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Effectiveness and safety of partial nephrectomy—no ischemia vs. warm ischemia: Systematic review and meta-analysis

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Purpose: This study aimed to determine the effectiveness and safety of partial nephrectomy (PN) without ischemia compared with PN with warm ischemia for reducing the deterioration in renal function in patients with cT1 renal tumors.
Materials and Methods: We conducted a systematic review that included patients over 18 years of age who underwent PN with or without warm ischemia for cT1 renal tumors. The primary outcome was impaired renal function. A search strategy was performed in MEDLINE, EMBASE, LILACS, CENTRAL, the article reference lists, and the unpublished literature to reach saturation of the information. We assessed the risk of bias with the methodological index for nonrandomized studies (MINORS) tool, and we performed a meta-analysis according to the type of variable.
Results: We found a total of 5,682 articles, of which 14 met the inclusion criteria. Seven studies evaluated renal function, identifying a difference in means (MD) of 3.50 (95% confidence interval [CI], 1.16 to 5.83), favoring no ischemia. We did not find any significant differences regarding intraoperative bleeding or operative time (MD, 55 mL; 95% CI, -33.16 to 144.08; and MD, 1.87; 95% CI, -20.47 to 24.21; respectively).
Conclusions: In this study, PN without ischemia showed a decrease in deterioration of the estimated glomerular filtration rate compared with warm ischemia.

Keywords: Cold ischemia; Meta-analysis; Nephrectomy; Systematic review; Warm ischemia

INTRODUCTION

Kidney cancer, although not prevalent in the general population, has an annual incidence of 214,000 cases worldwide, with an estimated 143,000 deaths, making it the 16th leading cause of death [1].

The incidence of small renal tumors is increasing as a consequence of incidental findings secondary to the widespread use of imaging studies, which has allowed early diagnosis [2]. In the US, most renal masses are diagnosed at clinical stage cT1, with an average size of 3.5 cm [3]. The decision to treat at stage T1a (<4 cm) allows a variety of options, such as surgery, ablation, or active surveillance, which should be the subject of discussion between the patient and his or her physician, with weighing of the risks and benefits [4].

At present, the clinical practice guidelines of the Euro-

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pean Association of Urology (EAU), the American Urological Association (AUA), and the National Comprehensive Cancer Network (NCCN) recommend partial nephrectomy (PN), if it is anatomically possible, or radical nephrectomy for the treatment of small renal masses [5-7].

Multiple retrospective observational studies, clinical trials, and even meta-analyses show that PN preserves renal function. It has similar oncologic results and reduces the incidence of chronic kidney disease [4,8].

The preservation of renal function after PN is of great importance, mainly in patients with a single kidney or preexisting chronic kidney disease. However, PN per se is associated with a certain degree of deterioration in renal function, with an approximate 10% decrease in the global glomerular filtration rate (GFR) secondary to renal mass loss and irreversible ischemic damage due to clamping of the renal hilum during the procedure [9,10]. In contrast to this hypothesis, recent studies have shown that the kidney may be more tolerant to ischemia than previously thought and even that the majority of nephrons recover after ischemia during PN [11,12].

There are three types of clamping time of the renal hilum during PN: warm ischemia (clamping time <30 minutes), cold ischemia (clamping time >30 minutes), and no ischemia. Different studies have indicated that ischemia times >30 minutes lead to deterioration in the GFR and subsequent renal atrophy [10,11]. The dissection of a renal tumor and subsequent nephrorrhaphy without clamping of the renal artery poses a challenging surgical field for a surgeon, but compared with warm ischemia, this technique may improve the preservation of renal function in well-selected patients [13-15].

It is necessary to determine whether PN without clamping of the renal hilum offers benefits not provided through PN with warm ischemia, because the former involves greater surgical complexity and higher intraoperative risks for patients owing to increased blood loss [2,13,15,16].

The objective of the present study was to determine the effectiveness and safety of PN without ischemia compared with PN with warm ischemia in patients with cT1 renal tumors in decreasing impaired renal function.

MATERIALS AND METHODS

We performed this study according to the Cochrane recommendations, and we registered the protocol in PROSPERO CRD42019121991.

1. Inclusion criteria

Clinical experiments (randomized controlled trials [RCTs]), quasi-experiments, and cohort studies were included (prospective and retrospective). Patients were older than 18 years who underwent PN with warm ischemia or without (Zero) ischemia for T1 renal tumors. Studies had to compare PN without ischemia with PN with warm ischemia.

2. Exclusion criteria

Studies and patients with PN of lesions of nononcologic origin and studies for which data were unavailable were excluded.

