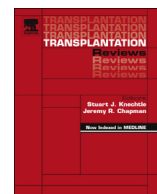


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Review article

Surgical learning curve in kidney transplantation: A systematic review and meta-analysis

Loubna Outmani, Jan N.M. IJzermans, Robert C. Minnee *

Department of Surgery, Division of HPB & Transplant Surgery, Erasmus University Medical Center (Erasmus MC), Doctor Molenwaterplein 40, 3015GD Rotterdam, Netherlands

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ABSTRACT

Aim: To assess the impact of the learning curve of kidney transplantation on operative and postoperative complications.

Methods: A literature search was systematically conducted to evaluate the significance of the learning curve on complications in kidney transplantation. Meta-analyses of the effect of the learning curve on warm ischemic time, total operating time (TOT), vascular and urological complications, postoperative bleeding, lymphocele and infection.

Results: Nine studies met the inclusion criteria and 2762 patients were included in the present meta-analyses. Surgeons at the beginning of the learning curve were found to have longer TOT (mean difference 41.77 (95% CI: 4.48–79.06; $P = .03$) and more urological complications (risk ratio 3.93; 95% CI: 1.87–8.25; $P < .01$). No differences were seen in warm ischemic time, postoperative bleeding, lymphocele, and vascular complications.

Conclusion: Surgeons at the beginning of their learning curve have a longer TOT and more urological complications, without an effect on postoperative bleeding, lymphocele, infection and vascular complications. For interpretation of the outcomes, the quality and sample size of the evidence should be taken into consideration.

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Abbreviations: ATN, Acute tubulus necrosis; DGF, Delayed graft function; IFTA, Interstitial fibrosis and tubular atrophy; KTx, Kidney transplantation; NOS, Newcastle-Ottawa Scale; PNF, Primary non function; PRISMA, Preferred Reporting Items for Systematic Reviews; TOT, Total operative time; WIT, Warm ischemic time.

* Corresponding author at: Department of surgery, Doctor Molenwaterplein 40, 3015 GD Rotterdam, Netherlands.

E-mail address: r.minnee@erasmusmc.nl (R.C. Minnee).

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1. Introduction

Kidney transplantation is the treatment of choice for patients with end-stage renal failure. [1] With 90,000 surgeries performed worldwide, kidney transplantation has become a substantial part of modern medicine. [2] Despite wide-ranging precautions to ensure patient safety, medical errors are still a source of complications and hospital costs. [3,4] Over the years, surgical techniques in kidney transplantation have changed substantially to improve quality of care and minimise complications. The learning curve is particularly important in surgery where a constant stream of new skills must be acquired safely and efficiently. Higher caseload proved better outcomes in various other fields of surgery such as oncological surgery, cardiothoracic surgery. [5,6] However, little is known about the impact of the learning curve in kidney transplantation, its effect on complications and patient outcome. Data on learning associated morbidity and mortality is needed to develop structured training programs and increase patient safety during these learning curves. Our aim is to systematically search the literature and analyse the impact of the learning curve of kidney transplantation and to assess its effect on intra- and postoperative complications.

2. Methods

The design of this systematic review was based on the criteria and guidelines mentioned in the Preferred Reporting Items for Systematic Reviews (PRISMA). [7] A systematic literature search of Embase, Medline Epub (Ovid), Cochrane Central, Web of Science and Google Scholar was constructed on June 14, 2019, to identify all studies on learning curve in kidney transplantation. The queries were constructed using suitable terms concerning surgeon experience, the surgical learning curve and kidney transplantation and. (See appendix A).

Titles, abstract and full-text articles were screened independently by two investigators. Predefined exclusion criteria included studies focusing on human subjects under the age of 18 or animals or in vitro studies, specific types of articles (e.g. conference abstracts, letters to the editor, replies, editorials, case reports, guidelines and reviews). Duplicate articles were removed.

Articles were screened on relevance based on the title and abstract. The remaining studies were assessed for relevance by evaluation of full-text articles. The reference lists of the included studies were examined to identify the studies that might have been missed during the search. These articles were included in this systematic review.

