Beni-Suef University Journal of Basic and Applied Sciences

REVIEW

Open Access

A prototype variable corresponding to the proportion of ischemia for the comparison between robotic and open partial nephrectomy: a meta-analysis accompanied by sensitivity analysis

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Abstract

Background The primary objective of this study involves the formulation of a novel variable, derived from initial data related to ischemia duration and operative time in partial nephrectomies. The aim was to determine the proportion of ischemia for the comparison between robotic and open approaches in terms of their relative ischemic requirements.

Main body The literature search was conducted from August 2022 to June 2023, primarily encompassing non-randomized comparative studies in the English language. Ultimately, a total of 62 studies involving data from 26,072 patients were included. Following appropriate transformation of the original data under the assumption of normal distribution, the proportion of ischemia (*I*) was formulated for each study and comparison arm, using estimator functions. Subsequent analysis of the generated data was performed for both the original variables and the *I* outcome. Statistical significance was only observed regarding the surgical duration, with a mean difference of 19.74 min ($CI_{95\%}$ = [11.56; 27.92]) in favor of robotic access. The mean difference in *I* was estimated on the entire dataset as well as carefully selected subgroups based on publication year, patient matching, the number of referral centers, and risk of bias class. Additionally, meta-regression analysis and four-level sensitivity analysis were conducted. In none of these investigations did statistically significant differences emerge between the two surgical approaches. These findings lead us to hypothesize that the proportion of ischemia in partial nephrectomies may represent an inherent characteristic of the procedure, typically manifesting as baseline ischemia (12–13% of operative time), with fluctuations depending on the chosen strategy or the complexity of the specific intervention.

Short conclusion There is no difference in the proportion of ischemia between robotic and open partial nephrectomies. In overall, ischemia time appears to be primarily determined by the overall duration of the procedure and the effectiveness in achieving adequate hemostasis.

Keywords Robotic partial nephrectomy, Open partial nephrectomy, Surgical precision, Ischemia, Operative time, Meta-analysis

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1 Background

Partial nephrectomy (PN) represents a nephron-sparing surgery (NSS) technique for the treatment of localized kidney tumors, primarily aiming at kidney function preservation compared to radical nephrectomy (RN) [1]. Various approaches, including open (OPN), laparoscopic (LPN), and robot-assisted partial nephrectomy (RAPN), are utilized. In particular, RAPN offers comparable perioperative outcomes to LPN but with improved precision in tumor excision. The R.E.N.A.L. nephrometry score is used to categorize kidney masses based on size, location, and depth, although there is limited data for highly complex tumors [1]. Guidelines from the American Urological Association (AUA) recommend PN for localized T1a-b renal tumors, and there has been an increased utilization of NSS in recent years, mainly due to the rise in robotic technology availability [2]. Ongoing research is exploring outcomes for robotic, open, and laparoscopic PN [2]. NSS is commonly employed for renal masses, with OPN preferred in cases involving a solitary kidney due to its field visualization and access advantages. RPN is gaining popularity and has demonstrated safety and effectiveness, even for complex tumors in solitary kidneys [3]. Renal cell carcinoma (RCC) is a life-threatening condition, and NSS is the currently most preferred approach. OPN has traditionally been the standard approach for treating RCC. However, the adoption of minimally invasive techniques like LPN has been limited due to the complexity of the procedure. In contrast, RAPN has emerged as a viable alternative, offering improved surgical capabilities and ergonomic benefits [4]. Several studies have shown that RAPN provides superior surgical precision compared to OPN and LPN, but the varied methodologies and outcome measures used, unavoidably limit broader conclusions [5–7].

In this study, our objective was to compare RAPN and OPN in terms of surgical precision, specifically in the context of intraoperative applied ischemia. The international literature consistently highlights the detrimental effects of prolonged ischemia on postoperative kidney function recovery [8]. Conversely, ischemia is crucial to achieve adequate hemostasis and optimize the visualization of the surgical field, ultimately enhancing the precision of surgical maneuvers [9]. The contribution of minimally invasive techniques to prolonging ischemia duration in PN compared to open surgery has been frequently discussed, although this position does not universally represent the body of relevant literature. Given the conflicting impact of ischemia duration on renal function and surgical precision, we considered the proportion of ischemia, defined as the ratio of ischemia time (IT) to operative time (OT), as a parameter that could provide a more objective basis for comparing the two surgical approaches in terms of their relative demands for intraoperative ischemia. Consequently, we conducted a meta-analysis using available data from the literature to obtain an overall estimation of the comparative effect within the maximum feasible set of studies.

2 Materials and methods

2.1 Main concept

We've previously elucidated the relationship between ischemia time (IT), renal function preservation, and hemostasis. In our analysis, we considered the impact of IT normalized to the procedure's total duration. We argue that the proportion of ischemia better reflects surgical precision, supported by international literature showing that RAPN typically has a longer operative time (OT) compared to OPN [10, 11]. Assuming IT and OT are collinear, indicating a non-zero correlation coefficient, we chose to compare RAPN and OPN precision using the ratio of these variables, denoted as "*I*". The newly introduced outcome, expressed as a dimensionless measure, essentially signifies the proportion of ischemia, effectively indicating the ischemic requirements associated with each approach. More specifically, it was considered to have a negative impact on surgical precision, aligning with literature advocating for improved postoperative outcomes by minimizing ischemia duration within a specified procedure timeframe [12]. In summary, our hypothesis proposes that when comparing RAPN and OPN, greater surgical precision can be offered by the approach that minimizes *I*.

2.2 Literature search and study selection

Between August 2022 and June 2023, a comprehensive literature search was conducted to identify relevant studies comparing RPN or RAPN with OPN based on their titles. Inclusion in the analysis was contingent upon the availability of simultaneous comparative data for the original variables: IT (ischemia time) and OT (operative time). These variables were combined as a quotient to derive the proportion of intraoperatively applied ischemia, the primary outcome of interest. The literature search encompassed multiple databases, including "Medline," "Scopus," "ScienceDirect," "CENTRAL," and "Google Scholar". Monthly alerts were set within these databases throughout the search period to ensure adequate coverage. The study protocol was meticulously formulated in advance and is accessible on the Prospero website (https://www.crd.york.ac.uk/prospero) [13], identified as CRD42022354959. In accordance with the original study protocol, two distinct interventions were implemented. Firstly, the protocol's title was succinctly condensed. And

secondly, the investigation was expanded to encompass a broader range of databases to conduct a more thorough examination of the available literature.

The preselected search strategy (SS) played a pivotal role in determining the study selection criteria. The original SS can be accessed online at the following URL: https://www.crd.york.ac.uk/PROSPEROFILES/354959_STRATEGY_20220821.pdf. In summary, this SS utilized keywords such as "robotic", "robot-assisted", "open", and "partial nephrectomy" in various combinations. To manage the extensive amount of data generated during the initial exploration of potential studies for the RPN/RAPN versus OPN comparison, these filters were applied exclusively to study titles. After applying the SS sequentially to each database, distinct sets of studies were identified and imported into the Sysrev electronic platform (https://sysrev.com) [14] in ".ris" format. The inclusion criteria were then applied, focusing on studies conducted exclusively in English, non-duplicated studies with accessible full-text, and comparative studies providing sufficient data for both arms of the comparison, enabling the calculation of "ischemia minutes per operative minute". Non-comparative studies, those lacking statistically assessable data, or studies reporting findings solely for one arm of the comparison were excluded. The application of these inclusion criteria to individual studies primarily occurred within the Sysrev online platform. The entire project is accessible online at the URL: https://sysrev.com/p/119881. Furthermore, an additional criterion was introduced post-initial evaluation, focusing on the exclusion of studies based on the outcome of interest. Within the Sysrev platform, each study underwent an initial assessment considering a set of binary qualitative variables, followed by the assignment of specific labels according to its field of interest. A PRISMA flowchart illustrating the processes of study exclusion or inclusion is available in the Sect. 3.

2.3 Evidence acquisition and quality assessment

The classification of studies obtained from the databases commenced within the Sysrev environment. This classification process involved three levels. Initially, studies were assessed using basic binary parameters based on their methodological profile, and they were then labeled according to their specific field of interest. At the third level, a list of variables was compiled for each study, focusing on relevant statistical data needed for comparative purposes between RAPN and OPN. A member of the authoring team ([SA]), oversaw this three-level process, which included study classification, labeling, and outcome identification. Subsequently, two reviewers ([DA] and [IK]) tabulated studies that met the eligibility criteria, creating the corresponding file in ".csv" format. It's important to note that missing data affected a total of 1093 patients, with 472 in the experimental arm (RPN/RAPN) and 621 in the control arm (OPN). Addressing these missing data was crucial in constructing the patient populations for comparison in each case.

Following data acquisition, the extraction of the necessary statistical parameters for each variable under comparison was conducted manually, without the use of automation tools. Alongside numerical data, metadata related to specific study features were also recorded. These included the study's author, publication year, patient matching implementation, number of referral centers involved, study duration, risk of bias, confounding issues, and other pertinent information. Upon completion of data and metadata tabulation from each individual study, three reviewers ([DA], [IK], and [KT]) performed an overall evaluation and applied two qualitative classification scales. Firstly, the Newcastle–Ottawa Scale (NOS) was employed for an overview grading, followed by the more detailed ROBINS-I tool for non-randomized comparative studies [15, 16]. This dual-scale approach was chosen for two primary reasons. Firstly, it allowed for the comprehensive assessment of different critical aspects since each scale addresses distinct factors. And secondly, it aimed to achieve a thorough evaluation of the study quality while minimizing the risk of underestimating bias.

2.4 Outcomes

The primary aim of this study was to estimate the proportion of ischemia (I), a measure derived through statistical estimations, as explained below. Additionally, the analysis involved two secondary outcomes: ischemia time (IT) and operative time (OT), both measured in minutes (min). These parameters are well-documented in the international literature, particularly in the context of RAPN versus OPN comparison. To achieve these objectives, a substantial number of studies meeting the inclusion criteria were collected, allowing for the exploration of inherent differences between RAPN and OPN within a diverse patient population. Given the extensive volume of data and adherence to the predefined study protocol, no additional variables beyond the mentioned ones were pursued. However, a comprehensive examination of potential deviations in comparability among integrated studies was conducted, with a specific focus on statistically significant differences in baseline characteristics between patient groups being compared. These variations are succinctly presented in the relevant table of included studies, available in the Sect. 3.

2.5 Statistical analysis

The estimation of the ischemia proportion (*I*) followed a standardized stepwise process, utilizing the expected value (EV) and standard error (SE) of the original outcomes. The analysis assumed a normal distribution and relied on summary statistics from the IT and OT variables. Each included study and arm under comparison (RPN/RAPN and OPN) were considered in the estimation process, accounting for missing data to form the respective patient populations. The statistical parameters EV and SE of *I* were derived using estimator functions (1) and (2), as previously reported by van Kempen and van Vliet in their computational analysis of fluoroscopy data [17]. These functions were implemented with the assumption that each study provided a single sample ($n=1$) for each arm under comparison, and all calculations were performed accordingly. To facilitate computation, the original variables (IT and OT) needed to be presented in the format "EV–SE," with units in minutes (min). In cases where the initial data were in a non-standard format, a transformation was applied following the "rule of thumb", assuming a normal distribution [18]. This assumption was supported by the extensive database of studies, which allowed the central limit theorem to be valid [19]. Additionally, when both cold and warm ischemia were applied, a weighted average between the two approaches was calculated based on the concept of the maximum effect from ischemia. The equations used for these computations are provided in analytical form below:

$$\mathrm{EV}\left\{\frac{\overline{x}}{\overline{y}}\right\} \approx \frac{m_x}{m_y} + \frac{1}{n}\left(\mathrm{var}(y)\frac{m_x}{m_y^3} - \frac{\mathrm{cov}(x,y)}{m_y^2}\right) \quad (1)$$

$$\mathrm{SE}\left\{\frac{\overline{x}}{\overline{y}}\right\} \approx \left(\mathrm{var}\left(\frac{\overline{x}}{\overline{y}}\right)\right)^{1/2} \approx \left[\frac{1}{n}\left(\frac{\mathrm{var}(x)}{m_y^2} + \frac{m_x^2\mathrm{var}(y)}{m_y^4} - \frac{2m_x\mathrm{cov}(x,y)}{m_y^3}\right)\right]^{1/2} \quad (2)$$

$$\mathrm{cov}(x,y) = rs_xs_y = r\mathrm{var}(x)^{1/2}\mathrm{var}(y)^{1/2} \quad (3)$$

The equations provided above involve the following variables: "*x*" represents ischemia time (IT), "*y*" represents operative time (OT), "*m*" represents the mean, "*s*" represents the standard deviation (SD), "*n*" represents the number of samples per arm, "cov" represents the covariance, and "*r*" represents the Pearson correlation coefficient between IT and OT [20]. The use of the correlation coefficient in the calculations is evident in Eq. (3) presented earlier. To obtain accurate *r* values, a Monte Carlo simulation with 1000 repetitions was conducted for each study and each compared arm, based on the EV and SE of the original variables [21]. The physiological significance of the correlation coefficient lies in the covariance between IT and OT when assumed to follow a bivariate normal distribution [22]. The theoretical range of *r* values extends from − 1 to + 1. For positive *r* values (approximating + 1), both IT and OT increase simultaneously, or they show an exact opposite pattern. This suggests scenarios related to the difficulty in performing partial nephrectomy (PN). In technically demanding procedures, both the total duration of the operation and the application of ischemia are expected to be extended to facilitate tumor removal, and vice versa. Conversely, for negative *r* values (approximating − 1), IT increases while OT is constrained, or IT decreases while OT is prolonged. In PN, the main goal is to limit ischemia duration, and the disproportionate use of ischemia likely reflects a strategic choice by the surgeon to implement hemostasis measures, despite its impact on postoperative renal function recovery. Following the calculations for the proportion of ischemia (*I*), the resulting data were re-tabulated by three reviewers: [SA], [DA], and [IS].

The estimation of the Pearson correlation coefficient (r) was performed collectively for each arm under comparison (RAPN vs. OPN) across all available studies, utilizing the expected values (EVs) of IT and OT. Subsequently, two coefficients were obtained, one for each arm, and these coefficients underwent statistical inference to estimate both their difference and their deviation from zero. It's important to note that we initially considered the likelihood of collinearity between the original variables, implying that as the duration of the surgery increases, so does the absolute time of ischemia application. Therefore, in case of a statistically significant difference in r between RAPN and OPN, it was predetermined to use these two correlation coefficients to calculate *I* for each arm, remaining constant as a pair across all available studies. This assumption was considered necessary, as determining r under a bivariate normal distribution through Monte Carlo simulations tends to be more conservative in revealing a substantial correlation between the two variables involved [23].

The generated *I* variable served as a suitable representation of the level of surgical precision in tissue handling and hemostasis during PN. It was also considered to adequately reflect the impact of intraoperative ischemic measures on postoperative renal function recovery. To estimate the overall effect of the comparison between RAPN and OPN, a meta-analyses methodology was employed, with the mean difference of *I* (MD_I) serving as the effect size. Given the inclusion of a substantial number of studies, made possible by the increased availability of data for the original variables, a random effects

model was adopted, following the Hartung and Knapp modification [24, 25]. In the forthcoming meta-regression plots, each study was visually represented as a circle with a radius proportional to the accuracy of its reported results, based on the typical rendering standard. Additionally, linear regression models based on the restricted maximum likelihood (REML) estimation were applied [26, 27]. Heterogeneity within the data was assessed using the statistical parameters I^2 and Cochran's Q [28, 29]. The statistical analysis was conducted using the R programming language version 4.3.1 [30]. This comprehensive approach enabled the systematic and objective evaluation of the precision of surgical maneuvers during RAPN and OPN, based on the proportion of ischemia implemented in each case.

The evaluation for potential publication bias (PB) was conducted through the utilization of appropriate funnel and radial plots. To enhance the robustness of its significance assessment, rigorous application of the Egger's test was carried out. Special attention was given to the impact of small studies, as they represented a substantial portion of the non-randomized studies included in the analysis. To explore additional sources of heterogeneity, subgroup analysis (SGA) was undertaken. This analysis was based on several factors, including the year of publication, the implementation of patient matching protocols, the involvement of multiple referral centers, and the risk of bias (ROB) classification according to the ROBINS-I tool. Furthermore, meta-regression analysis (MRA) was conducted to investigate the change in the comparative effect concerning both the publication year and the quality rating based on the Newcastle–Ottawa Scale (NOS). These parameters were treated as moderators for the respective analysis. MRA was applied to the entire set of studies and also separately for each of the aforementioned subgroups. This comprehensive approach allowed for a thorough examination of potential sources of variation in the overall effect between RAPN and OPN.

A sensitivity analysis (SA) was performed at four distinct levels to enhance the robustness and validity of the findings. At the first level, a subset of studies was isolated by applying a predefined cut-off to the range of the 95% confidence interval ($CI_{95\%}$) around the mean difference in I (MD_I) to assess the impact of individual studies on the overall effect size. At the second level, studies characterized by favorable methodological features and low risk of bias were selected. These studies applied patient matching and were classified as having low ROB according to the ROBINS-I tool, to draw more reliable conclusions regarding the comparative effect between RAPN and OPN. At the third level, a subset of studies with a larger patient population than the average of the initial dataset was chosen to address potential small study effects and enhance result reliability. At the fourth level, a sensitivity analysis was conducted by exploring a range of consecutive values of the correlation coefficient (r) between IT and OT, which is crucial in the estimation of I. This analysis involved examining the comparative effect between RAPN and OPN on MD_I as the coefficient (r values) varied from -0.99 to $+0.99$, providing insights into the sensitivity of results to different correlation levels. These four levels of sensitivity analysis collectively ensured the reliability and validity of the overall results by accounting for individual study impact and the interconnection between IT and OT, while addressing potential sources of variability.

The present study meticulously adhered to the guidelines provided on the PRISMA website (http://prisma-statement.org/Extensions/Protocols) to ensure compatibility with the PRISMA 2020 Checklist. Results are presented in the format: MD_I–$CI_{95\%}$, with a confidence level of $\alpha = 0.05$. To promote transparency and reproducibility, all primary and secondary data are available in ".csv" files, and the analytical code is accessible in ".txt" files. These materials are publicly accessible on a Github repository, through the URL: https://github.com/sotbike/I.git. Each code file's specific purpose and settings for reproducing the results are detailed in corresponding ".txt" files within the repository. Sharing these data and analytical code is intended to encourage open science practices, facilitate scrutiny of the findings, and promote further research in this domain.

3 Results

3.1 Study retrieval

The PRISMA flowchart illustrating the literature search process, is presented in Fig. 1. The initial search yielded 582 studies, and after eliminating duplicates, non-English studies, and those with ineligible titles or abstracts, 178 studies remained for screening. Of these, 24 studies were excluded due to the unavailability of their full text, resulting in 154 studies included for investigation into comparative data on RPN/RAPN versus OPN. Nine of these studies lacked statistically exploitable data and were subsequently excluded from further analysis. Therefore, a total of 145 records underwent a comprehensive eligibility assessment. Among these, six were excluded as meta-analyses or simple systematic reviews, while 50 were excluded for lacking comparative data. Additionally, 26 studies were excluded as they did not contain data on the outcome of interest for the present analysis. It's worth noting that those studies excluded based on the latter criterion were initially considered eligible based on their general content. However, they did not simultaneously include comparative data for both original variables (IT and OT), which was necessary for estimating I.

