found that the resection technique was a significant predictor of PSMs, grade 2 surgical complications, and trifecta achievement. Unfortunately, the SIB score has several limitations and is not very user-friendly. These limitations have prevented its widespread diffusion.

3.2. *Noncomparative studies*

Five studies analyzed the impact of the resection technique used on outcomes of interest. Mottrie et al. [12] reported on a series of 17 patients who underwent robot-assisted enucleoresection. The authors underlined that owing to compression of the tumor on the normal renal parenchyma, a pseudocapsule of healthy parenchyma a few millimeters away from the tumor usually offered a safe plane for blunt dissection. No patients had PSMs at final pathology.

Minervini et al. [13] described a series of 127 patients who underwent robot-assisted enucleation (median thickness of healthy margin 0.57 mm). The authors reported that a distinct peritumoral pseudocapsule was present in 121 tumors (95%). In terms of oncological outcomes, three patients had a PSM (2.4%), but no cases of recurrence at the enucleation site were recorded at median follow-up of 61 mo.

Mari et al. [14] studied the predictors of disease recurrence in a cohort of 259 patients who underwent enucleation according to the Florentine University endoscopic robot-assisted simple enucleation (ERASE) technique. Notably, the resection technique was classified according to the SIB score (only SIB 0–1 included in the analysis). The PSM rate was 2.7% (seven patients). Overall, three patients (1.1%) experienced local recurrence in the tumor resection bed at median follow-up of 36 mo (IQR 27–51).

Dong et al. [15] retrospectively analyzed a cohort of 146 patients with localized kidney cancer who underwent tumor enucleation performed via a minimally invasive laparoscopic approach (either pure or robot-assisted). Pseudocapsule invasion was reported for 50 tumors (34%) and PSMs were found in three of 146 tumors (2.1%). At median follow-up of 66 mo, two patients (1.4%) had experienced local recurrence.

Bertolo et al. [16] described a series of 11 patients who underwent off-clamp simple enucleation single-layer renorrhaphy RPN. The resection technique was categorized using the SIB score: eight patients (72.7%) underwent enucleation, two (18.2%) enucleoresection, and one (9.1%) standard resection. No patients had PSMs. The authors reported that enucleation had a synergistic effect in maximizing vision, notwithstanding the clampless approach. Moreover, 100% of the patients underwent single-layer renorrhaphy.

3.3. *Comparative studies*

Fifteen comparative studies were retrieved and involved different comparator arms were considered (Table 2). Satkunasivam et al. [17] reported a retrospective analysis of 179 patients undergoing anatomic RPN at a tertiary academic institution. Patients were grouped into three cohorts according to clamping management (super-selective clamping vs unclamped) and surgical experience (learning curve vs mature experience). The authors detailed the technique for “minimal-margin” PN performed for procedures without renal artery clamping. They concluded that the anatomic plane of dissection immediately adjacent to the tumor capsule (termed the minimal-margin plane) appears to be histologically and oncologically safe, with a lower risk of hemorrhage and higher likelihood of an off-clamp approach. The technical aim was to maintain a 1-mm sliver of parenchymal tissue on the tumor capsular surface rather than completely exposing the capsule, as would be the goal during enucleation. The percentage kidney tissue preserved was greater and the margin width was narrower with this technique ($p < 0.05$). At 1 mo after surgery, the median percentage reduction in estimated glomerular filtration rate (eGFR) was similar for the groups; however, new-onset chronic kidney disease (CKD) stage >3 occurred less frequently after the clampless minimal-margin approach [17].

Minervini et al. [18] conducted a retrospective analysis comparing patients treated with ERASE to patients treated with pure laparoscopic enucleation of a renal mass. The robotic approach reduced the need for clamping, ischemia time, blood loss, and length of stay. There was no significant difference in PSM rate (1.8% laparoscopy versus 2.2% robotic; $p = 0.4$). In a matched-pair analysis of 101 laparoscopic enucleations versus 101 ERASE procedures, Zhao et al. [19] found that the robotic approach was associated with shorter operative time, shorter warm ischemia time, and a lower rate of intraoperative complication, with similar PSM and recurrence rates.

Oh et al. [20] conducted a propensity score–matched study to compare open versus robotic PN with a focus on surgical margin width and multivariate logistic analysis to identify predictors of a peritumoral surgical margin of <1 mm. In both the unmatched and the matched cohorts, the mean peritumoral surgical margin was greater with the open approach. Multivariate analysis confirmed surgical approach as a significant factor in narrowing the surgical margin to <1 mm. After propensity score matching, the peritumoral healthy margin was wider after open PN (2.67 ± 2.14 mm) than after RPN (2.25 ± 2.03 mm; $p = 0.016$). The PSM rate was 1.8% for open PN versus 1.3% for RPN. At median follow-up of 48 mo, two patients who underwent open PN had experienced recurrence in the tumor bed.

Lu et al. [21] also conducted a propensity score–matched analysis to investigate differences in perioperative, functional, and oncological outcomes for robot-assisted simple enucleation with and without renal arterial cold perfusion. Although there was no difference in ischemia time, the change in eGFR significantly differed between the two groups at 3 mo and 12 mo ($p < 0.038$). Patients without cold perfusion were more likely to experience CKD upstaging (17% vs 41%; $p = 0.043$). On multivariable analysis, preoperative eGFR and the type of procedure were predictive factors for a >10% change in eGFR at 3 mo after surgery.

