



Laparoscopic Versus Open Partial Nephrectomy: A Systemic Review and Meta-Analysis of Surgical, Oncological, and Functional Outcomes

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You C, Du Y, Wang H, Peng L, Wei T, Zhang X, Li X and Wang A (2020) Laparoscopic Versus Open Partial Nephrectomy: A Systemic Review and Meta-Analysis of Surgical, Oncological, and Functional Outcomes. Front. Oncol. 10:583979. doi: 10.3389/fonc.2020.583979 **Purpose:** To summarize and analyze the current evidence about surgical, oncological, and functional outcomes between laparoscopic partial nephrectomy (LPN) and open partial nephrectomy (OPN).

Materials and Methods: Through a systematical search of multiple scientific databases in March 2020, we performed a systematic review and cumulative meta-analysis. Meanwhile, we assessed the quality of the relevant evidence according to the framework in the Cochrane Handbook for Systematic Reviews of Interventions.

Results: A total of 26 studies with 8095 patients were included. There was no statistical difference between the LPN and OPN in the terms of operation time (p=0.13), intraoperative complications (p=0.94), recurrence (p=0.56), cancer-specific survival (p=0.72), disease-free survival (p=0.72), and variations of estimated glomerular filtration rate (p=0.31). The LPN group had significantly less estimated blood loss (P<0.00001), lower blood transfusion (p=0.04), shorter length of hospital stay (p<0.00001), lower total (p=0.03) and postoperative complications (p=0.02), higher positive surgical margin (p=0.005), higher overall survival (p<0.00001), and less increased serum creatinine (p=0.002). The subgroup analysis showed that no clinically meaningful differences were found for T1a tumors in terms of operation time (p=0.11) and positive surgical margin (p=0.23). In addition, the subgroup analysis also suggested that less estimated blood loss (p<0.0001) and shorter length of hospital stay (p<0.0001) and shorter length of hospital stay (p<0.0001) and shorter length of hospital survives surgical margin (p=0.02). The subgroup analysis showed that no clinically meaningful differences were found for T1a tumors in terms of operation time (p=0.11) and positive surgical margin (p=0.23). In addition, the subgroup analysis also suggested that less estimated blood loss (p<0.0001) and shorter length of hospital stay (p<0.00001) were associated with the LPN group for T1a tumors.

Conclusions: This meta-analysis revealed that the LPN is a feasible and safe alternative to the OPN with comparable surgical, oncologic, and functional outcomes. However, the results should be applied prudently in the clinic because of the low quality of evidence. Further quality studies are needed to evaluate the effectiveness LPN and its postoperative quality of life compared with OPN.

Keywords: kidney neoplasm, laparoscopy, nephrectomy, surgical procedures, treatment outcomes

INTRODUCTION

For T1 (\leq 7 cm) renal masses, partial nephrectomy (PN) is the preferred surgical treatment, which is suggested by guidelines (1–3). On the one hand, PN is similar to radical nephrectomy in oncological safety (4, 5). On the other hand, PN protects kidney function better and reduces the incidence of cardiovascular diseases (4, 6). Although laparoscopic PN (LPN) is an enormous technical challenge and has a steep learning curve, it is obviously becoming a feasible alternative to open PN (OPN) with less blood loss, fewer complications, and comparable oncologic and functional outcomes (7–11).

With the development of laparoscopic techniques, the robotic technique has been frequently reported (12, 13). However, the robotic technology has not been fully popularized because of the limitations of economics or cognitions. Recently, hybrid transvaginal note nephrectomy also brought about widespread attention due to the superiority of sexual function, especially in the female population, but it needs further verification (14, 15). Therefore, the LPN is the first choice for primarily experienced centers because of better cost-efficacy (16).

There is always a lack of systemic evidence for LPN versus OPN even though the numbers of studies on it have increased recently. It is high time to perform a meta-analysis of outcomes for LPN versus OPN even though there are no randomized studies. Consequently, we conducted a systemic review and meta-analysis for LPN versus OPN, including surgical, oncological, and functional outcomes.

METHODS

The protocol of this review was registered prospectively (CRD42020178120) in the PROSPERO database (University of York, York, United Kingdom). The study was performed according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement (17).

Literature Search and Study Selection

In April 2020, a comprehensively systematic literature search was conducted by using PubMed, the Cochrane Library, and Embase databases. The different search strategies were used for corresponding research engines, respectively. Search terms combined participant terms (kidney or renal neoplasm, kidney or renal cancer, kidney or renal carcinoma, kidney or renal tumor), intervention terms (partial nephrectomy or nephronsparing surgery), and comparison terms (laparoscopic or laparoscopy, open). What is more, additional records were identified through manually searching references in the selected manuscripts or in the review articles. Literature searching imposed restrictions including being published in the English language and published from 2000 to 2020.

The studies focused on patients with kidney cancer and comparing surgical, oncological and functional outcomes between LPN and OPN were included. The studies involving patients with kidney tumor >7 cm were excluded to minimize the

differences caused by the size of tumor. To eliminate discrepancies from the surgical approach, only the patients who underwent LPN were included. The studies that reported hand-assisted or robot-assisted laparoscopic technology were excluded. Meanwhile, letters, cases, reviews, conference abstracts, and studies that are irrelevant to the theme or lack complete data were excluded in order to enhance the feasibility and quality of the conclusions.

All included studies were assessed according to the methodological index for nonrandomized studies (MINORS) with a total of 24 points, which involves 12 items (18). In addition, the level of evidence of each study was assessed by the Oxford Centre of Evidence Based Medicine criteria (19). In addition, the risk of bias of each study included was independently assessed using the Risk of Bias in Non-Randomized Studies of Interventions tool (ROBINS-I) for comparative studies (20).

In addition, a subgroup analysis was performed in the patients with clinical T1a stage tumor to compare the two surgical techniques simply because the size of tumor is associated with surgical outcomes.

Data Extraction

All outcomes of interest were collected in a piloted form, including the characteristics of selected studies, surgical, oncological, and functional outcomes. For the characteristics, the following items were included: author's name, study design, number of patients, mean age, gender ratio, tumor location, tumor pathology, tumor size, and follow-up duration. The surgical outcomes included operation time, estimated blood loss (EBL), blood transfusion, length of hospital stay (LOS), and complications (total, intraoperative, and postoperative). The oncological outcomes contained positive surgical margin (PSM); recurrence; and survival results, including overall survival (OS), cancer-specific survival (CSS), and disease-free survival (DFS). The items of variations of estimated glomerular filtration rate (eGFR) and serum creatinine (sCr) were recorded for the functional outcomes. For survival data, we excavated data from Kaplan-Meier curve using Engauge Digitizer version 4.1 (http:// digitizer.sourceforge.net/) for the studies without direct survival data.

The above two steps (literature search and data extraction) were completed by three of us (CY, YD, HW) independently. All disagreements were resolved by a senior author (AW) after public discussion.

Data Analysis

The Review Manager software (RevMan) version 5.3 (the Cochrane Collaboration) was used for statistical analysis in our study. The mean difference (MD) and odds ratio (OR) were calculated for continuous and dichotomous variables, respectively, with 95% confidence intervals (CIs). In addition, the hazard radio (HR) with 95% CIs was used for CSS and DFS. We used special statistical methods for studies that presented merely continuous data as median and range values (21). The heterogeneity between studies was assessed by using the chi-squared and I- squared test. Random-effects models were used

for cumulative analyses, which had high heterogeneity ($I^2>90\%$). Otherwise, fixed-effects models were used for analyses. Finally, *P* values of <0.05 were considered as a statistical significance for the meta-analysis.

What is more, the level of evidence for the outcomes was assessed using the framework in the Cochrane Handbook for Systematic Reviews of Interventions (22). A funnel plot was used to assess the risk of publication bias for outcomes that included at least 10 statistically significant studies.

RESULTS

Initially, a total of 1406 studies were identified by our search strategy. First, 478 records were excluded because of duplication. Second, 863 studies were excluded that were irrelevant to our inclusion criteria by screening records. Third, 39 records of the remaining 65 were excluded by reading the full text (13 included irrelevant patients, 8 without reporting outcomes, 9 reviewers, 7 without complete data, and 2 duplicate publication). Finally, the remaining 26 studies were included with 8095 patients in our meta-analysis (**Figure 1**).

The characteristics of the included studies are shown in **Supplementary Table 1**. All the included studies—6 prospective

studies (23–28) and 20 retrospective studies (22, 29–47)—were cohort observational studies with no randomization. There were 3292 and 4803 patients in the LPN and OPN groups, respectively. The mean ages ranged from 49.3 to 63.7 years and from 46.2 to 65 years in LPN and OPN, respectively. The mean MINORS scores of all the included studies were 11.9 (from 6 to 18). Twelve included studies (22, 27, 29, 31, 33, 36–38, 40, 42, 43, 46) were found to have a high risk of bias because of the selection of patients, performance bias, and observer bias of outcomes according to the ROBINS-I tool. The others had a moderate risk of bias (in **Supplementary Table 2**).

Surgical Outcomes

There was no statistical difference between LPN and OPN for operation time (p=0.13, MD: 11.15 min, 95% CI: -3.27, 25.57, **Figure 2A**). Meanwhile, no clinically meaningful differences were found when T1a (p=0.11, MD=20.06 min, 95% CI: -4.75, 44.87, **Figure 2B**) was analyzed in subgroup analyses. The quality of evidence was low because of high heterogeneity and the potential of performance biases.