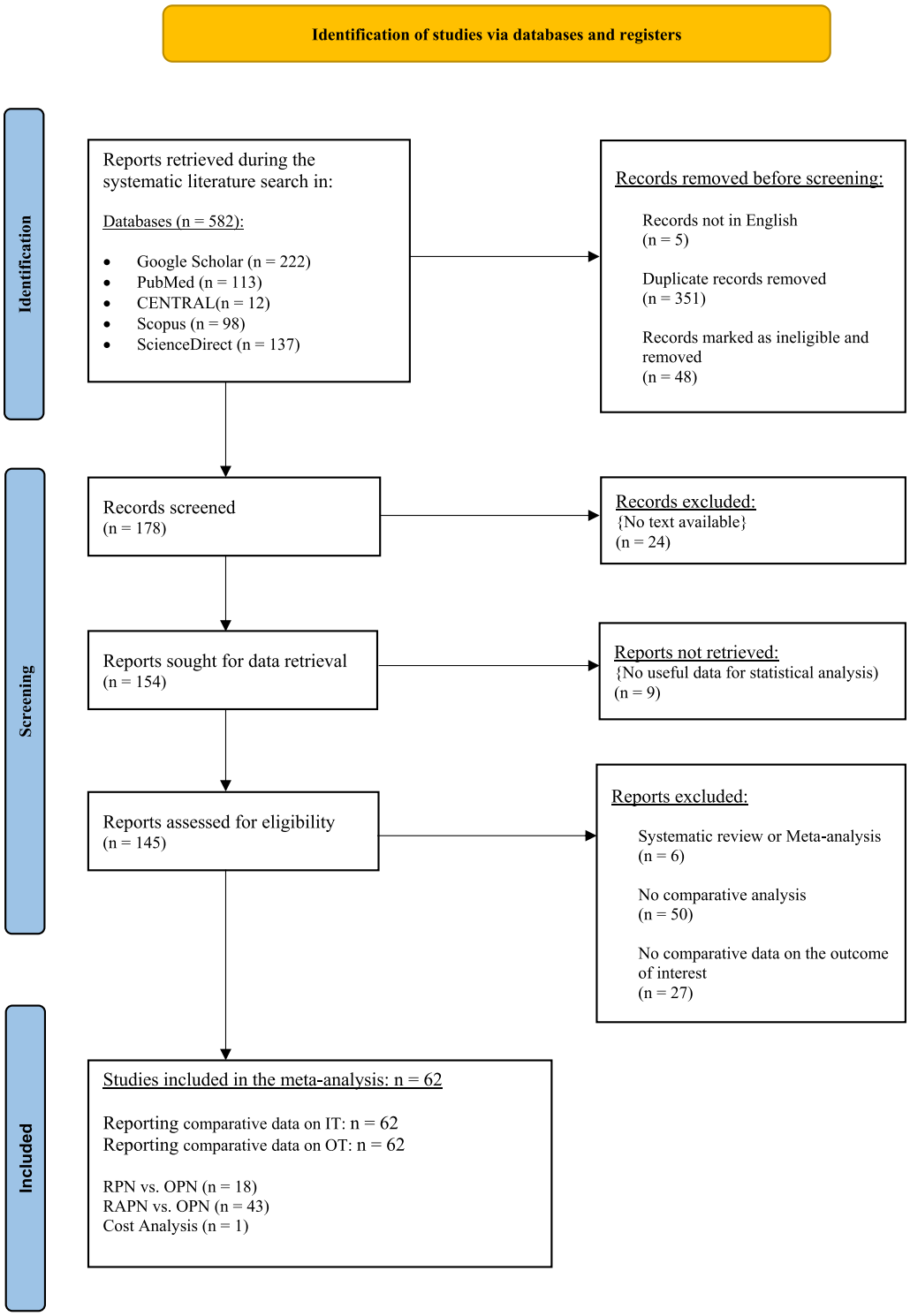

Fig. 1 Flow-chart of studies according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1136/bmj.n71

Through the inclusion–exclusion process described above, a total of 62 studies were identified as having suitable data for analysis. Among these, 18 studies focused on the comparison between RPN versus OPN, 43 compared RAPN versus OPN, and one study involved cost analysis. This final study-set provided data for a total of 26,072 patients, with 14,596 in the experimental group (RPN/RAPN) and 11,476 in the control group (OPN).

3.2 Study demographics

In this subsection, a comprehensive description of demographic metadata derived from the isolated studies is provided. Regarding the country of origin for both study and patient-level data, the primary sources were from the United States of America, Korea, and Japan. Additional contributions came from Italy and France within the European region. The percentage

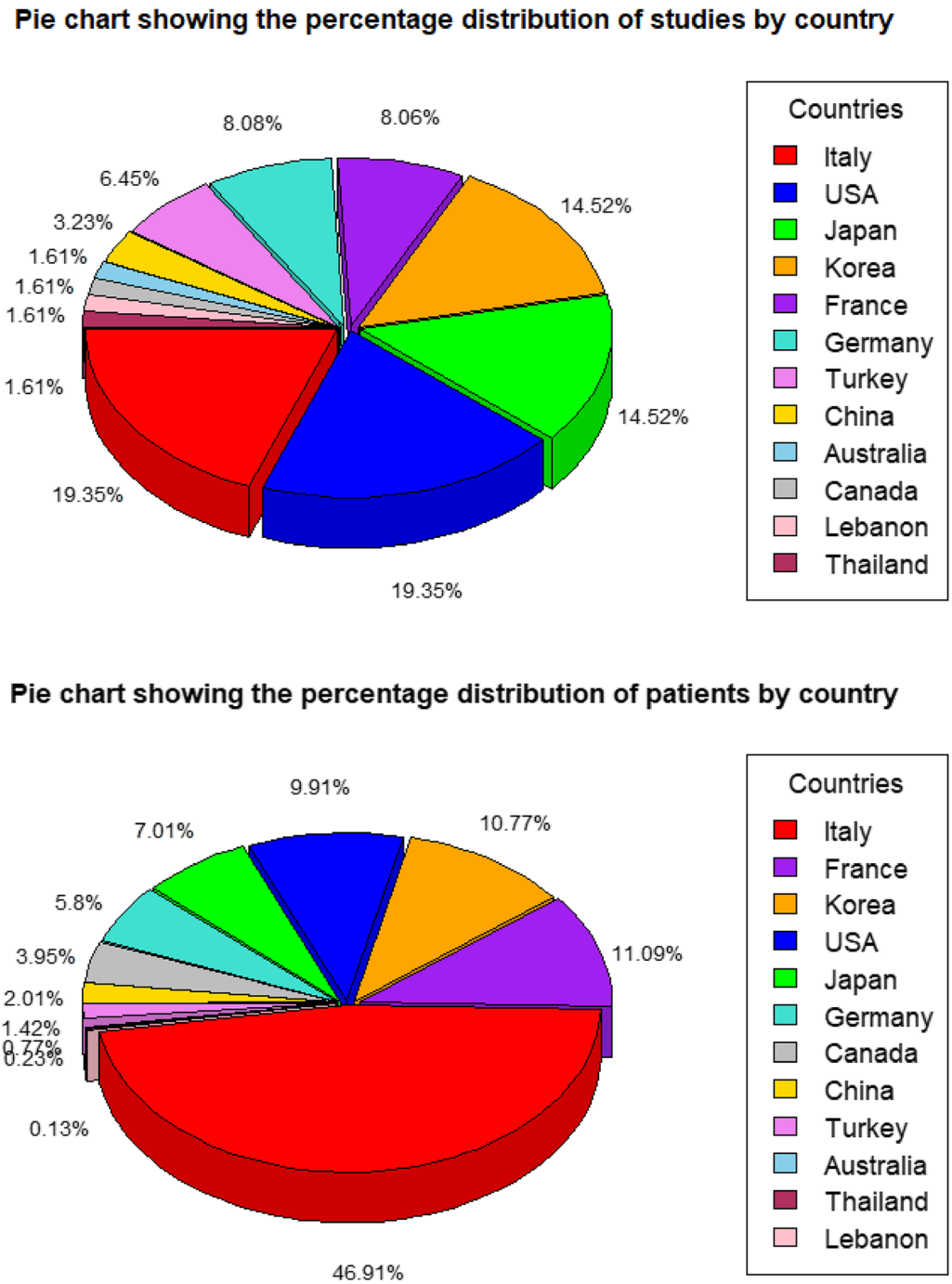

Fig. 2 Comprehensive pie charts displaying the percentage distributions of studies and patients by their respective countries of origin

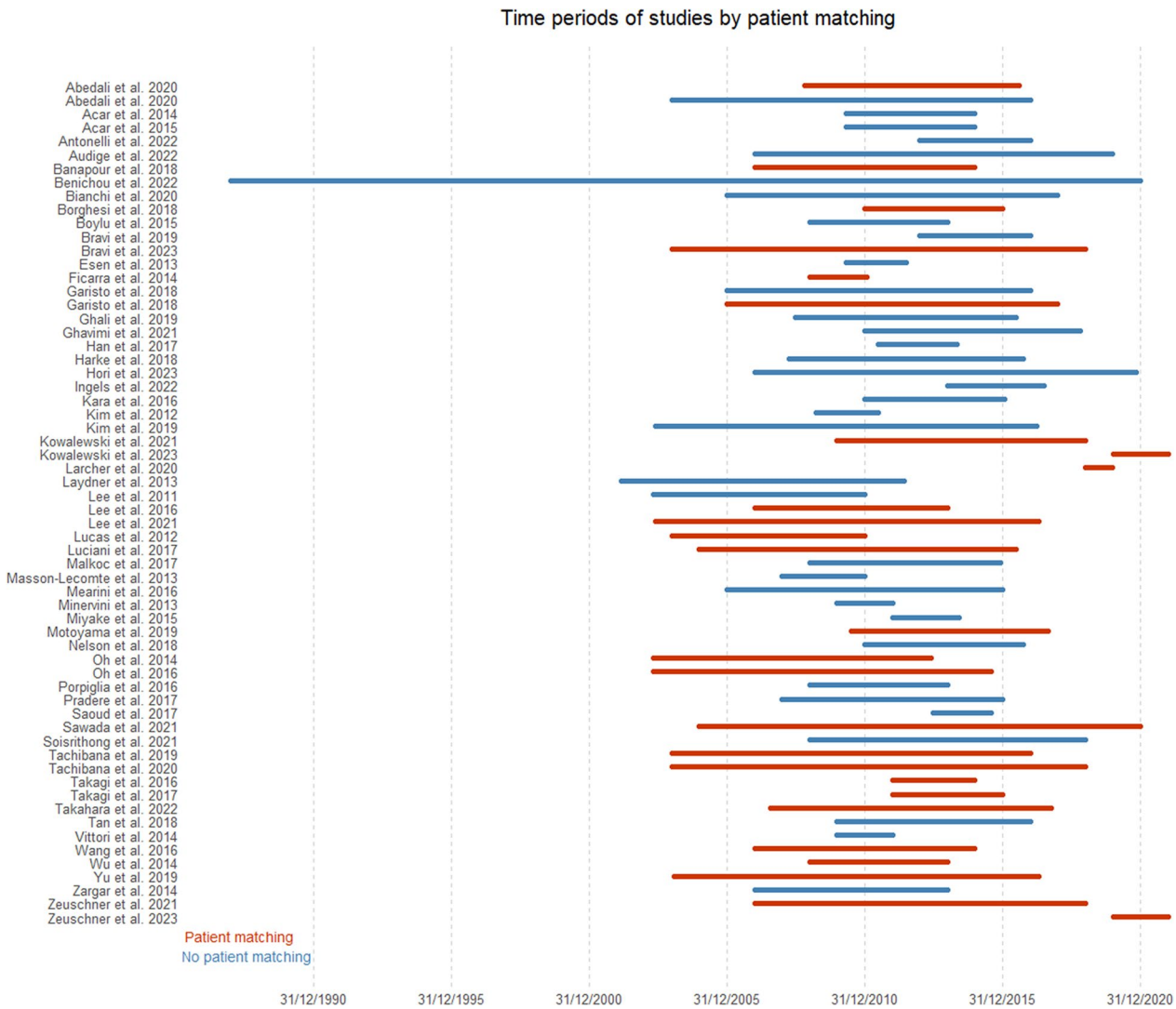

Fig. 3 Concise diagram illustrating the temporal activity intervals of the included studies by patient matching

distribution of acquired data at both levels is visually depicted in the relevant pie charts shown in Fig. 2. For further clarity, corresponding map charts are provided in Additional file 1: Fig. 1. Concerning the time periods of activity covered by the incorporated studies, the majority spanned the decade between 2006 and 2016. Figure 3 illustrates the specific timeframes and durations during which each study was in progress, based on the implementation of patient matching. These data are presented in Additional file 1: Fig. 2, with a focus on the number of referral centers involved and the classification according to the ROBINS-I tool. Importantly, no deviations were found regarding the duration of studies for any of the subgroups under investigation, indicating a uniform distribution in this regard. As for the parameter of publication year, 53.23% of the studies, accounting for 76.34% of the patient data, were published after the year 2018. This specific year was selected as the cutoff point, being the median publication year for all the included studies. Subsequent analysis according to patient matching implementation, revealed that 43.55% of data at the study level and 52.53% at the patient level involved the utilization of such methodology. Consequently, the analyzed data were considered balanced with respect to patient matching. The corresponding pie charts are presented in Fig. 4. Furthermore, in terms of referral centers, approximately 32.26% of the studies, accounting for 65.88% of the included patient data, were associated with a multicenter type of analysis. Lastly, concerning the ROB assessment using the ROBINS-I tool, approximately 31.7% of the incorporated studies, representing 54.46% of the patient data, belonged to

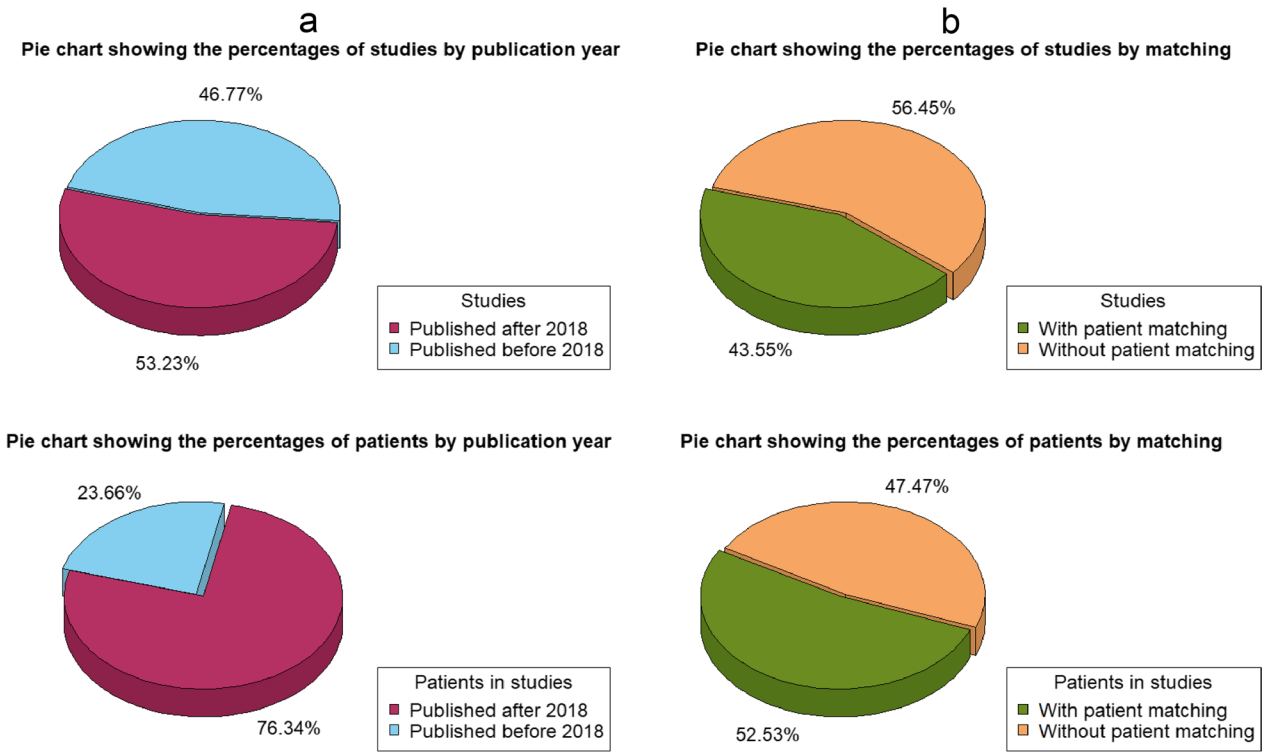

Fig. 4 Pie charts depicting the percentage distribution of available data for studies and patients categorized by publication year (**a**) and the adoption of patient matching (**b**)

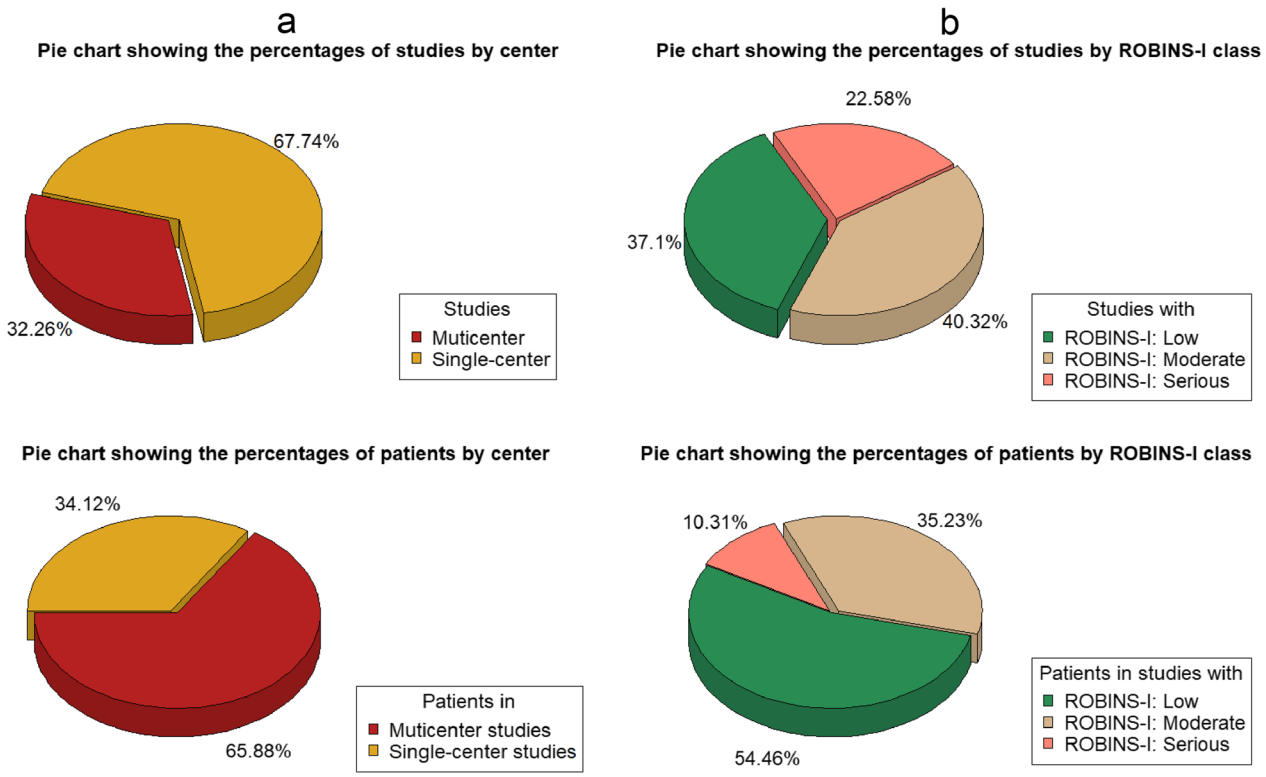

Fig. 5 Pie charts depicting the percentage distribution of available data for studies and patients categorized by the number of referral centers involved (**a**) and ROBINS-I class (**b**)