Campi et al. [22] performed a retrospective analysis comparing the outcomes of open versus RPN for highly complex renal masses with a focus on predictors of trifecta failure. Data for 113 patients were extracted from the prospectively maintained SIB International Consortium database (42% open PN versus 58% RPN). Resection techniques were classified as enucleation, enucleoresection, or resection. Trifecta outcomes were achieved in significantly more patients after RPN (70% vs 43%; $p = 0.004$). Multivariable analysis suggested that surgical approach (open versus robotic, OR 2.62, 95% CI 1.11–6.15; $p = 0.03$) and tumor complexity (OR for each additional PADUA score point 2.27, 95% CI

Table 2 – Summary of surgical outcomes in the comparative studies

Study	Surgical access	Ischemia type	RR and HA	Operative time (min)	WIT (min)	Surgical complications	Functional results	PSM rate (%)
Satkunasivam 2015 [17]	TPL/RPL	Group 1: SSC, LC experience Group 2: SSC, mature experience Group 3: minimal margin, clampless EUC: NR	RR: NR HA: NR	Group 1 vs 2 vs 3[a] 272 (126–507) vs 289 (133–534) vs 260 (87–516)	Group 1 vs 2 vs 3 NR	Group 1 vs 2 vs 3 EBL: 200 vs 225 vs 150 ml BT: 15 (21%) vs 14 (23%) vs 2 (4%) UL: 4 (5.7%) vs 0 vs 2 (4.0%); CD ≥1: 10 (14%) vs 5 (8%) vs 9 (18%)	Group 1 vs 2 vs 3 63 vs 74 vs 76 ml/min/1.73 m^2	Group 1 vs 2 vs 3 0 (0%) vs 2 (3%) vs 0 (0%)
Minervini 2015 [18]	TPL/RPL	Ischemia: on-clamp/ off-clamp EUC: yes	RR: NR HA: yes (TachoSil and FloSeal)	Lap TE vs ERASE 146.2 ± 45.3 vs 153.4 ± 50.1	Lap TE vs ERASE 20.3 ± 6.9 vs 17.3 ± 5.6	Lap TE vs ERASE EBL: 170 ± 130.6 vs 111 ± 95.0 ml BT: NR UL: 4 (6.3 %) vs 1 (1.0%) CD ≥1: 5 (7.9 %) vs 7 (6.9 %).	Lap TE vs ERASE Change in creatinine: 0.1 ± 0.2 vs 0.1 ± 0.2 mg/dl	Lap TE vs ERASE 1.8% vs 2.2%
Oh 2016 [20]	NR	Ischemia: NR EUC: NR	RR: NR HA: NR	OPN vs RPN 140.15 ± 46.83 vs 138.83 ± 72.44	OPN vs RPN 17.30 ± 7.37 vs 20.59 ± 7.61	OPN vs RPN EBL: 214.26 ± 202.66 vs 167.16 ± 236.63 ml BT: 12 (3.1%) vs 5 (1.6%) UL: NR CD ≥1: 40 (10.4%) vs 15 (4.7%)	OPN vs RPN NR	OPN vs RPN 7 (1.8%) vs 4 (1.7%)
Zhao 2018 [19]	TPL	Ischemia: on-clamp/ off-clamp EUC: yes	RR: single-layer, interrupted HA: NR	RPN vs LPN 171.9 ± 50.1 vs 188.2 ± 45.1	RPN vs LPN 20.9 ± 7.4 vs 24.2 ± 6.3	RPN vs LPN EBL: 174.2 vs 184.8 ml BT: NR; UL: NR CD 1–2: 27 (9.7%) vs 11 (10.5%) CD 3–4: 3 (1.1%) vs 2 (1.9%)	RPN vs LPN 94.9 vs 90.8 ml/min/1.73 m^2	RPN vs LPN 5 (1.8%) vs 3 (2.9%)
Lu 2021 [21]	TPL	Ischemia: NR EUC: NR	RR: double-layer, interrupted HA: no	cpERASE vs ERASE 264.1 ± 55.7 vs 206.9 ± 64	cpERASE vs ERASE 34.8 ± 9.4 vs 32.8 ± 7.2	cpERASE vs ERASE EBL: 208.3 ± 93.8 vs 230.7 ± 135.7 ml BT: NR; UL: NR CD ≥1: 13.8% vs 24.1%	cpERASE vs ERASE eGFR decrease [a]: −6.3 (−10.3 to −2.4) vs −12.0 (−17.5 to−6.7) ml/min/1.73 m^2	cpERASE vs ERASE 1 (3.4%) vs 0 (0%)
Campi 2022 [22]	TPL 23 (49%) for OPN vs 60 (91%) for RPN RPL 24 (51%) for OPN vs 6 (9%) for RPN	Ischemia: on-clamp EUC: NR	RR: NR HA: NR	OPN vs RPN [a] 135 (110–180) vs 150 (120–196)	OPN vs RPN [a] 23 (18–33) vs 18 (15–24)	OPN vs RPN EBL [a]: 200 (150–300) vs 150 (50–250) ml CD ≥3 surgical complications: 5 (10.6%) vs 2 (3.0%)	OPN vs RPN ΔGFR [a]: −12.8 (−25.8 to −1.7) vs −6.9 (−14.6 to −2.9) ml/min/1.73 m^2 pAKI: 20 (42.6%) vs 14 (21.2%)	OPN vs RPN 2 (4.3) vs 3 (4.5)
Comparison of TE versus standard PN								
Blackwell 2016 [23]	NR	Ischemia: on-clamp TE 25 (43.9%), standard RPN 52 (98.1%) EUC: NR	R: Double-layer; HA: NR.	TE vs RPN NR	TE vs RPN [a] 24.0 (20.0–29.0) vs 26.5 (21.5–29.0)	TE vs RPN EBL: NR; BT: NR; UL: NR CD 1/2/3: NR	TE vs RPN 73.3 vs 68.9 ml/min/1.73 m^2	TE vs RPN 0 vs 3 (5.7%)
Takagi 2017 [24]	NR	Ischemia: on-clamp EUC: no	RR: double-layer, running HA: yes (TachoSil)	TE vs RPN 189 ± 37 vs 193 ± 43	TE vs RPN 24 ± 12 vs 20 ± 6.4	TE vs RPN EBL: 129 ± 211 vs 117 ± 337 ml BT: 1 (2%) vs 2 (4%) UL: NR CD ≤2: 5 (11%) vs 9 (20%) CD 3: 2 (4%) vs 8 (18%)	TE vs RPN Decrease in eGFR (%): 5.6 ± 13 vs 12 ± 17	TE vs RPN 1 (2%) vs 0 (0%)
Lu 2019 [25]	TPL/RPL	Ischemia: on-clamp EUC: NR	RR: double-layer,	RPN vs TE	RPN vs TE	RPN vs TE	RPN vs TE	RPN vs TE