Less EBL was associated with the LPN group in the total analysis (P<0.00001, MD: -66.16 mL, 95% CI: -74.56, -57.77, **Figure 2C**) and subgroup analysis (p<0.0001, MD: -51.79 mL, 95% CI: -74.88, -28.71, **Figure 2D**), respectively. Similarly, a



| | Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% C | | IV | Rando | m, 95% CI | |
|---|---|---|--|--|--|--|---|--|---|------|-------|--|---------------------------------|-------------|
| | Beasley 2004 | 210 | 76 | 27 | 144 | 24 | 22 | 4.1% | 66.00 [35.63, 96.37] | | | | | |
| | Becker 2014 | 188.7 | 55.8 | 82 | 1/5 | 52.3 | 211 | 4.8% | 13.70 [-0.29, 27.69] | | | | | |
| | Chang 2018 | 241 9 | 40.0 90 | 122 | 172.5 | 40.9 64 | 122 | 5.0% 4.6% | -6.70 [-11.46, -1.92] 69 40 [49 80 89 00] | | | | - | |
| | Gill 2003 | 180 | 45.1 | 100 | 231.2 | 49.6 | 100 | 4.9% | -51.20 [-64.34, -38.06] | - | - | | | |
| | Gong 2008 | 225.1 | 63.8 | 76 | 193 | 62.9 | 77 | 4.6% | 32.10 [12.02, 52.18] | | | | | |
| | Jeon 2012 | 203.5 | 72.6 | 31 | 161 | 63.6 | 102 | 4.2% | 42.50 [14.12, 70.88] | | | | | _ |
| | Kartal 2020 | 160 | 39.3 | 22 | 120 | 27.7 | 41 | 4.7% | 40.00 [21.52, 58.48] | | | | | |
| | Liu 2013 | 94.3 | 19.8 | 40 | 117.6 | 22.6 | 23 97 | 4.0% | -23 30 [-29 07 -17 53] | | | - | | |
| | Lucas 2012 | 195 | 66.7 | 15 | 147 | 47.4 | 54 | 3.9% | 48.00 [11.96, 84.04] | | | | | |
| | Luciani 2016 | 186 | 49 | 70 | 145 | 59 | 73 | 4.7% | 41.00 [23.25, 58.75] | | _ | | | - |
| | Marszalek 2009 | 86.7 | 26.3 | 100 | 154 | 43.6 | 100 | 5.0% | -67.30 [-77.28, -57.32] | | - | 1 | | |
| | Park 2010 | 221 | 84 | 273 | 131.2 | 68 | 279 | 4.9% | 37.00 [24.23, 49.77] | | | | | |
| | Permpongkosol 2006 | 225 | 85.1 | 85 | 276 | 80.7 | 58 | 4.3% | -51.00 [-78.54, -23.46] | | | - | | |
| | Porpiglia 2016 | 129.7 | 30.4 | 57 | 138.3 | 45 | 133 | 4.9% | -8.60 [-19.59, 2.39] | | | | | |
| | Rezaeetalab 2016 | 180 | 61.8 | 34 | 127 | 61.8 | 31 | 4.2% | 53.00 [22.92, 83.08] | | | | | |
| | Springer 2012 | 145.3 | 62.4 45.4 | 50 170 | 248.9 | 45 35.6 | 28 170 | 4.5% | -07.80 [-91.14, -44.46] -9.90 [-18.57 -1.23] | | | | | |
| | Xu 2014 | 154.1 | 141.2 | 42 | 126.2 | 91.3 | 187 | 3.4% | 27.90 [-16.76, 72.56] | | | - | | |
| | Xu 2015 | 142.1 | 74.6 | 19 | 126.6 | 28.1 | 18 | 3.9% | 15.50 [-20.47, 51.47] | | | - | · · · · | |
| | Total (05% CI) | | | 2200 | | | 2740 | 100.0% | 44 46 5 2 27 26 671 | | | | | |
| | Heterogeneity: Tau ² = | 1067 60 | · Chi² = | 2309 545 18 | df = 21 | (P < 0 | 2/40 |). I ² = 969 | 11.15[-3.27, 23.57] | ⊢ | | | ─ | |
| | Test for overall effect: | Z = 1.52 | (P = 0. | 13) | | | | ,, | - | -100 | -50 | | 0PN 50 | 100 |
| | | | | | | | | | | | | | * | |
| В | Study or Subgroup | Mean | LPN SD | Total | 0 Mean | PN SD | Total | Weight | Mean Difference | | IV. | Rando | terence m. 95% Cl | |
| | Beasley 2004 | 210 | 76 | 27 | 144 | 24 | 22 | 12.9% | 66.00 [35.63, 96.37] | | | | | |
| | Becker 2014 | 188.7 | 55.8 | 82 | 175 | 52.3 | 211 | 15.2% | 13.70 [-0.29, 27.69] | | | ł | • | |
| | Gong 2008 | 225.1 | 63.8 | 76 | 193 (| 62.9 | 77 | 14.5% | 32.10 [12.02, 52.18] | | | | _ | |
| | Minervini 2013 Park 2010 | 143 | 56.9 84 | 140 273 | 131.2 : | 58.1 68 | 140 279 | 15.2% 15.3% | 11.80 [-1.67, 25.27] | | | | · | |
| | Rezaeetalab 2016 | 180 | 61.8 | 34 | 127 (| 61.8 | 31 | 12.9% | 53.00 [22.92, 83.08] | | | | _ | |
| | Romero 2008 | 181.1 | 62.4 | 56 | 248.9 | 45 | 28 | 14.0% | -67.80 [-91.14, -44.46] | | - | - | | |
| | Total (95% CI) | | | 688 | | | 788 | 100.0% | 20 06 [-4 75 44 87] | | | | • | |
| | Heterogeneity: Tau ² = | 1004.0 | 0: Chi² : | = 78.14. | df = 6 (| P < 0. | 00001) | : l ² = 92% | 20.00 [-4.75, 44.87] | H | + | | • + | |
| | Test for overall effect: | Z = 1.5 | 8 (P = 0 | 11) | | | , | | | -200 | 100 | 0 | 100 |) 200 |
| ~ | | | | , | | | | | | -200 | -100 | LPN | OPN | |
| | | | | , | 0 | DN | | | Mean Difference | 200 | -100 | LPN Mean Di | OPN fference | |
| | Study or Subgroup | Mean | LPN SD | Total I | Ol Mean | PN SD | Total | Weight | Mean Difference IV, Fixed, 95% | | -100 | LPN Mean Di IV. Fixed | OPN fference d. 95% Cl | |
| , | Study or Subgroup Adamy 2010 | Mean 241 | LPN SD 201 | <u>Total 1</u> 182 | O Mean 379 | PN SD 357 | Total 805 | Weight 5.6% | Mean Difference IV. Fixed, 95% -138.00 [-176.22, -99.78 | | -100 | LPN Mean Di IV, Fixed | OPN fference 1. 95% Cl | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 | Mean 241 165 | LPN SD 201 137.5 | <u>Total I</u> 182 625 | 01 <u>Mean</u> 379 200 1- | PN SD 357 48.6 | Total 805 682 | Weight 5.6% 33.7% | Mean Difference IV. Fixed, 95% -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.49 -0.20 (-46.07, 24.43 | | -100 | LPN Mean Di IV. Fixed | OPN fference 1. 95% Cl | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 | Mean 241 165 196.1 141.7 | LPN 201 137.5 142 75.2 | Total I 182 625 122 1 100 2 | 01 379 200 1 206.4 266.7 1 | PN 357 48.6 135 88.1 | Total 805 682 122 100 | Weight 5.6% 33.7% 6.7% 5.1% | Mean Difference IV, Fixed, 95% -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -125.00 [-164.70, -85.30 | | -100 | LPN Mean Di IV. Fixed | OPN fference 1.95% Cl | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 | Mean 241 165 196.1 141.7 395.2 | LPN 201 137.5 142 75.2 297 | Total 182 625 122 : 100 : 31 - | Of 379 200 1- 206.4 266.7 1- 440.6 3 | PN 357 48.6 135 88.1 27.9 | Total 1 805 682 122 100 102 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% | Mean Difference IV. Fixed, 95% -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -125.00 [-164.70, -85.30 -45.40 [-167.79, 76.98 | | -100 | LPN Mean Di IV. Fixed | OPN fference d. 95% Cl | _ |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 | Mean 241 165 196.1 141.7 395.2 525 | LPN 201 137.5 142 75.2 297 288 | Total I 182 625 122 : 100 : 31 - 22 (| 01 379 200 1 206.4 266.7 1 440.6 3 612.5 | PN 357 48.6 135 88.1 27.9 404 | Total 1 805 682 122 100 102 41 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.3% | Mean Difference IV. Fixed. 95% -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -125.00 [-167.79, 76.98 -87.50 [-260.06, 85.06 -04.06 (-167.79) [-16.79] | | | LPN Mean Di IV. Fixed | OPN fference d. 95% Cl | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liu 2013 | Mean 241 165 196.1 141.7 395.2 525 163 126 9 | LPN SD 201 137.5 142 75.2 297 288 179 41.8 | Total I 182 625 122 2 100 31 22 48 115 1 | Ol 379 200 1 206.4 266.7 1 440.6 3 512.5 367 232.3 | PN 357 48.6 135 88.1 27.9 404 286 86.7 | Total 1 805 682 122 100 102 41 23 97 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.3% 0.5% 22.8% | Mean Difference IV. Fixed, 95%, -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -125.00 [-164.70, -85.96 -87.50 [-260.06, 85.06 -204.00 [-331.38, -76.65 -204.00 [-321.38, -76.65 | | - 100 | LPN Mean Di IV. Fixed | OPN fference 1, 95% Cl | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liu 2013 Lucas 2012 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 | LPN 201 137.5 142 75.2 297 288 179 41.8 111.1 | Total I 182 625 122 : 100 : 31 - 22 : 48 115 : 5 | Ol 379 200 1 206.4 266.7 1 440.6 3 612.5 367 232.3 2 250 2 | PN <u>SD</u> 357 48.6 135 88.1 27.9 404 286 86.7 22.2 | Total 9 805 682 122 100 102 41 23 97 54 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.3% 0.5% 22.8% 1.2% | Mean Difference IV. Fixed, 95% 138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -125.00 [-164.70, -85.30 -45.40 [-167.79, 76.96 -75.50 [-260.06, 85.06 -204.00 [-331.38, -76.62 -105.40 [-124.27, -86.53 -105.00 [-213.69, -68.31 | | | LPN Mean Di IV, Fixed | OPN fference 1.95% CI | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liu 2013 Lucas 2012 Lucas 2012 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 | LPN SD 201 137.5 142 75.2 297 288 179 41.8 111.1 307 105 | Total I 182 625 625 122 100 31 22 6 48 115 15 70 | Ol 379 200 1 206.4 266.7 1 440.6 3 512.5 367 232.3 5 250 2 275 | PN 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 | Total 805 682 122 100 102 41 23 97 54 73 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 22.8% 1.2% 0.7% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.61, -19.46 -10.30 [-450.7, 24.47 -125.00 [-184.70, -86.35 -87.50 [-260.06, 85.06 -264.00 [-313.37, -76.62 -105.40 [-124.27, -86.55 -150.00 [-231.69.48.31 -41.00 [-68.85, 150.65 | | | LPN Mean Di IV, Fixed | OPN fference 1.95% CI | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Kartal 2020 Kartal 2020 Lucas 2012 Luciani 2016 Permpongkosol 2006 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166 7 | LPN <u>SD</u> 201 137.5 142 75.2 297 288 179 41.8 111.1 307 430.3 76 | Total I 182 625 625 122 100 2 31 - 22 6 48 115 15 70 85 - | Ol Mean 379 200 1. 