Table 1 Included studies, detailing title, author, publication year, methodology, duration of activity, quality assessment, patient population in each arm of the comparison, and baseline differences between populations

Title	Author	Study	Population	Duration	Quality	Baseline differences
Robotic and open partial nephrectomy for intermediate and high complexity tumors: A matched-pairs comparison of surgical outcomes at a single institution	Abedali et al. (USA) [42]	Single-center with patient matching (RAPN vs. OPN)	$N_{exp}=148$ $N_{ctrl}=74$ (Total: 222)	2829 days (1/11/2008–31/7/2016)	NOS: 8 ROBINS-I: Low	Highly complex tumors No differences
Robotic and open partial nephrectomy for tumors in a solitary kidney	Abedali et al. (USA) [3]	Multicenter without patient matching (RAPN vs. OPN)	$N_{exp}=11$ $N_{ctrl}=12$ (Total: 23)	4748 days (1/1/2004–31/12/2016)	NOS: 6 ROBINS-I: Moderate	Solitary kidney No differences
Open versus robotic nephron-sparing surgery: 4-year results and determinants of decision making	Acar et al. (Turkey) [43]	Single-center without patient matching (RAPN vs. OPN)	$N_{exp}=53$ $N_{ctrl}=64$ (Total: 117)	1705 days (1/5/2010–31/12/2014)	NOS: 5 ROBINS-I: Serious	No special population OPN: older pts, higher ASA score, higher RENAL & PADUA scores
Comparison of the Trifecta outcomes of robotic and open nephron-sparing surgeries performed in the robotic era of a single institution	Acar et al. (Turkey) [44]	Single-center without patient matching (RAPN vs. OPN)	$N_{exp}=59$ $N_{ctrl}=74$ (Total: 133)	1705 days (1/5/2010–31/12/2014)	NOS: 7 ROBINS-I: Moderate	No special population OPN: older pts, higher RENAL & PADUA scores
Prediction of significant renal function decline after open, laparoscopic, and robotic partial nephrectomy: External validation of the Martini's nomogram on the RECORD2 project cohort	Antonelli et al. (Italy) [39]	Multicenter without patient matching (RAPN vs. OPN)	$N_{exp}=981$ $N_{ctrl}=886$ (Total: 1867)	1460 days (1/1/2013–31/12/2016)	NOS: 8 ROBINS-I: Low	No special population OPN: retroperitoneal approach RAPN: enucleation, on-clamp technique
Clinical and oncological outcomes of open partial nephrectomy versus robot assisted partial nephrectomy over 15 years	Audige et al. (France) [45]	Multicenter without patient matching (RAPN vs. OPN)	$N_{exp}=201$ $N_{ctrl}=204$ (Total: 405)	4747 days (1/1/2007–31/12/2019)	NOS: 7 ROBINS-I: Moderate	No special population OPN: older pts, higher CCI, lower RENAL score
Nephrometry score matched robotic vs. laparoscopic vs. open partial nephrectomy	Banapour et al. (USA) [46]	Multicenter with patient matching (RPN vs. OPN)	$N_{exp}=163$ $N_{ctrl}=176$ (Total: 339)	2921 days (1/1/2007–31/12/2014)	NOS: 6 ROBINS-I: Moderate	No special population OPN: older pts, higher CCI (matched for RENAL score)
Partial nephrectomy in solitary kidneys: Comparison between open surgery and robotic-assisted laparoscopy on perioperative and functional outcomes (UroCCR-54 study)	Benichou et al. (France) [47]	Multicenter without patient matching (RAPN vs. OPN)	$N_{exp}=82$ $N_{ctrl}=68$ (Total: 150)	12,053 days (1/1/1988–31/12/2020)	NOS: 6 ROBINS-I: Serious	Solitary kidney RAPN: higher preoperative eGFR
Which patients with clinical localized renal mass would achieve the Trifecta after partial nephrectomy? The impact of surgical technique	Bianchi et al. (Italy) [48]	Single-center without patient matching (RAPN vs. OPN)	$N_{exp}=83$ $N_{ctrl}=243$ (Total: 326)	4382 days (1/1/2006–31/12/2017)	NOS: 7 ROBINS-I: Moderate	No special population OPN: higher RENAL score
Retroperitoneal robot-assisted versus open partial nephrectomy for cT1 renal tumors: A matched-pair comparison of perioperative and early oncological outcomes	Borghesi et al. (Italy) [40]	Multicenter with patient matching (RAPN vs. OPN)	$N_{exp}=52$ $N_{ctrl}=52$ (Total: 104)	1825 days (1/1/2011–31/12/2015)	NOS: 8 ROBINS-I: Low	Retroperitoneal approach RAPN: posterior tumor location

Table 1 (continued)

Title	Author	Study	Population	Duration	Quality	Baseline differences
Comparison of surgical outcomes of open, laparoscopic, and robotic partial nephrectomy	Boylu et al. (Turkey) [49]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 46 N_{ctrl} = 20 (Total: 66)	1825 days (1/1/2009–31/12/2013)	NOS: 7 ROBINS-I: Moderate	No special population RAPN: higher ASA score OPN: higher RENAL score
Perioperative outcomes of open, laparoscopic, and robotic partial nephrectomy: A prospective multicenter observational study (The RECORd 2 Project)	Bravi et al. (Italy) [50]	Multicenter without patient matching (RPN vs. OPN)	N_{exp} = 789 N_{ctrl} = 682 (Total: 1471)	1460 days (1/1/2013–31/12/2016)	NOS: 9 ROBINS-I: Low	No special population OPN: older pts, higher PADUA score, higher rate of solitary kidneys
The IRON study: Investigation of robot-assisted versus open nephron-sparing surgery	Bravi et al. (Italy) [51]	Multicenter with patient matching (RAPN vs. OPN)	N_{exp} = 2404 N_{ctrl} = 1063 (Total: 3467)	5478 days (1/1/2004–31/12/2018)	NOS: 8 ROBINS-I: Low	No special population OPN: older pts, lower preoperative eGFR, higher rate of solitary kidneys
Morphometric profile of the localized renal tumors managed either by open or robot-assisted nephron-sparing surgery: The impact of scoring systems on the decision-making process	Esen et al. (Turkey) [52]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 32 N_{ctrl} = 23 (Total: 55)	791 days (1/5/2010–30/6/2012)	NOS: 7 ROBINS-I: Moderate	No special population OPN: older pts, higher RENAL & PADUA scores
A multicenter matched-pair analysis comparing robot-assisted versus open partial nephrectomy	Ficarra et al. (Italy) [53]	Multicenter with patient matching (RPN vs. OPN)	N_{exp} = 200 N_{ctrl} = 200 (Total: 400)	760 days (1/1/2009–31/1/2011)	NOS: 8 ROBINS-I: Low	No special population No differences
Robotic versus open partial nephrectomy for highly complex renal masses: Comparison of perioperative, functional, and oncological outcomes	Garisto et al. (USA) [1]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 203 N_{ctrl} = 76 (Total: 279)	4017 days (1/1/2006–31/12/2016)	NOS: 6 ROBINS-I: Serious	Highly complex tumors No differences
Cold ischemia technique during robotic partial nephrectomy: A propensity score-matched comparison with open approach	Garisto et al. (USA) [54]	Single-center with patient matching (RPN vs. OPN)	N_{exp} = 51 N_{ctrl} = 102 (Total: 153)	4382 days (1/1/2006–31/12/2017)	NOS: 8 ROBINS-I: Low	Cold ischemia technique No differences
Robotic partial nephrectomy for clinical T2a renal mass is associated with improved Trifecta outcome compared to open partial nephrectomy: A single surgeon comparative analysis	Ghali et al. (USA) [55]	Single-center without patient matching (RPN vs. OPN)	N_{exp} = 59 N_{ctrl} = 91 (Total: 150)	2921 days (1/7/2008–30/6/2016)	NOS: 6 ROBINS-I: Moderate	cT2a renal tumors No differences
Achieving the "Trifecta" with open versus minimally invasive partial nephrectomy	Ghavimi et al. (Canada) [56]	Multicenter without patient matching (RPN vs. OPN)	N_{exp} = 284 N_{ctrl} = 746 (Total: 1030)	2860 days (1/1/2011–31/10/2018)	NOS: 7 ROBINS-I: Moderate	No special population OPN: larger tumor size, lower preoperative eGFR
Comparison of hand-assisted laparoscopic vs. robot-assisted laparoscopic vs. open partial nephrectomy in patients with T1 renal masses	Han et al. (Korea) [41]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 147 N_{ctrl} = 354 (Total: 501)	1034 days (1/7/2011–30/4/2014)	NOS: 6 ROBINS-I: Moderate	cT1 renal tumors RAPN: higher BMI, higher rate of endophytic tumors

Table 1 (continued)

Title	Author	Study	Population	Duration	Quality	Baseline differences
Are there limits of robotic partial nephrectomy Trifecta outcomes of open and robotic partial nephrectomy for completely endophytic renal tumors?	Harke et al. (Germany) [57]	Multicenter without patient matching (RAPN vs. OPN)	N_{exp} = 64 N_{ctrl} = 76 (Total: 140)	3104 days (1/4/2008–30/9/2016)	NOS: 7 ROBINS-I: Moderate	Endophytic tumors OPN: higher rate of solitary kidneys RAPN: higher CCI
Perioperative outcomes of open and robot-assisted partial nephrectomy in patients with renal tumors of moderate to high complexity	Hori et al. (Japan) [58]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 77 N_{ctrl} = 43 (Total: 120)	5051 days (1/1/2007–30/10/2020)	NOS: 7 ROBINS-I: Moderate	Moderately & highly complex tumors RAPN: older pts, transperitoneal approach
Comparison of open and robotic-assisted partial nephrectomy approaches using multicentric data (UroCCR-47 study)	Ingels et al. (France) [59]	Multicenter without patient matching (RPN vs. OPN)	N_{exp} = 1409 N_{ctrl} = 560 (Total: 1969)	1276 days (1/1/2014–30/6/2017)	NOS: 8 ROBINS-I: Moderate	No special population No differences
Comparison of robot-assisted and open partial nephrectomy for completely endophytic renal tumors: A single center experience	Kara et al. (USA) [60]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 87 N_{ctrl} = 56 (Total: 143)	1856 days (1/1/2011–31/1/2016)	NOS: 6 ROBINS-I: Moderate	Endophytic tumors OPN: higher rate of solitary kidneys
Comparison of robot-assisted partial nephrectomy and open partial nephrectomy: Clinical outcome and complication analysis	Kim et al. (Korea) [61]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 67 N_{ctrl} = 83 (Total: 150)	820 days (1/4/2009–30/6/2011)	NOS: 5 ROBINS-I: Serious	No special population OPN: older pts, higher rate of endophytic tumors
Comparison of robotic and open partial nephrectomy for highly complex renal tumors (RENAL nephrometry score ≥ 10)	Kim et al. (Korea) [62]	Single-center without patient matching (RPN vs. OPN)	N_{exp} = 85 N_{ctrl} = 64 (Total: 149)	5052 days (1/6/2003–31/3/2017)	NOS: 7 ROBINS-I: Moderate	Highly complex tumors RPN: larger tumor size
Robotic-assisted versus conventional open partial nephrectomy (Robocop): A propensity score-matched analysis of 249 patients	Kowalewski et al. (Germany) [63]	Single-center with patient matching (RAPN vs. OPN)	N_{exp} = 83 N_{ctrl} = 166 (Total: 249)	3286 days (1/1/2010–31/12/2018)	NOS: 8 ROBINS-I: Moderate	No special population No differences
Randomized controlled feasibility trial of robot-assisted versus conventional open partial nephrectomy: The ROBOCOP II study	Kowalewski et al. (Germany) [64]	Single-center with patient matching (RAPN vs. OPN)	N_{exp} = 25 N_{ctrl} = 25 (Total: 50)	731 days (1/1/2020–1/1/2022)	NOS: 9 ROBINS-I: Low	No special population No differences
The Iron study: Investigation of robot-assisted versus open nephron-sparing surgery	Larcher et al. (Italy) [65]	Multicenter with patient matching (RAPN vs. OPN)	N_{exp} = 2405 N_{ctrl} = 1063 (Total: 3468)	365 days (31/12/2018–31/12/2019)	NOS: 8 ROBINS-I: Low	No special population No differences
Robotic, laparoscopic and open partial nephrectomies: Comparison of surgical outcomes at a single institution	Laydner et al. (USA) [66]	Single-center without patient matching (RPN vs. OPN)	N_{exp} = 554 N_{ctrl} = 204 (Total: 758)	3744 days (1/3/2002–31/5/2012)	NOS: 7 ROBINS-I: Moderate	No special population OPN: larger tumor size, lower preoperative eGFR
Open versus robot-assisted partial nephrectomy: Effect on clinical outcomes	Lee et al. (Korea) [67]	Single-center without patient matching (RPN vs. OPN)	N_{exp} = 69 N_{ctrl} = 234 (Total: 303)	2801 days (1/5/2003–31/12/2010)	NOS: 6 ROBINS-I: Serious	No special population RPN: higher BMI

Table 1 (continued)

Title	Author	Study	Population	Duration	Quality	Baseline differences
Comparison of renal function between robot-assisted and open partial nephrectomy as determined by Tc 99 m-DTPA renal scintigraphy	Lee et al. (Korea) [68]	Single-center with patient matching (RAPN vs. OPN)	N_{exp} = 84 N_{ctrl} = 84 (Total: 168)	2556 days (1/1/2007–31/12/2013)	NOS: 7 ROBINS-I: Low	No special population OPN: higher rate of endophytic tumors, higher RENAL score
Open partial nephrectomy vs. robot-assisted partial nephrectomy for a renal tumor larger than 4 cm: A propensity score matching analysis	Lee et al. (Korea) [69]	Single-center with patient matching (RAPN vs. OPN)	N_{exp} = 67 N_{ctrl} = 67 (Total: 134)	5082 days (1/6/2003–30/4/2017)	NOS: 8 ROBINS-I: Low	Tumors larger than 4 cm No differences
A comparison of robotic, laparoscopic and open partial nephrectomy	Lucas et al. (USA) [70]	Single-center with patient matching (RPN vs. OPN)	N_{exp} = 27 N_{ctrl} = 54 (Total: 81)	2556 days (1/1/2004–31/12/2010)	NOS: 7 ROBINS-I: Moderate	No special population No differences
Robotic-assisted partial nephrectomy provides better operative outcomes as compared to the laparoscopic and open approaches: Results from a prospective cohort study	Luciani et al. (Italy) [2]	Single-center with patient matching (RAPN vs. OPN)	N_{exp} = 110 N_{ctrl} = 73 (Total: 183)	4198 days (1/1/2005–30/6/2016)	NOS: 6 ROBINS-I: Serious	No special population RAPN: higher preoperative Hb
Robotic and open partial nephrectomy for localized renal tumors larger than 7 cm: A single-center experience	Malkoc et al. (USA) [71]	Single-center without patient matching (RPN vs. OPN)	N_{exp} = 54 N_{ctrl} = 56 (Total: 110)	2524 days (1/1/2009–30/11/2015)	NOS: 7 ROBINS-I: Serious	Tumors larger than 7 cm No differences
A prospective comparison of the pathologic and surgical outcomes obtained after elective treatment of renal cell carcinoma by open or robot-assisted partial nephrectomy	Masson-Lecomte et al. (France) [4]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 42 N_{ctrl} = 58 (Total: 100)	1095 days (1/1/2008–31/12/2010)	NOS: 7 ROBINS-I: Moderate	No special population OPN: higher RENAL score
Margin and complication rates in clampless partial nephrectomy: A comparison of open, laparoscopic and robotic surgeries	Mearini et al. (Italy) [72]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 31 N_{ctrl} = 80 (Total: 111)	3651 days (1/1/2006–31/12/2015)	NOS: 6 ROBINS-I: Serious	No special population RAPN: higher ASA score, higher CCI
Robotic-assisted versus open partial nephrectomy: A prospective multicenter comparison study of perioperative outcomes (AGILE project)	Minervini et al. (Italy) [73]	Multicenter without patient matching (RAPN vs. OPN)	N_{exp} = 104 N_{ctrl} = 198 (Total: 302)	729 days (1/1/2010–31/12/2011)	NOS: 8 ROBINS-I: Moderate	No special population OPN: larger tumor size RAPN: higher CCI
Partial nephrectomy for hilar tumors: Comparison of conventional open and robot-assisted approaches	Miyake et al. (Japan) [74]	Single-center without patient matching (RAPN vs. OPN)	N_{exp} = 16 N_{ctrl} = 15 (Total: 31)	881 days (1/1/2012–31/5/2014)	NOS: 7 ROBINS-I: Moderate	Hilar tumors No differences
Early single-center experience with robotic partial nephrectomy using the da Vinci Xi: Comparative assessment with conventional open partial nephrectomy	Motoyama et al. (Japan) [75]	Single-center with patient matching (RAPN vs. OPN)	N_{exp} = 37 N_{ctrl} = 37 (Total: 74)	2618 days (1/7/2010–31/8/2017)	NOS: 7 ROBINS-I: Low	No special population OPN: retroperitoneal approach

Table 1 (continued)