Table 2 (*continued*)

Study	Surgical access	Ischemia type	RR and HA	Operative time (min)	WIT (min)	Surgical complications	Functional results	PSM rate (%)
			interrupted HA: NR	121.3 ± 11.48 vs 107.1 ± 10.35	20.47 ± 3.46 vs 17.5 ± 3.69	EBL: 143.3 vs 90.8 ml BT: 4% vs 0% UL: 3% vs 0% CD 1: 2.8% vs. 2.1% CD 2: 11.1% vs. 2.1% CD 3: 2.8% vs 0%.	6-mo eGFR decrease: −3.8 vs −3.5 ml/min/1.73 m^2	1 (1.4%) vs 1 (1.1%)
Guo 2019 [26]	RPL	Ischemia: on-clamp EUC: no	RR: double-layer, running HA: no	2 vs 5 mm ER 81 ± 17.63 vs 79 ± 15.89	2 vs 5 mm ER 22.45 ± 5.08 vs 20.17 ± 4.7	2 vs 5 mm ER EBL: 77.41 ± 37.26 vs 75.38 ± 38.62; BT: NR UL: 0 vs 0 CD ≥1: 0 vs 0	2 vs 5 mm ER eGFR decrease: 11.48 ± 3.05 vs 20.53 ± 4.61 ml/min/1.73 m^2	2 vs 5 mm ER 0 (0%) vs 0 (0%)
Minervini 2020 [5]	NR	Ischemia: on-clamp EUC: yes	RR: NR HA: NR	TE vs ER vs RPN [a] 150 (110–190) vs 140 (100–176) vs 150 (114–180)	TE vs ER vs RPN [a] 17 (14–23) vs 18 (14–23) vs 17 (14–20)	TE vs ER vs RPN EBL [a]: 200 (100–300) vs 150 (80–300) vs 175 (50–180) ml BT: NR; UL: NR CD1: 11.7% vs 14.7% vs 9.9% CD2: 4.2% vs 10.7% vs 3.3% CD3: 3% vs 4% vs 5.5% CD4: 0% vs 0% vs 0%.	TE vs ER vs RPN eGFR loss at discharge [a]: 4.1 (1.9–13.8) vs 8.9 (0.0–21.1) vs 7.3 (0.0–19.2) ml/min/1.73 m^2	TE vs ER vs RPN 13 (4.9%) vs 15 (10%) vs 2 (2.2%)
Culpan 2021 [27]	NR	Ischemia: 251 (23.46%) off-clamp; 697 (65.14%) warm, 73 (6.82%) cold on-clamp EUC: NR	RR: NR HA: NR	TE vs RPN [a] 165 (110−180) vs 120 (90−180)	TE vs RPN >25 min WIT: 179 (21.5%) vs 23 (12.2%)	TE vs RPN EBL [a]: 180 (100−300) vs 200 (130−250) ml BT: NR; UL: NR CD ≥1: 79 (9.3%) vs 20 (9.0%)	TE vs RPN eGFR decrease >10%: 441 (52.0%) vs 133 (59.9%)	TE vs RPN 62 (7.3%) vs 13 (5,9%)
Minoda 2021 [28]	TPL/RPL	Ischemia: on-clamp EUC: yes	RR: double-layer, running HA: NR	TE vs RPN 140 ± 44 vs 167 ± 40	TE vs RPN 23 ± 14 vs 21 ± 8	TE vs RPN EBL: 56 ± 101 vs 86 ± 104 ml BT: NR; UL: NR CD ≥1: 0 (0%) vs 2 (4.4%)	TE vs RPN eGFR decline >10%: 12 (27%) vs 19 (42%)	TE vs RPN 3 (6.7%) vs 1 (2.2%)
Zhao 2021 [29]	TPL	Ischemia: on-clamp or off-clamp EUC: no	RR: single-layer, running HA: NR	ERASE vs RPN 197.7 ± 54.6 vs 215.6 ± 61.6	ERASE vs RPN 21.2 ± 6.4 vs 24.1 ± 6.9	ERASE vs RPN EBL: 230.5 ± 207.0 vs 269.8 ± 273.3 ml BT: NR; UL: NR CD ≤2: 13 (9.4%) vs. 7 (10.9%) CD >2: 1 (0.7%) vs. 2 (3.1%)	ERASE vs RPN Change in eGFR (%): −14.0 ± 18.7 vs −15.0 ± 16.1	ERASE vs RPN 2.2% vs 6.3%
Patel 2022 [30]	TPL/RPL	Ischemia: on-clamp in 108 (62.4) vs 274 (96.5) EUC: NR	RR: NR HA: yes	TE vs RPN [a] 151 (116−190) vs 212 (177−254)	TE vs RPN [a] 15 (10−22) vs 23 (16.5−29)	TE vs RPN EBL: 25 vs 150 ml BT: NR; UL: NR CD ≤2: 17 (9.7%) vs 60 (20.6%) CD >2: 2 (1.1%) vs 22 (7.6%).	TE vs RPN eGFR at 3–12 mo: 74.6 vs 68.1 ml/min/1.73 m^2	TE vs RPN 12 (8.5%) vs 8 (3.4%)

HA = hemostatic agent; RR = renorrhaphy; SSC = superselective clamping; LC = learning curve; EBL = estimated blood loss; EUC = early unclamping; CD = Clavien-Dindo complications; TE = tumor enucleation; ERASE = endoscopic robot-assisted simple enucleation; PN = partial nephrectomy; OPN = open PN; RPN = robotic PN; LPN = laparoscopic PN; cpERASE = endoscopic robot-assisted simple enucleation with cold arterial perfusion; ER = enucleoresection; NR = not reported; PSM = positive surgical margin; RPL = retroperitoneal; TPL = transperitoneal; WIT = warm ischemia time; ΔGFR = preoperative GFR − discharge GFR; pAKI = postoperative acute kidney injury; BT = blood transfusion; UL = urinary leakage.

