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A Systematic Review and Meta-Analysis of Minimally Invasive Partial Nephrectomy Versus Focal Therapy for Small Renal Masses

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Background: Minimally invasive partial nephrectomy (MIPN) and focal therapy (FT) are popular trends for small renal masses (SRMs). However, there is currently no systematic comparison between MIPN and FT of SRMs. Therefore, we systematically study the perioperative, renal functional, and oncologic outcomes of MIPN and FT in SRMs.

Methods: We have searched the Embase, Cochrane Library, and PubMed for articles between MIPN (robot-assisted partial nephrectomy and laparoscopic partial nephrectomy) and FT {radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation (CA), irreversible electroporation, non-thermal [irreversible electroporation (IRE)] ablation, and stereotactic body radiation therapy (SBRT)}. We calculated pooled mean difference (MD), odds ratios (ORs), and 95% confidence intervals (CIs) (CRD42021260787).

Results: A total of 26 articles (n = 4,420) were included in the study. Compared with MIPN, the operating time (OP) of FT had significantly lower (SMD, −1.20; CI, −1.77 to −0.63; I^2 = 97.6%, P < 0.0001), estimated blood loss (EBL) of FT had significantly less (SMD, −1.20; CI, −1.77 to −0.63; I^2 = 97.6%, P < 0.0001), length of stay (LOS) had shorter (SMD, −0.90; CI, −1.26 to −0.53; I^2 = 92.2%, P < 0.0001), and estimated glomerular filtration rate (eGFR) of FT was significantly lower decrease (SMD, −0.90; CI, −1.26 to −0.53; I^2 = 92.2%, P < 0.0001). However, FT possessed lower risk in minor complications (Clavien 1–2) (OR, 0.69; CI, 0.45 to 1.07; I^2 = 47%, P = 0.023) and overall complications (OR, 0.71; CI, 0.51 to 0.99; I^2 = 49.2%, P = 0.008). Finally, there are no obvious difference between FT and MIPN in local recurrence, distant metastasis, and major complications (P > 0.05).

Conclusion: FT has more advantages in protecting kidney function, reducing bleeding, shortening operating time, and shortening the length of stay. There is no difference in local recurrence, distant metastasis, and major complications. For the minimally invasive era, we need to weigh the advantages and disadvantages of all aspects to make comprehensive choices.

Systematic Review Registration: https://www.crd.york.ac.uk/PROSPERO/#recordDetails, identifier PROSPERO (CRD42021260787).

Keywords: minimally invasive, focal therapy, ablation techniques, kidney, nephrectomy, meta-analysis

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INTRODUCTION

Small renal masses (SRMs) represent a group of heterogeneous tumors covering the entire metastatic potential, including malignant, indolent, and benign tumors. Among them, kidney cancer already accounts for 2%–3% of all cancers, and the incidence is increasing year by year (1, 2). The American Urological Association (AUA) and European Association of Urology (EAU) guidelines both recommend partial nephrectomy for SRMs (3). In addition, minimally invasive partial nephrectomy (MIPN) including robot-assisted partial nephrectomy (RAPN) and laparoscopic partial nephrectomy (LPN) is the current trend. However, OPN is selected, most of which are intraoperatively converted from LPN or RAPN to OPN for SRMs. In addition, it has recently been fully developed in the clinic.

With the clinical application of ablation techniques, focal therapy (FT) {radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation (CA), irreversible electroporation, and non-thermal [irreversible electroporation (IRE)] ablation} has been fully developed (4). FT has the advantages of less trauma, less bleeding, and shorter hospital stay (5). The guidelines of AUA and EUA recommend FT replacing PN for kidney mass < 3 cm in size, and it is suitable for patients with kidney masses who are forbidden to operate or have serious comorbidities (6, 7). Therefore, the comparative study on MIPN and FT is very meaningful. However, there are main systematic reviews about ablative therapies versus partial nephrectomy for small renal masses at present (8). Therefore, the purpose of this study is to compare the perioperative period, renal function, and oncologic outcomes of MIPN and FT in SRMs.

METHODS

Protocol and Guidance

The study was performed according to Preferred Reporting Items for Systematic Reviews and the meta-analysis (PRISMA) (9). The protocol for this review has been registered on PROSPERO (CRD42021260787).

Search Strategy

This study involved literature published in the Embase, PubMed, and Cochrane Library up to January 26, 2022. We defined the eligibility criteria according to the population (P), intervention (I), comparator (C), outcome, and study design approach (O). P, the patients with SRMs; I, undergoing MIPN; C, FT was performed as a comparator; O, one or more of the following outcomes: perioperative, renal functional, and oncologic outcomes. The search terms included (robot-assisted partial nephrectomy OR robotic partial nephrectomy OR RAPN OR RPN OR laparoscopic partial nephrectomy OR LPN OR Minimally invasive) AND ["Renal Neoplasm" (MeSH) OR renal masses] AND ["radiofrequency ablation" (MeSH) OR "Cryoablation" (MeSH) OR microwave ablation OR RFA OR irreversible electroporation OR CRA OR MWA OR IEP OR "Stereotactic body radiation therapy" (MeSH) OR SBRT]. The search strategy was not limited by language or year. It was not requested by the ethics or institutional review committee due to the study being designed as a systematic review and meta-analysis.