3. Primary and secondary outcomes

The primary outcome was impaired renal function, defined as the decrease in the postoperative GFR compared with that in the preoperative period. Secondary outcomes were 1) intraoperative bleeding, defined as the blood volume (in mL) lost during the procedure; 2) operative time, defined as the duration of the procedure; and 3) postoperative urine leakage, defined as the percentage of patients reporting postoperative urine leakage at the nephrorrhaphy site.

4. Search sources

We performed a search strategy in the following databases from inception to the present: MEDLINE, EMBASE, LILACS, and the Cochrane Central Register of Controlled Trials (CENTRAL) (Supplementary material).

We searched in other electronic sources to find additional studies such as Clinicaltrials.gov, DARE, PROSPERO, conference abstracts, Google Scholar, Open Grey database, thesis databases, and reference lists. When information was missing, we contacted the authors to expand our knowledge of published or unpublished reports. There were no language restrictions.

5. Extraction and analysis of data

The two researchers identified and independently and blindly selected titles and abstracts obtained from electronic searches. The two evaluators analyzed their relevance by using a standardized eligibility format that included the predefined inclusion and exclusion criteria. We solved discrepancies for the inclusion of an article by consensus.

6. Extraction of information and management of data

The researchers extracted the data independently using a standard format. We obtained the following data: name of the first author, year of publication, country, year of study, type of study, sample size, outcome, and sociodemographic and clinical variables such as the number of patients per treatment arm, clinical stage, surgical technique, the mea-

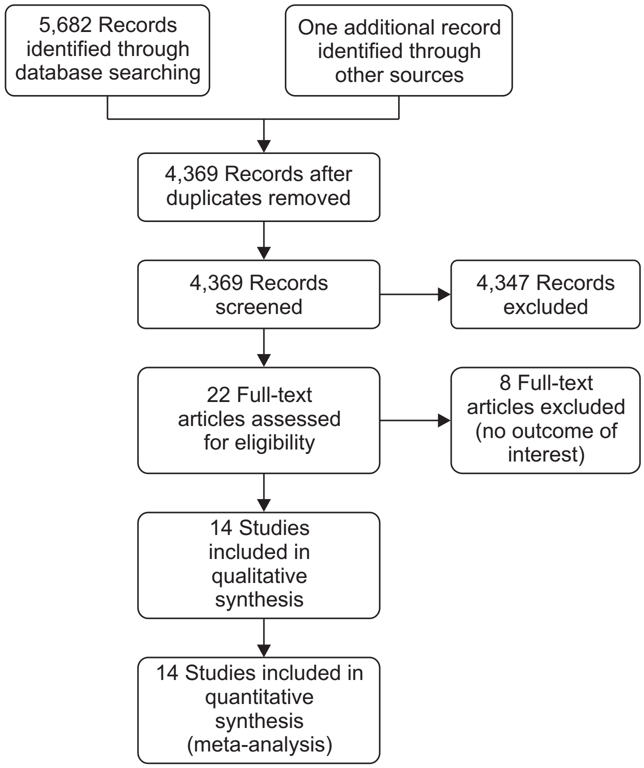

Fig. 1. Flowchart of study selection.

surement method of renal function, operative time, and postoperative urine leakage.

7. Evaluation of the risk of bias in the included studies

We evaluated the quality of the studies on the basis of study methodology and reporting, according to the recommendations of the methodological index for nonrandomized studies (MINORS) tool. For clinical experiments, we used the Cochrane Risk of Bias tool.

8. Statistical analysis

We performed a statistical analysis in Review Manager ver. 5.4. We described the outcomes in terms of the difference in means (MD) with the corresponding confidence interval. We used a random-effects model according to the heterogeneity found in the studies. We reported the results in forest plots.

9. Sensitivity analysis

We performed a sensitivity analysis based on the type of study (RCT vs. nonrandomized) and the weighted studies.

RESULTS

1. Selection of studies

With the search strategy, we found 5,682 articles. After eliminating duplicates, we included 14 articles (Fig. 1).

2. Characteristics of the included studies

We included 13 observational studies, in which there was a description of functional and oncologic results in patients undergoing PN without ischemia compared with PN with warm ischemia [15,17-28], and one clinical trial [29] (Table 1) [15,17-29].

Eight of the included studies allowed evaluation of the primary outcome because data was provided on the change in estimated GFR (eGFR); in a smaller proportion of studies, the proposed secondary outcomes could be evaluated (Table 2) [15,17-29].