[a] Median (interquartile range).

1.27–4.06; $p = 0.006$) were significant predictors of trifecta failure. The resection technique was not a predictor of PSMs, surgical complications, or trifecta achievement (contradicting prior findings by the same group [5]).

3.3.1. *Quantitative synthesis: enucleation versus resection*

Owing to the similarity of the treatment groups compared, nine studies focusing on differences between enucleation and standard resection were included in a quantitative synthesis [5,23–30]. The highest sample size was available for PSM analysis (1763 enucleation vs 1113 resection). Pooled analysis of data did not identify significant differences between enucleation and standard resection in operative time, warm ischemia time, estimated blood loss, transfusion rate, or the PSM rate. Conversely, significant differences favoring enucleation were found for clamping management (OR for renal artery clamping 3.51, 95% CI 1.13–10.88; $p = 0.03$), overall complications (OR for occurrence 0.55, 95% CI 0.34–0.87; $p = 0.01$), major complications (OR 0.39, 95% CI 0.19–0.79; $p = 0.009$), length of stay (WMD −0.72 d, 95% CI −0.99 to −0.45; $p < 0.001$), and decrease in eGFR (WMD −2.64 ml/min, 95% CI −5.15 to −0.12; $p = 0.04$; Fig. 3A, B).

3.4. Discussion

The first PN was performed in 1884 by Wells [34] to remove a perirenal fibrolipoma, followed by Czerny [35], who was the first to excise a renal neoplasm, in 1887. The intervention was initially received with much enthusiasm, but it was soon abandoned owing to excessive postoperative morbidity. Interest in PN as a surgical option in the treatment of renal masses was revived in 1950 by Vermooten [36], who suggested that PN could be a viable choice for peripheral renal carcinomas, even in patients with a normal contralateral kidney.

The Cleveland Clinic under the leadership of Novick pioneered PN as an option by demonstrating that although radical nephrectomy was preferred as the optimal curative therapy for patients with localized renal cell carcinoma and a normal contralateral kidney, PN could be considered as the treatment of choice for localized renal masses in patients with bilateral tumors, a solitary kidney, or kidney disease affecting the contralateral kidney [37]. Initially, the wider the margin of excision, the lower was the chance of leaving residual disease [3]. This can be accomplished when there is abundant healthy tissue (as in the bowel), but for PN a wider excision margin means greater loss of healthy parenchyma, and thus lower residual renal function [38].

While a minimum 1-cm margin during resection was suggested in early PN practice, contemporary studies indicate that the thickness of the healthy peritumoral tissue excised during PN may not impact oncological outcomes if no tumor remains [39,40]. Such revolutionary thinking paved the way to greater diffusion of “anatomic” minimal-margin/no-margin PN resection techniques, namely enucleoresection and enucleation, that showed comparable oncological outcomes to those with standard PN and radical nephrectomy [41,42]. Apart from the comparable oncological efficacy to standard resection, some enucleation advocates argued that tumor enucleation may have additional distinct benefits over “standard” PN. Specifically, it was suggested that enucleation allows the surgeon to excise the tumor under optimal visualization of its contours, potentially reducing the risk of PSMs and of violation of the urinary collecting system and/or renal sinus. In line with this, some studies (including results from the present review) identified tumor enucleation as a factor predicting avoidance of renal artery clamping [16,17,43] and a “facilitator” of “nephron-sparing” renorrhaphy.

There are no certainties about the impact of clamping management on renal function [44], but a more anatomic resection strategy such as enucleation, which follows a relatively avascular dissection plane, could facilitate minimal renal reconstruction, with benefits that include preservation of renal function and minimization of perioperative complications, as shown by recent literature reviews [45,46].

However, skepticism regarding tumor enucleation remained. Some groups published histopathological analyses for patients who required salvage nephrectomy for ipsilateral recurrences. Antonelli et al. [47] found that such recurrences were mostly caused by incomplete resection of the primary tumor or (in a minority of cases) local spread of the tumor via microvascular embolization, which leads to relapse in the same portion of the kidney as the primary tumor. The issue of microembolization of cancer cells was also raised by Bertolo et al. [48] after an analysis of histopathological data for a salvage nephrectomy case series from the Cleveland Clinic.

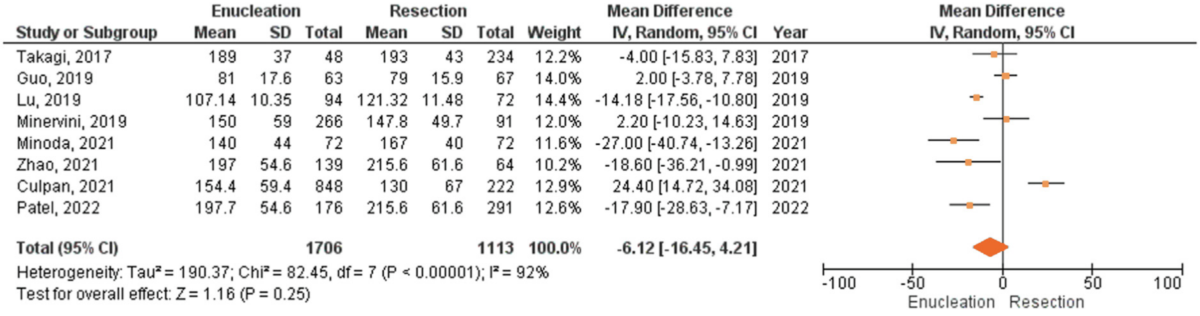
Of paramount importance is the systematic review by Minervini et al. [49], whose pooled analysis of 11 000 patients showed that enucleation was at least noninferior to standard PN in terms of the PSM rate and tumor bed recurrences. A more recent prospective multicenter study led by the University of Florence showed that resection techniques does impact perioperative (and early functional and oncological) outcomes in patients with localized renal masses. The resection technique (as assessed using the SIB score) was the only significant predictor of PSM status and one of the strongest predictors of grade ≥2 surgical complications and trifecta achievement [5].