2.1. Data extraction

The data extraction was performed independently by two reviewers. Study parameters collected for data included were: warm ischemic time (WIT), total operating time (TOT), urological complications, postoperative bleeding, infection, lymphocele and vascular complications.

2.2. Categories

To compare the results of the studies, two groups were created: less experienced and well experienced surgeons. Surgeons in the less experienced group had performed between 0 and 30 kidney transplantations and those in the well experienced group had completed over 30 kidney transplantations. The cut off of 30 was chosen as the majority of studies published on this subject refers to this number.

2.3. Quality of evidence assessment

Quality assessment was performed using an adjusted version of the Newcastle-Ottawa Scale for observational studies (NOS). [8] The included articles were scored in three different sections namely the selection process, the comparison and the outcome. For each section, questions regarding quality were answered and points were awarded if the criteria were met. The maximum amount of points that could be obtained was nine. Studies with seven or more points were considered to be of good quality. Studies with four to six were scored as moderate quality and studies with three or less points were scored as poor quality.

2.4. Statistical analyses

We performed meta-analysis on six outcomes (WIT, TOT, urological complications, postoperative bleeding, lymphocele and vascular complications) using Review Manager 5.3. The pooled risk ratios (RR) and 95% confidence intervals (CI) were assessed using the DerSimonian-Laird method, a binary random effects method. A *P*-value below 0.05 was considered statistically significant. Potential variance due to heterogeneity between studies was estimated by the statistic I^2 which was defined as low (25%), moderate (50%) or high (75%).

3. Results

3.1. Study selection

The PRISMA flow diagram of articles included in the present review is depicted in Fig. 1. A total of 1090 potentially eligible articles were identified. Nine articles met our inclusion criteria and were included in this systematic review. [9–17] The baseline characteristics of all nine included studies are shown in Table 1. The results of the intra- and postoperative complications are showcased in Table 2. Six studies provided data for meta-analysis. [9,13–17]

3.2. Quality assessment

The results of the quality assessment are shown in Table 3. Three studies were rated as good quality. [13,15,17] The quality of the remaining six studies was considered moderate. [9–12,14,16]

3.3. Warm ischemic time

Four studies measured warm ischemic time (WIT) including 3 studies with quantitative data (Fig. 2). [9,13,14] A total of 916 patients were included of which 55.6% (509/916) in the less experienced group and 44.4% (407/916) in the experienced group. The pooled mean difference in minutes was 8.20 (95% CI: -1.80, 18.20; *P* = .11) and showed no significant lower WIT in the experienced group. The I^2 heterogeneity was 99% with a *P*-value of less than 0.01.

3.4. Total operative time

Four studies measured total operative time (TOT) including 2 studies with quantitative data (Fig. 3). [9,14] A total of 497 patients were included of which 84.9% (422/497) in the less experienced group and 15.1% (75/497) in the experienced group. The mean difference in minutes was significant shorter in the experienced group 41.77 (95% CI:

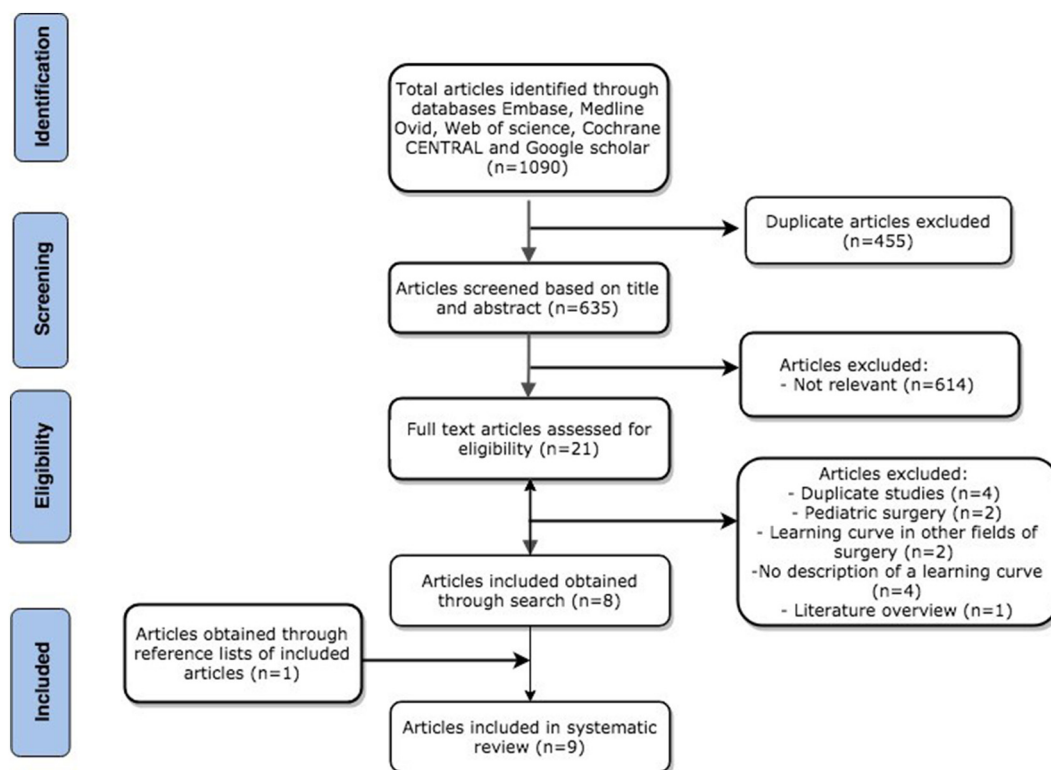


Fig. 1. Flowchart of search strategy and selection process.

Table 1
Characteristics of included studies.

Author	Thomas et al [9]	Wolff et al [10]	Weng et al [11]	Oitchayomi et al [12]	Cash et al [13]	Fechner et al [14]	Seow et al [15]	Dlugosz et al [16]	Kulu et al [17]
Year of publication	2013	2014	2015	2014	2011	2012	2012	1999	2018
Country	Germany	Switzerland	Taiwan	France	Germany	Germany	United Kingdom	Poland	Germany
Mean volume of KTx per year	61	41	222 ^a	105	27	15	107	20	86
Number of patients	184	1496	1779	738	484	392	322	225	1462
Number of surgeons	16	33	142	90	13	18	–	143	–
Number of groups	4	8	2	3	2	5	2	2	5
Division of groups	Trainees, low-experienced: 30 supervised interventions, medium: 30 unsupervised interventions, high-experienced	Number of surgeries divided per 10	low-volume < 33 transplant, medium/high volume > 33	Juniors 1, Juniors 2, Seniors	Inexperienced > 30 surgeries, experienced > 30 surgeries	Number of surgeries divided per 10	Trainees vs trained	Learning group vs seniors	Inexperienced < 25, experienced > 25
Follow-up time (in months)	3	12	120	60	12	12	6	36	3
Period of follow-up	2010–2012	1962–2003	1999–2007	2006–2012	1988–2005	1985–2010	1998–2001	1985–1995	2000–2016
Living or deceased donors	Deceased donors	73% deceased donors	Deceased donors	–	Deceased donors	Deceased donors	Deceased donors	Deceased donors	66% deceased donors
Ureterovesical anastomosis, with or without stent	–	Lich Gregoir, with stent	–	Lich Gregoir, with stent	Politano Leadbetter, with stent	Lich Gregoir, with stent	Lich Gregoir, with stent ^b	–	Lich Gregoir, with stent
Mean age recipients	57	47	–	53.6	47.7	48	–	–	48.5
Mean age donors	58	41	–	56.6	48.7	42.5	–	–	51.2

^a Nationwide study in which 35 hospitals participated.

^b Stent was added in January 2000.