3. Evaluation of the risk of bias

During the evaluation of the quality of the studies with the MINORS tool, we identified a high risk of bias in prospective data collection, the impartial assessment of the primary outcome, and calculation of the sample size. For the other items, the evaluation yielded mostly a low risk of bias (Fig. 2A, B) [15,17-28]. For Andersen 2019, we found an unclear risk of bias for blinding since there was no clear description of this issue. We assessed the other items as having a low risk of bias (Fig. 2C, D) [29].

4. Primary outcome: renal function

We included seven studies in the meta-analysis, including 567 patients in the group without ischemia and 824 patients in the warm ischemia group. The analysis yielded a favorable outcome for techniques without ischemia compared with techniques with warm ischemia, with an MD of 3.50 mL/min/1.73 m^2 (95% confidence interval [CI], 1.16 to 5.83; I^2=56%) (Fig. 3A) [18,19,22,23,26,27,29].

5. Secondary outcomes: intraoperative bleeding

For the evaluation of intraoperative bleeding, we included 10 studies; the comparison between techniques without ischemia and those with warm ischemia did not identify statistically significant differences, with an MD of 55.46 mL (95% CI, -33.16 to 144.08; I^2=97%) (Fig. 3B) [17-23,27-29].

6. Operative time

Eight of the included studies comparatively evaluated the operative time between techniques with warm ischemia and without ischemia, which showed an MD of 1.87 minutes

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Table 1. Characteristics of the included studies

Author (year)	No. of patients without ischemia/ warm ischemia	Clinical stage	Surgical technique	Measurement method for renal function	Renal function outcome measure	Median follow-up (mo)
Bhayani et al. [17] (2004)	42/48 patients	No information	LPN	Serum creatinine	Difference in mean Cr pre- and postsurgery	6 months
Wang et al. [18] (2016)	22/22 patients	T1a	LPN	eGFR	GFR changes	1 week postsurgery
George et al. [19] (2013)	150/180 patients	T1a-T1b	LPN	eGFR	GFR changes	6 months
Koo et al. [20] (2010)	11/10 patients	T1a	LPN	Serum creatinine	Difference in mean Cr pre- and postsurgery	NA
Kopp et al. [21] (2012)	64/164 patients	No information	LPN	eGFR	GFR changes	<12 months
Lee et al. [22] (2014)	39/201 patients	T1a	OPN	eGFR	GFR changes	12 months
Tanagho et al. [23] (2012)	29/29 patients	T1a	RAPN	eGFR	GFR changes	12 months
Peyronnet et al. [24] (2017)	26/104 patients	T1a	RAPN	eGFR	GFR changes	6 months
Thompson et al. [15] (2010)	96/362 patients	T1a	LPN and OPN	eGFR	GFR changes	1 month
Simone et al. [25] (2018)	485/221 patients	T1a-T1b	All	eGFR	GFR changes	No information
Salevitz et al. [26] (2015)	95/236 patients	No information	All	eGFR	GFR changes	<3 months
Smith et al. [27] (2011)	192/116 patients	T1a	All	eGFR	GFR changes	12 months
Akca et al. [28] (2014)	35/206 patients	T1a	RAPN	eGFR	GFR changes	12 to 24 months
Anderson et al. [29] (2019)	40/40 patients	T1a	RAPN	eGFR	GFR changes	3 months

LPN, laparoscopic partial nephrectomy; eGFR: estimated glomerular filtration rate; NA, not available; OPN, open partial nephrectomy; RAPN, robot-assisted partial nephrectomy.