Title	Author	Study	Population	Duration	Quality	Baseline differences
Robotic cold ischemia achieves comparable functional outcomes to open cold ischemia during partial nephrectomy for complex kidney tumors	Nelson et al. (USA) [32]	Single-center without patient matching (RPN vs. OPN)	$N_{exp} = 31$ $N_{ctrl} = 170$ (Total: 201)	2099 days (1/1/2011–30/9/2016)	NOS: 6 ROBINS-I: Serious	Cold ischemia technique No differences
Comparison of robotic and open partial nephrectomy: Single-surgeon matched cohort study	Oh et al. (Korea) [76]	Single-center with patient matching (RPN vs. OPN)	$N_{exp} = 100$ $N_{ctrl} = 100$ (Total: 200)	3683 days (1/5/2003–31/5/2013)	NOS: 8 ROBINS-I: Low	No special population No differences
Comparison of the width of peritumoral surgical margin in open and robotic partial nephrectomy: A propensity score matched analysis	Oh et al. (Korea) [77]	Single-center with patient matching (RPN vs. OPN)	$N_{exp} = 299$ $N_{ctrl} = 299$ (Total: 598)	4474 days (1/5/2003–31/7/2015)	NOS: 7 ROBINS-I: Serious	No special population No differences
Partial nephrectomy in clinical T1b renal tumors: Multicenter comparative study of open, laparoscopic and robot-assisted approach (the RECORd Project)	Porpiglia et al. (Italy) [78]	Multicenter without patient matching (RAPN vs. OPN)	$N_{exp} = 95$ $N_{ctrl} = 133$ (Total: 228)	1825 days (1/1/2009–31/12/2013)	NOS: 9 ROBINS-I: Low	No special population OPN: older pts
Perioperative outcomes between open and robot-assisted partial nephrectomy for cystic masses: An international multicentric study	Pradere et al. (France) [79]	Multicenter without patient matching (RAPN vs. OPN)	$N_{exp} = 137$ $N_{ctrl} = 131$ (Total: 268)	2921 days (1/1/2008–31/12/2015)	NOS: 6 ROBINS-I: Serious	Cystic tumors RAPN: older pts, higher CCI, higher preoperative Cr, lower RENAL score, smaller tumor size
Comparative analysis of robotic-assisted partial nephrectomy versus open partial nephrectomy during the initial robotic learning curve: Does the end justify the means?	Saoud et al. (Lebanon) [80]	Single-center without patient matching (RAPN vs. OPN)	$N_{exp} = 15$ $N_{ctrl} = 19$ (Total: 34)	760 days (1/7/2013–31/7/2015)	NOS: 5 ROBINS-I: Serious	No special population OPN: higher RENAL score
Comparative analysis of perioperative outcomes between robot-assisted partial nephrectomy and open partial nephrectomy: A propensity-matched study	Sawada et al. (Japan) [38]	Single-center with patient matching (RAPN vs. OPN)	$N_{exp} = 58$ $N_{ctrl} = 58$ (Total: 116)	5843 days (1/1/2005–31/12/2020)	NOS: 7 ROBINS-I: Low	No special population No differences
Comparative outcomes and predictive assessment of Trifecta in open, laparoscopic, and robotic-assisted partial nephrectomy cases with renal cell carcinoma: A 10-year experience at Ramathibodi hospital	Soisrithong et al. (Thailand) [81]	Single-center without patient matching (RAPN vs. OPN)	$N_{exp} = 41$ $N_{ctrl} = 18$ (Total: 59)	3651 days (1/1/2009–31/12/2018)	NOS: 7 ROBINS-I: Serious	No special population No differences
Robot-assisted partial nephrectomy is superior in terms of postoperative acute kidney injury, as compared to open partial nephrectomy	Tachibana et al. (Japan) [82]	Single-center with patient matching (RAPN vs. OPN)	$N_{exp} = 248$ $N_{ctrl} = 248$ (Total: 496)	4748 days (1/1/2004–31/12/2016)	NOS: 7 ROBINS-I: Moderate	No special population No differences

Table 1 (continued)

Title	Author	Study	Population	Duration	Quality	Baseline differences
Lower incidence of postoperative acute kidney injury in robot-assisted partial nephrectomy than in open partial nephrectomy: A propensity score-matched study	Tachibana et al. (Japan) [83]	Multicenter with patient matching (RAPN vs. OPN)	$N_{exp} = 368$ $N_{ctrl} = 368$ (Total: 736)	5478 days (1/1/2004–31/12/2018)	NOS: 8 ROBINS-I: Low	No special population No differences
A propensity score-matched comparison of surgical precision obtained by using volumetric analysis between robot-assisted laparoscopic and open partial nephrectomy for T1 renal cell carcinoma: A retrospective non-randomized observational study of initial outcomes	Takagi et al. (Japan) [6]	Single-center with patient matching (RAPN vs. OPN)	$N_{exp} = 48$ $N_{ctrl} = 48$ (Total: 96)	1095 days (1/1/2012–31/12/2014)	NOS: 7 ROBINS-I: Low	cT1 renal tumors No differences
Robot-assisted laparoscopic versus open partial nephrectomy in patients with chronic kidney disease: A propensity score-matched comparative analysis of surgical outcomes	Takagi et al. (Japan) [84]	Single-center with patient matching (RAPN vs. OPN)	$N_{exp} = 40$ $N_{ctrl} = 40$ (Total: 80)	1460 days (1/1/2012–31/12/2015)	NOS: 8 ROBINS-I: Low	Pts with CKD No differences
Perioperative and long-term functional outcomes of robot-assisted versus open partial nephrectomy: A single-center retrospective study of a Japanese cohort	Takahara et al. (Japan) [85]	Single-center with patient matching (RAPN vs. OPN)	$N_{exp} = 39$ $N_{ctrl} = 39$ (Total: 78)	3713 days (1/8/2007–30/9/2017)	NOS: 7 ROBINS-I: Low	No special population No differences
Comparison of perioperative, renal and oncologic outcomes in robot-assisted versus open partial nephrectomy	Tan et al. (Australia) [86]	Single-center without patient matching (RAPN vs. OPN)	$N_{exp} = 145$ $N_{ctrl} = 55$ (Total: 200)	2556 days (1/1/2010–31/12/2016)	NOS: 8 ROBINS-I: Moderate	No special population OPN: older pts, higher preoperative eGFR, lower RENAL score
Open versus robotic-assisted partial nephrectomy: A multicenter comparison study of perioperative results and complications	Vittori et al. (Italy) [87]	Multicenter without patient matching (RAPN vs. OPN)	$N_{exp} = 105$ $N_{ctrl} = 198$ (Total: 303)	729 days (1/1/2010–31/12/2011)	NOS: 9 ROBINS-I: Low	No special population OPN: larger tumor size RAPN: higher CCI
Robotic and open partial nephrectomy for complex renal tumors: A matched-pair comparison with a long-term follow-up	Wang et al. (China) [88]	Multicenter with patient matching (RPN vs. OPN)	$N_{exp} = 190$ $N_{ctrl} = 190$ (Total: 380)	2921 days (1/1/2007–31/12/2014)	NOS: 8 ROBINS-I: Low	Moderately & highly complex tumors No differences
A propensity-score matched comparison of perioperative and early renal functional outcomes of robotic versus open partial nephrectomy	Wu et al. (China) [89]	Single-center with patient matching (RPN vs. OPN)	$N_{exp} = 51$ $N_{ctrl} = 94$ (Total: 145)	1825 days (1/1/2009–31/12/2013)	NOS: 8 ROBINS-I: Low	No special population No differences
Predictors of renal function after open and robot-assisted partial nephrectomy: A propensity score-matched study	Yu et al. (Korea) [90]	Single-center with patient matching (RPN vs. OPN)	$N_{exp} = 303$ $N_{ctrl} = 303$ (Total: 606)	4837 days (1/2/2004–30/4/2017)	NOS: 7 ROBINS-I: Moderate	No special population No differences

Table 1 (continued)

Title	Author	Study	Population	Duration	Quality	Baseline differences
Comparison of perioperative outcomes of robot-assisted partial nephrectomy and open partial nephrectomy in patients with a solitary kidney	Zargar et al. (USA) [91]	Multicenter without patient matching (RAPN vs. OPN)	N_{exp} = 40 N_{ctrl} = 85 (Total: 125)	2556 days (1/1/2007–31/12/2013)	NOS: 5 ROBINS-I: Serious	Solitary kidney No differences
Open versus robot-assisted partial nephrectomy: A longitudinal comparison of 880 patients over 10 years	Zeuschner et al. (Germany) [92]	Single-center with patient matching (RAPN vs. OPN)	N_{exp} = 500 N_{ctrl} = 313 (Total: 813)	4382 days (1/1/2007–31/12/2018)	NOS: 6 ROBINS-I: Moderate	No special population OPN: larger tumor size, higher PADUA score
Last resort from nursing shortage? Comparative cost analysis of open versus robot-assisted partial nephrectomies with a focus on the costs of nursing care	Zeuschner et al. (Germany) [93]	Single-center with patient matching (Cost Analysis)	N_{exp} = 198 N_{ctrl} = 61 (Total: 259)	730 days (1/1/2020–31/12/2021)	NOS: 8 ROBINS-I: Low	No special population OPN: larger tumor size, higher CCI, higher PADUA score

RAPN robot-assisted partial nephrectomy, *OPN* open partial nephrectomy, *NOS* Newcastle–Ottawa Scale, *ROBINS-I* Risk of Bias in Non-randomized Studies of Interventions, N_{exp} patient population in experimental arm (RAPN), N_{ctrl} patient population in control arm (OPN)

Fig. 6 Summary plot illustrating the evaluation of all incorporated studies using the ROBINS-I tool, presenting their percentages corresponding to the risk level within each of its seven domains (**a**). ROBINS-I assessment stratified by patient matching (**b**)

the "ROBINS-I: Low" category. For studies classified as having moderate and serious ROB, the corresponding percentages were 68.3% and 45.54%, respectively. The relevant results are visually presented in Fig. 5.

The comprehensive compilation of the included studies is presented in Table 1, detailing their specific characteristics. These features encompass the publication year, patient matching utilization, number of referral centers, timeframe of activity, NOS grading, ROBINS-I class, and any deviations observed concerning baseline characteristics among the compared populations. Upon analysis of the pooled studies, common baseline differences were related to older patients and higher complexity renal masses in the OPN group. However, in general, no significant differences were observed between the compared surgical approaches. Regarding the ROB assessment, the ROBINS-I grading forms for each individual study are included as Additional file 2. For the tabulation and visualization of the results of this assessment, the statistical package "Robvis" in the R programming language was employed [31]. Figure 6a presents a summary plot for the entire dataset, graphically depicting the percentages of studies in each risk category, spanning the 7 domains of the ROBINS-I tool. In Fig. 6b, similar summary plots are provided, stratifying the data according to patient matching. From the examination of these specific diagrams, it can be deduced that in overall there were no significant deviations from intended interventions. The most notable risk percentages were observed in the domains of "confounding", "classification of interventions" and "selection bias", each accounting for 40% of the pooled studies, encompassing both moderate and serious ROB. Concerning those studies with patient matching, it becomes apparent that the overall ROB is notably suppressed. Conversely, in studies without the application of a patient matching protocol, bias in all three aforementioned domains is inflated, with their respective percentages now being 75%, 65%, and 60%. A complementary analysis was conducted to account for the subgroups as well. The results demonstrated better performance in terms of ROB, in studies published after 2018 compared to older ones (ROBINS-I: Low: 40% vs. 30%), and in multicenter over single-center studies (ROBINS-I: Low: 50% vs. 30%). The outcomes at the subgroup level align with the expected theoretical differences between the respective groups, affirming the likely appropriate application of the ROBINS-I tool. The summary plots for the subgroups, as well as the traffic light plots showing the grading of each study for each of the 7 domains of the tool, are available as Additional file 1: Fig. 3 and Additional file 1: Figs. 4–10, respectively.

3.3 Correlation coefficient

In the initial phase of data analysis, the investigation focused on the role of the correlation coefficient (r), and the relevant examination was conducted at two stages. Firstly, it was performed on the pooled data by utilizing the expected value of I (EV_I) in both RPN/RAPN and OPN arms collectively. Subsequently, the analysis was carried out for each arm of every study individually, employing a Monte Carlo simulation for indirect determination. Regarding the first level of estimation, Fig. 7 showcases the scatterplots of IT–OT pairs for each compared group. A visual observation of these diagrams confirms the initially hypothesized correlation between IT and OT. Notably, in the OPN group, the correlation appears to be stronger, with longer ischemia times compared to RAPN for operations lasting more than 200 min. The correlation coefficients derived from the expected values of IT (EV_{IT}) and OT (EV_{OT}) from all studies in the RAPN and OPN groups were found to be 0.256 and 0.644, respectively. The difference in correlation coefficients between the two groups was found to be statistically significant (z value = − 2.7353, p value = 0.0062). Additionally, both coefficients were significantly different from zero (RAPN group: t-value = 2.0122, p value = 0.0487; OPN group: t-value = 5.8804, p value < 0.0001). These findings hold physiological significance through statistical inference, as they indicate that in both approaches, the absolute time of intraoperatively applied ischemia increases with the duration of the operation, with a stronger correlation observed in open surgery cases. As per the relevant strategy formulated in the section 2, this specific pair of coefficients for the RAPN and OPN groups will be used to estimate the EV_I and SE_I in each arm of every included study.

In the subsequent stage, a Monte Carlo simulation with 1000 repetitions was conducted for every study and each arm of the comparison, utilizing the corresponding patient populations [21]. The primary objective of this simulation was to generate a bivariate normal distribution for the original variables, aiming to determine the most probable correlation coefficient in each case. Upon completing the calculations, a dataset with coefficients on the order of magnitude of E(-3) (i.e., 10 to the power of − 3) was obtained, which can be practically considered as negligible. These findings indicate a lack of significant correlation between IT and OT, a pattern that is not globally representative, as demonstrated in the previous inference. Consequently, in the following analysis, special emphasis is placed on the estimation of I using the pair of correlation coefficients obtained for the RAPN and OPN groups at the first level of the present investigation, as presented above. This approach enables a more accurate

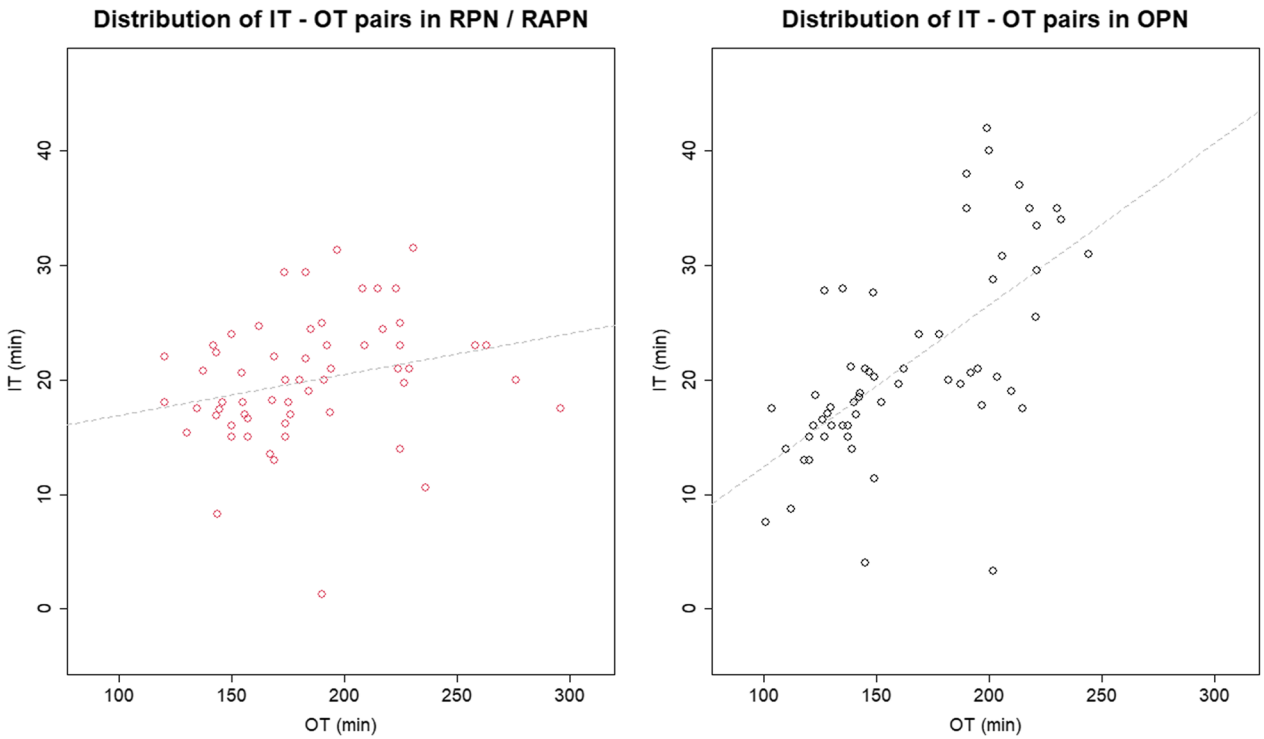

Fig. 7 Scatter plots depicting the IT–OT pairs for the two compared surgical approaches (RAPN–OPN) in partial nephrectomy. Each diagram is accompanied by the corresponding correlation, represented by a dashed line. It is noted that the plots were constructed using the expected values for each variable from each arm of every included study

and reliable estimation of the relationship between IT and OT, and its impact on *I* in each arm of every included study, leading to more robust conclusions.

3.4 Exploratory meta-analysis

This subsection involves the presentation of results from the meta-analysis for the original variables (IT, OT), *I*, and MD_I, utilizing a random effects model. In this analysis, the pair of correlation coefficients established above were employed to compare the outcomes of RAPN and OPN. The dataset encompassed a total of 24,507 patients, with 14,124 falling within the experimental group (RPN/RAPN) and 10,383 within the control group (OPN). Initially, the impact of the two surgical approaches was assessed individually, for each of the IT and OT variables. For IT, in the overall pool of available studies and within the RAPN group, the expected value (EV_{IT}) stood at 19.95 min, with a corresponding 95% confidence interval ($CI_{95\%}$) of [18.61; 21.28]. Conversely, within the OPN group, the EV_IT was determined to be 21.05 min, with a $CI_{95\%}$ of [18.89; 23.21]. A preliminary inspection of the above findings suggests that there is no statistically significant distinction in the absolute duration of ischemia between RAPN and OPN. With respect to the OT variable in the RAPN group, EV_{OT} was calculated as 181.7 min, with a $CI_{95\%}$ of [172.1; 191.3]. In comparison, in the OPN group, EV_{OT} was found to be 161.5 min, with a $CI_{95\%}$ of [151.6; 171.4]. This analysis reveals a notable inclination toward a shorter surgical duration in OPN cases; however, this trend does not reach a level of absolute statistical significance. The forest plots of the aforementioned results are provided as Additional file 1: Figs. 11–14.

Furthermore, within the context of preceding analyses, an examination of the mean differences in IT and OT was conducted. Concerning the former, the mean difference in IT (MD_{IT}) was calculated as − 1.11 min, with $CI_{95\%} = [-2.92; -0.70]$. In terms of the latter, the mean difference in OT (MD_{OT}) was determined to be 19.74 min, with $CI_{95\%} = [11.56; 27.92]$. The above comparison between RAPN and OPN underscores the absence of substantial deviation in the absolute duration of ischemia. However, it is evident that the robotic approach entails an approximately 20-min lengthier process. Given this observation and mindful of the correlation between the original variables, the inquiry now pertains to whether the additional 20 min of surgical time in the context of RAPN engender a significant alteration in the proportion of ischemia, a parameter deemed inherent in each surgical approach. The pertinent outcomes are delineated

in the Additional file 1: Figs. 15–16, presented as forest plots. Finally, the results acquired for the *I* variable were subjected to a similar analytical methodology. Accordingly, as for the expected value of *I* (EV_I) within the RAPN group, it stood at 0.121, with $CI_{95\%}$ = [0.111; 0.130]. On the contrary, within the OPN group, the corresponding EV_I was determined to be 0.131, with $CI_{95\%}$ = [0.121; 0.141]. These findings offer valuable insights into the disparity observed in MD_I, warranting further exploration. Essentially, they imply a lack of statistical significance between the robotic and open approaches in relation to the ischemia proportion required for the seamless conduct of the PN procedure. The corresponding results are visually depicted as forest plots, accessible through Additional file 1: Figs. 17–18.