Inclusion and Exclusion Criteria

We have included the literature by the following criteria. Comparative data were available on the treatment of SRMs through MIPN (RAPN and LPN) and FT (RFA, CA, MWA, and IRE). Outcome indexes should include at least one of the following: perioperative period, renal function, and oncologic outcomes. Any study that did not confirm the above inclusion criteria was excluded.

Data Extraction and Outcome Measures

Two researchers (LY and LX) independently have reviewed the retrieved literature by the inclusion and exclusion criteria. The third researcher (ZZJ) was asked to participate in the discussion to decide whether to include when disagreements were encountered. The extracted data included the first author, publication, country, study type, group, age (if mentioned), follow-up, female proportion, and renal nephrectomy score (**Table 1**).

Statistical Analysis

Statistical analysis was performed by Review Manager, version 5.2 (The Cochrane Collaboration, Oxford, UK) Stata v.12.0 (Stata Corp LLC, College Station, TX, USA). For this meta-analysis, if the heterogeneity test was $I^2 > 50\%$, $P < 0.1$, then we used the random effect model; if the heterogeneity test was $I^2 < 50\%$, $P > 0.1$, then we used the fixed utility model. The combined r-values and 95% confidence intervals (CIs) of each study were calculated, and the forest map displayed the characteristics of each study result. The quality of the included literature was evaluated using the Newcastle–Ottawa scale (NOS). The Begg's and Egger's tests were used to test the publication bias. The $P < 0.05$ was indicated statistically significant.

RESULTS

Eligible Studies and Study Characteristics

We initially searched 1,206 records. A total of 385 literature studies that were published repeatedly and cross-published were deleted. After reading the title and abstract, 760 articles were excluded. After the remaining 61 pieces of literature were searched for full text, reading, and quality assessment, 26 pieces of literature (10–35) (4,420 participants: MIPN: 2031 vs. FT: 2389) were eventually included (**Figure 1**). The detailed information of this literature was listed in **Table 1**.

Abbreviations: MIPN, minimally invasive partial nephrectomy; FT, focal therapy; SRMs, small renal masses; RFA, radiofrequency ablation; MWA, microwave ablation; CA, cryoablation; IRE, irreversible electroporation; SBRT, stereotactic body radiation therapy; MD, mean difference; ORs, odds ratios; CIs, confidence intervals; AUA, American Urological Association; EAU, European Association of Urology; RAPN, robot-assisted partial nephrectomy; LPN, laparoscopic partial nephrectomy; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; NOS, Newcastle–Ottawa scale; OP, operating time; EBL, estimated blood loss; LOS, length of stay.

TABLE 1 | Characteristics of the included studies.

Author	Year	End points	Publication	Country	Study design	Study interval	Group	Cases	Malignant tumour, n (%)	Tumour grade (1-2),n (%)	Clinical T1, n (%)	Clavien grade (0-2), n (%)	Age	Male proportion(%)	BMI (Body mass index) (kg/m2)	Comorbidities ASA(%)	tumour size (cm)	Pathology (Ma/Be/Un)	R.E.N.A.L Nephrometry score	Follow-up (months)	Confounders adjustment	NOS score (max:9)
Bensalah (10)	2007	Survival, recurrence, complications	BJU international	USA	R	2000-2006	LPN	50	41 (82)	37 (90)			56.5 ± 11.7	62	31.1 ± 8.0	≥3(53%)	2.6 ± 0.9	N/A	N/A	25	No	8
							LRFA	38	29 (80)	20 (95)			62 ± 17.5	58	29.6 ± 4.8	≥ 3(26%)	2.3 ± 0.7			15		
Bertolo (11)	2019	Survival, recurrence, complications, renal function	Urologic Oncology	USA	R	2006-2016	RAPN	65			65(100)	16 (25)	79.3 ± 3.3	66	27.4 ± 4.9	3.0 (0.5)	2.9 ± 1.0	54/11/0	6.9 ± 1.9	37 (29-44)	No	7
							CA	65			65(100)	5 (8)	79.3 ± 4.1	60	27.9 ± 5.9	2.9 (0.6)	3.0 ±1.0	48/17/0	6.4 ± 2.0	46 (38-53)		
Bianchi, L (12).	2021	Survival, recurrence, complications, renal function	Int J Urol	Italy	R	2007-2019	MIPN	137	2.4 (2–3)				72 (62–77)	66.4	26 (24–29)		2.4 (2–3)	107/30/0		52 (32–99)	Yes (propensity score matching)	7
							Ablation	137	2.3 (1.8–2.9)				72 (65–79)	65.7	26 (24–28)		2.3 (1.8–2.9)	106/19/12		62 (47–79)		
Bird (13)	2009	Survival, recurrence, complications, renal function	Journal of Endourology	USA	R	2002-2007	LPN	33	20 (60.6)				57.8 (27–77)	55	28.45	2.2	3.1	.20/13/0	N/A	27 (6–58)	No	7
							LRFA	36	26 (72.3)				75.2 (56–86)	61	30.08	2.8	2.8	26/13/0		12 (6–23)		
Caputo (14)	2017	Survival, recurrence, complications	European Urology	USA	P	1999-2014	RAPN	31	28 (90)	8 (36.5)	31 (100)	30 (96.8)	61 (52–68)	67	30.6 (26.6–35.4)	3 (2–3)	5.0 (4.5–5.6)	28/3/0	9.0 (8–10)	13.0 (3.19–19.2)	Yes (propensity score matching)	8
							CA	31	22 (71)	12 (42.6)	31 (100)	27 (87.1)	68 (64–76)	81	30.6 (26.3–37.4)	3 (3–3)	4.3 (4.2–4.7)	.22/8/1	8.0 (6–9)	30.1 (13.2–64.0)		
Desai (15)	2005	Survival, recurrence, complications	Urology	USA	P	1999-2003	LPN	153					60.59 ± 13.19	58	29.06 ± 6.42	≥3(46)	2.25 ± 0.67	N/A	N/A	5.8 (1–36)	No	6
							LCA	89					65.55 ± 12.69	69	27.43 ± 5.59	≥3(75)	2.05 ± 0.56			24.6 (1–60)		
Emara (16)	2014	Survival, recurrence, complications, renal function	BJU international	UK	P	2010-2012	RAPN	47	33 (70)				60.5 (38–80)	80	N/A	N/A	3.278 ± 1.787	33/14/0	5.77 ± 0.25	16.50 ± 0.946	No	8
							CA	56	39 (70)				69.75 (42–90)	66			2.559 ± 0.958	.9/9/8	5.75 ± 0.23	31.30 ± 1.802		
Fossati (17)	2015	Survival, recurrence, complications, renal function	European urology focus	Italy	R	2000-2013	MIPN	206	153 (74)			194 (94)	60 (51–70)	69	26 (23–28)	≥3(17)	2.5 (2.0–3.4)	153/53/0	N/A	43	No	8
							LCA	166	105 (63)			136 (82)	66 (57–73)	73	25 (23–29)	≥3(30)	2.0 (1.5–2.5)	105/43/18		39		
Garcia, R. G (18).	2021	Recurrence, complications	CardioVascular and Interventional Radiology	Brazil	R	2008-2017	RAPN	69			69 (100)	2 (3)	54.8 ± 11.9	72.4	27.5 ± 3.8	≥3(0)	N/A	N/A	N/A	22.1	No	7
							PCA	63			63 (100)	0 (0)	62.5 ± 14.1	76.2	28.3 ± 4.5	≥3(24.5)				22.1		