Table 2. Variables in the included studies

Study	Technique	Operative time (min)	Estimated blood loss (mL)	eGFR, preoperative	eGFR, postoperative	Change in eGFR (<6 mo)	Postoperative urine leakage
Bhayani et al. [17] (2004)	Without ischemia	190 (67–370)	390±457	No information	No information	No information	No information
	Warm ischemia	153 (75–280)	301±261	No information	No information	No information	No information
Wang et al. [18] (2016)	Without ischemia	No information	134±70	86±19	84±21	-1.5±4.7	0.00%
	Warm ischemia	No information	70±79	90±21	84±28	-6.4±3.8	0.00%
George et al. [19] (2013)	Without ischemia	137 (35–441)	338 (50–1,700)	93.8 (28–292)	No information	-3.9 (-80.2–181.5)	No information
	Warm ischemia	141 (31–400)	250.8 (5–1,300)	97 (32–384)	No information	-8.6 (-59.5 to 83.2)	No information
Koo et al. [20] (2010)	Without ischemia	174±54.6	159±153	No information	No information	No information	No information
	Warm ischemia	232±27	165±110	No information	No information	No information	No information
Kopp et al. [21] (2012)	Without ischemia	No information	200 (150–400)	No information	No information	No information	3.10%
	Warm ischemia	No information	300 (200–440)	No information	No information	No information	7.30%
Lee et al. [22] (2014)	Without ischemia	No information	200 (40–1,700)	79.2 (34.6–125.1)	73.8 (35.5–111.4)	-7.9 (-57.1 to 24.1)	No information
	Warm ischemia	No information	200 (20–1,300)	80.7 (40.2–133.7)	63.7 (12.5–102.1)	-20.8 (-83.1 to 24.2)	No information
Tanagho et al. [23] (2012)	Without ischemia	127.0±37.9	146.4 (99.2)	84.8 (26.7)	79.9 (25.0)	-4.9 (8.9)	No information
	Warm ischemia	123.8±33.7	103.9 (81.7)	85.8 (21.3)	74.1 (21.1)	-11.7 (12.3)	No information
Peyronnet et al. [24] (2017)	Without ischemia	No information	284.6	78.4	No information	-0.2	No information
	Warm ischemia	No information	266.4	84.9	No information	-6.9	No information
Thompson et al. [15] (2010)	Without ischemia	No information	No information	54 (16–95)	No information	No information	1.00%
	Warm ischemia	No information	No information	61 (11–133)	No information	No information	5.00%
Simone et al. [25] (2018)	Without ischemia	No information	No information	86.4±17.7	78.5	No information	No information
	Warm ischemia	No information	No information	86.4±15.4	79.2	No information	No information
Salevitz et al. [26] (2015)	Without ischemia	143±65	No information	73.1±22.3	67.1±23.8	-6±15.5	No information
	Warm ischemia	172±49	No information	80.0±20.0	72.9±21.3	-6.07±13.5	No information
Smith et al. [27] (2011)	Without ischemia	226.5 (181–265)	500 (250–1,000)	72.2 (57.1–86.9)	66.3 (52.9–78.3)	-9.8 (-19–0)	4.70%
	Warm ischemia	192 (144–262)	200 (100–700)	77.5 (61–88.8)	68.9 (55.7–78.5)	-12.3 (-20.9–0.3)	0.80%
Akca et al. [28] (2014)	Without ischemia	180±63.3	210 (100–400)	78.3±26.3	75.5±25.1	No information	No information
	Warm ischemia	180±54	150 (100–250)	85.1±22.4	75±22.6	No information	No information
Anderson et al. [29] (2019)	Without ischemia	178±44.4	184.1±193.3	85.8 ±21	76 ±23.3	-10.7±17.5	No information
	Warm ischemia	156±40.6	178.5±207.5	92±21.6	81.8±19.3	-9.4±14.8	No information

Values are presented as mean (range) or number only or mean±standard deviation.
eGFR, estimated glomerular filtration rate.