The most interesting results from our review corroborate previous findings. We focused on RPN, which is now the preferred approach in centers where the technology is available. First, according to the pooled analysis, PSM rates did not differ between enucleation and standard resection (138/1763, 7.8% vs 77/1166, 6.6%; OR for PSM 1.89, 95% CI 0.57–6.29; $p = 0.3$), confirming data from single reports.

Impressively, quantitative synthesis showed that when enucleation was performed, a clampless approach (as aforementioned) was chosen more often and the risk of overall and major complications was lower. This probably contributed to the shorter length of stay favoring enucleation. Finally, enucleation was associated with a lower decrease in eGFR (WMD −2.64 ml/min, 95% CI −5.15 to −0.12; $p = 0.04$) although we share the view that the clinical relevance of this finding may be limited. Information about new-onset CKD events would undoubtedly have been a more reliable outcome measure.

We acknowledge that our study has limitations. First, specific to the topic investigated, nomenclature issues

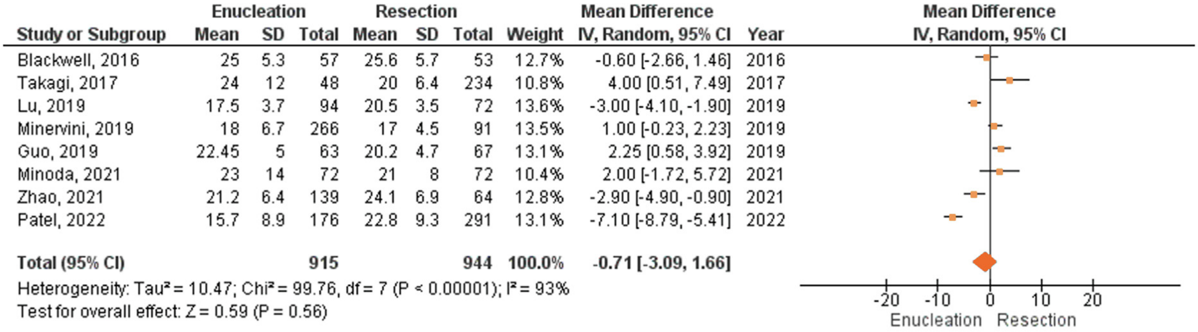
Operative time



Study or Subgroup	Enucleation Mean	SD	Total	Resection Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Takagi, 2017	189	37	48	193	43	234	12.2%	-4.00 [-15.83, 7.83]	2017
Guo, 2019	81	17.6	63	79	15.9	67	14.0%	2.00 [-3.78, 7.78]	2019
Lu, 2019	107.14	10.35	94	121.32	11.48	72	14.4%	-14.18 [-17.56, -10.80]	2019
Minervini, 2019	150	59	266	147.8	49.7	91	12.0%	2.20 [-10.23, 14.63]	2019
Minoda, 2021	140	44	72	167	40	72	11.6%	-27.00 [-40.74, -13.26]	2021
Zhao, 2021	197	54.6	139	215.6	61.6	64	10.2%	-18.60 [-36.21, -0.99]	2021
Culpan, 2021	154.4	59.4	848	130	67	222	12.9%	24.40 [14.72, 34.08]	2021
Patel, 2022	197.7	54.6	176	215.6	61.6	291	12.6%	-17.90 [-28.63, -7.17]	2022
Total (95% CI)			**1706**			**1113**	**100.0%**	**-6.12 [-16.45, 4.21]**	

Heterogeneity: Tau² = 190.37; Chi² = 82.45, df = 7 (P < 0.00001); I² = 92%
Test for overall effect: Z = 1.16 (P = 0.25)

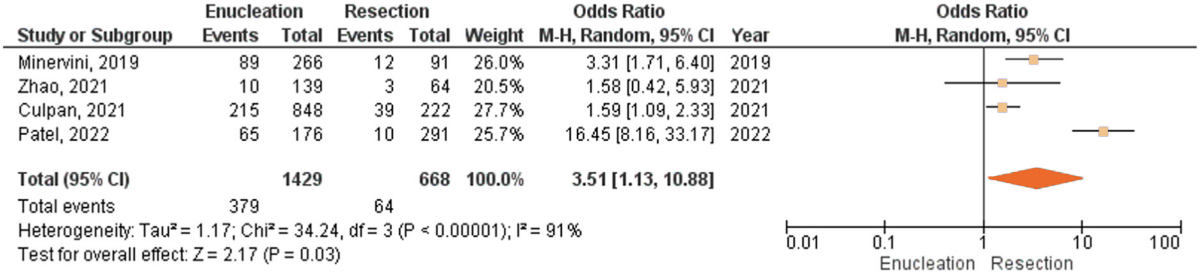
Ischemia time



Study or Subgroup	Enucleation Mean	SD	Total	Resection Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Blackwell, 2016	25	5.3	57	25.6	5.7	53	12.7%	-0.60 [-2.66, 1.46]	2016
Takagi, 2017	24	12	48	20	6.4	234	10.8%	4.00 [0.51, 7.49]	2017
Lu, 2019	17.5	3.7	94	20.5	3.5	72	13.6%	-3.00 [-4.10, -1.90]	2019
Minervini, 2019	18	6.7	266	17	4.5	91	13.5%	1.00 [-0.23, 2.23]	2019
Guo, 2019	22.45	5	63	20.2	4.7	67	13.1%	2.25 [0.58, 3.92]	2019
Minoda, 2021	23	14	72	21	8	72	10.4%	2.00 [-1.72, 5.72]	2021
Zhao, 2021	21.2	6.4	139	24.1	6.9	64	12.8%	-2.90 [-4.90, -0.90]	2021
Patel, 2022	15.7	8.9	176	22.8	9.3	291	13.1%	-7.10 [-8.79, -5.41]	2022
Total (95% CI)			**915**			**944**	**100.0%**	**-0.71 [-3.09, 1.66]**	