Table 2
Results of intra- and postoperative complications.

Author	Thomas et al [9]	Wolff et al [10]	Weng et al [11]	Oitichayomi et al [12]	Cash et al [13]	Fechner et al [14]	Seow et al [15]	Dlugosz et al [16]	Kulu et al [17]
Warm ischemic time in minutes	Significantly lower in experienced surgeons	-	-	Significantly lower in experienced surgeons	N.S ^a	Significantly lower in most experienced group	-	-	-
Total operative time in minutes	Significantly lower in experienced surgeons	-	-	Significantly lower in experienced surgeons	-	Significantly lower in most experienced group	-	-	Significantly lower in experienced surgeons
Lymphocele	N.S	N.S.	-	-	N.S.	N.S.	N.S.	-	-
Urological complications	N.S.	-	-	N.S.	Significantly lower in experienced surgeons	N.S	Significantly lower in experienced surgeons	N.S.	-
Vascular complications	N.S.	N.S.	-	N.S.	N.S.	N.S.	N.S.	-	Significantly lower in experienced surgeons
Post-operative bleeding	N.S.	-	-	-	N.S.	N.S.	N.S.	-	-
Wound infection	N.S.	-	-	-	-	-	N.S.	-	-

^a N.S. = not significant.

Table 3
Quality assessment of included studies.

Author	Selection	Comparability	Outcome	Total Quality		
	The study population is a representative of the population undergoing kidney transplantation (*)	Were surgeons divided in two groups? (*)	Correction for case selection was done. (*)	Assessment of outcome was from independent blind assessment or record linkage. (*)		
	The study population received a kidney from living and deceased donor. (*)	Were surgeons divided in two groups? (*)	Correction for case selection was done. (*)	Quantative data of parameters was available. (**)		
				Follow-up was long enough for outcomes to occur. (*)		
				Was loss of follow-up after baseline less than 20%? (*)		
1 Thomas et al [9]	*	-	-	*	6	Moderate
2 Wolff et al [10]	*	-	*	*	6	Moderate
3 Weng et al [11]	*	-	*	*	5	Moderate
4 Oitichayomi et al [12]	*	-	-	*	4	Moderate
5 Cash et al [13]	*	-	*	*	7	Good
6 Fechner et al [14]	*	-	-	*	6	Moderate
7 Seow et al [15]	*	-	*	*	7	Good
8 Dlugosz et al [16]	*	-	-	*	6	Moderate
9 Kulu et al [17]	*	*	-	*	7	Good

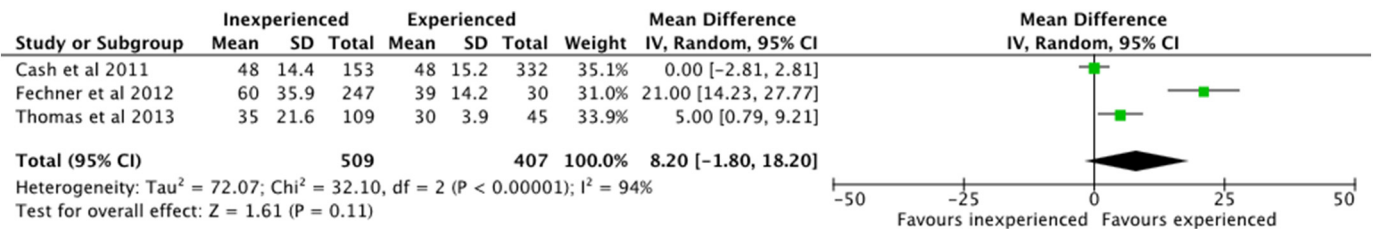


Fig. 2. Meta-analysis of warm ischemic time.