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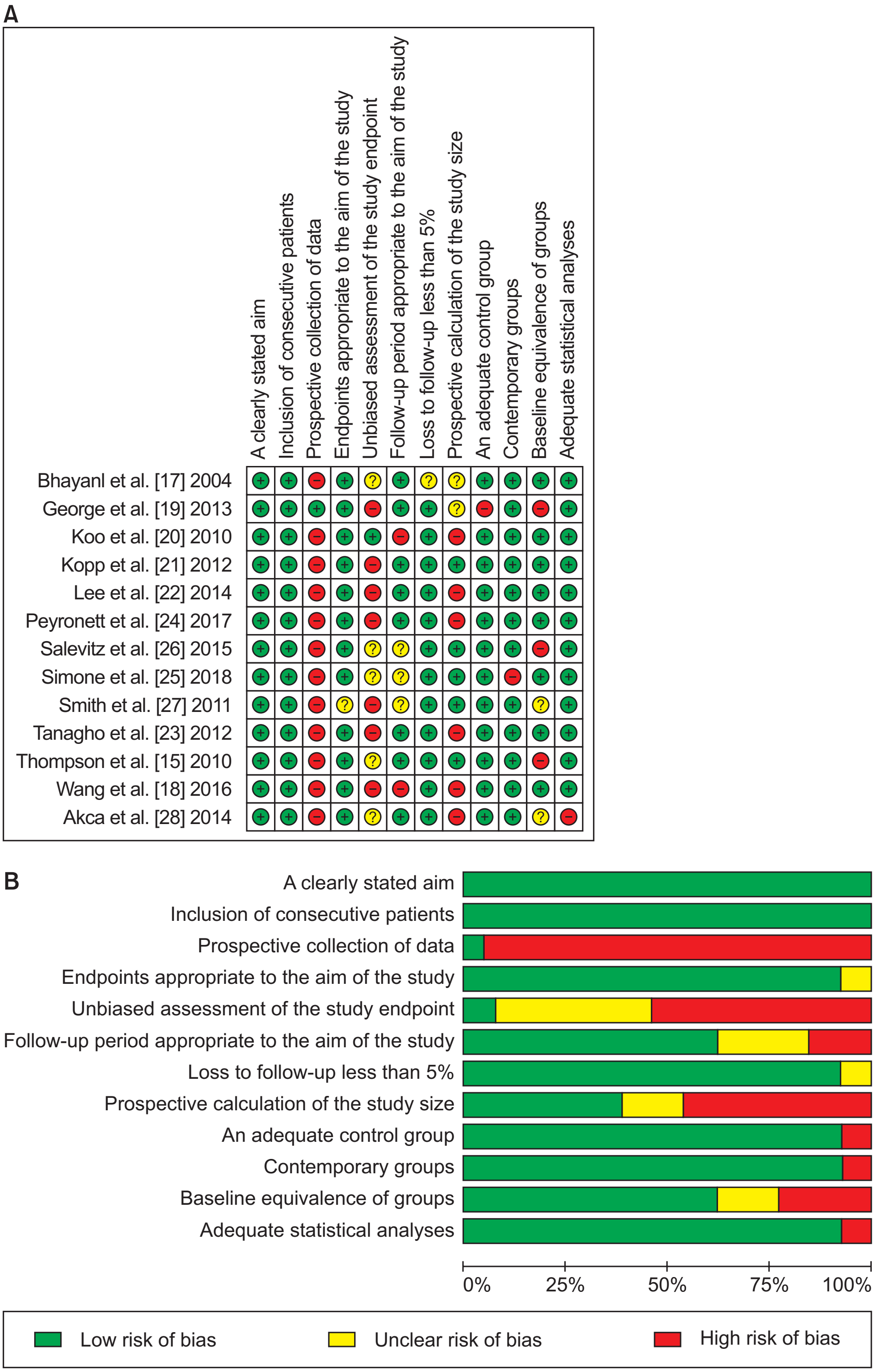

Fig. 2. (A) Risk of bias within studies: observational. (B) Risk of bias across studies: observational. (C) Risk of bias within studies: experimental. (D) Risk of bias across studies: experimental.

(95% CI, -20.47 to 24.21), with no statistically significant differences (Fig. 3C) [17,19,20,23,26-29].

7. Urine leakage

When assessing postoperative urine leakage, we found that only 4 of the 13 studies included evaluated postoperative urine leakage. An odds ratio of 0.74 was found (95% CI, 0.12 to 4.62). No statistically significant differences were observed (Fig. 3D) [15,18,21,27].

8. Sensitivity analysis

There were no changes in the results when we performed a sensitivity analysis based on the type of study (RCT vs. nonrandomized) and the weighted studies.