3.5 Meta-analysis, subgroup analysis and meta-regression analysis

In this section, the meta-analysis (MA) conducted for MD_I using the previously implemented random effects model with the Hartung and Knapp adjustment is presented. The comprehensive examination of the comparison between RAPN and OPN on the *I* variable, based on the aggregated studies, yielded an overall mean difference of: $MD_I = -0.0105$, accompanied by a $CI_{95\%}$ of [− 0.0212; 0.0002]. This outcome highlights a trend of insignificance regarding the superiority of RAPN over OPN in terms of the proportion of intraoperatively applied ischemia. The visualization of this finding can be observed through the forest plot presented in Fig. 8. However, it is imperative to acknowledge the high degree of heterogeneity observed (Cochran's $Q = 2522.67$, Higgins $I^2 = 97.6\%$, $CI_{95\%}$ = [97.3%; 97.9%]). This heterogeneity level can be ascribed to several underlying factors. Primarily, the inclusion of numerous studies is expected to introduce anticipated disparities. Furthermore, the utilization of estimator functions results in condensed standard errors (SE) compared to population standard deviations (SD), consequently amplifying inter-study variation (τ^2). Lastly, the incorporation of non-randomized comparative analyses, coupled with a substantial proportion of small studies marked by low accuracy in reported results, contributes significantly to the observed heterogeneity. In overall, the above suggest that a significant proportion of the observed variability can be attributed to genuine differences in effect sizes rather than just random error, as inter-study variation is estimated at: $\tau^2 = 0.0017$, with $CI_{95\%}$ = [0.0012; 0.0025].

Figure 9a illustrates the funnel plot designed to evaluate the presence of publication bias (PB), while incorporating a regression curve to model small study effects. The corresponding graph demonstrates a notable degree of symmetry around the overall estimate of the effect across all encompassed studies. Additional file 1: Fig. 19 depicts the same funnel plot, augmented with contours indicating statistical significance. Additionally, an evaluation was undertaken using the Egger's test to gauge the significance of asymmetry. The resulting magnitude of bias (MB) was computed as − 0.2385, accompanied by an SE of 1.5575. Employing linear regression yielded a *t* value of − 0.15, and the associated p-value stood at 0.8788. This outcome underscores the absence of a statistically significant PB. In summary, the amalgamation of results and their collective interpretation, suggest a lack of compelling evidence for asymmetry within the funnel plot analysis. This outcome indicates that the observed estimates of effect size remain relatively unaffected by potential factors such as PB or other systematic sources of distortion. Further scrutiny was applied to investigate the potential impact of small study effects. The respective test does not provide strong substantiation to infer that publication bias or other related biases from small studies considerably sway the outcomes of the meta-analysis. This is further supported by the Q–Q' value of 0.99, and a corresponding *p* value of 0.3209. For an in-depth exploration of PB, Fig. 9b introduces a radial plot integrated with the solid regression line derived from Egger's test.

Subsequent to the primary investigation, a subgroup analysis (SGA) was meticulously conducted, encompassing various stratifications based on distinct factors, including publication year, patient matching, the number of referral centers involved, and the ROB assessment employing the ROBINS-I tool. For studies published post-2018, the MD_I exhibited a value of − 0.014, accompanied by a $CI_{95\%}$ spanning [− 0.029; 0.002]. On the other hand, for studies predating this period, the MD_I was determined as − 0.007, with a corresponding $CI_{95\%}$ of [− 0.023; 0.009]. The outcomes regarding patient matching unveiled an MD_I of − 0.007 within the $CI_{95\%}$ range of [− 0.026; 0.013] for matched analyses, whereas the non-matched studies displayed an MD_I of − 0.013, enclosed within the $CI_{95\%}$ bounds of [− 0.025; − 0.001]. Additionally, for multicenter studies, the MD_I stood at − 0.016 within the $CI_{95\%}$ interval of [− 0.031; − 0.001], while single-center studies yielded an MD_I of − 0.008 within the $CI_{95\%}$ bounds of [− 0.022; 0.007]. Further subdivision based on the ROB assessment revealed intriguing findings. For studies categorized as "ROBINS-I: Low", the MD_I was estimated at − 0.016, with a $CI_{95\%}$ of [− 0.032; 0.001]. Similarly, studies classified as "ROBINS-I: Moderate" displayed an MD_I of − 0.004 within the $CI_{95\%}$ of [− 0.020; 0.013]. Lastly, for studies categorized as "ROBINS-I: Serious", the MD_I stood at − 0.015, encompassing the $CI_{95\%}$ interval of [− 0.046; 0.015]. In a systematic manner, the outcomes of the subgroup analysis collectively, do not present robust statistical significance

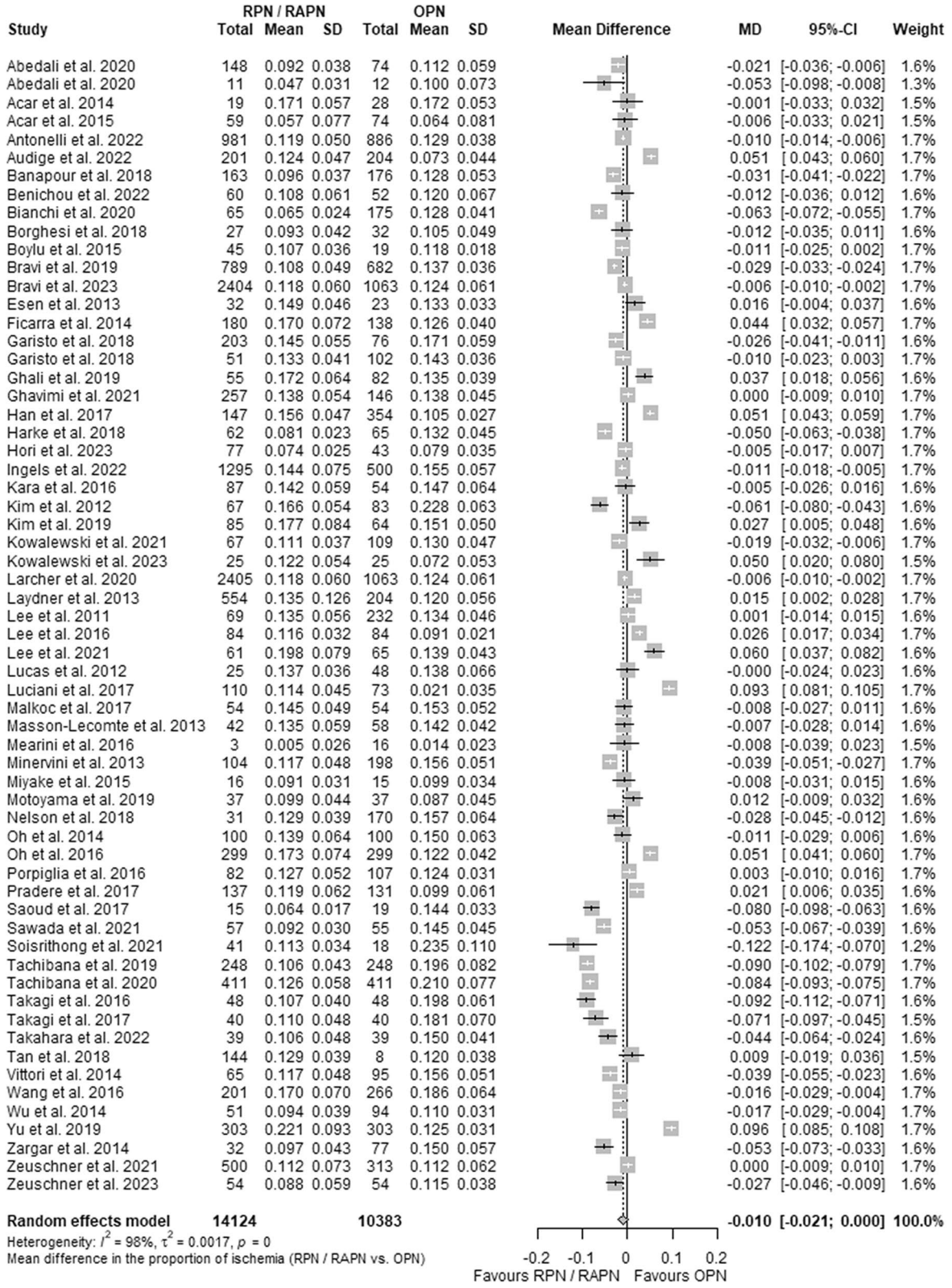

Fig. 8 Forest plot showing the comparative effect as the mean difference of I (MD_I) between RAPN and OPN for all included studies

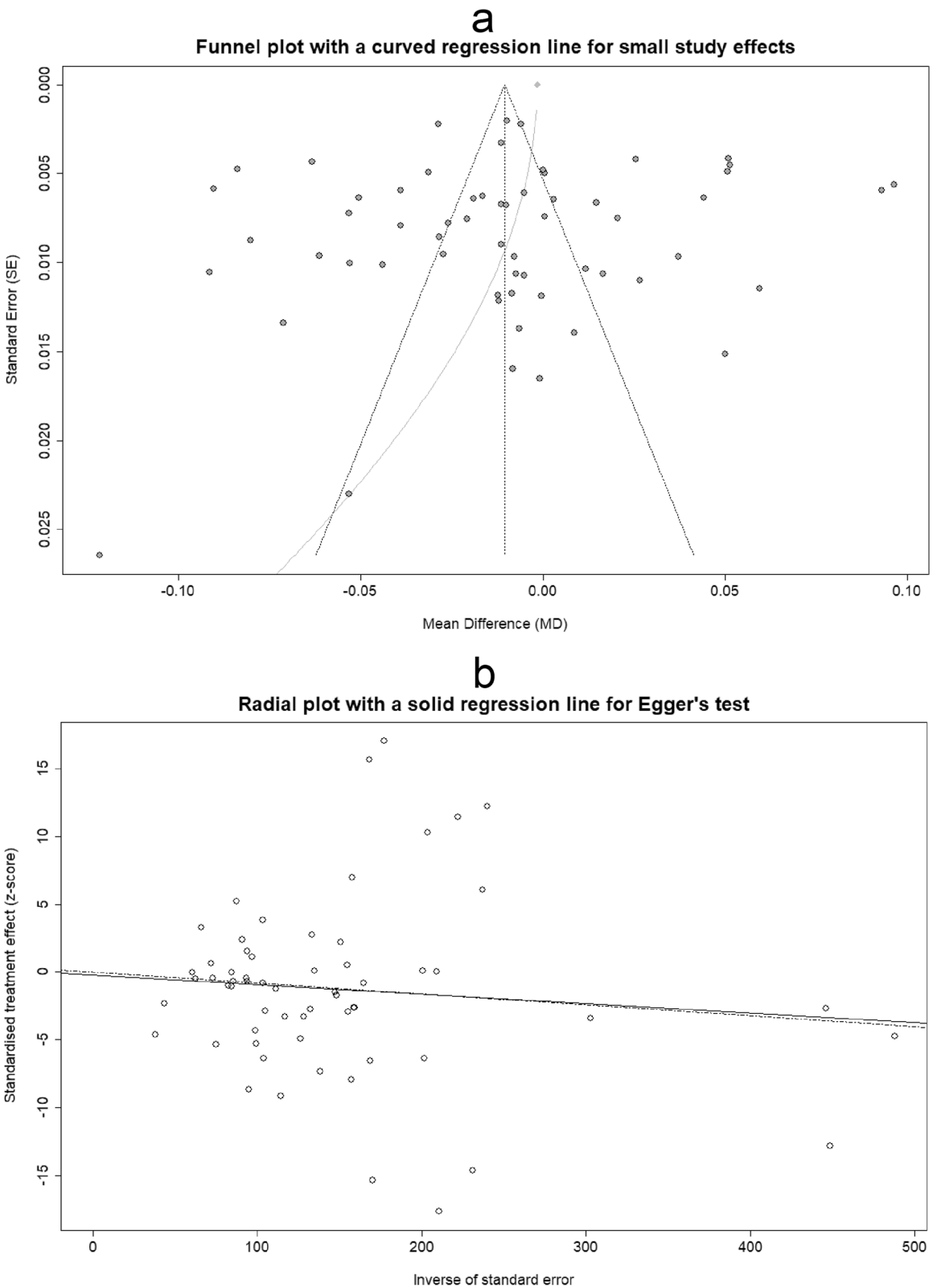

Fig. 9 Funnel plot presenting publication bias assessment in all the examined studies, incorporating a curved regression line to investigate for small study effects (**a**). Radial plot complemented with an integrated regression line, to assess the significance of publication bias using Egger's test (**b**)

regarding the distinction between RAPN and OPN as for the proportion of ischemia (*I*). The above discerning findings aptly demonstrate the equivalence of the two surgical approaches in terms of the per minute requirement for intraoperative ischemia during PN. The relevant SGA results are provided as forest plots in Additional file 1: Figs. 20–23, while the pooled analysis results are presented concisely as percentages of IT over OT in the first section of Table 2.

Conclusively, a meta-regression analysis (MRA) was complementarily conducted at both the pooled data and subgroup levels, employing a restricted maximum likelihood linear model. This model facilitated the construction of regression lines to represent the change in corresponding effects. Illustratively, Fig. 10a portrays the overall comparative effect of RAPN versus OPN concerning the MD_I, juxtaposed against the publication year. Similarly, Fig. 10b showcases the same comparative

Table 2 The meta-analysis results for the complete set of studies that were isolated

Analysis level	Data level	Mean difference (MD) (%)	95% Confidence interval ($CI_{95\%}$)
Pooled Analysis (All available studies)	Pooled data	− 1.0	[− 2.1%; 0.0%]
	Studies published after 2018	− 1.4	[− 2.0%; 0.2%]
	Studies published before 2018	− 0.7	[− 2.3%; 0.9%]
	Studies with patient matching	− 0.7	[− 2.6%; 1.3%]
	Studies without patient matching	**− 1.3**	**[− 2.5%; − 0.1%]**
	Multicenter studies	**− 1.6**	**[− 3.1%; − 0.1%]**
	Single-center studies	− 0.8	[− 2.2%; 0.7%]
	Studies of class: ROBINS-I: Low	− 1.6	[− 3.2%; 0.1%]
	Studies of class: ROBINS-I: Moderate	− 0.4	[− 0.2%; 1.3%]
	Studies of class: ROBINS-I: Serious	− 1.5	[− 4.6%; 1.5%]
Sensitivity Analysis (Level 1): (Studies with optimal $CI_{95\%}$ range, providing increased accuracy of results)	Pooled data	− 0.8	[− 2.2%; 0.6%]
	Studies published after 2018	− 1.9	[− 3.7%; 0.0%]
	Studies published before 2018	0.6	[− 1.7%; 2.8%]
	Studies with patient matching	− 0.3	[− 2.8%; 2.2%]
	Studies without patient matching	− 1.3	[− 3.0%; 0.4%]
	Multicenter studies	− 1.3	[− 3.1%; 0.6%]
	Single-center studies	− 0.5	[− 2.7%; 1.7%]
	Studies of class: ROBINS-I: Low	− 1.5	[− 3.2%; 0.2%]
	Studies of class: ROBINS-I: Moderate	− 0.7	[− 3.4%; 1.9%]
	Studies of class: ROBINS-I: Serious	0.5	[− 4.8%; 5.7%]
Sensitivity Analysis (Level 2): (Studies with patient matching & of "ROBINS-I: Low" class, providing enhanced credibility)	Pooled data	− 1.5	[− 3.5%; 0.5%]
Sensitivity Analysis (Level 3): (Studies with patient populations above the pooled average, providing improved statistical power)	Pooled data	0.1	[− 2.6%; 2.8%]
	Studies published after 2018	− 0.8	[− 4.3%; 2.7%]
	Studies published before 2018	2.5	[− 2.6%; 7.7%]
	Studies with patient matching	− 0.7	[− 5.9%; 4.5%]
	Studies without patient matching	1.0	[− 1.9%; 3.8%]
	Multicenter studies	− 1.2	[− 3.9%; 1.5%]
	Single-center studies	2.0	[− 4.6%; 8.7%]
	Studies of class: ROBINS-I: Low	− 2.5	[− 5.6%; 0.6%]
	Studies of class: ROBINS-I: Moderate	1.4	[− 3.2%; 6.0%]
	Studies of class: ROBINS-I: Serious*	**5.1**	**[4.1%; 6.0%]**

The first three levels of sensitivity analysis are included for each subgroup under investigation. Statistically significant findings are highlighted in bold. However, absolute statistical significance was considered of low clinical significance, as the proportion of ischemia in both RPN and OPN was determined to be around 12–13% of the total surgical time

An asterisk (*) implies the presence of a single study in the subgroup of interest

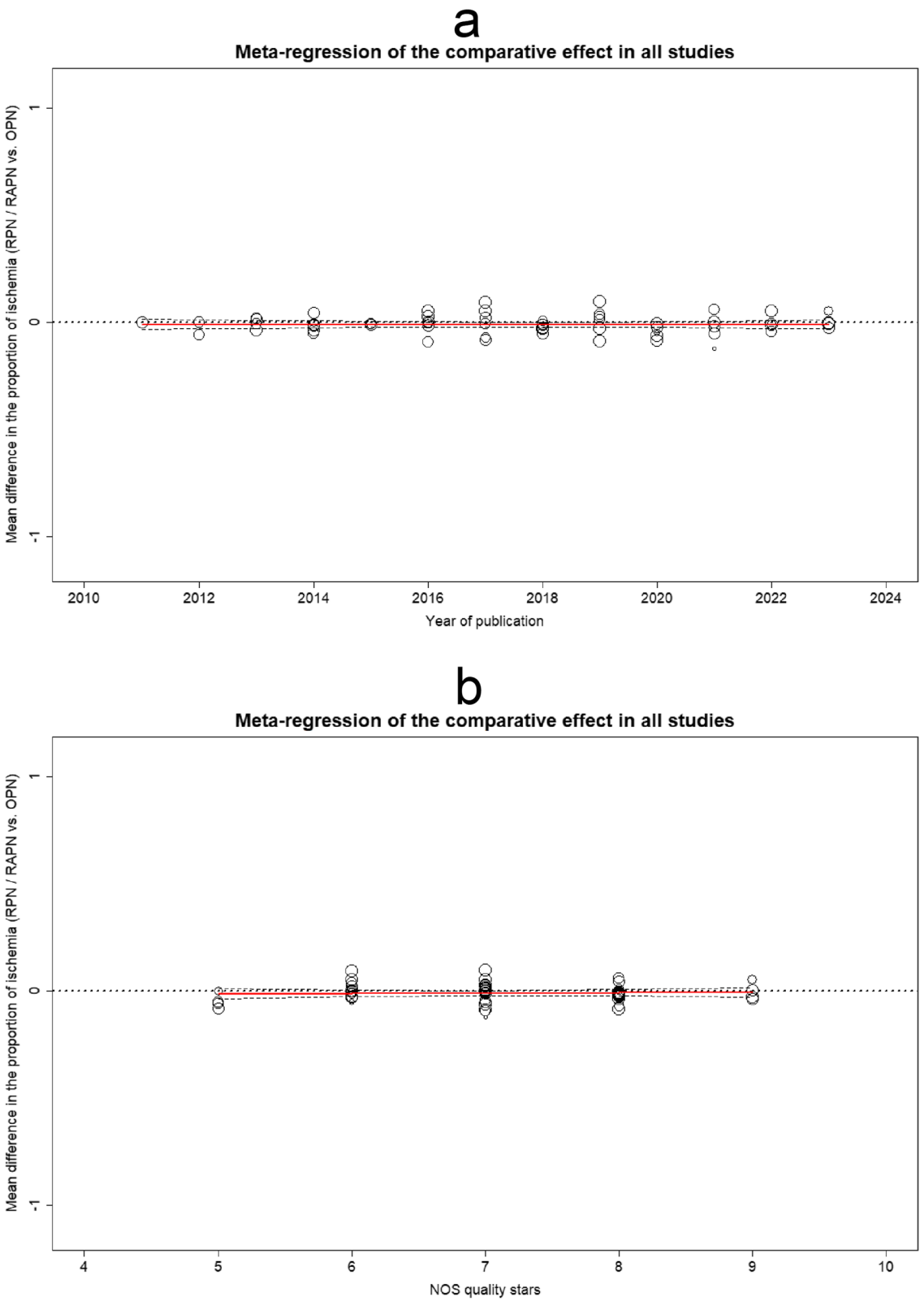

Fig. 10 Meta-regression analysis plots showing the change in the comparative effect (MD_I) between RAPN versus OPN, along with the $CI_{95\%}$, in the aggregated studies, using as moderator the publication year (**a**) and the score in quality stars based on the NOS scale (**b**)

analysis, this time in relation to the quality assessment score, as measured through NOS. In both graphical representations, the observed effects exhibit a consistent pattern, irrespective of the publication year or the awarded number of quality stars. Notably, the quantitative trend revolves around the zero line, suggesting a neutral effect. The scope of the MRA was further extended to encompass subgroup levels as previously defined. Across these subgroups, the comparative effect consistently maintains its neutrality, reinforcing the uniformity of the above findings. Collectively, the analysis presented above points towards the absence of a significant disparity between RAPN and OPN with regard to the novel *I* variable. This lack of distinction holds true regardless of the publication year or the assessed quality level established through the NOS scale. The respective results are presented in Additional file 1: Figs. 24–26 (Fig. 11).