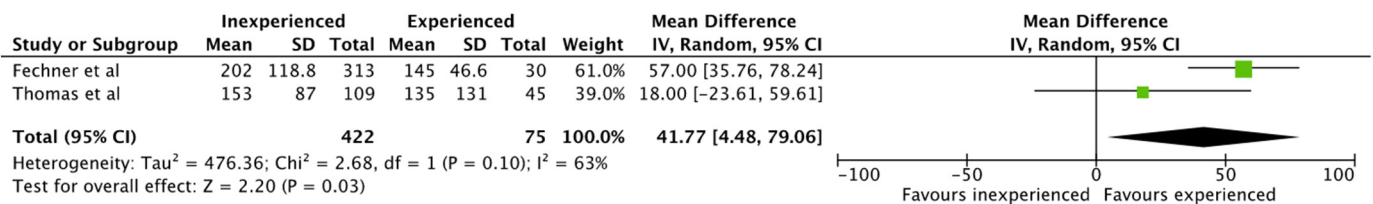


Fig. 3. Meta-analysis of total operative time.

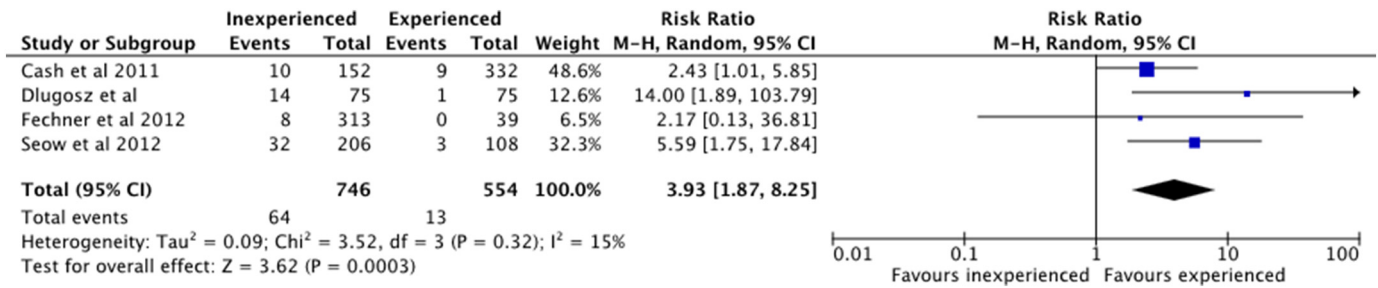


Fig. 4. Meta-analysis of urological complications.

4.48–79.06; P = .03). The I² heterogeneity was 63% with a P-value of 0.10.

3.5. Urological complications

Six studies implemented urological complications as outcome including 4 studies with quantitative data (Fig. 4). [13–16] A total of 1300 patients were included of which 57.4% (746/1300) in the less experienced group and 42.6% (554/1300) in the experienced group. The risk of an urological complication was almost 4 times higher in the less experienced group RR 3.93 (95% CI: 1.87–8.25; P = .01). The I² heterogeneity was 15% with a P-value of 0.32.

3.6. Postoperative bleeding

Four studies measured postoperative bleeding including 2 studies with quantitative data (Fig. 5). [13,14] A total of 827 patients were included of which 56.2% (465/827) in the less experienced group and 43.8% (362/827) in the high experienced group. The pooled RR showed no significant higher postoperative bleeding in the less experienced group RR 0.97 (95% CI: 0.45–2.12; P = .94). The I² heterogeneity was 0% with a P-value of 0.89.

3.7. Infection

Two studies reported that there was no difference in infection rate between the experienced and less experienced groups. [9,15]

3.8. Lymphocele

Five studies measured lymphocele including 2 studies with quantitative data (Fig. 6). [13,14] A total of 827 patients were included of which 56.2% (465/827) in the less experienced group and 43.8% (362/827) in the high experienced group. The pooled RR was not significantly different between experienced and less experienced surgeons with a RR 0.87 (95% CI: 0.43–1.73; P = .68). The I² heterogeneity was 0% with a P-value of 0.46.