206.4 266.7 1. 440.6 3. 612.5 367 232.3 2. 275 275 275 200 4 | PN 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 22.8% 1.2% 0.7% 0.6% 7.8% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -10.30 [-45.07, 24.47 -125.00 [-184.77, 76 59 -87.50 [-260.06, 85.06 -204.00 [-331.38, -76.65 -155.40 [-124.27, -86.55 -155.40 [-124.27, -86.55 -155.40 [-124.27, -86.55 -155.40 [-24.55, 150.86 -9.20 [-105.54, 124.34 -33.30 [-65.27, -27.55] | | | LPN Mean Di IV. Fixed | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Katal 2020 Klassen 2014 Liu 2013 Luciani 2016 Permpongkosol 2006 Porpiglia 2016 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 | LPN SD 201 137.5 142 75.2 297 288 179 41.8 111.1 307 430.3 76 123.1 | Total 1 182 625 625 122 100 31 22 6 48 115 15 70 85 57 170 27 | 01 379 200 1 206.4 266.7 1 440.6 3 512.5 367 232.3 2 235 275 427.7 2 200 1 240.2 1 | PN SD 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 170 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.3% 0.5% 22.8% 1.2% 0.7% 0.6% 7.8% 10.7% | Mean Difference IV. Fixed. 95% | | - | LPN Mean Di IV, Fixed | OPN fference 1,95% Cl | , |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Katal 2020 Klaassen 2014 Liu 2013 Luciani 2016 Permpongkosol 2006 Porpiglia 2016 Springer 2012 Webb 2015 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 | LPN SD 201 137.5 142 75.2 297 288 179 41.8 111.1 307 430.3 76 123.1 77.7 | Total 1 182 625 625 122 100 31 22 1 48 115 105 70 85 - 57 170 31 - | Ol 379 200 1 206.7 1 440.6 3 512.5 367 232.3 5 250 2 275 2 427.7 2 200 1 240.2 1 383.3 3 | PN 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 57.8 | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 170 21 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 22.8% 1.2% 0.7% 0.6% 7.8% 10.7% 0.3% | Mean Difference IV. Fixed. 95% | | - | LPN Mean Di IV, Fixed | OPN fference 1.95% Cl | , |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liucas 2012 Luciani 2016 Permpongkosol 2006 Porpigila 2016 Springer 2012 Webb 2015 Xu 2014 Xu 2014 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.4 | LPN SD 2011 137.55 142 75.2 297 288 179 41.8 111.1 307 430.3 76 123.1 77.7 166 202 | Total 1 182 625 625 122 100 31 22 1 48 115 15 70 85 - 57 170 31 - 42 - | Ol 379 200.1 206.4 266.7 11 440.6 3612.5 367 232.3 255 275 2427.7 2 200 1 240.2 1 383.3 3 231.5 2 200 200 1 | PN 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 57.8 22.5 52.7 | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 170 21 187 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 0.5% 0.5% 22.8% 1.2% 0.7% 0.6% 7.8% 10.7% 0.3% - 2.3% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-450.72, 44 -10.30 [-450.72, 44 -45.40 [-167.79, 75.95 -87.50 [-260.06, 85.00 -204.00 [-313.83, -76.62 -105.40 [-124.27, -86.53 -150.00 [-231.69, -86.31 -40.01 [-68.55, 150.85 9.20 [-105.94, 124.34 -33.30 [-458.52, -1.05 -82.70 [-110.21, -55.15] -82.30 [-143.67, -127.84 -40.40 [-99.88, 19.00 | | - | LPN Mean Di IV. Fixed | OPN fference , 55% CI | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Katati 2020 Klassen 2014 Lucas 2012 Lucasi 2016 Permpongkosol 2006 Porpigla 2016 Springer 2012 Webb 2015 Xu 2014 Xu 2015 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 | LPN SD 2011 137.5 142 75.2 297 288 179 41.8 111.1 307 430.3 76 123.1 77.7 166 108.2 | Total I 182 625 625 122 100 31 22 48 115 15 70 85 57 170 31 42 19 1 | Ol 379 200.4 266.7 1 440.6 3 512.5 367 232.3 255 275 275 275 275 275 275 275 275 275 | PN 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 57.8 22.5 52.7 | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 170 21 187 18 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 0.5% 0.5% 0.5% 0.7% 0.6% 7.8% 10.7% 0.3% -2.3% 1.1% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -10.30 [-45.07, 24.47 -125.00 [-184.77, 76 95 -87.50 [-260.06, 85.00 -204.00 [-231.88, -76 62 -105.40 [-124.27, -86 53 -150.00 [-231.68, -76 62 -105.40 [-124.27, -86 53 -150.00 [-231.68, -76 62 -33.30 [-65.52, -106 -82.70 [-110.21, -55 15 283.30 [-438, 76, -127 44 -40.40 [-98.81, 906 -127.20 [-212.89, -41 51 | | - | LPN Mean Di IV. Fixer | OPN fference , 95% Cl | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Katal 2020 Klaassen 2014 Liu 2013 Lucas 2012 Luciani 2016 Porrpiglia 2016 Porpiglia 2016 Springer 2012 Webb 2015 Xu 2014 Xu 2015 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 | LPN 201 137.5 142 75.2 297 41.8 111.1 307 430.3 76 123.1 77.7 166 108.2 | Total I 182 625 622 1 100 31 22 48 115 1 70 85 57 70 31 31 42 1 170 31 42 19 1734 1734 | 01 379 200 1 200 4 206 4 206 4 206 4 206 7 1 440.6 3 512.5 232.3 250 2 275 2275 2275 2200 1 240.2 1 383.3 3 231.5 2 2223.3 1 | PN 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 57.8 22.5 52.7 | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 170 21 187 18 2686 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 22.8% 1.2% 0.7% 0.6% 7.8% 10.7% 0.3% 1.7% 10.7% 11% | Mean Difference IV. Fixed, 95%, 1 -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -10.30 [-45.07, 24.47 -45.40 [-167.79, 76.99 -87.50 [-260.06, 85.06 -204.00 [-31.38, -76.65 -105.40 [-124.27, -86.55 -105.40 [-124.27, -86.55 -105.40 [-124.27, -86.55 -105.00 [-231.69, -88.31 -33.30 [-65.52, -127.48, -127.48, 19.06 -127.20 [-212.89, -41.51 -68.35 [-77.36, -59.35 | | - | LPN Mean Di IV. Fixed | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klassen 2014 Liu 2013 Lucas 2012 Lucas 2012 Jeon 2012 Kartal 2020 Klassen 2014 Lucas 2012 Verba 2015 Xu 2014 Xu 2015 Total (95% CI) Heterogeneity: Chi ^P 9 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 | LPN 201 137.5 142 75.2 297 288 179 41.8 111.1 307 430.3 76 123.1 77.7 166 108.2 = 15 (P | Total 1 182 625 625 122 100 31 22 48 115 57 57 57 170 31 42 19 19 1734 <0.000040 | Ol 379 200 1 206 4 206 4 206 7 1 440.6 3 512.5 220.3 250 2 275 2275 2275 2200 1 240.2 1 383.3 3 231.5 2 2223.3 1 240.2 1 383.3 3 231.5 2 223.3 1 2001; I ² = 8 | PN SD 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 57.8 22.5 52.7 34% | Total N 805 682 122 100 100 102 41 23 97 54 73 58 133 170 21 187 18 18 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 22.8% 1.2% 0.7% 0.6% 7.8% 0.3% 1.2% 10.7% 0.3% 1.1% | Mean Difference IV. Fixed. 