Heterogeneity: Tau² = 10.47; Chi² = 99.76, df = 7 (P < 0.00001); I² = 93%
Test for overall effect: Z = 0.59 (P = 0.56)

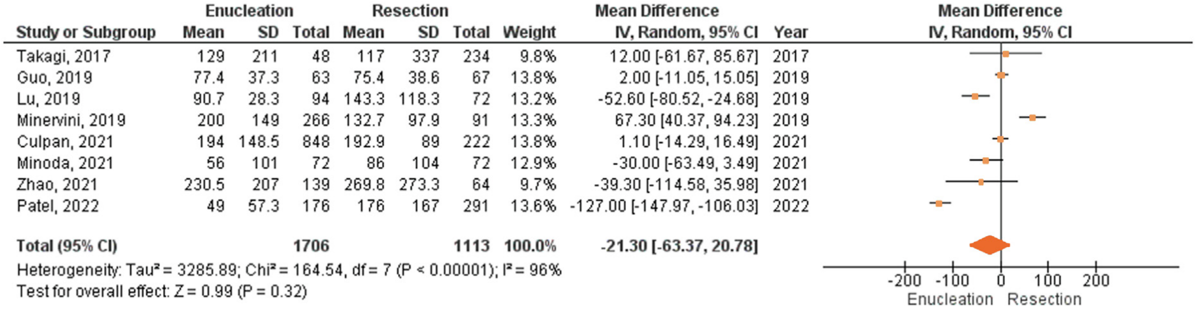
Clampless approach



Study or Subgroup	Enucleation Events	Total	Resection Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Minervini, 2019	89	266	12	91	26.0%	3.31 [1.71, 6.40]	2019
Zhao, 2021	10	139	3	64	20.5%	1.58 [0.42, 5.93]	2021
Culpan, 2021	215	848	39	222	27.7%	1.59 [1.09, 2.33]	2021
Patel, 2022	65	176	10	291	25.7%	16.45 [8.16, 33.17]	2022
Total (95% CI)		**1429**		**668**	**100.0%**	**3.51 [1.13, 10.88]**	
Total events	379		64				

Heterogeneity: Tau² = 1.17; Chi² = 34.24, df = 3 (P < 0.00001); I² = 91%
Test for overall effect: Z = 2.17 (P = 0.03)