3.6 Sensitivity analysis

In the last part of this section, we present the results of the sensitivity analysis (SA) that was conducted at four distinct levels.

Initially, a subset of studies was isolated through exclusion criteria targeting studies with low accuracy of reported results. The precision of each study's findings was ascertained through the utilization of the inverse variance method, visually represented through the range of 95% confidence intervals ($CI_{95\%}$) presented in the respective forest plots. Following the determination of summary statistics for $CI_{95\%}$ across the entire array of studies, a permissible range equivalent to 2 SDs was established based on previously conducted calculations. Consequently, 25 studies were deemed ineligible and excluded from the analysis, resulting in a final cohort of 37 studies with a more compacted profile pertaining to

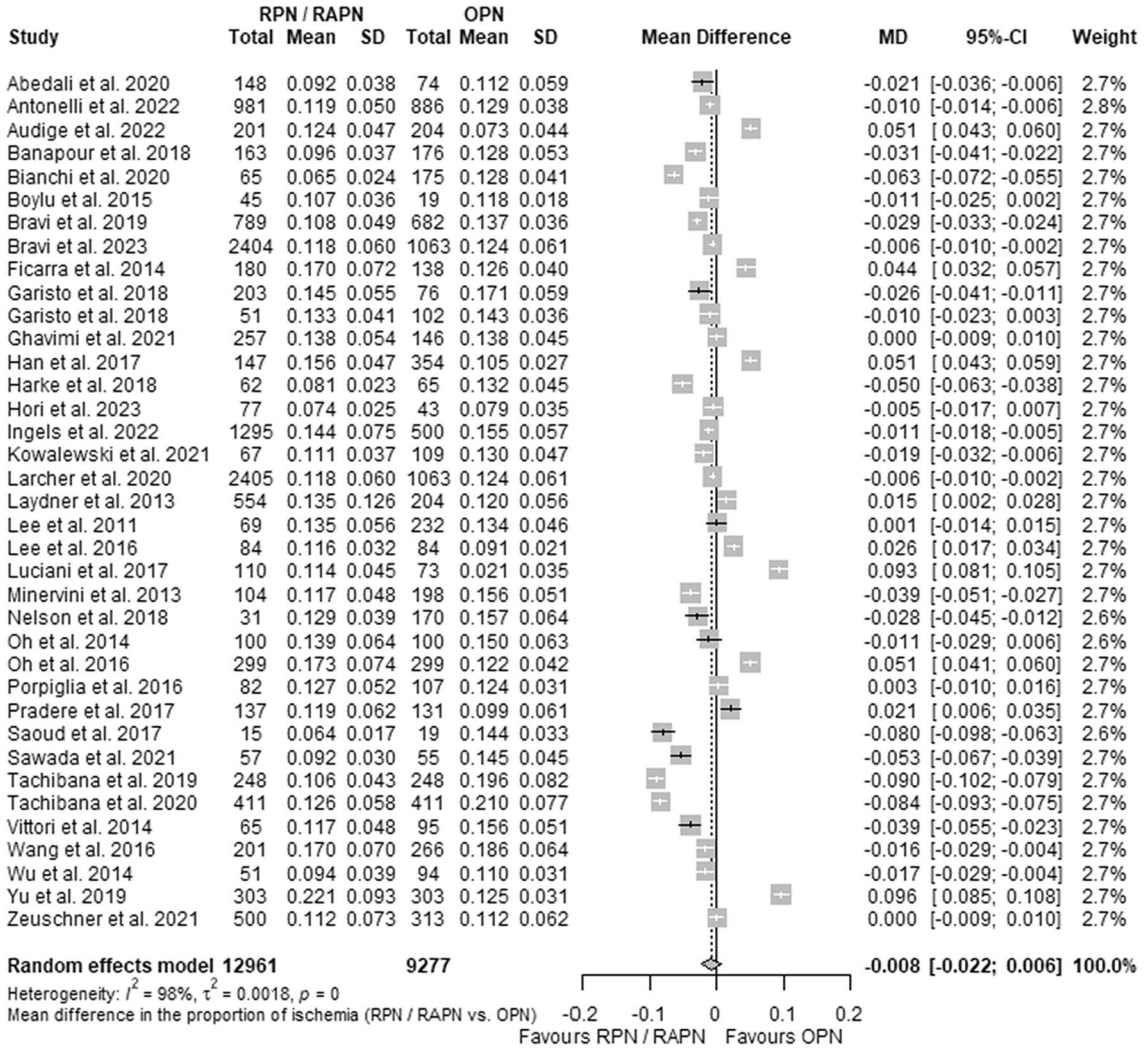

Fig. 11 Forest plot showing the comparative effect as the mean difference of *I* (MD_I) between RAPN and OPN in the subset of studies with increased accuracy of reported results, for the first level of the sensitivity analysis

the precision of reported *I* estimates. In aggregate, data emanating from a total of 22,238 patients were analyzed, with 12,961 individuals allocated to the experimental group and 9277 assigned to the control group. The pooled effect estimate was computed as follows: $MD_I = -0.008$, with $CI_{95\%} = [-0.022; 0.006]$. Despite efforts to enhance accuracy, substantial heterogeneity persisted (Cochran's $Q = 2255.36$, Higgins $I^2 = 98.4\%$, $CI_{95\%} = [98.2\%; 98.6\%]$), corroborated by inter-study variance: $\tau^2 = 0.0018$, with $CI_{95\%} = [0.0012; 0.0030]$. This degree of heterogeneity can be attributed to variability in the method of data retrieval for *I*, emphasizing the pronounced disparity in the strategies employed for implementing intraoperative ischemia across the amalgamated studies. A revised funnel plot characterized by relative symmetry surrounding the overall effect estimate is presented in Fig. 12a. The implementation of the Egger's test for PB assessment resulted in an MB of 0.4362, with an SE of 3.0206. The ensuing linear regression analysis yielded a *t* value of − 0.14 and a *p* value of 0.8860. Consequently, the statistical insignificance of PB is reaffirmed, a conclusion further reinforced by the visual symmetry evident in the corresponding plot. Moreover, the absence of substantial small study effects is also evident ($Q–Q'$ statistic = 1.34, *p* value = 0.2465). In Fig. 12b, the radial plot delineates the refined compilation of 37 studies, incorporating a solid regression line derived from the Egger's test. The minimal deviation of this regression line from the dashed line representing actual data suggests a similarity between the present analysis and the initial findings.

The scope of the sensitivity analysis was expanded to encompass previously scrutinized subgroups. In studies published subsequent to 2018, the comparative effect manifested as follows: $MD_I = -0.019$, with $CI_{95\%} = [-0.037; -0.0001]$. Conversely, for studies previously published, the effect estimate was: $MD_I = -0.006$, with a corresponding $CI_{95\%}$ of [− 0.017; 0.028]. In instances where patient matching protocols had been employed, the resultant effect was: $MD_I = -0.003$, accompanied by a $CI_{95\%}$ of [− 0.028; 0.022]. Conversely, for studies that deviated from such a protocol, the observed effect was: $MD_I = -0.013$, with $CI_{95\%} = [-0.030; 0.004]$. Upon further analysis, for studies conducted across multiple centers, the effect MD_I equaled − 0.013, along with a corresponding $CI_{95\%}$ of [− 0.031; 0.006]. On the other hand, for analyses confined to a single center, the effect was ascertained as: $MD_I = -0.005$, with a $CI_{95\%}$ of [− 0.027; 0.017]. Moreover, upon stratification according to the ROBINS-I tool, studies classified as "ROBINS-I: Low" exhibited an effect estimate of: $MD_I = -0.015$, with a $CI_{95\%}$ of [− 0.032; 0.002]. Similarly, studies classified as "ROBINS-I: Moderate" yielded an effect estimate of: $MD_I = -0.007$, accompanied by a $CI_{95\%}$ of [− 0.034; 0.019]. For the subgroup characterized as "ROBINS-I: Serious", the effect estimate was calculated as: $MD_I = 0.005$, with a $CI_{95\%}$ of [− 0.048; 0.057]. In light of these findings, within the confines of these meticulously selected subgroups characterized by adherence to reporting accuracy, no statistically significant differences are evident in terms of normalized ischemia time (*I*) between the two surgical techniques under comparison. A comprehensive compilation of these outcomes is provided in Additional file 1: Fig. 27. The relevant results are summarized as percentages of IT over OT, at the first level of SA in Table 2. The initial phase of the SA was also augmented by the inclusion of an MRA. Figure 13a displays the alteration in the comparative effect vis-à-vis the year of publication, while Fig. 13b portrays the effect in relation to the quality stars assigned according to the NOS assessment. Analogous to the findings in the primary analysis, MD_I appears to exhibit a consistent pattern irrespective of the moderating variables, maintaining alignment with the horizontal axis of neutrality. These uniform outcomes were consistently replicated across all the pre-defined subgroups. Detailed graphical representations of the MRA results can be found in Additional file 1: Figs. 28–29.

In the second level of SA, a distinct study selection criterion was employed for analysis. Specifically, studies that applied patient matching and concurrently evaluated as "ROBINS-I: Low" were isolated, to enhance the reliability of ensuing outcomes. This combined criterion yielded a novel set comprising 19 studies, encompassing 10,213 patients, with 6423 undergoing RPN/RAPN and 3790 undergoing OPN. From the analysis of aggregated data concerning the comparative effect, the following finding emerged: $MD_I = -0.015$, with a $CI_{95\%} = [-0.035; 0.005]$, confirming our initial findings indicating the absence of significant disparity in terms of the proportion of ischemia in the RAPN versus OPN comparison. The pertinent results are presented in Fig. 14, and the respective field concerning the second level of SA in Table 2. Regarding heterogeneity, the following emerged: Cochran's $Q = 584.49$, Higgins $I^2 = 96.9\%$ with a $CI_{95\%} = [96.1\%; 97.6\%]$, and $\tau^2 = 0.00017$ with a $CI_{95\%} = [0.0009; 0.0038]$, without substantial differentiation from our prior findings. In Fig. 15a, the relevant funnel plot for assessing PB and small study effects is depicted, which in this case seems to exert significant impact ($Q–Q'$ statistic = 13.35, *p* value = 0.0003). Subsequently, Fig. 15b displays the corresponding radial plot with the solid line denoting the Egger's test. In this instance, the outcome was: MB = − 1.5110 with SE = 2.3966, whereas through linear regression analysis it was: *t* value = − 0.63, and *p* value = 0.5368, demonstrating the absence of substantial PB. The final phase of this

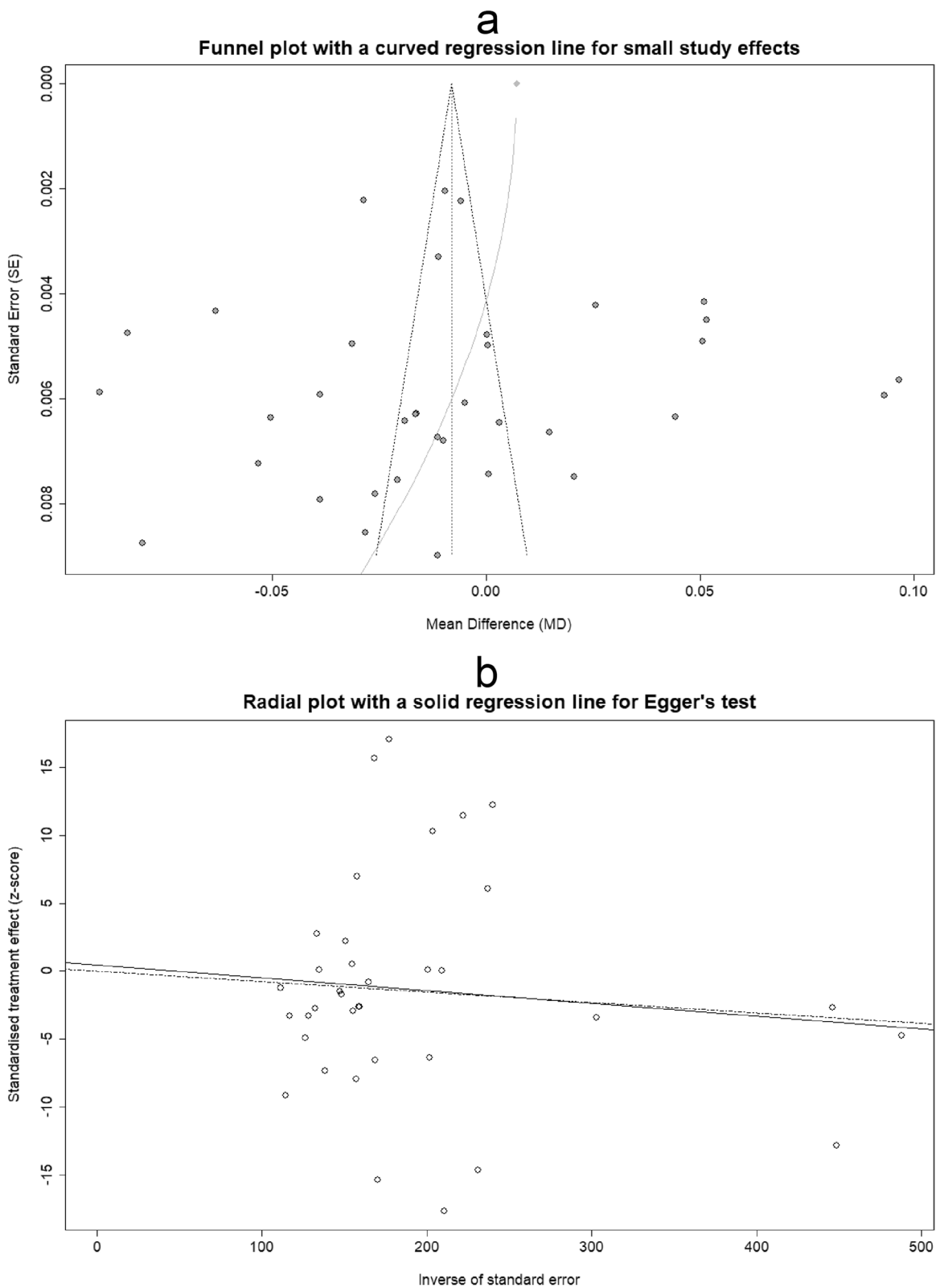

Fig. 12 Funnel plot presenting publication bias assessment in the subset of studies corresponding to the first level of sensitivity analysis, that incorporates a curved regression line to investigate for small study effects (**a**). The respective radial plot with an embedded regression line, to assess the significance of publication bias using Egger's test (**b**)

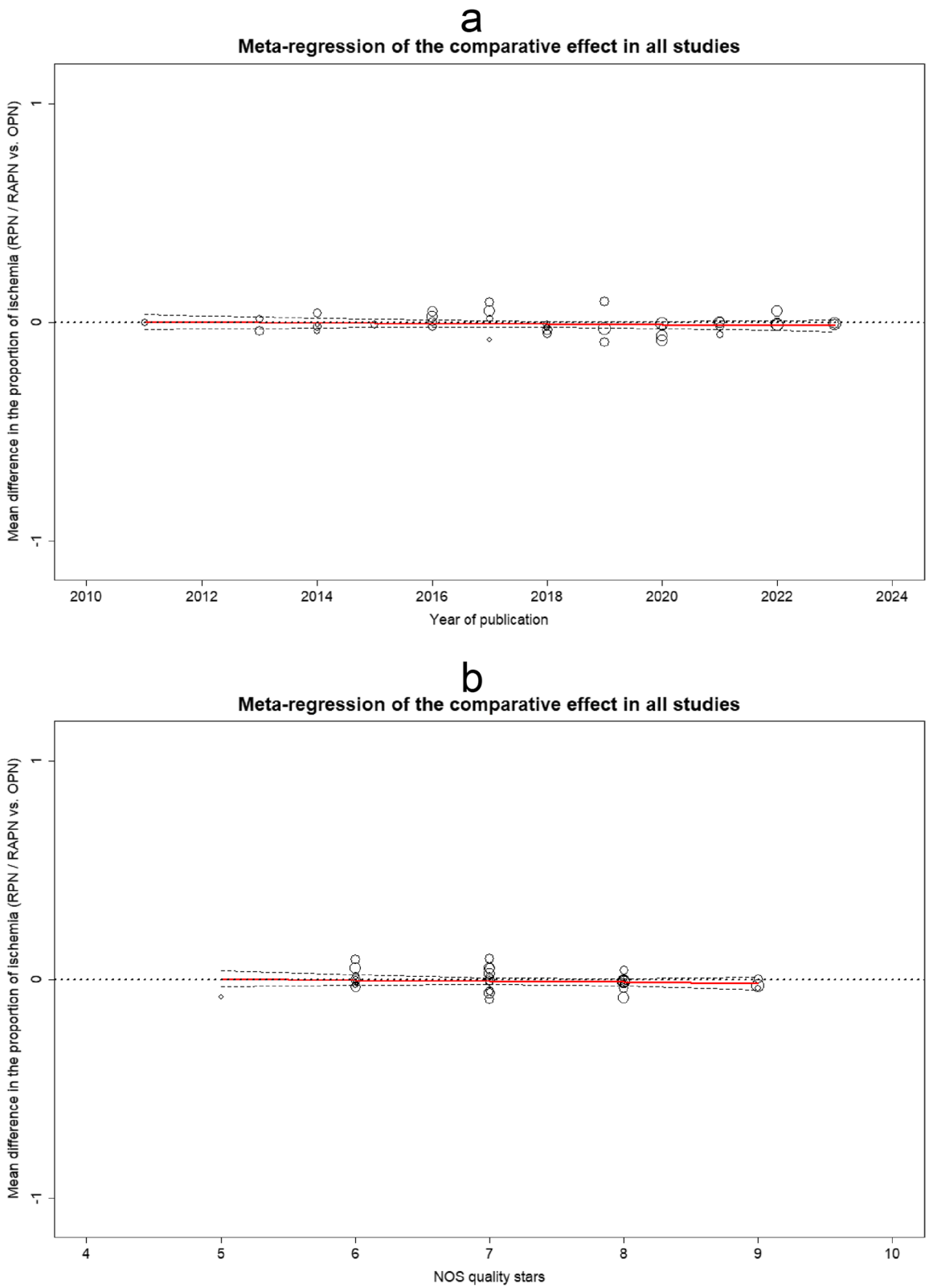

Fig. 13 Meta-regression analysis plots showing the change in the comparative effect (MD_l) between RAPN versus OPN, along with the $CI_{95\%}$, in the subset of studies corresponding to the first level of sensitivity analysis using as moderator the publication year (**a**) and the score in quality stars based on the NOS scale (**b**)