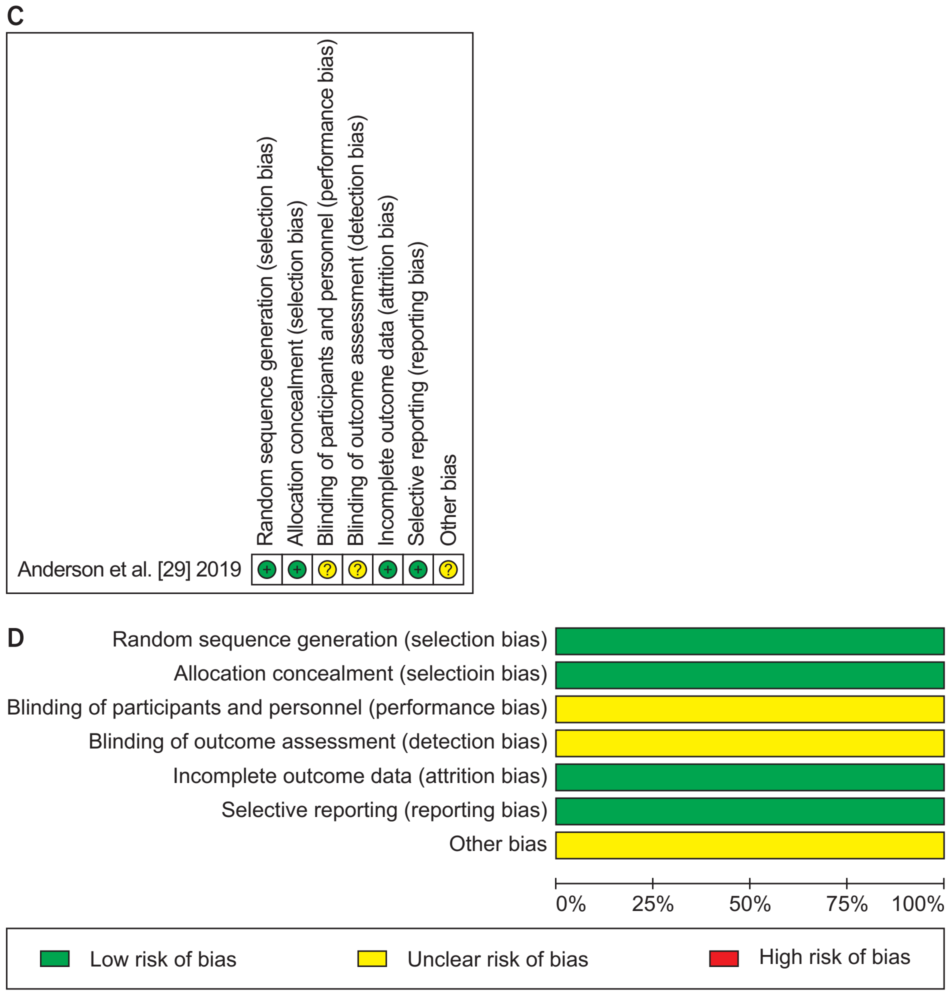

Fig. 2. Continued.

DISCUSSION

1. Summary of the main findings

We found a statistically significant difference in the decrease in deterioration of the eGFR, favoring techniques without ischemia. Nonetheless, this difference was not clinically meaningful. There were no statistically significant differences between intraoperative bleeding and operative time. In our evaluation of the proposed third secondary objective, postoperative leakage, we found no significant differences in the results for the two techniques described; however, only four studies assessed this outcome.

2. Contrast with the literature

The impact of ischemia time in PN has been the subject of many debates, considering that the injury caused by the ischemia-reperfusion process is the leading cause of impaired renal function, independent of resected renal tissue, because it leads to hyperfiltration and secondary nephrosclerosis [10,11]. Given the above, the approach of PN without ischemia as the therapeutic option could minimize the deterioration in renal function in patients undergoing this intervention.

In a systematic review, Greco et al. [30] assessed functional and oncologic outcomes in patients who underwent PN. That study included all types of studies (e.g., case series), which permitted the inclusion of a higher number of studies. Besides, it did not have a risk of bias analysis, making unclear the quality of the included studies. The previous finding limits the generalization of the results in the population. Therefore, we decided to perform the current research by use of international recommendations for conducting systematic reviews to obtain the best evidence for treating our patients.

Our study results demonstrate the lowest impact on deterioration in the eGFR in patients undergoing PN without ischemia compared with those undergoing PN with warm ischemia, including studies with different surgical techniques (open, laparoscopic, and robot-assisted PN) [31,32]. However, this difference was not clinically significant. It is essential to mention that four of the included studies in which the change in eGFR was evaluated had a follow-up

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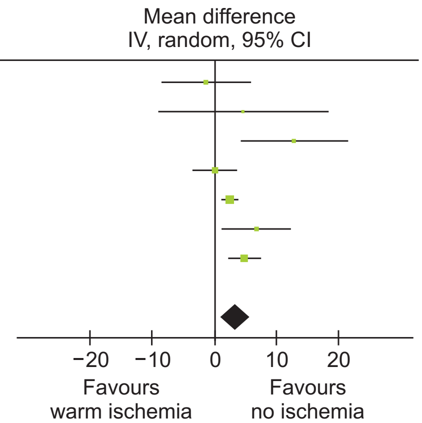
A

Study or subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Anderson et al. [29] 2019	−10.7	17.5	40	−9.4	14.8	40	8.1%	−1.30 [−8.40, 5.80]
George et al. [19] 2013	−3.9	76.9	150	−8.6	41.5	180	2.7%	4.70 [−9.02, 18.42]
Lee et al. [22] 2014	−7.9	23.5	39	−20.8	30.9	201	6.1%	12.90 [4.38, 21.42]
Salevitz et al. [26] 2015	−6.0	15.5	95	−6.07	13.5	236	18.6%	0.07 [−3.49, 3.63]
Smith et al. [27] 2011	−9.8	5.48	192	−12.3	6.14	116	29.4%	2.50 [1.14, 3.86]
Tanagho et al. [23] 2012	−4.9	8.9	29	−11.7	12.3	29	11.5%	6.80 [1.27, 12.33]
Wang et al. [18] 2016	−1.5	4.7	22	−6.4	3.8	22	23.6%	4.90 [2.37, 7.43]
Total (95% CI)			567			824	100.0%	3.50 [1.16, 5.83]