(Continued)

TABLE 1 | Continued

Author	Year	End points	Publication	Country	Study design	Study interval	Group	Cases	Malignant tumour, n (%)	Tumour grade (1-2),n (%)	Clinical T1, n (%)	Clavien grade (0-2), n (%)	Age	Male proportion(%)	BMI (Body mass index) (kg/m2)	Comorbidities ASA(%)	tumour size (cm)	Pathology (Ma/Be/Un)	R.E.N.A.L Nephrometry score	Follow-up (months)	Confounders adjustment	NOS score (max:9)
Guillotreau (19)	2012	Recurrence, complications, renal function	European Urology	USA	R	1998-2010	RAPN	210	156 (74)			36 (17)	57.8 ± 11.8	58	30.1 ± 6.4	≥3(51)	2.4 ± 0.8	N/A	N/A	4.8 (1–7.9)	Yes (multivariable logistic regression for complications)	8
							LCA	226	181 (77)			19 (8)	67.4 ± 11.3	71	29.3 ± 6.2	≥3(80)	2.2 ± 0.9			44.5 (8.7–66.8)		
Haber (20)	2012	Survival, recurrence, complications, renal function	BJU international	USA	R	1998-2008	LPN	48			48 (100)		60.6 ± 13.7	52.1	30.1 ± 6.2	2.7 ± 0.5	3.2 ± 1.33	31/17/0	N/A	42.7 ± 30.8	No	8
							LCA	30			30 (100)		60.9 ± 11.4	73.3	31.5 ± 5.8	2.7 ± 0.8	2.6 ± 1.08	25/5/0		60.2 ± 46.3		
Haramis (21)	2012	Survival, recurrence, complications	Journal of Laparoendoscopic and Advanced Surgical Techniques	USA	R	2005-2008	LPN	92				10 (10.9)	58.8 (37–85)	60.8	N/A	N/A	1.9 (0.3–4.5)	N/A	N/A	21.8 (1–48)	No	6
							LCA	75				5 (0.07)	69.2 (19–84)	62.7		1.9 (1–3)	2.0 (0.4–7.5)			14 (1–34)		
Ji (22)	2016	Recurrence, complications	Urologia internationalis	China	R	2006-2015	LPN	74					57.3 (25–76)	55.4	N/A	1.7 (1–3)	2.9 (1.4–3.8)	103/2/0	N/A	2.2 (1.7–3.3)	No	6
							LRFA	105					64.2 (42–81)	62.9		2.3 (1–3)	2.2 (1.7–3.3)	71/3/0		78 (60–106)		
Kim (23)	2015	Survival, recurrence, complications, renal function	Asian journal of surgery	South Korea	R	2005-2011	RAPN	27					60.33 ± 15.61	70.4	25.9 ± 3.4	N/A	1.77 ± 0.96	24/3/0	6.5 ± 1.7	10.9 ± 7.0	Yes (propensity score matching)	6
							RFA	27					58.67 ± 11.60	81.5	26.6 ± 3.1		1.8 ± 0.81	.3/2/24	6.3 ± 1.6	16.7 ± 10.5		
Kiriluk (24)	2011	Complications, renal function	Journal of Endourology	USA	P	2002-2008	LPN	51	41 (80.3)			6 (11.8)	66.0 (23–83)	51	29.1 (18.2–24)	N/A	2.27 (0.80–5.10)	N/A	N/A	18.3 (13.0–26.8)	No	7
							LAT	51	26 (50.9)			12 (23.5)	65.7 (27–75)	51	30.0 (12.1–56.9)		2.35 (0.99–4.90)			27.9 (0.4–40.0)		
Lian (25)	2010	Recurrence, complications, renal function	Chinese journal of surgery	China	R	2005-2009	LPN	29					61 (55-68)	66	N/A	N/A	2.8 (2.0-4.5)	N/A	N/A	27 (3-36)	No	6
							LCA	18					63 (41-73)	78			2.9 (1.5-5.0)			16 (6-21)		
Link (26)	2006	Recurrence	Journal of Endourology	USA	R	2004-2005	LPN	217					N/A	N/A	N/A	N/A	2.6 ± 1.3	N/A	N/A	N/A	No	7
							LCA	28									2.4 ± 0.9					
Liu (27)	2021	Survival, recurrence, complications, renal function	Diagnostics	China	R	2008, 2015	RAPN	55	32 (58.2)		53 (96.4)	0 (0)	57.27 ± 13.28	52.7	25.29 ± 4.58	≥3(23.6)	4.06 ± 2.01	N/A	N/A	33.20 ± 19.55	Yes: matching	7
							LCA	55	27 (49.1)		54 (98.2)	3 (5.5)	59.44 ± 14.77	52.7	25.04 ± 4.23	≥3(20)	3.86 ± 2.13			54.96 ± 34.59		