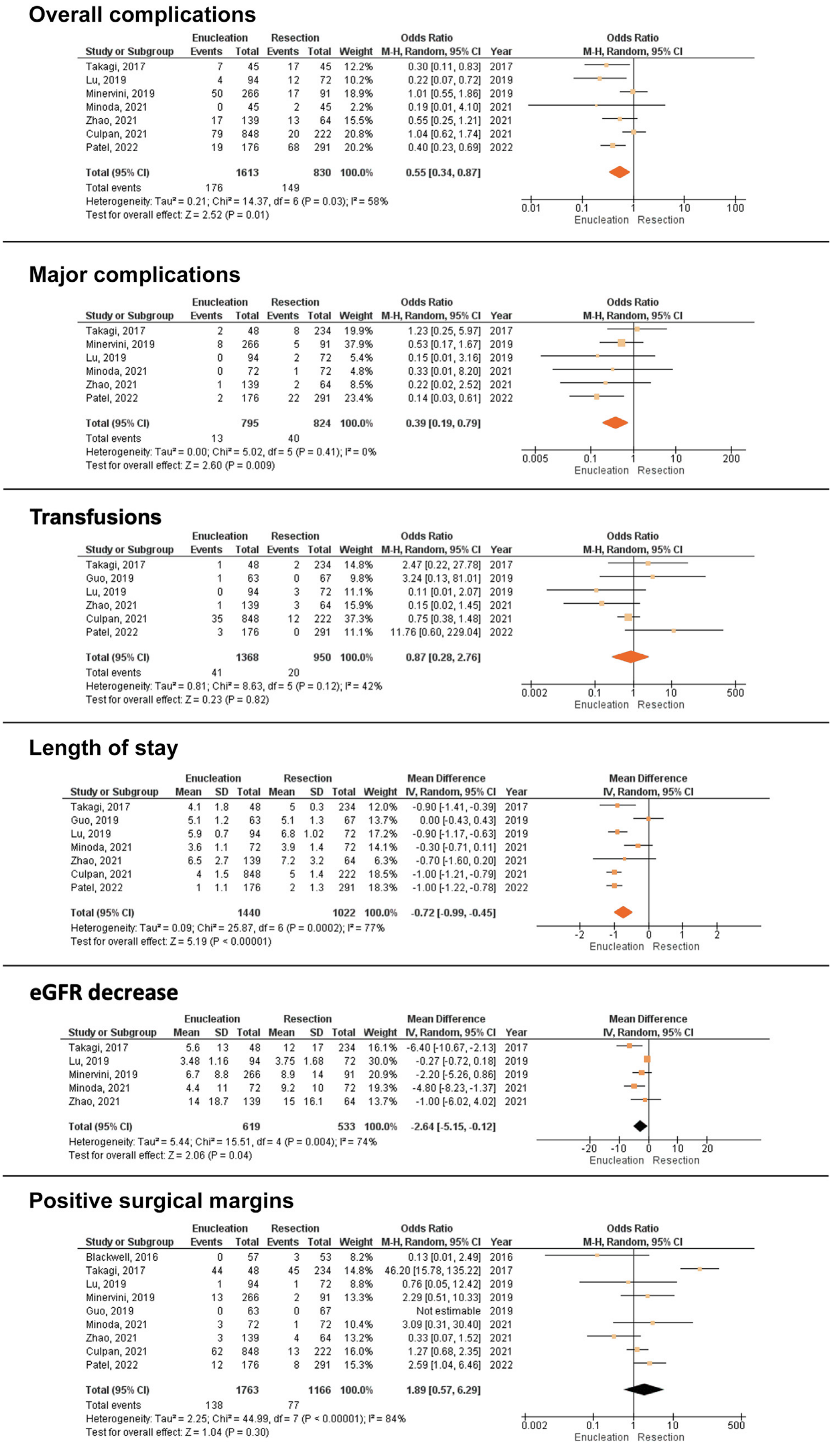
Estimated blood loss



Study or Subgroup	Enucleation Mean	SD	Total	Resection Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Takagi, 2017	129	211	48	117	337	234	9.8%	12.00 [-61.67, 85.67]	2017
Guo, 2019	77.4	37.3	63	75.4	38.6	67	13.8%	2.00 [-11.05, 15.05]	2019
Lu, 2019	90.7	28.3	94	143.3	118.3	72	13.2%	-52.60 [-80.52, -24.68]	2019
Minervini, 2019	200	149	266	132.7	97.9	91	13.3%	67.30 [40.37, 94.23]	2019
Culpan, 2021	194	148.5	848	192.9	89	222	13.8%	1.10 [-14.29, 16.49]	2021
Minoda, 2021	56	101	72	86	104	72	12.9%	-30.00 [-63.49, 3.49]	2021
Zhao, 2021	230.5	207	139	269.8	273.3	64	9.7%	-39.30 [-114.58, 35.98]	2021
Patel, 2022	49	57.3	176	176	167	291	13.6%	-127.00 [-147.97, -106.03]	2022
Total (95% CI)			**1706**			**1113**	**100.0%**	**-21.30 [-63.37, 20.78]**	

Heterogeneity: Tau² = 3285.89; Chi² = 164.54, df = 7 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.99 (P = 0.32)

Fig. 3 – Comparison of enucleation versus (standard) resection during robotic partial nephrectomy: pooled analysis of (A) intraoperative and (B) postoperative data. SD = standard deviation; IV = inverse variance; CI = confidence interval; df = degrees of freedom; M-H = Mantel-Haenszel method; eGFR = estimated glomerular filtration rate.



Overall complications

	Enucleation		Resection			Odds Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Takagi, 2017	7	45	17	45	12.2%	0.30 [0.11, 0.83]	2017
Lu, 2019	4	94	12	72	10.2%	0.22 [0.07, 0.72]	2019
Minervini, 2019	50	266	17	91	18.9%	1.01 [0.55, 1.86]	2019
Minoda, 2021	0	45	2	45	2.2%	0.19 [0.01, 4.10]	2021
Zhao, 2021	17	139	13	64	15.5%	0.55 [0.25, 1.21]	2021
Culpan, 2021	79	848	20	222	20.8%	1.04 [0.62, 1.74]	2021
Patel, 2022	19	176	68	291	20.2%	0.40 [0.23, 0.69]	2022
Total (95% CI)		**1613**		**830**	**100.0%**	**0.55 [0.34, 0.87]**	
Total events	176		149				

Heterogeneity: Tau² = 0.21; Chi² = 14.37, df = 6 (P = 0.03); I² = 58%
Test for overall effect: Z = 2.52 (P = 0.01)

Major complications

	Enucleation		Resection			Odds Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Takagi, 2017	2	48	8	234	19.9%	1.23 [0.25, 5.97]	2017
Minervini, 2019	8	266	5	91	37.9%	0.53 [0.17, 1.67]	2019
Lu, 2019	0	94	2	72	5.4%	0.15 [0.01, 3.16]	2019
Minoda, 2021	0	72	1	72	4.8%	0.33 [0.01, 8.20]	2021
Zhao, 2021	1	139	2	64	8.5%	0.22 [0.02, 2.52]	2021
Patel, 2022	2	176	22	291	23.4%	0.14 [0.03, 0.61]	2022
Total (95% CI)		**795**		**824**	**100.0%**	**0.39 [0.19, 0.79]**	
Total events	13		40				

Heterogeneity: Tau² = 0.00; Chi² = 5.02, df = 5 (P = 0.41); I² = 0%
Test for overall effect: Z = 2.60 (P = 0.009)

Transfusions

	Enucleation		Resection			Odds Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Takagi, 2017	1	48	2	234	14.8%	2.47 [0.22, 27.78]	2017
Guo, 2019	1	63	0	67	9.8%	3.24 [0.13, 81.01]	2019
Lu, 2019	0	94	3	72	11.1%	0.11 [0.01, 2.07]	2019
Zhao, 2021	1	139	3	64	15.9%	0.15 [0.02, 1.45]	2021
Culpan, 2021	35	848	12	222	37.3%	0.75 [0.38, 1.48]	2021
Patel, 2022	3	176	0	291	11.1%	11.76 [0.60, 229.04]	2022
Total (95% CI)		**1368**		**950**	**100.0%**	**0.87 [0.28, 2.76]**	
Total events	41		20				

Heterogeneity: Tau² = 0.81; Chi² = 8.63, df = 5 (P = 0.12); I² = 42%
Test for overall effect: Z = 0.23 (P = 0.82)

Length of stay

	Enucleation			Resection				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Takagi, 2017	4.1	1.8	48	5	0.3	234	12.0%	-0.90 [-1.41, -0.39]	2017
Guo, 2019	5.1	1.2	63	5.1	1.3	67	13.7%	0.00 [-0.43, 0.43]	2019
Lu, 2019	5.9	0.7	94	6.8	1.02	72	17.2%	-0.90 [-1.17, -0.63]	2019
Minoda, 2021	3.6	1.1	72	3.9	1.4	72	14.1%	-0.30 [-0.71, 0.11]	2021
Zhao, 2021	6.5	2.7	139	7.2	3.2	64	6.3%	-0.70 [-1.60, 0.20]	2021
Culpan, 2021	4	1.5	848	5	1.4	222	18.5%	-1.00 [-1.21, -0.79]	2021
Patel, 2022	1	1.1	176	2	1.3	291	18.3%	-1.00 [-1.22, -0.78]	2022
Total (95% CI)			**1440**			**1022**	**100.0%**	**-0.72 [-0.99, -0.45]**	