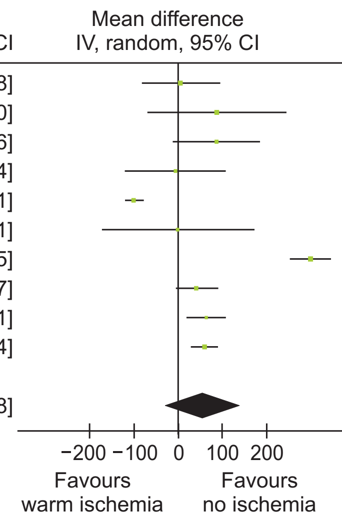
Heterogeneity: $Tau^2=4.34$; $chi^2=13.76$, df=6 (p=0.03); $I^2=56\%$
Test for overall effect: Z=2.94 (p=0.003)



B

Study or subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Anderson et al. [29] 2019	184.1	193.3	40	178.5	207.5	40	10.0%	5.60 [−82.28, 93.48]
Bhayanl et al. [17] 2004	390	457	42	301	261	48	8.3%	89.00 [−67.70, 245.70]
George et al. [19] 2013	338	500.9	150	250.8	391.4	180	9.8%	87.20 [−11.26, 185.66]
Koo et al. [20] 2010	159	153	11	165	110	10	9.4%	−6.00 [−119.24, 107.24]
Kopp et al. [21] 2012	200	75.3	64	300	69.5	164	11.1%	−100.00 [−121.29, −78.71]
Lee et al. [22] 2014	200	516.7	39	200	392.6	201	7.9%	0.00 [−171.01, 171.01]
Smith et al. [27] 2011	500	219.4	192	200	182.5	116	10.8%	300.00 [254.55, 345.45]
Tanagho et al. [23] 2012	146.4	99.2	29	103.9	81.7	29	10.8%	42.50 [−4.27, 89.27]
Wang et al. [18] 2016	134	70	22	70	79	22	10.8%	64.00 [19.89, 108.11]
Akca et al. [28] 2014	210	87.3	35	150	43.9	206	11.0%	60.00 [30.46, 89.54]
Total (95% CI)			624			1,016	100.0%	55.46 [−33.16, 144.08]

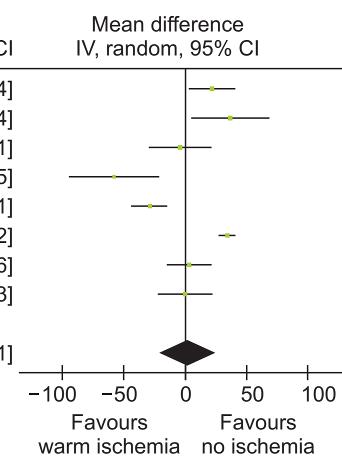
Heterogeneity: $Tau^2=18,340.12$; $chi^2=280.89$, df=9 (p<0.00001); $I^2=97\%$
Test for overall effect: Z=1.23 (p=0.22)



C

Study or subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Anderson et al. [29] 2019	178	44.4	40	156	40.6	40	13.0%	22.00 [3.36, 40.64]
Bhayanl et al. [17] 2004	190	87.8	42	153	59.5	48	11.2%	37.00 [5.56, 68.44]
George et al. [19] 2013	137	120.7	150	141	108.7	180	12.1%	−4.00 [−29.01, 21.01]
Koo et al. [20] 2010	174	54.6	11	232	27	10	10.4%	−58.00 [−94.35, −21.65]
Salevitz et al. [26] 2015	143	65	95	172	49	236	13.5%	−29.00 [−43.49, −14.51]
Smith et al. [27] 2011	226.5	11.1	192	192	34.2	116	14.2%	34.50 [28.08, 40.92]
Tanagho et al. [23] 2012	127	37.9	29	123.8	33.7	29	13.1%	3.20 [−15.26, 21.66]
Akca et al. [28] 2014	180	63.3	35	180	54	206	12.5%	0.00 [−22.23, 22.23]
Total (95% CI)			594			865	100.0%	1.87 [−20.47, 24.21]

Heterogeneity: $Tau^2=906.80$; $chi^2=92.03$, df=7 (p<0.00001); $I^2=92\%$
Test for overall effect: Z=0.16 (p=0.87)