3.9. Vascular complications

Five studies measured vascular complications including 3 studies with quantitative data (Fig. 7). [13,14,17] A total of 2289 patients were included of which 45.3% (1038/2289) in the less experienced group and 54.9% (1251/2289) in the high experienced group. The pooled RR showed no statistical significant difference for risk of vascular complications with a RR 2.31 (95% CI: 0.55–10.78; P = .29). The I² heterogeneity was 0% with a P-value of 0.02.

4. Discussion

Our systematic review and meta-analysis revealed that experienced surgeons had a shorter TOT and lower risk of urological complications.

This analysis uses case volume as a surrogate marker for experience. Prior studies in other disciplines have mentioned the importance of

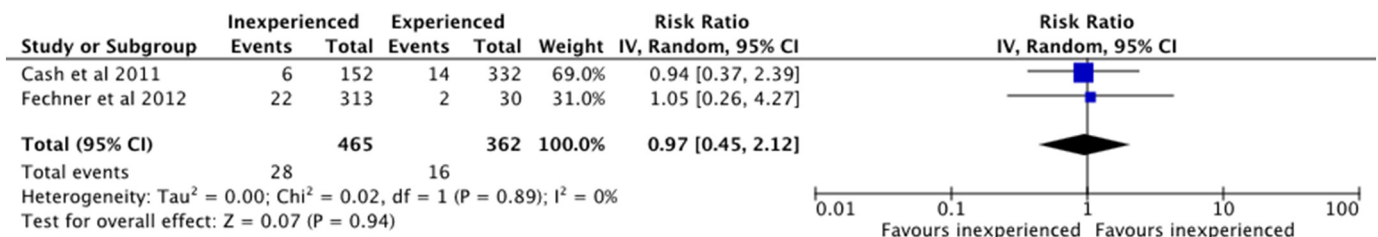


Fig. 5. Meta-analysis of postoperative bleeding.

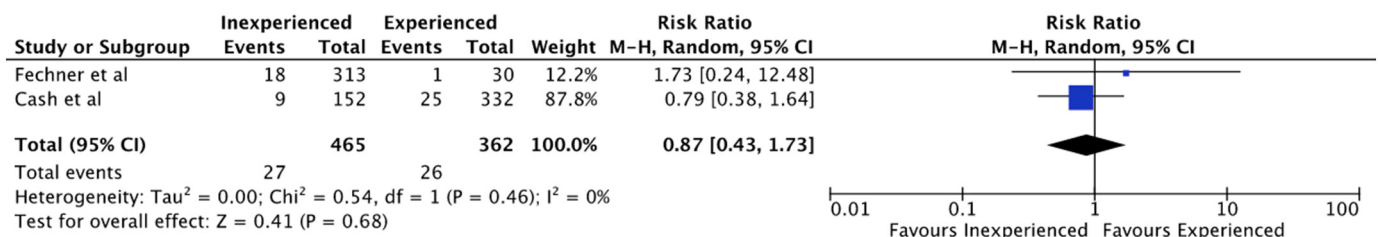


Fig. 6. Meta-analysis of lymphocele.

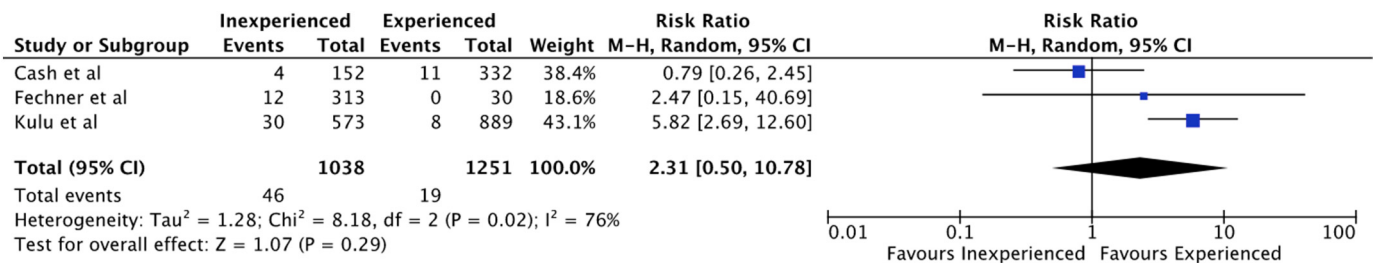


Fig. 7. Meta-analysis of vascular complications.