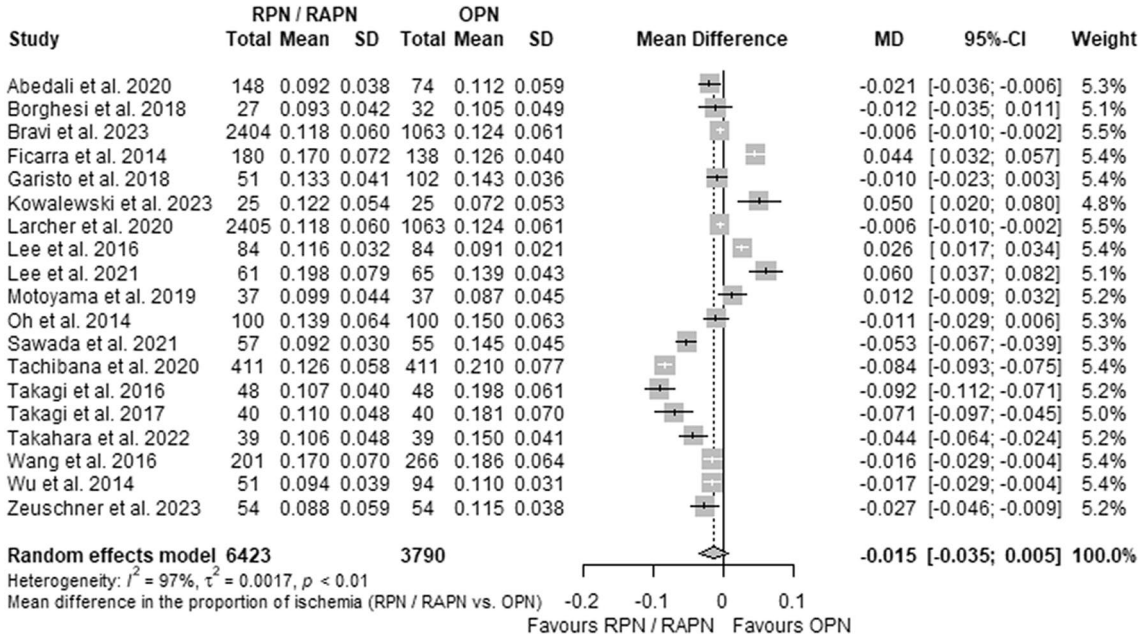

Fig. 14 Forest plot showing the comparative effect as the mean difference of I (MD_I) between RAPN and OPN in the subset of "ROBINS-I: Low" studies with patient matching, for the second level of the sensitivity analysis

level of SA was augmented by MRA, where no significant deviations were observed compared to the already presented findings. Specifically, in this study set, the comparative effect was uniformly distributed around zero, both in terms of publication year and the qualitative status of the included studies according to the NOS. The relevant diagrams are presented in Fig. 16.

At the third level of SA, the total population of integrated patients served as the sole criterion for study selection. Specifically, after initially calculating the average population across the initial study set, records were isolated where the sum of populations in their experimental and control arms exceeded this average. The aim of this specific analysis was the complete elimination of small studies, thereby enabling the estimation of comparative effects from analyses of larger feasible size, with the presumption that they provide the most robust results. The final set included 15 studies, encompassing a total of 17,937 patients, with 10,995 in the RPN/RAPN arm and 6942 in the OPN arm. Pooled data analysis yielded the following result: $MD_I = 0.001$ with a $CI_{95\%} = [-0.026; 0.028]$, as depicted in Fig. 17. From the above, it became evident that even in the case of large studies, no difference emerges between RAPN and OPN concerning the I variable. However, heterogeneity remained at previously high levels (Cochran's $Q = 1409.54$, Higgins $I^2 = 99\%$ with a $CI_{95\%} = [98.8\%; 99.2\%]$, and $\tau^2 = 0.0024$ with a $CI_{95\%} = [0.0013; 0.0060]$). In this case as well, PB did not exhibit significant impact based on the Egger's test (t value = 0.90, p value = 0.3847), while the relevant funnel and radial plots are provided in Additional file 1: Fig. 30. This analysis was extended to the subgroup level, where for studies published after 2018, the result was: $MD_I = -0.008$ with a $CI_{95\%} = [-0.043; 0.027]$, while for previously published studies it was: $MD_I = 0.025$ with a $CI_{95\%} = [-0.026; 0.077]$. Additionally, for studies with patient matching, it was: $MD_I = -0.007$ with a $CI_{95\%} = [-0.059; 0.045]$, whereas for those without patient matching, it was: $MD_I = 0.010$ with a $CI_{95\%} = [-0.019; 0.038]$. Furthermore, for multicenter studies, it was: $MD_I = -0.012$ with a $CI_{95\%} = [-0.039; 0.015]$, while for single-center analyses, it was: $MD_I = 0.020$ with a $CI_{95\%} = [-0.046; 0.087]$. Lastly, regarding the ROB assessment, in those studies classified as "ROBINS-I: Low", the result was: $MD_I = -0.025$ with a $CI_{95\%} = [-0.056; 0.006]$, for those categorized as "ROBINS-I: Moderate", it was: $MD_I = 0.014$ with a $CI_{95\%} = [-0.032; 0.060]$, while the group "ROBINS-I: Serious" included only one study. The relevant results are presented in Additional file 1: Fig. 31. In Table 2, all the above findings are summarized comprehensively as a percentage of IT over OT, in the respective fields pertaining to the third level of SA. Finally, during the MRA on pooled data, a similar pattern of uniform zero-comparative effect emerged, as shown in Fig. 18. Analogous results were also obtained during MRA at the subgroup level, as presented in Additional file 1: Fig. 32–33.

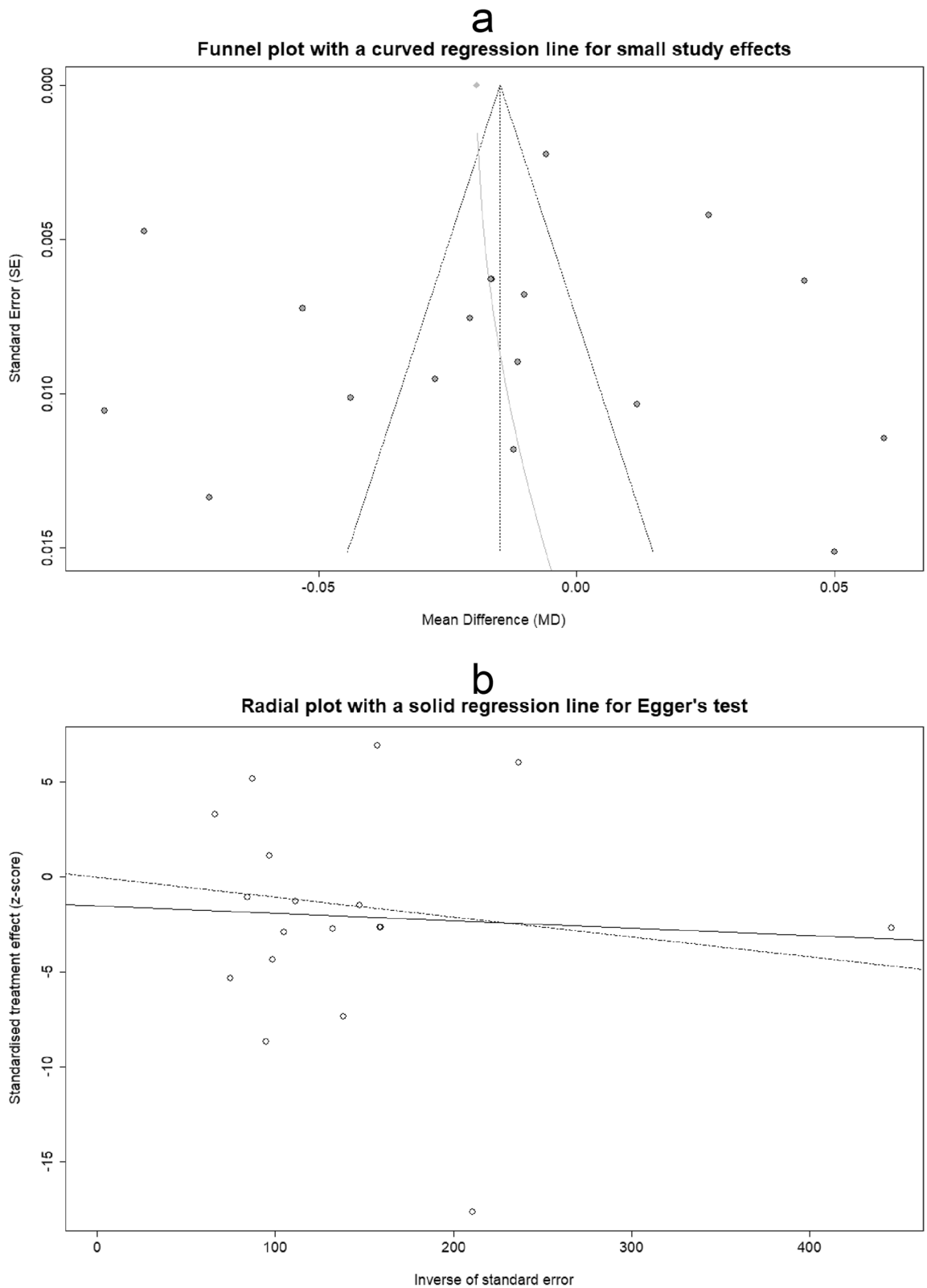

Fig. 15 Funnel plot presenting publication bias assessment in the subset of studies corresponding to the second level of sensitivity analysis, that incorporates a curved regression line to investigate for small study effects (**a**). The respective radial plot with an embedded regression line, to assess the significance of publication bias using Egger's test (**b**)

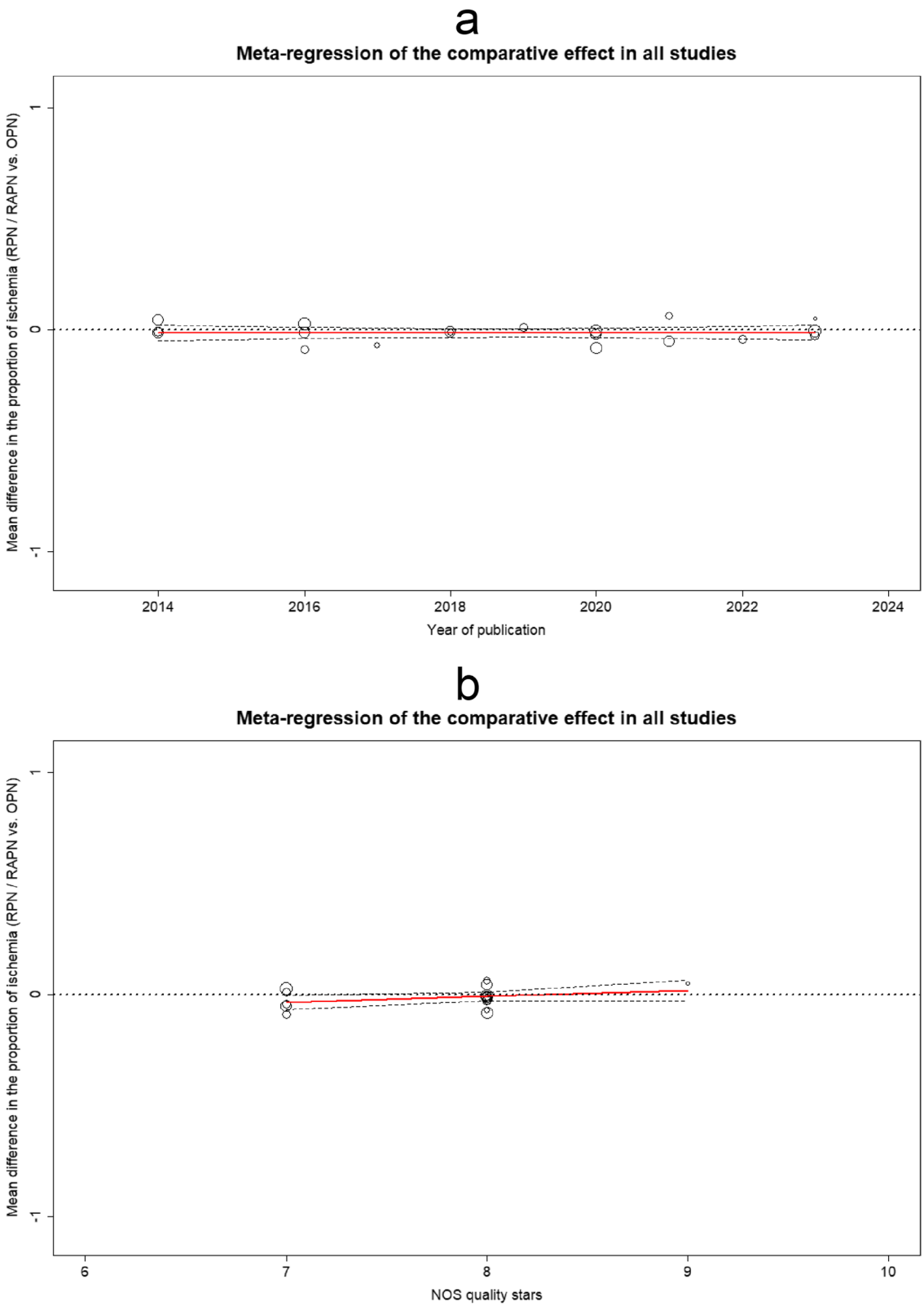

Fig. 16 Meta-regression analysis plots showing the change in the comparative effect (MD_I) between RAPN versus OPN, along with the $CI_{95\%}$, in the subset of studies corresponding to the second level of sensitivity analysis using as moderator the publication year (**a**) and the score in quality stars based on the NOS scale (**b**)

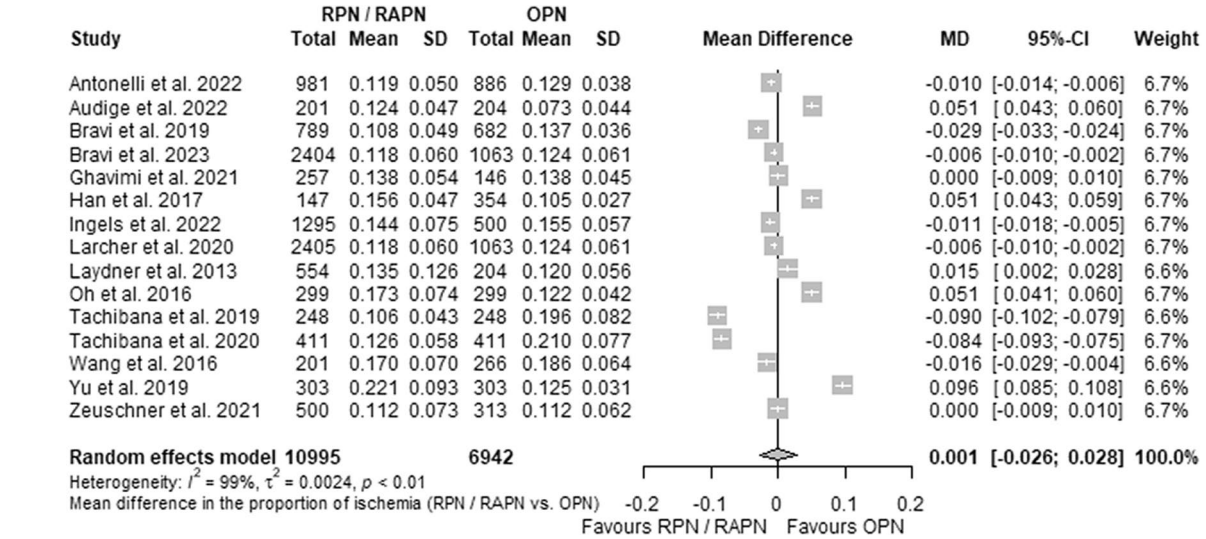

Fig. 17 Forest plot showing the comparative effect as the mean difference of I (MD_I) between RAPN and OPN in the subset of studies with a total population above the average of the original study set, for the third level of the sensitivity analysis

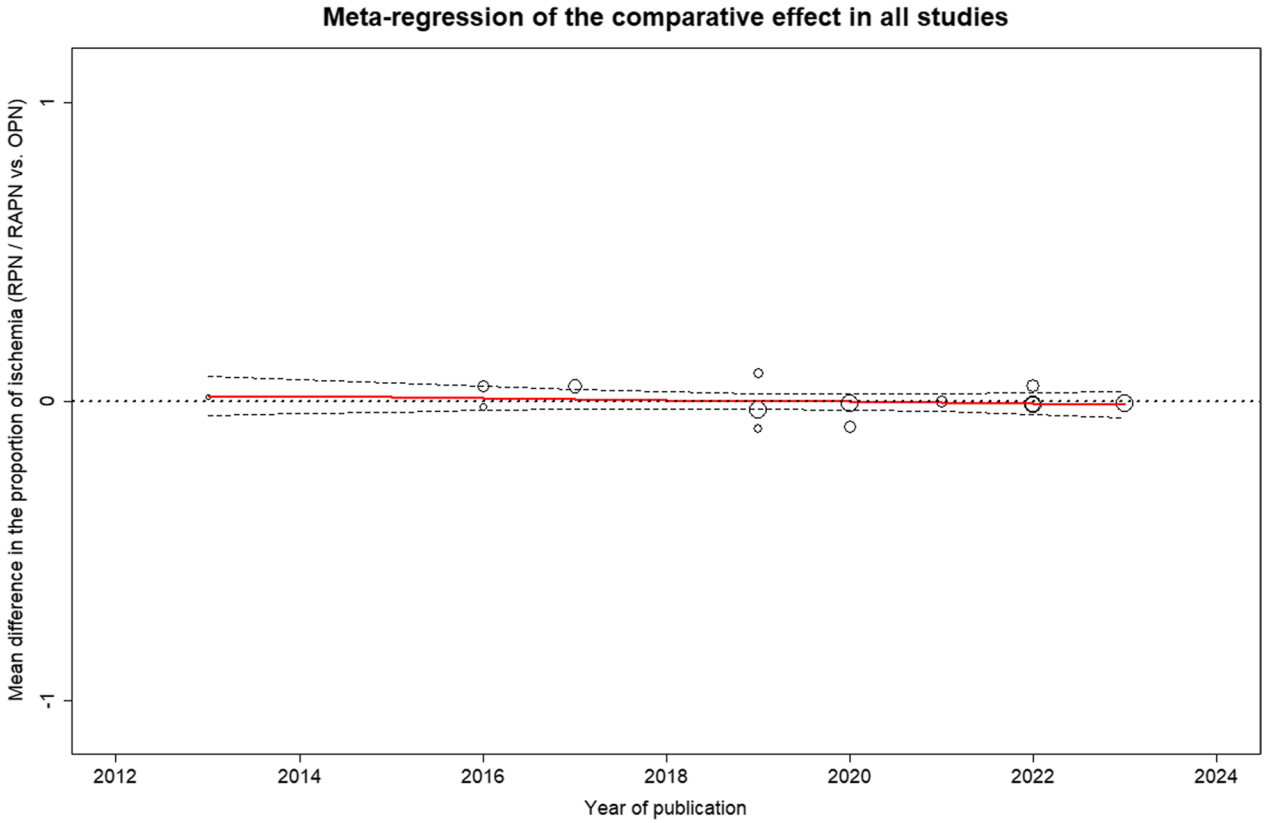

Fig. 18 Meta-regression analysis plots showing the change in the comparative effect (MD_I) between RAPN versus OPN, along with the $CI_{95\%}$, in the subset of studies corresponding to the third level of sensitivity analysis using as moderator the publication year

The fourth and final level of SA involve the theoretical exploration of the variation in MD_I between RAPN and OPN, for a range of successive values of the correlation coefficient (*r*) between the original variables (IT, OT). In this case, the two compared groups (RAPN, OPN) share a common coefficient, with *r* sequentially taking values from − 0.99 to + 0.99. The aim was to verify whether a substantial difference exists in the MD_I between the extreme values of *r*, followed by the interpretation of the physiological impact of the resulting findings. In the section 2, the hypothesis was formulated that the most positive *r* values (i.e. those proximal to + 1) are related to the level of difficulty in performing the PN, with the expected consequence of an increase in IT with an increase in OT, and vice versa. On the other hand, the most negative *r* values (i.e. those proximal to − 1) are theoretically associated with the specific strategy regarding ischemia application from the perspective of the treating surgeon. Figure 19 illustrates the variation of the comparative effect (MD_I) between RAPN and OPN for successive values of *r*, as previously described. From a careful examination of the diagram, a nearly constant comparative effect is observed across the entire spectrum of *r* values. Interpreting this finding, it can be concluded that the difference between the aforementioned surgical approaches in terms of normalized ischemia time (*I*) is not influenced by the difficulty in performing PN, nor by the intraoperative choices of the surgeon. Additionally, based on the findings derived earlier, it can be asserted that the proportion of ischemia (*I*) is an inherent characteristic of both RAPN and OPN, without a substantial difference between the two approaches. Extending this reasoning, it could be further hypothesized that the *I* variable constitutes a distinct characteristic of PN itself, essentially serving as a constant. However, drawing secure conclusions in this regard requires further investigation and lies beyond the scope of this study.