D

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M−H, random, 95% CI
Kopp et al. [21] 2012	2	64	12	164	37.7%	0.41 [0.09, 1.88]
Smith et al. [27] 2011	9	192	1	116	30.8%	5.66 [0.71, 45.23]
Thompson et al. [15] 2010	1	96	18	362	31.5%	0.20 [0.03, 1.53]
Wang et al. [18] 2016	0	22	0	22		Not estimable
Total (95% CI)		374		664	100.0%	0.74 [0.12, 4.62]
Total events	12		31			

Heterogeneity: $Tau^2=1.73$; $chi^2=5.82$, df=2 (p=0.05); $I^2=66\%$
Test for overall effect: Z=0.33 (p=0.74)

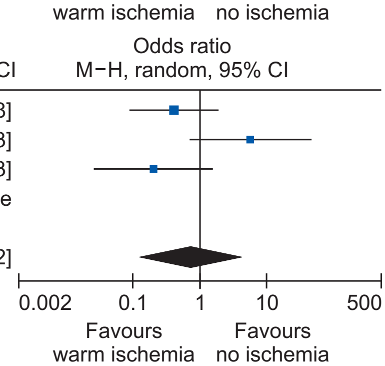


Fig. 3. (A) Decrease in estimated glomerular filtration rate. (B) Intraoperative bleeding. (C) Operative time. (D) Urine leakage. SD, standard deviation; IV, inverse of variance; CI, confidence interval.

time of fewer than 6 months, which could be a confounding factor when assessing the real impact of GFR deterioration with different techniques.

The transfusion of red blood cells and all the risks that this involves (infectious and immunological) is one of the main concerns of current transfusion medicine, which explains the strict guidelines and the motivation to search for strategies to reduce intraoperative bleeding and with this the need for transfusion [33]. Liu et al. in 2014 [32] reported an increase in the need for transfusions in patients undergoing PN without ischemia. In our study, although the need for transfusion was not evaluated, we did not find statistically significant differences in intraoperative bleeding between the two groups. However, there was a tendency toward more significant bleeding associated with PN without ischemia. Also, there were no significant differences in postoperative urine leakage, which shows that the reported major complications for PN without ischemia do not differ from those for PN with warm ischemia.

Trehan in 2014 [31] showed no differences concerning the operative time when comparing the two PN techniques. We confirmed this finding in this study, and the evolution of laparoscopic and robotic procedures explains it.

There is a need for extensive prospective randomized studies with long-term follow-up that compare PN techniques with and without warm ischemia, with pre- and postoperative measurements of renal function with dimercaptosuccinic acid (DMSA), not with eGFR only. This idea would allow better discrimination of renal function and determination of the real impact of the technique used. We found one protocol published by Cindolo et al. in 2019 [34] (The CLOCK randomized phase III study); however, there have been no data until now.

3. Strengths and limitations

Our study, unlike the previously conducted studies, had a clear methodological strategy, and the quality of the included studies was evaluated to give our study greater scientific rigor. One of the limitations of our study was the short follow-up of the patients in the included studies. We found follow-ups of up to 1 postoperative week, which may mask the real impact of the different techniques used in PN. The retrospective observational characteristics of the studies and the lack of evaluation of adverse effects related to PN techniques, which did not allow us to estimate the impact of this item, are other limitations. The small sample size in most studies is another significant limitation. Besides, there was a high clinical and statistical heterogeneity that may prevent the generalization of these results.

CONCLUSIONS

PN without ischemia showed reduced deterioration in the eGFR compared with that for PN with warm ischemia. There were no statistically significant differences in intraoperative blood loss and operative time between the two surgical techniques. Nonetheless, there were important limitations that may prevent the extrapolation of these results in clinical settings.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Sergio Hernando Mina-Riascos, Gonzalo Vitagliano, and Herney Andrés García-Perdomo. Data acquisition: Sergio Hernando Mina-Riascos and Herney Andrés García-Perdomo. Statistical analysis: Sergio Hernando Mina-Riascos and Herney Andrés García-Perdomo. Data analysis and interpretation: Sergio Hernando Mina-Riascos, Gonzalo Vitagliano, and Herney Andrés García-Perdomo. Drafting of the manuscript: Sergio Hernando Mina-Riascos, Gonzalo Vitagliano, and Herney Andrés García-Perdomo. Critical revision of the manuscript: Sergio Hernando Mina-Riascos, Gonzalo Vitagliano, and Herney Andrés García-Perdomo. Approval of the final manuscript: Sergio Hernando Mina-Riascos, Gonzalo Vitagliano, and Herney Andrés García-Perdomo.

SUPPLEMENTARY MATERIAL

Supplementary material can be found via https://doi.org/10.4111/icu.20190313.

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