35%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [45.07, 24.47 -10.30 [45.07, 24.47 -45.40 [-167.79, 76.95 -45.40 [-167.79, 76.95 -45.50 [-26.06, 85.06 -204.00 [-231.83, -76.65 -150.00 [-231.69, -68.37 -150.00 [-231.69, -68.37 -40.40 [-9.88, 19.06 -40.40 [-9.88, 19.06 -127.20 [-21.29, -41.51 -68.35 [-77.36, -59.35 | | | LPN Mean Di IV. Fixed | OPN fference 1.95% CI | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liu 2013 Lucas 2012 Lucas 2012 Permpongkosol 2006 Porpiglia 2016 Springer 2012 Webb 2015 Xu 2014 Xu 2015 Total (95% CI) Heterogeneity: Chi ² = 9 Test for overall effect: 2 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 3.38, df 2 = 14.87 | LPN 201 137.5 142 297 288 179 41.8 111.1 307 430.3 76 123.1 77.7 166 108.2 = 15 (P (P < 0.1) | Total 1 182 625 122 1 100 3 220 48 115 5 57 57 170 3 19 3 19 1 1734 < 0.000(00001) | Ol 379 200 1 206.4 266.7 1 440.6 3 367 232.3 5 250 2 275 427.7 2 200 1 275 427.7 2 200 1 240.2 1 383.3 3 231.5 2 223.3 1 3231.5 2 223.3 1 01); I ² = 8 | PN <u>SD</u> 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 57.8 22.5 52.7 34% | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 170 21 187 18 2686 - | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 0.5% 22.8% 22.8% 1.2% 0.6% 0.6% 0.6% 0.6% 0.6% 0.3% - 2.3% 1.1% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-450.7, 24.47 -10.30 [-450.7, 24.47 -125.00 [-180.70, 78.69 -87.50 [-260.06, 85.0 -204.00 [-313.33, -76 62 -105.40 [-124.27, -86.55 -150.00 [-231.69, 86.83 -41.00 [-68.85, 150.86 -9.20 [-105.94, 124.34 -33.30 [-68.55, 24, 106 -82.70 [-110.21, -55.15 -82.30 [-438.76, -127.84 -40.40 [-99.88, 19.06 -127.20 [-212.89, -41.51 -68.35 [-77.36, -59.35 | | | LPN | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klassen 2014 Lucas 2012 Luciani 2016 Porrippigla 2016 Springer 2012 Webb 2015 Xu 2014 Xu 2015 Total (95% CI) Heterogeneily: Chi ² = 9 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 3.38, df 2 = 14.87 | LPN SD 2011 137.5 142 297 288 179 41.8 171.1 307 430.3 7.7 166 123.1 77.7 166 108.2 = 15 (P < 0.1 LPN | Total 1 182 625 122 1 31 - 48 15 15 70 85 - 57 31 42 15 170 31 42 19 1931 - 1734 <0.000001) | Ol Mean 379 200 1 266.7 1 266.7 1 266.7 1 267.7 2 275 275 275 277.7 2 277.7 2 2 2 2 2 2 2 2 2 2 2 2 2 2 | PN 357 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 52.5 52.7 34% | Total No. 805 682 122 100 102 41 23 97 54 73 58 133 170 21 187 18 2686 18 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 0.3% 22.8% 22.8% 1.2% 0.6% 0.6% 0.6% 0.6% 1.2% 0.6% 1.2% 0.6% 1.2% 0.6% 1.2% 0.6% 1.2% 0.6% 1.2% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5 | Mean Difference IV. Fixed, 95%. -138.00 [-106.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -10.30 [-45.07, 24.47 -125.00 [-184.77, 97.69 -87.50 [-260.06, 85 -024.00 [-331.38, -76.62 -105.40 [-124.27, -86.55 -105.40 [-124.27, -86.55 -105.40 [-124.27, -86.55 -105.40 [-124.27, -86.55 -105.40 [-124.27, -86.55 -105.40 [-124.27, -86.55 -20.10 [-20.54, -124.24 -33.30 [-65.52, -10 -42.70 [-110.21, -55.15 -68.35 [-77.36, -59.35 Mean Difference | | | LPN Mean Di IV. Fixer | OPN fference | , , , |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klassen 2014 Liu 2013 Lucas 2012 Lucas 2012 Lucas 2012 Lucas 2012 Valot 2015 Total (95% CI) Heterogeneily: Ch ² = 9 Study or Subgroup Brandar 2001 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 3.38, df = 14.87 | LPN SD 201 137.5 142 297 75.2 297 41.8 111.1 77.7 430.3 76 123.1 166 108.2 = 15 (P < 0.1 LPN SD 275 297 41.8 109 109 109 109 109 109 109 109 | Total I 182 625 122 : 100 : 31 - 48 15 170 : 31 - 48 15 70 31 42 : 1701 : 311 - 42 : 19 : 1734 < | Ol Mean 379 200 1. 266.7 1. 266.7 1. 267.7 2. 250 2. 275 2. 275 2. 277.7 2. 277.7 2. 277.7 2. 277.7 2. 227.3 1. 383.3 3. 321.5 2. 2223.3 1. 1)1); I ² = E O O Mean 221.5 2. 222.3 1. 222.3 1. 223.5 1. | PN 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 52.7 35.4 52.7 34% PN 5D | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 58 133 77 21 187 18 2686 7 202 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 0.5% 0.5% 0.7% 0.7% 0.7% 0.7% 0.7% 0.7% 0.3% 1.1% 10.7% 1.1% 100.0% Weight | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -10.30 [-45.07, 24.47 -132.50 [-160.06, 85.06 -204.00 [-131.33, -76.65 -37.50 [-260.06, 85.00 -204.00 [-231.69, -88.31 -105.40 [-124.27, -86.55 -150.00 [-231.69, -88.31 -33.30 [-65.52, -1.06 -82.70 [-110.21, -85.15 283.30 [-45.52, -1.06 -82.70 [-110.21, -85.15 -68.35 [-77.36, -59.35 Mean Difference IV. Fixed, 95%. | | | LPN Mean Di IV. Fixer LPN Mean Di IV. Fixer | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liu 2013 Lucas 2012 Lucas 2012 Lucas 2012 Springer 2012 Webb 2015 Xu 2014 Xu 2014 Study or Subgroup Beasley 2004 Chol 2019 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 3.38, df 433.8, df 157.5 100 191.1 96.1 3.38, df 164.8 | LPN <u>SD</u> 2011 137.5 1422 297 75.2 297 41.8 111.1 307 41.8 111.1 307 41.8 111.1 307 166 108.2 = 15 (P () (P < 0.) LPN <u>SD</u> 250 122.1 123.1 123.1 123.1 123.1 123.1 123.1 125.1 | Total 1 182 625 122 : : 100 : : 22 : : 31 : : 22 : : 48 : 115 : : 15 : 70 : : 31 : : 42 : : 19 : : 1734 < | O() Mean 2000 1. 2006 4. 2006 4. 2006 4. 2006 4. 2006 4. 2007 2. 2007 4. 2007 2. 2007 4. 2007 2. 2007 4. 2007 4. 2 | PN SD 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 371.7 49.9 35.4 57.8 52.7 343 343 343 | Total 1 805 682 122 100 102 41 23 97 54 73 58 133 170 21 187 18 2686 1 22 285 | Weight 5.6% 33.7% 6.7% 0.5% 0.3% 0.5% 22.8% 0.7% 0.6% 1.2% 0.6% 2.3% 1.1% 100.0% Weight 1.8% 61.1% | Mean Difference IV. Fixed, 95%, -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.77, 24.47 -125.00 [-167.79, 76.96 -87.50 [-260.08, 85.06 -204.00 [-231.38, -76.65 -105.40 [-124.27, -86.55 -105.00 [-231.99, -88.31 -41.00 [-88.5150.86 -9.20 [-105.94, 124.34 -33.30 [-65.52, -10 -40.40 [-99.88, 19.06 -127.20 [-212.89, -41.51 -68.35 [-77.36, -59.35 Mean Difference IV. Fixed, 95%, -84.00 [-255.57, 87.5] | | | LPN Mean Di IV. Fixes LPN LPN | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liu 2013 Lucas 2012 Lucas 2012 Lucas 2012 Lucas 2014 Lucas 2015 Pernpongkosol 2006 Porpiglia 2016 Springer 2012 Xu 2015 Total (95% CI) Heterogeneity: Ch ² = 9 Study or Subgroup Beasley 2004 Chi 2019 Gong 2008 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 100 191.1 96.1 3.38, df Mean 2500 164.8 211.9 | LPN 2011 137.5 142 75.2 297 41.8 111.1 307 430.3 76 123.1 77.7 166 108.2 = 15 (P < 0. LPN <u>5D</u> 2500 122.6 251.3 | Total 1 182 625 625 122 : 100 : 22 : 31 - 22 : 48 15 70 31 : 57 70 : 31 : 57 170 : 31 : 19 : 19 : 1734 <0.000() | OI Mean 379 200 1. 200.4 312.5 232.3 275 2272 200.1 383.3 3231.5 222.3.3 11); I² = E Mean 334 173 1355.4 | PN SD 357 48.6 135 88.1 27.9 404 286 86.7 22.2 362 71.7 49.9 35.4 57.8 52.5 52.7 34% PN SD 343 343 343 343 | Total 1 805 682 122 100 41 23 97 54 73 54 73 53 53 170 21 187 187 187 187 22 2855 77 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.3% 22.8% 1.2% 0.6% 7.8% 0.6% 7.8% 10.7% 0.3% 2.3% 1.1% 100.0% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-450.7, 24.47 -125.00 [-184.70, -85.53 -87.50 [-260.06, 85.00 -204.00 [-331.33, -76.62 -105.40 [-124.27, -86.53 -150.00 [-231.69, -88.51 -33.30 [-45.52, -1.02 -42.70 [-110.21, -55.16 -82.70 [-110.21, -55.16] -82.30 [-438.76, -127.84 -40.40 [-99.88, 19.06 -127.20 [-212.89, -41.51 -68.35 [-77.36, -59.35 Mean Difference IV. Fixed, 95% -84.00 [-255.57, 87.57 -82.00 [-37.72, 21.37] | | | LPN Mean Di IV. Fixes Mean Di UV. Fixes | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klassen 2014 Liu 2013 Luciani 2016 Porripiglia 2016 Porripiglia 2016 Porrigilia 2016 Porrigoria 2012 Webb 2015 Xu 2014 Xu 2015 Total (95% CI) Heterogeneity: CIP = 9 Study or Subgroup Beasley 2004 Charl 2019 Gong 2008 Park 2010 | Mean 241 165 196.1 141.7 395.2 525 163 126.9 166.7 157.5 100 191.1 96.1 3.38, df 42 14.87 2500 164.8 211.9 293 | LPN SD 2011 137.55 2977 2888 179 41.8 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 307 430.3 231 108 40 40 40 40 40 40 40 40 40 40 | Total 1 182 625 122 1 100 31 22 1 15 70 31 31 48 115 170 31 31 42 19 1734 1734 <0.0000 | Oin 379 379 2001 12064 3667 367 367 322.3 275 2001 240.2 383.3 321.5 2223.3 11); IP = E O Mean 334 1773 1773 418 | PN SD 357 48.6 135 88.1 27.9 404 286 86.7 362 362 71.7 49.9 362 35.4 57.8 22.5 52.7 34% PN SD 343 343 343 343 341 57.8 20.5 52.7 | Total 1 805 682 122 100 41 23 97 54 73 58 170 21 133 170 21 187 18 7 8 2686 7 77 2285 77 7279 | Weight 5.6% 33.7% 6.7% 6.7% 0.5% 0.5% 0.5% 1.2% 0.3% 1.2% 0.3% 1.2% 0.3% 1.2% 0.3% 1.1% 10.0% Weight 1.1% 7.8% 2.3% 0.1% 7.8% 2.3% 0.5% 0.7% | Mean Difference IV. Fixed, 95%. -138.00 [-106.