(Continued)

TABLE 1 | Continued

Author	Year	End points	Publication	Country	Study design	Study interval	Group	Cases	Malignant tumour, n (%)	Tumour grade (1-2),n (%)	Clinical T1, n (%)	Clavien grade (0-2), n (%)	Age	Male pro-portion(%)	BMI (Body mass index) (kg/m2)	Comorbidities ASA(%)	tumour size (cm)	Pathology (Ma/Be/Un)	R.E.N.A.L Nephrometry score	Follow-up (months)	Confounders adjustment	NOS score (max:9)
O'Malley (28)	2007	Recurrence, complications	BJU International	USA	R	2003-2005	LPN	15					75.7 ± 4.6	79	27.1 ± 3.9	≥3(53)	2.5 ± 1.0	N/A	N/A	9.83 ± 8.8	Yes: matching	8
							LCA	15					76.1 ± 4.5	57	29.1 ± 6.8	≥3(62)	2.7 ± 1.3			11.9 ± 7.2		
Pantelidou (29)	2016	Recurrence, complications, renal function	CardioVascular and Interventional Radiology	UK	R	2005-2013	RAPN	63	59 (93.7)			10 (15.9)	54 ± 7	N/A	N/A	2 (2–3)	2.88 ± 0.13	63/0/0	7.38 ± 0.16	18.5 (6.2–29.5)	No	7
							RFA	63	63 (100)			4 (6.3)	61 ± 21			2 (2–3)	2.11 ± 0.19	59/0/4	7.38 ± 0.16	47.5 (11.8–80.2)		
Park (30)	2018	Survival, recurrence, complications	European radiology	Republic of Korea	R	2008-2016	RAPN	63	54 (85.7)			3 (4.8)	57.7 ± 10.8	75	N/A	1.8 ± 0.3	2.0 ± 0.6	63/0/0	7.1 ± 1.7	24.6 (1-90)	Yes: matching	8
							RFA	63	48 (76.2)			3 (4.8)	57.1 ± 13.1	65		1.8 ± 0.7	2.1 ± 0.5	63/0/0	7.2 ± 1.5	21 (1-65)		
Tanagho (31)	2013	Recurrence, complications, renal function	Journal of Endourology	USA	R	2007-2012	RAPN	233	80 (52.3)				57.4 ± 11.9	54.5	30.1 ± 6.0	N/A	2.9 ± 1.5	185/48/0	7.3 ± 1.9	21.9 ± 18.8	No	
						2000-2003	CA	267	185 (79.4)				69.3 ± 11.0	61	30.4 ± 7.8		2.5 ± 1.0	80/73/114	6.4 ± 1.7	39.8 ± 34.3		
Turna (32)	2009	Survival, recurrence, complications, renal function	The Journal of urology	USA	R	1997-2006	LPN	36	23 (63.8)				60.3 ± 15.5	58	30.5 ± 7.1	≥3(66.7)	3.7 ± 1.9	N/A	N/A	80	No	8
							RFA	36	22 (73.3)				64.1 ± 11.1	64	31.3 ± 5.7	≥3(77.7)	2.5 ± 1.1			80		
Uemura, T (33).	2021	Survival, recurrence, complications, renal function	In Vivo	Japan	R	2016-2019	RAPN	78	58 (74.3)		78 (100)	76 (97.4)	61 (52-69)	63	23 (21-25)	≥3(1.3)	1.9 (1.5-2.3)	N/A	≥10(3.8)	18.5 (12-30)	No	7
							PCA	48	41 (85.4)		48 (100)	47 (97.9)	78 (70-82)	41	23 (21-26)	≥3(33.3)	2.6 (2.0-3.4)		≥10(10.8)	12 (6-32)		
Yanagisawa (34)	2020	Survival, recurrence, complications, renal function	Urologic oncology	Japan	R	2011-2019	LPN	90	65 (72)		90 (100)	87 (96.7)	69.5 (63-75)	81	N/A	N/A	28.8 ± 9.5	88/0/2	6 (5-8)	18	Yes: matching	7
							PCA	90	88 (97.8)		90 (100)	89 (98.9)	68.5 (61 –76)	76			27.6 ± 9.7	65/25/0	6 (5-7)	26.5		
Yu (35)	2020	Survival, recurrence, complications, renal function	Radiology	China	R	2006-2017	LPN	185			185 (100)		60.4 ± 14.1	74.6	N/A	N/A	2.3 ± 0.9	185/0/0	N/A	40.6 (25.1–63.4)	Yes: matching	8
							MWA	185			185 (100)		63.2 ± 15.2	74			2.3 ± 0.5	185/0/0		42.0 (23.5–69.3)		