Heterogeneity: Tau² = 0.09; Chi² = 25.87, df = 6 (P = 0.0002); I² = 77%
Test for overall effect: Z = 5.19 (P < 0.00001)

eGFR decrease

	Enucleation			Resection				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Takagi, 2017	5.6	13	48	12	17	234	16.1%	-6.40 [-10.67, -2.13]	2017
Lu, 2019	3.48	1.16	94	3.75	1.68	72	30.0%	-0.27 [-0.72, 0.18]	2019
Minervini, 2019	6.7	8.8	266	8.9	14	91	20.9%	-2.20 [-5.26, 0.86]	2019
Minoda, 2021	4.4	11	72	9.2	10	72	19.3%	-4.80 [-8.23, -1.37]	2021
Zhao, 2021	14	18.7	139	15	16.1	64	13.7%	-1.00 [-6.02, 4.02]	2021
Total (95% CI)			**619**			**533**	**100.0%**	**-2.64 [-5.15, -0.12]**	

Heterogeneity: Tau² = 5.44; Chi² = 15.51, df = 4 (P = 0.004); I² = 74%
Test for overall effect: Z = 2.06 (P = 0.04)

Positive surgical margins

	Enucleation		Resection			Odds Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Blackwell, 2016	0	57	3	53	8.2%	0.13 [0.01, 2.49]	2016
Takagi, 2017	44	48	45	234	14.8%	46.20 [15.78, 135.22]	2017
Lu, 2019	1	94	1	72	8.8%	0.76 [0.05, 12.42]	2019
Minervini, 2019	13	266	2	91	13.3%	2.29 [0.51, 10.33]	2019
Guo, 2019	0	63	0	67		Not estimable	2019
Minoda, 2021	3	72	1	72	10.4%	3.09 [0.31, 30.40]	2021
Zhao, 2021	3	139	4	64	13.2%	0.33 [0.07, 1.52]	2021
Culpan, 2021	62	848	13	222	16.0%	1.27 [0.68, 2.35]	2021
Patel, 2022	12	176	8	291	15.3%	2.59 [1.04, 6.46]	2022
Total (95% CI)		**1763**		**1166**	**100.0%**	**1.89 [0.57, 6.29]**	
Total events	138		77				

Heterogeneity: Tau² = 2.25; Chi² = 44.99, df = 7 (P < 0.00001); I² = 84%
Test for overall effect: Z = 1.04 (P = 0.30)

Fig. 3 (*continued*)

remain and require attention. For example, "traditional" sharp resection (healthy parenchymal margin >5 mm) and "ultra-thin" parenchymal resection include many subtle variations in technique, and some authors who call their technique “enucleoresection” are actually performing enucleation. Second, the studies included in the review exhibit great heterogeneity, and most were single-center experiences in referral institutions. Mastery of RPN is an ongoing learning process for which prior experience does count [50]. Expert surgeons are more likely to perform enucleation than beginners, and we were unable to exclude the possibility that the potential advantages found for enucleation could be related to surgeon expertise rather than the resection technique.

Heterogeneity differed considerably among the outcome measurements considered in the pooled analysis, ranging from 0% for major complications to 96% for estimated blood loss. A possible explanation may be that all the studies included were nonrandomized, and thus were less standardized.

Third, low-level evidence was obtained. This should not be considered as a limitation in methodology but rather a limitation of the literature. For some endpoints such as renal function, very nuanced differences were found, so the results must be interpreted with caution, considering the relevance versus the significance of the finding itself. Moreover, the time points at which renal function was assessed ranged between 3 and 12 mo in the studies. Finally, very interesting outcomes such as tumor rupture were anecdotally reported.

Notwithstanding these limitations, our review provides a comprehensive overview of the literature regarding resection techniques during RPN. For the first time, a pooled analysis was conducted to compare perioperative outcomes of robotic enucleation versus standard resection.

Some research gaps were highlighted that represent a basis for future research. We anticipate that a more comprehensive model to catch the overall picture of tumor resection during RPN should pair the final resection technique used with the a priori intent (ie, the resection strategy).

Exciting studies in prostate cancer are emerging on assessment of the surgical margin and resection bed based on prostate-specific membrane antigen (PSMA)-expressing cancer cells and in vivo fluorescence imaging to guide additional resection of residual fluorescent tissue after prostatectomy. The same concept could be translated to the excision of renal masses, as PSMA is highly expressed on the cell surface of the microvasculature of several other solid tumors, including renal cell carcinoma [51]. This would be a potentially interesting imaging target for real-time monitoring of surgical margin status during PN.

4. Conclusions

Our analysis confirms that there is still heterogeneity in the reporting of resection techniques used during PN. The urological community must improve the quality of reporting and the research produced accordingly. Positive margins are not an issue related to the specific technique. Focusing on studies comparing standard resection versus enucleation, a pooled analysis revealed an advantage with tumor enucleation in terms of avoidance of renal artery clamping, overall and major complications, length of stay, and renal function. These data should be considered when planning the strategy for tumor resection in RPN.

Author contributions: Riccardo Bertolo had 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: Bertolo.
Acquisition of data: Pecoraro, Carbonara, Diana, Muselaers.
Analysis and interpretation of data: Bertolo.
Drafting of the manuscript: Bertolo.
Critical revision of the manuscript for important intellectual content: Campi, Marchioni.
Statistical analysis: Carbonara.
Obtaining funding: None.
Administrative, technical, or material support: Amparore.
Supervision: Mir, Antonelli, Badani, Breda, Challacombe, Kaouk, Mottrie, Porpiglia, Porter, Minervini.
Other: None.

Financial disclosures: Riccardo Bertolo certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

***Funding/Support and role of the sponsor*:** None.

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Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2023.03.008.

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