Remaining within the context of Fig. 19 and comparing it with the findings from earlier levels of the SA, it is noted that in the case of a common correlation coefficient between RAPN and OPN, there is an apparently significant advantage for the former in terms of the proportion of intraoperatively applied ischemia (*I*). Nevertheless, the relatively high heterogeneity level observed discourages acceptance of this finding as universally valid. This position is significantly reinforced by confirming the existence of different and non-zero correlation coefficients between RAPN and OPN groups.

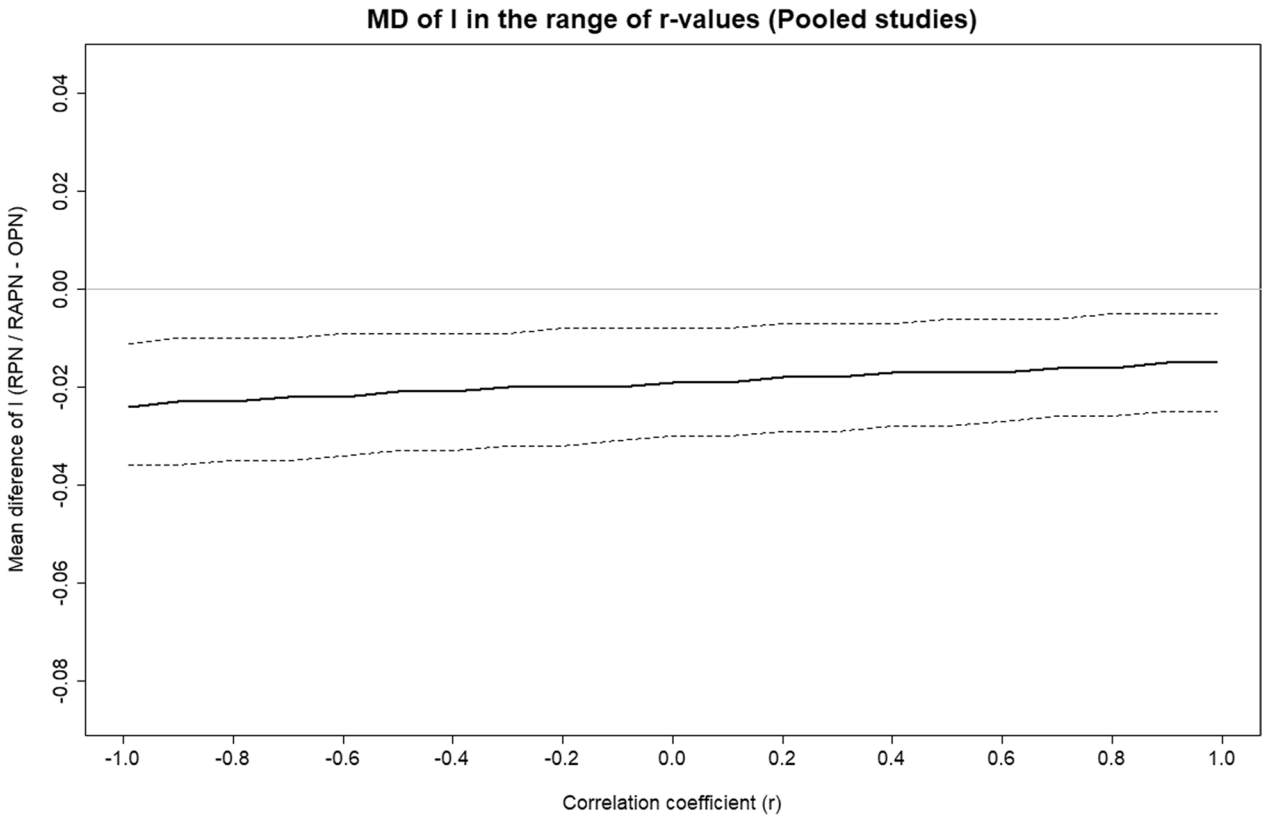

Fig. 19 Plot depicting the change in the comparative effect (MD_I) between RAPN and OPN, along with the $CI_{95\%}$, for consecutive *r* values, at the fourth level of the sensitivity analysis and for the total of included studies

Furthermore, the variation of MD_I across the range of *r* values within subgroup levels is presented in Additional file 1: Figs. 34–35. In this case, a similar possibly pseudo-significant advantage emerges, from studies published after 2018, those without patient matching, multicenter studies, and those of "ROBINS-I: Low" class.

Finally, animated plots were appropriately constructed to highlight the dynamic changes of PB and MD_I in both the aggregated data and the various subsets of investigated subgroups. Animated Plot 1 demonstrates the alteration of the funnel plot for PB estimation. The gradual accentuation of asymmetry suggests an increase in the impact from PB. In contrast, Animated Plot 2, depicting the corresponding radial plot change, doesn't reveal significant divergence between the solid line of Egger's test and the dashed line corresponding to the acquired data, which aligns with the non-statistically significant effect of PB on the overall effect estimation. In the context of MRA, Animated Plots 3–10 and Animated Plots 11–15 present the variation of MD_I using publication year and NOS quality stars as moderators, respectively. A common finding emerges from these: the initial trend of RAPN superiority over OPN in terms of the proportion of ischemia diminishes towards zero with the incremental shift of *r* from − 0.99 to + 0.99. In conclusion, it's worth noting the non-significant difference in MD_I between the extreme values of *r*, an observation that was thoroughly discussed previously.

4 Discussion

The present study introduces the novel variable of ischemia proportion (*I*) to facilitate the comparison of RAPN and OPN as for their relative ischemia requirements. The research addresses the limitations associated with using absolute ischemic time as the sole parameter for such a comparison. Notably, the analysis reveals a substantial discrepancy in OT, with RAPN generally requiring approximately 20 min more than OPN. Conversely, the difference in absolute IT proved statistically insignificant, with RAPN exhibiting only a marginal one-minute reduction compared to OPN. This observation does not suggest a significant physiological impact. Therefore, the study introduces the novel variable of normalized IT to OT to offer a nuanced perspective on ischemia application in PN procedures. The *I* variable is systematically computed across various studies and sensitivity analysis levels, consistently indicating no significant difference between RAPN and OPN. The mean difference in the proportion of ischemia (MD_I) tends to regress around zero, with only a faint inclination favoring RAPN in limiting ischemia. The expected value of *I* (EV_I) for both surgical approaches approximates 12–13%. However, forest plots present a remarkable degree of heterogeneity, warranting further investigation. This heterogeneity level may be attributed to variations in the definition of the novel variable, the inclusion of non-randomized and of low sample size studies, and variability in ischemia implementation strategies. Individual estimates within the forest plots reveal persistent residual heterogeneity, suggesting genuine disparities in *I* and MD_I among the included studies. This insight is particularly significant, implying that the strategy for implementing ischemia possibly differs across studies, leading to unabated heterogeneity. This variability could be explained by two primary technical aspects in conducting PN: one involving a more liberal approach to ensure hemostasis by employing ischemia, and the other aiming to optimize postoperative renal function recovery and prevent acute kidney injury (AKI) by minimizing intraoperative ischemia duration. While MD_I tends to approach zero even when a significant portion of surgical time is dedicated to ischemia in both RAPN and OPN, it is conceivable that a baseline ischemia duration is fundamental for PN procedures in general. However, this assumption cannot be definitively confirmed with the available data.

The international literature extensively explores the application of intraoperative ischemia in PN, revealing numerous variations in both duration and type [12, 32–34]. Additionally, ischemia duration (IT) plays a pivotal role in the composite outcome referred to as the "Trifecta", which assesses renal tumor excision quality by considering complication rates, resection margin status, and renal function changes. Two primary definitions of the Trifecta concept are prominent, primarily differing in the assessment of their impact on patients' renal function. Both definitions require the simultaneous fulfillment of three criteria: the first includes negative surgical margins, the absence of urological complications, and an ischemia duration of less than 20 min, while the second replaces IT with the percentage change in the estimated glomerular filtration rate (eGFR), which should generally remain below 10% [35–37]. These variations highlight the complexity involved in analyzing the impact from IT and the variability in ischemia application techniques. In a retrospective cohort study, Sawada et al. conducted a comparative analysis comparing RAPN to OPN for the treatment of small renal masses. Rigorously adjusting for individual patient and tumor characteristics, the researchers revealed RAPN's superiority over OPN in critical aspects such as estimated blood loss (EBL), IT, and hospital length of stay (LOS). Despite the fact that no statistically significant differences emerged in perioperative complications or positive surgical margin

rates, RAPN notably excelled in preserving renal function immediately post-surgery and at the three-month follow-up. This study provides valuable insights into specific aspects of the diverse range of ischemia techniques and underscores the pivotal role of ischemia duration in achieving favorable outcomes in PN [38]. Furthermore, the absolute IT remains a focal point of investigation concerning postoperative renal function in patients undergoing PN. In this regard, Antonelli et al. sought to validate Martini's nomogram, an estimator of post-PN renal function decline, using extensive data from multiple medical centers in Italy. Employing this nomogram across OPN, LPN, and RAPN procedures demonstrated strong predictive accuracy for the latter two techniques at 6-month and 12-month marks. However, predictive efficacy waned for OPN, a trend consistent across all approaches by the 48-month assessment. Notably, patients in higher-risk categories demonstrated an increased probability of experiencing renal function decline, although the nomogram's predictive accuracy fell below 70% at the 48-month checkpoint [39].

The above findings underscore the particular interest in investigating both the absolute ischemia duration and the technical aspects concerning its application within the context of international literature related to PN. Several studies have focused on comparing RAPN versus OPN in relation to the absolute IT [40, 41]. The current analysis represents an initial attempt to explore IT as a proportion of OT, as the aforementioned original variables appear to be significantly correlated. Our results have demonstrated equivalence between OPN and RAPN concerning the inherent need for ischemia, an anticipated outcome due to the relatively universally applicable strategies of IT minimization in PN procedures. The ultimate goal in the development of the prototype *I* variable also encompasses its further utilization in subsequent studies for detecting inherent differences in IT demands among various surgical approaches that involve ischemia application.

4.1 Strengths and limitations

The current investigation demonstrates several strengths and limitations, which this section thoroughly evaluates.

A primary strength lies in the introduction of the novel *I* variable, previously absent in the original data of the included studies. This variable aims to assess the comparative impact of RAPN versus OPN on the proportion of ischemia, a quantifiable metric crucial for evaluating ischemia duration within the context of PN and its direct correlation with surgical precision. This hypothesis was well-founded due to the dual influence of intraoperatively applied ischemia duration, driven both by surgical techniques and the inherent complexities of PN, on postoperative renal function. Another strength is the focus on a concise triad of variables: ischemia time (IT), operative time (OT), and the ischemia proportion (*I*), all subjected to thorough examination. The study draws upon a comprehensive dataset derived from an extensive body of international literature comparing RAPN and OPN. Methodological rigor is evident in the systematic literature search and the application of inclusion criteria, ensuring transparency and consistency, as detailed in the section 2. Furthermore, the present study conducts an extensive analysis using robust methodologies, encompassing both aggregate-level and subgroup-level assessments. Employing a multilevel approach, it utilizes meta-regression and sensitivity analyses to ensure a comprehensive and consistent extraction of insights from the compiled data. These strengths collectively enhance the validity and reliability of the study's findings.

However, the present analysis has notable limitations, primarily stemming from the computationally intensive nature of its methodology. It includes predominantly non-randomized comparative studies of RAPN versus OPN, often characterized by modest sample sizes. This extensive inclusion, coupled with repetitive calculations, results in a significant degree of heterogeneity, as discussed in the Sects. 3 and 4. The reliance on estimators and the assumption of normal distribution within each comparative arm of the included studies contribute to this level of heterogeneity. Additionally, limitations arise from the approximation of the correlation coefficient (*r*) between IT and OT, due to the unavailability of individual patient data for direct calculation. Despite these limitations, it's essential to recognize that the study's results align coherently with the underlying physiological rationale governing the original variables.

4.2 Future potential

Despite its inherent constraints, the present study holds significant implications concerning the introduced novel variable. As elucidated earlier, the marginal difference in *I* between RAPN and OPN, quantified as MD_I, appears to have minimal influence within the typical duration of PN. This finding suggests the possible existence of a fundamental baseline level of ischemia proportion intrinsic to PN, warranting comprehensive investigation across RAPN, LPN, and OPN. Future research could involve determining summary statistics for IT, OT, and the newly devised *I* variable within each patient cohort, enhancing the computation of the correlation coefficient (*r*) and refining the theoretical framework. It is worth noting that the *I* metric, primarily driven by the IT variable, may not fully capture the multidimensional nature of surgical precision in PN. Consequently, our future efforts will focus on comparatively investigating the multifaceted outcome

of surgical precision in the context of the per minute estimated blood loss (EBL), aiming to establish a comprehensive framework for robust interpretation and sound conclusion-drawing.

5 Conclusions

In the present investigation, we undertook a retrospective comparative analysis between RAPN and OPN with a focus on the ischemia proportion. To facilitate this examination, a novel variable denoted as *I* was thoroughly formulated, serving as a measure inversely reflecting surgical precision. Specifically, we leveraged essential data from primary comparative studies, isolating the original variables IT and OT, and ultimately estimating the pertinent statistical parameters for *I* through appropriate estimator functions. Subsequently, a meta-analysis was conducted to derive an overall effect estimate, gauged through the mean difference between the two surgical approaches under comparison. Upon subjecting the collected data to a rigorous multilevel analysis, no statistically significant disparity emerged between RAPN and OPN in terms of the normalized ischemia duration relative to the total operative time. Notably, this finding was reinforced by MRA, which underscored the stability of the finding across various dimensions such as publication year and quality assessment based on the NOS scale. Additionally, sensitivity analysis reaffirmed the consistency of the initial findings. Consequently, we inferred the presence of a fundamental baseline level of ischemia proportion within the majority of PN procedures. To explore this hypothesis more comprehensively, further investigations will be warranted in subsequent studies.

Abbreviations

AKI	Acute Kidney Injury
AUA	American Urological Association
CENTRAL	Cochrane Central Register of Controlled Trials
$CI_{95\%}$	95% Confidence Interval
CLT	Central Limit Theorem
EBL	Estimated Blood Loss
eGFR	Estimated Glomerular Filtration Rate
EV	Expected Value
I	Ischemia proportion (Normalized Ischemia Time)
IT	Ischemia Time
LOS	Length Of hospital Stay
LPN	Laparoscopic Partial Nephrectomy
MA	Meta-analysis
MB	Magnitude of (Publication) Bias
MD	Mean Difference
min	Minutes
MRA	Meta-regression Analysis
NOS	Newcastle–Ottawa Scale
NSS	Nephron Sparing Surgery
OPN	Open Partial Nephrectomy
OT	Operative Time
PB	Publication Bias
PN	Partial Nephrectomy
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-analyses
RAPN	Robot-assisted Partial Nephrectomy
RCC	Renal Cell Carcinoma
REML	Restricted Maximum Likelihood
RN	Radical Nephrectomy
ROB	Risk of Bias
ROBINS-I	Risk of Bias In Non-randomized Studies-of Interventions
RPN	Robotic Partial Nephrectomy
SA	Sensitivity Analysis
SD	Standard Deviation
SE	Standard Error
SGA	Subgroup Analysis
SS	Search Strategy

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s43088-023-00431-3.

Additional file 1. Supplementary figures.

Additional file 2. Supplementary ROBINS-I forms: Risk of bias assessment forms for all included studies based on the ROBINS-I tool.

Additional file 3. Supplementary SA forest plots: Forest plots produced from the pooled MA and SGA during the fourth level of SA, when determining the MDI between RAPN and OPN for each value of the correlation coefficient (r) between IT and OT.

Additional file 4. Supplementary animated plots.

Acknowledgements
Not applicable.

Author contributions
SA has given substantial contributions to the conceptualization, data curation, formal analysis, data investigation, methodology implementation, project administration, acquisition of resources, software utilization, procedure validation, visualization of results, original draft formulation, as well as the final review and editing of the present study. DA has given substantial contributions in data curation, formal analysis, data investigation, project administration, acquisition of resources, as well as procedure validation. IK has given substantial contributions in conceptualization, methodology implementation, software utilization, procedure validation, as well as critical review of the final manuscript. KT has given substantial contributions in supervision, data validation, as well as critical review of the final manuscript. GZ held the position of general supervisor during the elaboration of the present study. All authors have read and approved the final manuscript. [SA, IK] contributed to Conceptualization, Methodology and Software; [SA, DA] contributed to Data curation, Project administration, Writing—original draft and Formal Analysis; [] contributed to Funding acquisition; [SA, DA, IK] contributed to Investigation and Resources; [KT, GZ] contributed to Supervision; [SA, DA, KT] contributed to Validation; [SA] contributed to Visualization; [SA, DA, IK, KT] contributed to Writing—review and editing. All authors have read and approved the final manuscript.

Funding
All authors confirm that no funds, grants, or other support was received.

Availability of data and materials
All the data utilized and statistical code developed are available at the following link: https://github.com/sotbike/I.git.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 5 September 2023 Accepted: 8 October 2023
Published online: 14 October 2023

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