Matching: 1 - Age; 2 - BMI; 3 - ASA; 4 - Charlson; 5 - Gender; 6 - Pathological stage; 7 - Urinary diversion type. RARC, robot-assisted partial nephrectomy; LPN, laparoscopic partial nephrectomy; RFA, Radiofrequency ablation; CRA, Cryoablation; MWA, Microwave ablation; RCT, randomized controlled trial; R, Retrospective; P, Prospective; NA, data not available; NOS, score; Newcastle-Ottawa Scale score.

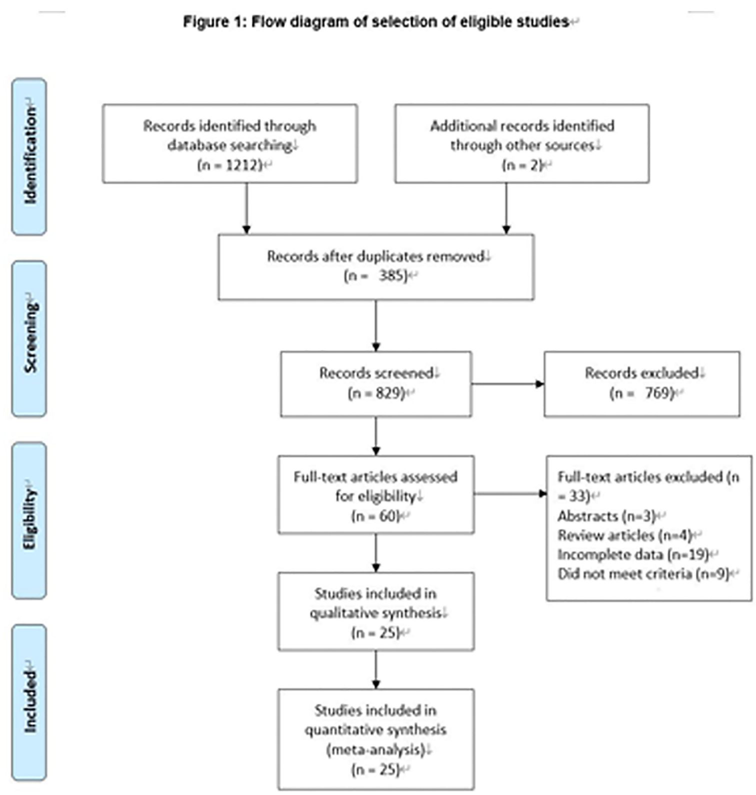

FIGURE 1 | Flowchart for records selection process of the meta-analysis [According to PRISMA template: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal. Pmed 1000097].

Perioperative Outcomes

Data on OP were reported in 17 studies (10, 11, 15, 17, 18, 20, 22, 24–28, 30–32, 34, 35). Compared with MIPN, patients who underwent FT had significantly lower OP (SMD, −1.20; CI, −1.77 to −0.63; I^2 = 97.6%, P < 0.0001) (**Figure 2A**). Owing to high heterogeneity (I^2 = 95%), we chose subgroup analysis. Compared with FT, patients who underwent LPN had significantly higher OP (SMD, −1.14; CI, −1.26 to −1.02; I^2 = 97.6%, P < 0.0001) and patients who underwent RAPN had significantly higher OP (SMD, −0.67; CI, −0.83 to −0.51; I^2 = 97.5%, P < 0.0001) (**Figure 2B**). Sensitivity analysis and subgroup analysis cannot reduce heterogeneity.

We included 13 studies (11, 15–17, 20, 22, 24, 25, 27, 28, 31, 32, 35) about EBL. Compared with MIPN, patients who underwent FT had significantly less EBL (SMD, −0.90; CI, −1.26 to −0.53; I^2 = 92.2%, P < 0.0001) (**Figure 2C**). Owing to high heterogeneity (I^2 = 92.2%), we chose subgroup analysis. Compared with FT, patients who underwent LPN had significantly higher EBL (SMD, −0.97; CI, −1.36 to −0.58; I^2 = 87.8%, P < 0.0001) and patients who underwent RAPN had significantly higher EBL (SMD, −1.00; CI, −1.44 to −0.55; I^2 = 73.4%, P = 0.01) (**Figure 2D**). We subgroup analysis by nephropathy recently published 2022 back to 2017 (5 years) vs. older studies. There is only subgroup analysis by nephropathy recently published in 2022 back to 2017 (5 years) (SMD, −0.95; CI, −1.11 to −0.78; I^2 = 26.8%, P = 0.247) vs. older studies (SMD, −0.44; CI, −0.56 to −0.32; I^2 = 92.2%, P = 0.0001) difference here for estimated blood loss (EBL). Sensitivity analysis cannot reduce heterogeneity.