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -10.30 [-45.07, 24.47 -125.00 [-161.79, 76.96 -87.50 [-260.06, 85.00 -204.00 [-331.38, -76.62 -105.40 [-124.27, -86.55 -150.00 [-21.42, -7, 86.55 -150.00 [-21.42, -7, 86.55 -33.30 [-65.52, -1.06 -42.70 [-110.21, -55.15 -40.40 [-99.88, 19.06 -127.20 [-212.89, -41.51 -68.35 [-77.36, -59.35 Mean Difference W. Fixed, 95%. -84.00 [-25.57, 87.57 -8.20 [-37.72, 21.33] -173.50 [-256.19, -90.83 -125.00 [-175.84, -74.11 | | | LPN Mean Di IV. Fixed LPN LPN Mean Di IV. Fixed | OPN fference | , , , |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klassen 2014 Liu 2013 Lucas 2012 Luciani 2016 Permpongkosol 2006 Porpiglia 2016 Porpiglia 2016 Vau 2014 Xu 2015 Total (95% CI) Heterogeneity: Chr ² = 9 Study or Subgroup Beasley 2004 Choi 2019 Gong 2008 Park 2010 Rezaeetalab 2016 | Mean 2411 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 01 191.1 96.1 3.38, df 42.2 164.2 164.2 164.3 3.38, df 164.8 250 164.8 211.9 293 3100 | LPN SD 2011 137.5 142 75.2 297 430.3 76 123.1 177.7 430.3 76 123.1 177.7 166 108.2 = 15 (P < 0. LPN 2500 122.6 251.3 223 221.6 | Total 1 182 625 122 1 100 31 22 1 15 7 170 31 42 31 1734 1734 27 96 76 76 273 34 56 76 | Oing 379 379 2001 1206.4 1206.4 3512.5 367 223.3 240.2 1383.3 231.5 2233.1 2233.3 11); I ² = E O Mean 334 1733 1733 385.4 418 324.4 418 324.4 | PN SD 357 48.6 1355 88.1 27.9 404 286 86.7 71.7 49.9 362 35.4 57.8 22.5 52.7 34% PN SD 343 343 370 221.6 370 221.6 | Total 1 805 682 122 100 102 41 23 97 55 58 133 170 21 187 187 18 22 2686 77 229 279 311 | Weight 5.6% 33.7% 6.7% 6.7% 0.5% 0.5% 0.3% 1.2% 0.7% 0.6% 7.8% 10.3% 1.1% 100.0% | Mean Difference IV, Fixed, 95%, -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.4 -10.30 [-45.07, 24.47 -10.30 [-45.07, 24.47 -125.00 [-184.77, 76.95 -87.50 [-260.06, 85.06 -204.00 [-231.89, -86.35 -150.00 [-231.69, -88.37 -150.00 [-231.69, -88.37 -40.20 [-98.8, 19.06 -42.70 [-110.21, -85.15 -83.30 [-65.52, -1.06 -42.70 [-110.21, -85.15 -84.00 [-21.89, -41.51 -68.35 [-77.36, -59.35 -84.00 [-255.57, 87.57 -84.00 [-255.77, 87.57] -84.00 [-255.77, 87.57] -82.00 [-37.72, 21.33 -173.50 [-256.19, -90.88, -74.11 -14.00 [-121.86, 39.38, -74.11 -14.00 [-121.86, 39.38, -74.11 -14.00 [-121.86, 39.38] | | | LPN Mean Di IV. Fixed LPN LPN Mean Di IV. Fixed | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klaassen 2014 Liu 2013 Lucas 2012 Lucas 2012 Lucas 2012 Springer 2012 Webb 2015 Xu 2014 Xu 2015 Total (95% CI) Heterogeneity: Ch² = 9 Study or Subgroup Beasley 2004 Choi 2019 Gong 2008 Park 2010 Rezaeetalab 2016 Romero 2008 | Mean 2411 165 196.1 141.7 395.2 525 163 126.9 100 316 436.9 166.7 157.5 163.38, df 2 141.7 96.1 3.38, df 250 164.8 250 164.8 210.9 283 310 280.9 | LPN 5D 2011 137.5 142 75.2 297 41.8 179 43.03 76 123.1 77.7 166 108.2 = 15 (P < 0. LPN 250 122.6 251.0 221.6 221.6 | Total I 182 625 122: 100: 31: 22: 48 115: 15: 57 70: 31: 57 170: 31: 57 170: 19: 1734 <0.000001) | Oi Oi 379 379 200 1 200 1 200 1 200 1 266.7 1 311 12.5 202 200 202.3 275 2 200 240.2 1 2223.3 1 3134 1 322 223.3 1); I* F* O O O Mean 34 3173 1 385.4 2 324 2 418 324 34112 2 | PN SD 357 48.6 135 27.9 404 286 88.1 27.9 404 286 88.7 22.2 362 352.4 57.8 57.8 52.5 52.7 34% PN SD 343 441.5 3370 370 221.6 274.6 | Total 805 682 122 100 102 41 23 97 55 58 133 170 21 187 187 18 2686 77 72 285 77 72 285 77 73 31 28 | Weight 5.6% 33.7% 6.7% 5.1% 0.5% 0.5% 2.8% 1.2% 0.6% 2.8% 1.2% 0.6% 1.2% 0.6% 1.2% 0.6% 2.8% 1.1% 100.0% Weight 1.8% 4.6% 4.6% 4.1% | Mean Difference IV. Fixed, 95%, | | | LPN Mean Di IV. Fixed LPN LPN Mean Di IV. Fixed | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klassen 2014 Liu 2013 Lucas 2012 Lucas 2012 Lucas 2012 Permpongkosol 2006 Porpiglia 2016 Springer 2012 Webb 2015 Xu 2015 Total (95% CI) Heterogeneity: Ch ² = 9 Study or Subgroup Beasley 2004 Choi 2019 Gong 2008 Park 2010 Rezaeetalab 2016 Romero 2008 Total (95% CI) | Mean 241 165 196.1 141.7 395.2 525 163 126.9 100 166.7 197.1 3.38, df 436.9 191.1 96.1 3.38, df 164.8 211.9 293 310 280.9 | LPN SD 2011 137:5 142 75:2 288 179 41.8 111.1 307 6 123.1 77.7 166 123.1 77.7 166 251.3 223 221.6 202.1 | Total I 1 182 625 625 122 : 100 : 31 - 48 15 : 57 15 170 : 55 - 57 31 : 42 : 19 : 19 : 1734 000001) 766 766 773 34 56 562 562 | Oi Oi 379 200 1. 379 200 1. 200 1. 200 1. 200 1. 260.7 1. 250 2.7 2 275 2203.1 2 200.1 1. 383.3 2 2 223.3 1 1); IP = E 0 0 0 Mean 335.4 2 4.18 385.4 2.4 4.18 2.24 4118 2.24 2.24 4.12.4 2 | PN SD 357 48.6 135 27.9 404 286 88.1 27.9 404 286.7 22.2 362 352.4 57.8 57.8 52.5 52.7 34% PN SD 343 441.5 3370 343 343 221.6 274.6 | Total 1 805 682 122 100 102 23 97 54 133 170 21 187 18 187 18 2686 22 285 777 279 31 28 722 | Weight 5.6% 5.1% 0.5% 0.5% 0.5% 0.5% 0.28% 0.7% 0.6% 0.7% 0.6% 0.7% 0.3% 1.2% 0.3% 1.2% 0.3% 0.3% 0.3% 0.3% 0.4% 0.3% 4.1% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-450.7, 24.47 -125.00 [-184.770, 75.69 -87.50 [-260.06, 85.00 -204.00 [-313.37, 76.62 -105.40 [-124.27, -86.53 -150.00 [-231.69, -88.31 -33.30 [-455.52, -106 -82.70 [-110.21, -55.16] -82.30 [-438.76, -127.84 -40.40 [-99.88, 19.06 -127.20 [-212.89, -41.51 -68.35 [-77.36, -59.35 Mean Difference IV. Fixed, 95% -84.00 [-255.57, 87.57 -8.20 [-37.72, 21.37] -14.00 [-12.48, -9.38, -131.50 [-246.16, -16.89 -51.79 [-74.88, -28.71] | | | LPN Mean Di IV. Fixed IV. Fixed LPN LPN Mean Di IV. Fixed | OPN fference | |
| | Study or Subgroup Adamy 2010 Bravi 2019 Chang 2018 Gill 2003 Jeon 2012 Kartal 2020 Klassen 2014 Liu 2013 Luciani 2016 Porripiglia 2016 Porripiglia 2016 Springer 2012 Webb 2015 Xu 2014 Xu 2015 Total (95% CI) Heterogeneity: CIP = 9 Study or Subgroup Beasley 2004 Chaz 2018 Gong 2008 Park 2010 Total (95% CI) Heterogeneity: CIP = 9 Study or Subgroup Rezaeetalab 2016 Romero 2008 Total (95% CI) Heterogeneity: CIP = 5 | Mean 241 165 196.1 1395.2 525 163 126.9 100 316 166.7 157.5 100 3.38, drf 250 166.7 166.7 157.5 100 3.38, drf 164.8 211.9 293 310 280.9 27.13, drf | LPN <u>SD</u> 2011 137.5 142 275.2 297 288 179 41.8 111.1 77.7 123.1 77.7 123.1 77.7 123.1 77.7 123.1 177.7 123.1 177.7 125.1 202 100.2 2 50.0 2 250.0 225.3 225.3 225.3 225.3 225.3 225.3 225.3 225.3 225.3 225.3 225.3 225.3 225.5 25.5 25. | Total I 1 182 625 625 122 : 100 : 31 - 48 115 : 15 57 170 : 57 173 : 31 : 42 : 19 : 1734 : 200001) Total I 27 96 76 76 34 562 <0.0002) | Oi 379 379 200 379 200 379 200 379 200 312 266.7 250 250 252 275 275 2201.5 231.5 223.3 11); IP = 6 Mean 334 335.4 418 324 412 412.4 412.4 2412.4 2412.4 | PN SD 357 48.6 135 88.1 27.9 404 88.1 27.9 404 88.7 71.7 49.9 35.4 57.8 362 71.7 35.4 52.7 34% PN SD 24% 24.6 84.7 34.3 52.2 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 34.3 52.7 52. | Total 1 805 682 122 100 102 41 23 97 58 133 170 21 187 18 2686 77 279 285 77 279 31 28 7722 | Weight 5.6% 6.7% 6.7% 6.7% 0.5% 0.5% 22.8% 1.2% 0.6% 2.3% 1.1% 10.7% 0.3% 2.3% 1.1% 100.0% | Mean Difference IV. Fixed, 95%. -138.00 [-176.22, -99.76 -35.00 [-50.51, -19.46 -10.30 [-45.07, 24.47 -125.00 [-164.70, -85.35 -87.50 [-260.06, 85.00 -204.00 [-331.38, -76.62 -105.40 [-124.27, -86.55 -150.00 [-231.69, -88.37 -150.00 [-231.69, -88.37 -33.30 [-65.52, -10 -82.70 [-110.21, -551 -82.30 [-105.94, 124.34 -40.40 [-99.88, 19.06 -127.20 [-212.89, -41.51 -68.35 [-77.36, -59.35 Mean Difference W. Fixed, 95%, -84.00 [-255.57, 87.51 -82.0 [-37.72, 21.37 -82.0 [-37.72, 21.37 -173.50 [-266.19, -90.8 -125.00 [-175.84, -74.11 -14.00 [-121.86, 39.38 -51.79 [-74.88, -28.71 | | | LPN Mean Di IV. Fixes LPN Mean Di IV. Fixes | OPN fference | |