We included 18 studies (10, 11, 13, 15–18, 20, 22–28, 30, 32, 34) on LOS. Compared with MIPN, patients who underwent FT had significantly less LOS (SMD, −0.90; CI, −1.26 to −0.53; I^2 = 92.2%, P < 0.0001) (**Figure 2E**). Owing to high heterogeneity (I^2 = 92.2%), we chose subgroup analysis. Compared with FT, patients who underwent RAPN had significantly higher LOS (SMD, −0.86; CI, −1.26 to −0.46; I^2 = 90.1%, P < 0.0001) and patients who underwent LPN had significantly higher LOS (SMD, −1.23; CI, −2.68 to 0.22; I^2 = 98.4%, P < 0.0001) (**Figure 2F**). Sensitivity analysis cannot reduce heterogeneity.

Compared with MIPN, patients who underwent FT had significantly less minor complication (Clavien 1–2) (OR, 0.69; CI, 0.45 to 1.07; I^2 = 47%, P = 0.023) (**Figure 2G**) and overall complication (OR, 0.71; CI, 0.51 to 0.99; I^2 = 49.2%, P = 0.008) (**Figure 2H**). There is a similarity between MIPN and FT for major complications (Clavien 3–5) (OR, 0.91; CI, 0.60 to 1.39; I^2 = 0%, P = 0.504) (**Figure 2I**).

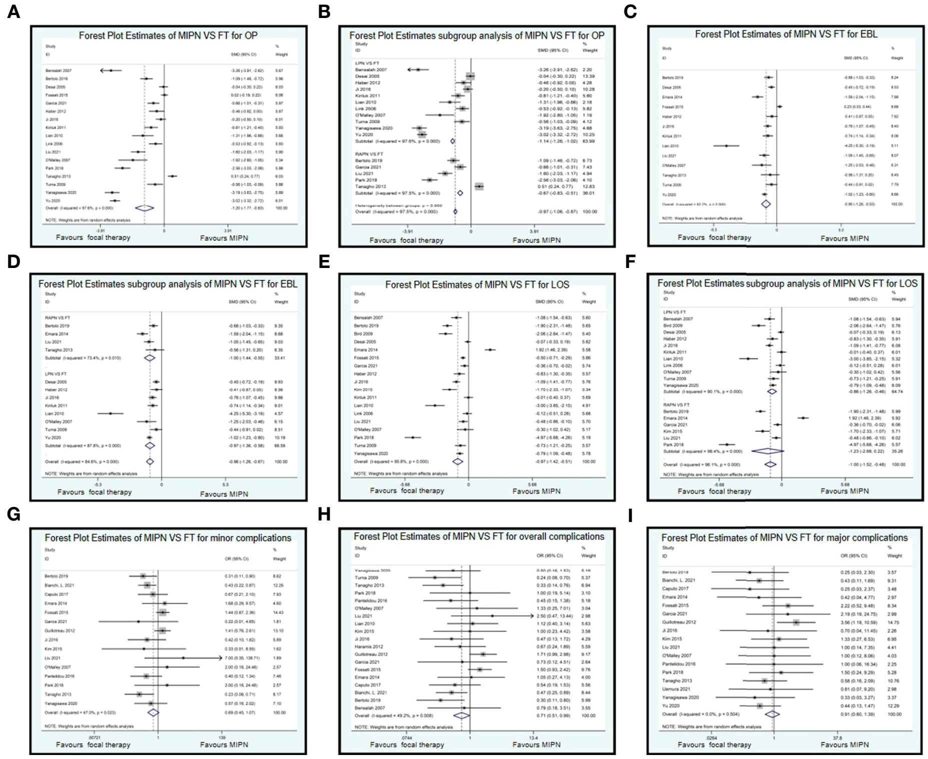

FIGURE 2 | Forest plots of perioperative outcomes: perioperative outcomes. Forest Plot Estimates of MIPN VS FT for OP **(A)**, EBL **(C)**, LOS **(E)**, minor complications **(G)**, overall complications **(H)**, and major complications **(I)**. Forest Plot Estimates subgroup analysis of MIPN VS FT for OP **(B)**, EBL **(D)**, and LOS **(F)**. MIPN, minimally invasive partial nephrectomy; FT, focal therapy; OP, operating time; EBL, estimated blood loss; LOS, length of stay.

Renal Functional Outcomes

For the functional results, we conducted a systematic analysis of eGFR. Data on eGFR were reported in seven studies. Compared with MIPN, patients who underwent FT had significantly reduced in eGFR (SMD, −0.94; CI, −1.32 to −0.57; I^2 = 83.9%, P < 0.0001) (**Figure 3A**). Owing to high heterogeneity (I^2 = 83.9%), we chose sensitivity analysis. After omitting the studies by Bensalah et al. (10), Kim et al. (23), and Tanagho et al. (31), as samples that were left out, the pooled results change substantially, but the heterogeneity was significantly reduced (SMD, −0.850; CI, −1.050 to −0.650; I^2 = 5.1%, P = 0.367) (**Figure 3B**).