lower blood transfusion rate was found in the LPN group (p=0.04, OR: 0.75, 95% CI: 0.57-0.99, **Figure 3A**). The quality of evidence for EBL and transfusion both were moderate.

For LOS, there was a statistically significant difference between the two surgical techniques (p<0.00001, MD: -2.01 days, 95% CI: -2.58, -1.45, **Figure 3B**). Moreover, subgroup analysis showed that a shorter LOS was related to LPN (p<0.00001, MD: -2.03 days, 95% CI: -2.43, -1.63, **Figure 3C**) for the clinical stage of T1a. The quality of evidence was judged to be moderate according to the Cochrane Handbook. No clinically meaningful differences were found between two groups for term of intraoperative complications (p=0.94, OR: 1.01, 95% CI: 0.69, 1.49, **Figure 4B**). However, fewer complications were found in terms of both total (p=0.03, OR: 0.80, 95% CI: 0.66, 0.98, **Figure 4A**) and postoperative complications (p=0.02, OR: 0.75, 95% CI: 0.59, 0.96, **Figure 4C**). The quality of evidence was graded as low because of no classification of complications and the potential of performance, detection, and attrition biases influencing the estimate of effect.

| A | LPN | T-4-1 | OPN | T - 4 - 1 | 14/-1 | Udds Katio | Odds Ratio |
|-----------------------------------|--------------------------|----------|------------------------|--------------------|--------------------------|------------------------|-----------------------------|
| Study or Subgroup | Events | lotal | Events | lotal | Weight | M-H, Fixed, 95% CI | M-H, Fixed, 95% Cl |
| Bravi 2019 | 33 | 625 | 41 | 682 | 32.0% | 0.87 [0.54, 1.40] | |
| Gong 2008 | 9 | 76 | 12 | 77 | 9.1% | 0.73 [0.29, 1.84] | |
| Jeon 2012 | 2 | 31 | 12 | 102 | 4.5% | 0.52 [0.11, 2.45] | - |
| Kartal 2020 | 2 | 22 | 0 | 41 | 0.3% | 10.12 [0.46, 220.70] | |
| Klaassen 2014 | 1 | 48 | 1 | 23 | 1.1% | 0.47 [0.03, 7.83] | |
| Liu 2013 | 5 | 115 | 3 | 97 | 2.7% | 1.42 [0.33, 6.12] | - |
| Luciani 2016 | 15 | 70 | 16 | 73 | 10.6% | 0.97 [0.44, 2.15] | _ |
| Park 2010 | 26 | 273 | 47 | 279 | 36.3% | 0.52 [0.31, 0.87] | |
| Springer 2012 | 2 | 170 | 4 | 170 | 3.4% | 0.49 [0.09, 2.73] | |
| Total (95% CI) | | 1430 | | 1544 | 100.0% | 0.75 [0.57, 0.99] | ◆ |
| Total events | 95 | | 136 | | | | |
| Heterogeneity: Chi ² | = 6.81. df = 8 | 6 (P = 0 | .56); l ² = | 0% | | + | |
| Test for overall effect | t: Z = 2.04 (F | P = 0.04 | 4) | | | 0.0 | 005 0.1 1 10 200 LPN OPN |
| в | LPN | | OF | N | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean SD | Total | Mean S | SD Tot | al Weigh | t IV. Random, 95% CI | IV. Random, 95% CI |
| Beasley 2004 | 2.9 1.5 | 27 | 6.4 1 | .8 2 | 22 5.6% | 6 -3.50 [-4.44, -2.56] | |
| Chang 2018 | 6.9 4.3 | 122 | 6.1 3 | 3.2 12 | 22 5.6% | 6 0.80 [-0.15, 1.75] | |
| Gill 2003 | 2.3 0.8 | 100 | 5.7 1 | .5 10 | 0 6.4% | 6 -3.40 [-3.73, -3.07] | - |
| Gong 2008 | 2.5 2.1 | 76 | 5.6 | 3 7 | 77 5.8% | 6 -3.10 [-3.92, -2.28] | |
| Jeon 2012 | 4.7 1.8 | 31 | 7.3 | 2 10 | 02 5.9% | 6 -2.60 [-3.34, -1.86] | |
| Kartal 2020 | 4.5 1 | 22 | 73 | 3.2 4 | 41 5.3% | 6 -2.50 [-3.56, -1.44] | |
| Klaassen 2014 | 1.9 1.7 | 48 | 3 1 | .8 2 | 23 5.7% | 6 -1.10 [-1.98, -0.22] | |
| Liu 2013 | 8.3 2.3 | 115 | 12.1 5 | 5.2 9 | 97 5.2% | 6 -3.80 [-4.92, -2.68] | |
| Luciani 2016 | 8 3 | 70 | 9 | 5 7 | 73 4.8% | 6 -1.00 [-2.35, 0.35] | |
| Marszalek 2009 | 5.3 0.8 | 100 | 7 1 | .5 10 | 0 6.4% | 6 -1.70 [-2.03, -1.37] | |
| Minervini 2013 | 5 3 | 140 | 6 | 3 14 | 40 6.0% | 6 -1.00 [-1.70, -0.30] | |
| Permpongkosol 2006 | 3.3 1.6 | 85 | 5.4 2 | 2.3 5 | 58 6.0% | 6 -2.10 [-2.78, -1.42] | - |
| Rezaeetalah 2016 | 4.6 2.3 | 34 | 4.1 2 | 23 - 2 0 0 - 7 | 11 52% 20 E20 | 6 0.50 [-0.62, 1.62] | |
| Romero 2006 | 3.2 1.0 | 170 | 0.3 4 | 1.0 4 | 20 5.27 | 0 -3.10 [-4.22, -1.96] | |
| Wobb 2015 | 4.0 2.1 | 31 | 43 3 | 0.0 II | 0 0.17 | 6 -2.10 [-2.75, -1.45] | |
| Xu 2014 | 85 31 | 42 | 9.3 2 | 18 18 | 27 539 | 6 -2.30 [-3.47, -1.13] | |
| Xu 2015 | 5.3 2.1 | 19 | 8.7 2 | 2.8 | 18 4.3% | 6 -3.40 [-5.00, -1.80] | |
| Xazoro | 0.0 2.1 | 10 | 0.1 | | 10 1.07 | 0.10[0.00, 1.00] | • |
| Total (95% CI) | | 1288 | | 141 | 10 100.0% | 6 -2.01 [-2.58, -1.45] | |
| Heterogeneity: Tau ² = | 1.26; Chi ² = | 171.72, | dt = 17 (P | < 0.000 | 001); I ² = 9 | 0% | -4 -2 0 2 4 |
| Test for overall effect: | Z = 6.99 (P < | 0.0000 | 1) | | | | LPN OPN |
| С | LPN | | O | PN | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean SD | Total | Mean | SD To | tal Weig | ht IV, Fixed, 95% CI | IV. Fixed, 95% Cl |
| Beasley 2004 | 2.9 1.5 | 27 | 6.4 | 1.8 | 22 18.1 | % -3.50 [-4.44, -2.56] | |
| Gong 2008 | 2.5 2.1 | 76 | 5.6 | 3 | 77 23.9 | % -3.10 [-3.92, -2.28] | |
| Minervini 2013 | 5 3 | 140 | 6 | 3 1 | 40 32.5 | % -1.00 [-1.70, -0.30] | |
| Rezaeetalab 2016 | 4.6 2.3 | 34 | 4.1 | 2.3 | 31 12.8 | % 0.50 [-0.62, 1.62] | - +- - |
| Romero 2008 | 3.2 1.6 | 56 | 6.3 | 2.8 | 28 12.8 | % -3.10 [-4.22, -1.98] | |
| Total (95% CI) | | 333 | | 2 | 98 100.0 | % -2.03 [-2.43, -1.63] | • |
| Heterogeneity: Chi ² = | 47.30, df = 4 | (P < 0. | 00001); l ^a | ^e = 92% | | - | |
| Test for overall effect | Z = 9.94 (P | < 0.000 | 01) | | | | -4 -2 U 2 4 |
| | | | | | | | |

Oncological Outcomes

The higher PSM was in connection with the LPN (p=0.005, OR: 1.51, 95% CI: 1.13, 2.01, **Figure 5A**). Nonetheless, no statistically significant difference was found in subgroup analysis (p=0.23, OR: 1.49, 95% CI: 0.78, 2.85, **Figure 5B**). The quality of evidence was judged to be low because of selection bias and inconsistency of results from populations.

There was no clinically meaningful differences for recurrence between the LPN and OPN (p=0.56, OR: 1.12, 95% CI: 0.76, 1.67, **Figure 5C**). The quality of evidence was moderate.

For survival outcomes, there was a statistically significant difference between the two surgical techniques regarding OS (p<0.00001, OR: 2.45, 95% CI: 1.79, 3.37, **Figure 5D**). The quality of evidence was graded as very low because of the potential of selection bias and circumstantial evidence. Yet, no significant difference was found for terms of CSS (p=0.72, HR: 1.13, 95% CI: 0.58, 2.18, **Figure 5E**) and DFS (p=0.72, HR: 1.14, 95% CI: 0.56, 2.36, **Figure 5F**). The quality of evidence was low because of the small sample size, the potential of performance, and detection biases, respectively.

Functional Outcomes

No statistically significant difference between the two surgical techniques regarding eGFR (p=0.31, MD: -1.60 mL/min/1.73m², 95% CI: -4.71, 1.51, **Figure 6A**). There was a clinically meaningful difference between the two groups for term of sCr (p=0.002, MD: -0.08 mg/dL, 95% CI: -0.14, -0.03, **Figure 6B**). The quality of evidence was low because of high heterogeneity and the potential of performance bias, respectively.

Publication Bias

We analyzed possible publication bias generating funnel plots used for the evaluated comparisons of outcomes. There was apparent publication bias in most of the outcomes. For example, we present the funnel plot of PSM showing the obvious asymmetry (**Figure 7**).

DISCUSSION

We believed that there is a different effect on surgical, oncological, and functional outcomes between LPN and OPN.



Due to lack of systematic evidence, we performed a meta-analysis and found several significant results after a systematic review of the literatures.

First, the results of surgical outcomes show that no significant difference was found pertaining to the operative time with high heterogeneity. Even so, some experienced centers report that shorter operative time has something to do with the LPN, which proves that the LPN has a great potential to transcend the OPN in terms of operative time for experienced centers (25, 39, 42, 43). Fu et al. prove that the retroperitoneal LPN has significantly less

operating time the transperitoneal LPN (48). No subgroup analysis was performed because lack of sufficient data. Therefore, the tumor size, initial experience, and peritoneal access play main roles in the high heterogeneity. In addition, a lower volume (66.16 ml) of EBL is associated with LPN, which is not necessarily of clinical significance unless the total blood loss is sufficient to transfuse. Hence, we further analyzed the difference in intraoperative blood transfusion rate between the two surgical techniques and found that 15% risk of transfusion was reduced by LPN. It is pneumoperitoneum and superior