Oncological Outcomes

The median or mean follow-up period of oncological outcomes of MIPN was 2.2 to 42.7 months, and FT was 14 to 78 months. Fourteen studies recorded on local recurrence rate, and six studies recorded on distant metastasis rate. There is a similarity between MIPN and FT for local recurrence rate (OR, 4.54; CI, 2.59 to 7.96; I^2 = 1.6%, P = 0.431) (**Figure 4A**) and distant metastasis rate (OR, 2.37; CI, 0.87 to 6.47; I^2 = 29.1%, P = 0.217) (**Figure 4B**).

Publication Bias

We conducted publication bias on more than 15 included studies using Egger's test. For OP, Egger's test results revealed that t = −2.39, P = 0.051 in **Supplementary Figure 1A** and funnel plots in **Supplementary Figure 1B**. For LOS, Egger's test results revealed that t = −1.73, P = 0.106 in **Supplementary Figure 1C** and funnel plots in **Supplementary Figure 1D**. For overall complication, Egger's test results revealed that t = 1.11, P = 0.281 in **Supplementary Figure 1E** and funnel plots in **Supplementary Figure 1F**. For major complications (Clavien 3–5), Egger's test results revealed that t = 0.97, P = 0.345 in **Supplementary Figure 1G** and funnel plots in **Supplementary Figure 1H**. There is no publication bias in the above.

DISCUSSION

In recent years, with the development of minimally invasive technology, SRMs were mainly treated by MIPN. For the clinical application of ablation technology, SRM ablation therapy has thus entered a new era (36, 37). The purpose of SRMs by MIPN or FT was to treat tumors while reducing perioperative complications, protecting the function of the kidney, and decreasing the postoperative recurrence rate (38). Therefore, the best treatment plan depends on the perioperative period, renal function, and tumor outcome. At present, there are few reports on the relationship between MIPN and FT.

MIPN has replaced the traditional radical nephrectomy with the increase of SRMs patients' willingness to protect the kidney

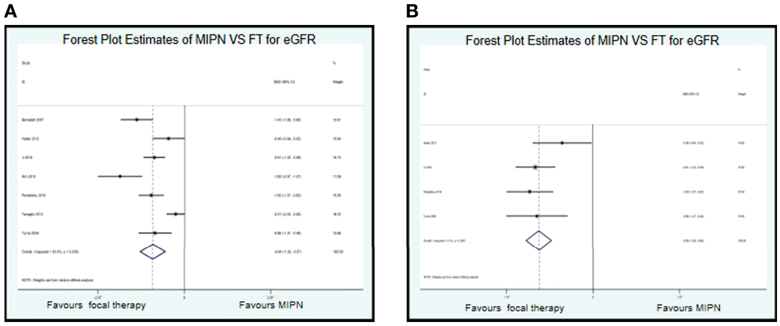

FIGURE 3 | Forest plots of perioperative outcomes: renal functional outcomes. Forest Plot Estimates of MIPN VS FT for eGFR **(A)** (I2=83.9%) and **(B)** (I2=5.1%). MIPN, minimally invasive partial nephrectomy; FT, focal therapy.

and the progress of corresponding surgical techniques in urology. A study has concluded that it is no statistically significant difference between MIPN and radical nephrectomy in terms of tumor control effects (39). At the same time, MIPN not only preserves the patient's nephrons but also is minimally invasive. Therefore, MIPN has become the main treatment for SRMs and early renal cancer. However, because MIPN requires renal artery block during the operation, the long-term renal function damage caused by this has also become a deficiency of MIPN (40–42). There have always been controversies regarding the treatment of SRMs between FT and MIPN, but unfortunately, due to the shortcomings of retrospective research, the level of credibility of the relevant conclusions is not high. To our knowledge, this study provides a new systematic review and meta-analysis comparing MIPN and FT for SRMs. Because of the lack of RCTs, we have investigated 25 non-randomized observational studies comparing MIPN and FT. The primary endpoint is the oncology outcome (local tumor recurrence and distant metastasis). The secondary endpoints are renal function and perioperative outcomes. Because of the short follow-up period, the meta-analysis of CSS and OS is inappropriate. However, a multi-center retrospective analysis showed that RAPN has good long-term oncologic and functional outcomes of the procedure, which duplicate those achieved in historical series of laparoscopic surgery (43).

The meta-analysis emphasizes that FT has a disadvantage in Oncological control compared to MIPN. Compared with patients who received MIPN, patients who have received FT had an OR of 2.43 for distant metastases and an OR of 6.59 for local recurrence. For the reasons, on the one hand, the overall follow-up period of the oncologic outcomes in the FT group is long, which may lead to a relatively high recurrence rate, especially metastasis rate. The different follow-up periods between MIPN and FT affect both distant metastasis rate and local recurrence rate. In addition, considering the secondary efficacy, which is the confirmed oncologic outcomes after the second FT, the risk of recurrence can be reduced (44). In one study, compared with MIPN, secondary FT seemed to be effective for cancer control and the metastasis rate was not high (45). However, there is no second FT in the included literature. Interestingly, matching studies with similar basic characteristics showed no difference in local recurrence rates between MIPN and FT (23, 29, 35). On the other hand, the firing diameter of FT covers the tumor edge 0.5–1 cm (46). In some anomalistic tumors, FT cannot guarantee complete coverage of the entire tumor. MIPN only needs to ensure that the tumor