| A Study or Subaroup | LPN Events | Total I | OPN Events 1 | otal | Weight | Odds Ratio M-H, Fixed, 95% Cl | | Udds M-H, Fixe | rtatio d. 95% CI | |
|---|---------------------------------|----------------------|-------------------------------|------------------|------------------|---|----------|-------------------|---------------------|-------|
| Becker 2014 | 2 | 57 | 3 | 154 | 2.0% | 1.83 [0.30, 11.25] | | | _ | |
| Bravi 2019 Chang 2018 | 56 5 | 625 122 | 48 | 682 122 | 54.8% 2.5% | 1.30 [0.87, 1.94] 2.56 [0.49, 13.48] | | - | | |
| Gill 2003 | 3 | 100 | 1 | 100 | 1.3% | 3.06 [0.31, 29.95] | | | | |
| Gong 2008 | 1 | 76 | 1 | 77 | 1.3% | 1.01 [0.06, 16.50] | | | | |
| Jeon 2012 Kartal 2020 | 3 | 23 | 2 | 75 41 | 0.3% 1.7% | 25.78 [1.28, 519.43] | | | | |
| Klaassen 2014 | 3 | 48 | 0 | 23 | 0.8% | 3.62 [0.18, 72.96] | | | · · · | |
| Lane 2010 | 5 | 499 | 2 | 762 | 2.1% | 3.85 [0.74, 19.90] | | | | |
| Lucas 2012 | 0 | 15 | 1 | 97 54 | 0.9% | 1.15 [0.04, 29.68] | | | | |
| Luciani 2016 | 3 | 70 | 0 | 73 | 0.6% | 7.62 [0.39, 150.30] | | | | • |
| Marszalek 2009 | 4 | 100 | 2 | 100 | 2.5% | 2.04 [0.37, 11.41] | | | | |
| Park 2010 | 4 12 | 273 | 7 | 279 | 6.4% 8.7% | 0.79 [0.21, 3.02] 1.79 [0.69, 4.61] | | - | | |
| Permpongkosol 2006 | 2 | 85 | 1 | 58 | 1.5% | 1.37 [0.12, 15.51] | - | | | |
| Porpiglia 2016 | 1 | 57 | 9 | 133 | 7.0% | 0.25 [0.03, 1.99] | | | | |
| Springer 2012 | 3 | 34 170 | 1 | 31 170 | 1.2% | 2.90 [0.29, 29.49] | _ | | | |
| | - | | - | | | , | | | • | |
| Total (95% CI) | 110 | 2631 | 3 | 171 | 100.0% | 1.51 [1.13, 2.01] | | | • | |
| Heterogeneity: Chi ² = | 112 12.87. df = 1 | 8 (P = 0 | 88).80); l ² = | 0% | | | | - | | |
| Test for overall effect: | Z = 2.80 (P | = 0.005 |) | | | | 0.05 | 0.2 1 | OPN 5 | 20 |
| | L DN | | ODN | | | Odda Batia | | Odda | Patia | |
| B Study or Subgroup | Events | Total | Events | Total | Weight | M-H. Fixed, 95% C | I | M-H. Fixe | ed. 95% CI | |
| Becker 2014 | 2 | 57 | 3 | 154 | 10.4% | 1.83 [0.30, 11.25] | | | • | _ |
| Gong 2008 | 1 | 76 | 1 | 77 | 6.5% | 1.01 [0.06, 16.50] | - | | | |
| Minervini 2013 Park 2010 | 4 | 140 273 | 5 | 140 279 | 32.4% 44.2% | 0.79 [0.21, 3.02] | | | | |
| Rezaeetalab 2016 | 3 | 34 | 1 | 31 | 6.4% | 2.90 [0.29, 29.49] | | | | |
| | | | | | | | | | | |
| Total (95% CI) | 22 | 580 | 17 | 681 | 100.0% | 1.49 [0.78, 2.85] | | 1 | | |
| Heterogeneity: Chi ² = | 1.43, df = 4 | (P = 0. | 84); l ² = 0 | % | | | <u> </u> | + | | 1 |
| Test for overall effect: | Z = 1.20 (P | = 0.23 |) | | | | 0.01 (| U.1 1 LPN | OPN | iu 10 |
| | I DN | | OPN | | | Odde Patio | | Odde | Patio | |
| C Study or Subgroup | Events | Total | Events | Fotal | Weight | M-H. Fixed, 95% Cl | | M-H, Fixe | d, 95% CI | |
| Chang 2018 | 6 | 122 | 4 | 122 | 8.4% | 1.53 [0.42, 5.55] | | | • | |
| Choi 2019 | 0 | 96 | 10 | 285 | 11.6% | 0.14 [0.01, 2.34] | ← | · | | |
| Jeon 2012 Lane 2010 | 2 | 31 499 | 27 | 102 762 | 2.9% | 2.28 [0.36, 14.28] | | - | - · | |
| Liu 2013 | 2 | 115 | 1 | 97 | 2.3% | 1.70 [0.15, 19.03] | | | - | |
| Marszalek 2009 | 3 | 100 | 4 | 100 | 8.5% | 0.74 [0.16, 3.41] | | | | |
| Park 2010 Bormpongkosol 2006 | 4 | 273 | 9 | 279 | 19.3% | 0.45 [0.14, 1.47] | | | | |
| T empongkosol 2000 | 2 | 00 | | 50 | 2.070 | 1.07 [0.12, 10.01] | | | | |
| Total (95% CI) | | 1321 | | 1805 | 100.0% | 1.12 [0.76, 1.67] | | • | | |
| Total events Heterogeneity: Chi ² = | 46 7 01 df = 7 | (P = 0 4 | 59 3): 1 ² = 09 | ~ | | | ++ | | | |
| Test for overall effect: | Z = 0.58 (P | = 0.56) | 5), 1 = 0 | 0 | | | 0.02 0.1 | 1 1 I DNI | OPN | 10 5 |
| | 1.01 | | 0.001 | | | Odda Datia | | O d de | Defin | |
| D Study or Subgroup | Events | Total | Events | Fotal | Weight | M-H. Fixed, 95% Cl | | M-H. Fixe | d. 95% CI | |
| Chang 2018 | 121 | 122 | 116 | 122 | 1.8% | 6.26 [0.74, 52.79] | | - | • | |
| Kartal 2020 | 21 | 22 | 38 | 41 | 2.2% | 1.66 [0.16, 16.96] | | | | |
| Lane 2010 Marszalek 2009 | 639 96 | 672 100 | 829 85 | 944 100 | 62.5% 6.3% | 2.69 [1.80, 4.01] | | | | _ |
| Park 2010 | 269 | 273 | 276 | 279 | 7.4% | 0.73 [0.16, 3.30] | | | | |
| Permpongkosol 2006 | 83 | 85 | 55 | 58 | 2.8% | 2.26 [0.37, 13.99] | | | | _ |
| Springer 2012 | 160 | 170 | 156 | 170 | 17.0% | 1.44 [0.62, 3.33] | | 1 | - | |
| Total (95% CI) | | 1444 | | 1714 | 100.0% | 2.45 [1.79, 3.37] | | | • | |
| Total events | 1389 | | 1555 | | | - | | | | |
| Heterogeneity: Chi ² = | 5.98, df = 6 | (P = 0.4 | 3); I ² = 0 | 6 | | | 0.01 0 |).1 1 | 1 | 10 10 |
| rescior overall effect: | ∠ - 0.04 (P | ~ 0.000 | 01) | | | | | LPN | OPN | |
| E | | | | | | Hazard Ratio | | Hazard F | Ratio | |
| Study or Subgroup | log[Ha | zard Ra | atio] S | E We | eight | IV, Fixed, 95% CI | | IV, Fixed, | 95% CI | |
| Chang 2018 Kartal 2020 | | | 0 1.9 | 53 74 | 3.0% 1 1.7% 5 | 1.00 [0.02, 45.69] 58 [0.04, 860 15] | | | | |
| Permpongkosol 2006 | 6 | (|).34 0.9 | 5 12 | 2.6% | 1.40 [0.22, 9.04] | | | | |
| Springer 2012 | | 0 | 0.06 0.3 | 7 82 | 2.8% | 1.06 [0.51, 2.19] | | - | _ | |
| T-4-1 (05%) 01 | | | | | 0.09/ | 4 4 2 10 50 0 403 | | | - | |
| I otal (95% CI) Heterogeneity: Chi2 - | - 0 47 df - 1 | 3 (P - 0 | 931- 12 - | 100 0% | 0.0% | 1.13 [U.58, 2.18] | | - | | |
| Test for overall effect | : Z = 0.36 (I | P = 0.72 | 2) | J /0 | | 0.0 | 0.1 | 1 | 1 | 0 10 |
| | | | • | | | | | LPN C | JPN | |
| F | 1 | | 4-1 07 | | | Hazard Ratio | | Hazard F | Ratio | |
| Study or Subgroup Chang 2018 | log[Ha | zard Ra | 50 2 / 4 | : We | ight / | 1V. FIXED, 95% CI | | IV, Fixed, | 95% CI | |
| Choi 2019 | | -1 -0 | .35 2.41 | 6 | | 0.66 [0.04, 11.16] | - | | | |
| Jeon 2012 | | 0 | .94 0.74 | 24 | .8% | 2.56 [0.60, 10.92] | | + | • | |
| Kartal 2020 | | -1 | .44 2.97 | 1 | .5% | 0.24 [0.00, 79.93] 🔶 | | | | |
| Liu 2013 Marszalok 2000 | | 0 | 31 3.81 | 0 | .9% 1.3 | 36 [0.00, 2386.21] * | | | | |
| Warszalek 2009 | | -0 -0 | .02 0.53 | , 4 , 48 | .0% | 0.98 [0.35. 2.77] | | - | _ | |
| Park 2010 | i | -0 | .23 1.09 | 11 | .4% | 1.26 [0.15, 10.66] | | | | |
| Park 2010 Permpongkosol 2006 | | | | | | - | | | | |
| Park 2010 Permpongkosol 2006 | | | | | | 4 4 4 70 70 | | | | |
| Park 2010 Permpongkosol 2006 Total (95% CI) | 2 /8 df - " | 7 (P - ^ | 03)-12 - | 100 | 0.0% | 1.14 [0.56, 2.36] | | + | • | |
| Park 2010 Permpongkosol 2006 Total (95% CI) Heterogeneity: Chi ² = Test for overall effect | = 2.48, df = 7 ; Z = 0.36 (F | 7 (P = 0 P = 0.72 | .93); I² = | 100 0% | 0.0% | 1.14 [0.56, 2.36] ⊢ 0.0 | 001 | 0.1 1 | 10 | 100 |





vision that contribute to reduce blood loss providing precise dissection (23, 25, 34). A lower transfusion rate is associated with postoperative survival in patients with renal cell carcinoma after nephrectomy and reduces potential risk factors, such as hemolysis in the clinic (49, 50). What is more, results of LOS are 2.01 days shorter for LPN than OPN with high heterogeneity because of lower complications, smaller wounds, and more rapid recovery (23, 34, 44). We believe that the discharge criteria, postoperative care management, and characteristics of patients are associated with high heterogeneity. Due to the lack of

scientific and strict classification of complications in most included studies and the lack of sufficient data, we only analyzed the complications classified into total, intraoperative, and postoperative complications according to the time of occurrence. Our cumulative analysis showed lower total and postoperative complications were related to the LPN compared with the OPN and showed no clinically meaningful differences were found for term of intraoperative complications. Marszalek et al. and Rezaeetalab et al. believe that shorter anesthesia and ischemia times are attributed to the lower perioperative complications, respectively (25, 28). On the other hand, some series thought the small difference in mean tumor size and tumor location were associated with fewer complications (26, 34, 35, 41). The fewer complications are beneficial to improve postoperative recovery and quality of life, which is more popular in the clinic.

Second, the analysis of oncological outcomes indicated that a higher PSM was found in the group of LPN. Subgroup analysis showed no significantly meaningful differences in term of PSM between two groups for T1a stage tumor. We believe that tumor size and learning curve play an important role in the discrepancy because the limited operation range of the laparoscope and less complete excision than open surgery was associated with high PSM for larger tumors. Current research suggests that a higher PSM is closely related to a higher incidence of local relapses, especially in large RCC, poorly differentiated, and/or more centrally located (51-53). However, the LPN and OPN accessed yield comparable in terms of recurrence, CSS, and DFS. It may be related to differences in pathological stage and follow-up time. In addition, we found that a high OS was associated with the LPN. Lane et al. thought that it had something to do with the renal functional outcomes (38). However, there is no clinical significance because of too many influences, such as underlying diseases and accidents.

Third, our results notably reveal that significant differences were found for postoperative change in sCr but not for postoperative changes in eGFR with moderate and high heterogeneity, respectively. The differences of patients' characteristics, ischemia technique, and time are associated with heterogeneity. Marszalek et al. believe that the functional outcomes were closely related to intraoperative renal perfusion, caused by either arterial clamping or capnoperitoneum or capnoretroperitoneum (25). In addition, Bravi et al. suggest that surgical manipulation and suture/hemostatic techniques may affect early postoperative renal function (23). In addition, ischemia technique and time are related to postoperative renal function (26, 28). Subgroup analysis was not possible due to the lack of data. Recently, a systematic review proved that functional outcomes had something to do with ischemia technique, but none of the available ischemia techniques could be recommended over the other (54). Yet, a 0.08 mg/dL less increased sCr has no significant difference in the clinic.

Few studies focused on quality of life after PN. Becker et al. report that LPN and OPN were equivalent with postoperative quality of life, which needs further argument (31). For cost, current studies suggested that LPN is more cost-effective than OPN because of shorter LOS (55).

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Although we performed this meta-analysis with the rigorous methodology of review and quantitative synthesis, some inherent limitations cannot be avoided. First, there were no prospective randomized controlled studies, which reduced the quality of evidence. Second, results should be applied carefully in clinical practice because of great heterogeneity in terms of operative time, LOS, and variations of eGFR. Third, some data were unsuitable to evaluate oncologic outcomes, including recurrence, OS, CSS, and DFS, because of insufficient follow-up period. Finally, there was evidence of the apparent publication bias. Computer-based literature searching could not include all relevant studies. Gray literature also could not be included.

CONCLUSIONS

This meta-analysis revealed that the LPN is a feasible and safe alternative to the OPN with comparable surgical, oncologic, and functional outcomes. However, the results should be applied prudently in the clinic because of the low quality of evidence. Further quality studies are needed to evaluate effectiveness of LPN and its postoperative quality of life compared with OPN.

DATA AVAILABILITY STATEMENT

All datasets presented in this study are included in the article/ Supplementary Material.

AUTHOR CONTRIBUTIONS

Conceived and designed the experiments: AW. Analyzed the data: CY, YD, LP, and HW. Contributed reagents/materials/ analysis: YD, LP, TW, and XZ. Wrote the manuscript: CY and YD. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2020. 583979/full#supplementary-material

SUPPLEMENTARY TABLE 1 | Characteristics and quality assessment of included studies.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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