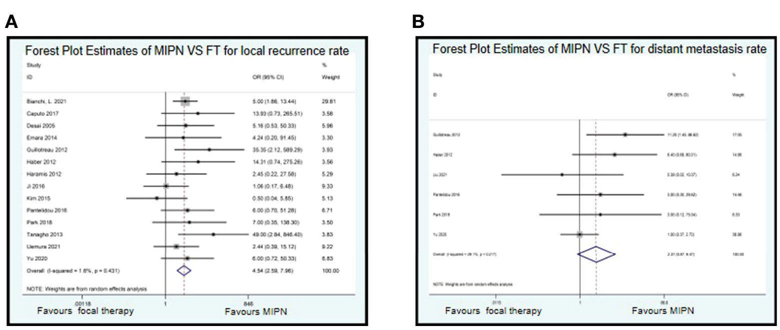

FIGURE 4 | Forest plots of perioperative outcomes: renal functional outcomes. Forest Plot Estimates of MIPN VS FT for local recurrence rate **(A)** and distant metastasis rate **(B)**. MIPN, minimally invasive partial nephrectomy; FT, focal therapy.

capsule is intact. Several studies have confirmed that MIPN is more effective in local recurrence rate and distant metastasis rate compared with FT (20, 35).

Conversely, for the meta-analysis results, we mainly describe the perioperative outcomes of MIPN and FT in SRMs. Patients who underwent FT had significantly lower OP of MD (60.34 min), lower EBL of MD (50.28 ml), and LOS of MD (1.95 day) compared with MIPN. For the renal functional outcomes, patients who underwent FT had significantly lower eGFR of WD (8.56 ml/ min/1.73m^2) compared with MIPN. There are two main reasons that FT has a lower OP, BEL, LOS, and eGFR than MIPN. On the one hand, FT has the advantages of convenient operation and small trauma (47). Research by Park et al. also confirmed that FT has the above results (30). On the other hand, compared with MIPN, FT does not need to block the renal artery, thereby reducing the renal warm ischemia time and ischemia-reperfusion injury and further preserving the advantages of renal function. A system analysis study also confirmed this view (44). Moreover, the EAU guidelines suggest that FT is feasible for renal insufficiency or isolated renal tumors (7). However, there is only subgroup analysis by nephropathy recently published in 2022 back to 2017 (5 years) vs. older studies difference here for EBL. The possible reason is that with the improvement of minimally invasive surgical techniques, the amount of surgical bleeding in 2022 back to 2017 has been significantly controlled. Therefore, compared with FT, there was no difference in the amount of EBL. In addition these are also explained in the discussion section of the article.

We used postoperative complication graded by Clavien Dindo classification for complication analysis (48). Interestingly, no matter one of the minor complications (Clavien 1–2), major complications (Clavien 3–5), and overall complications are similar between MIPN and FT. MIPN has a higher complication rate compared with FT in many studies (31, 35). Although the management of SRMs by MIPN has developed rapidly, the incidence of major complications is still higher than that of FT but not statistically significant. However, all overall complication rates, max complication rates, and minor complication rates in the FT group and MIPN group were lower. Moreover, it did not reach statistical significance.

Choosing MIPN or FT requires comprehensive consideration of the patient's underlying disease, tumor characteristics (size, number, and anatomical relationship), kidney disease stage, life expectancy, comorbidities, and other related factors (49, 50). The diameter of tumors reported in literature studies is about 2–3 cm, and a few studies are up to 7 cm in size (13, 51). Compared with MIPN, patients receiving FT have smaller average tumor size, relatively uncomplicated anatomical location, multiple renal tumors, endogenous tumors, and other factors (52, 53). Among the SRMs patients treated with FT, most of the patients' R.E.N.A.L nephrectomy scores showed that the complexity of the operation was Low or medium (11, 34). In adition, part of the literature included in this meta-analysis uses renal measurement scores to assess the complexity of surgery also confirms the appeal argument (11, 14, 16, 23, 29–31, 34). Therefore, we are considering whether to choose MIPN or FT treatment. The Charlson comorbidity index and tumor complexity score can replace the age and tumor size reference factors to make the most profitable decision (54).

Our meta-analysis has several limitations. First, none of the literature in this meta-analysis is a randomized controlled trial. Second, the meta-analysis mainly recorded observational studies and may be affected by factors such as bias and confounding. Third, the OP and LOS in this article are highly heterogeneous. The heterogeneity could not be ruled out after sensitivity analysis and subgroup analysis, so the random-effects model was selected. Fourth, we did not distinguish the surgical approach (laparoscopic vs. percutaneous vs. robotic). Moreover, the long-term prognosis of tumors cannot be fully assessed due to the lack of long-term and follow-up control studies of large cases.

CONCLUSION

FT has more advantages in protecting kidney function, reducing bleeding, shortening operating time, and shortening the length of stay. There is no difference in local recurrence, distant metastasis, and major complications. For the minimally invasive era, we need to weigh the advantages and disadvantages of all aspects to make comprehensive choices.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/**Supplementary Material**.

AUTHOR CONTRIBUTIONS

Conceptualization: LD and LiY. Data curation: LD, LuY, WLL, and WQ. Formal analysis: LD and LuY. Funding acquisition: LD. Methodology: LiY. Investigation: LD and LuY. Resources: WLL. Writing—original draft: WLL. Writing—review and editing: WQ. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2022.732714/full#supplementary-material

Supplementary Figure 1 | Egger's publication bias plot to detect publication bias and Funnel plot to detect publication bias.

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