experience and have established a positive correlation between higher case volume and improved outcomes. [5,6]

Kulu et al. described a correlation between experience and the predictive probability of developing vascular and haemorrhagic complications after kidney transplantation. [17] Their analysis revealed 26 as the best cut off number of previous KTxs to decrease the predicted probability of vascular and haemorrhagic complications. However, using case volume as a surrogate marker for experience does not take into account the technical skill level of individual surgeons. Heylen et al. examined an alternative measure of surgical skill using anastomosis time and demonstrated a correlation with kidney allograft function, suggesting that individual technical skill is a more accurate measure for surgeon related outcome instead of case volume. [18]

It is unclear whether short operative duration actually is a good measurement of the quality of surgery. [19] In a systematic review published by Cheng et al. the association between operative duration and complications across several surgical specialties was reviewed. [20] They concluded that increased operative duration was associated with a statistically significant increase in postoperative complications in both general surgery and urology. An increment of 30 min increased the risk of complications by 14% ($P < .001$).

However, in kidney transplantation, TOT is not as important as the anastomotic time. Three studies observed a longer WIT in less experienced surgeons compared to experienced surgeons. [9,12,14] This difference however, is not significant when all data is pooled. Transplant surgeons are advised to keep WIT as short as possible due to the damage longer WIT may have on kidney allografts. Longer WIT increases the risk of primary non-function (PNF) and is associated with delayed graft function (DGF) and acute tubular necrosis (ATN). [18,21] Heylen et al. found in an analysis of 669 kidney transplants that WIT above 35 min is associated with lower allograft function up to three years after transplantation ($P < .001$). [18] At one and two year after transplantation, allografts with WIT longer than 35 min had significantly more interstitial fibrosis and tubular atrophy (IFTA) ($p = .002$), which suggest that longer WIT also has an impact on chronic allograft injury. In two included studies, the mean WIT in both experienced and less experienced surgeons was well above the threshold of 35 min. [13,14]

Cash et al. and Seow et al. reported a higher risk of urological complications in less experienced surgeons. [13,15] This difference could be explained by their technique for the ureterovesical anastomosis. Cash et al. used the Politano Leadbetter technique. Previous studies have shown that this intravesical technique is more susceptible to complications compared to other techniques. [22] A systematic review by Alberts et al. concluded that the Lich-Gregoir ureterovesical anastomotic technique compared to the Politano Leadbetter technique results in significantly less postoperative urological complications. [23] The difference in urological complications could also be explained by the lack of a ureteric stent. Seow et al. state that the use of a ureteric stent was introduced halfway through their study and that routinely use of a stent had drastically reduced the urological complication rate. [15] This is in line with other studies that concluded that the use of ureteric stents results in less urological complications compared to no stent use. [24–26] A third explanation for the increase in urological complications is that

most kidney transplants are carried out by vascular or general surgeons. They have less experience in performing ureterovesical anastomoses compared to vascular anastomoses. That means that the learning curve observed in this study reflects the true learning curve surgeons go through, when they are trained for kidney transplantations. Considering that the ureteric anastomosis is the Achilles heel in transplant surgery, senior surgeons are advised to put more emphasis the ureteric anastomosis while training transplant surgeons. Complication caused by a poorly performed ureteric anastomosis can lead to decrease graft function or even graft loss. Less experienced surgeons should only perform ureterovesical anastomosis under strict supervision of a senior surgeon until they have mastered this skill.

Less experienced surgeons have an almost 2.5 folds increased risk of vascular complications (RR 2.31; 95% CI: 0.55–10.78; $P = .29$). However, this RR is not statistically significant. This is probably due to the small study population and the rare occurrence of vascular complications. As rare complications have lower statistical power, larger number of patients are needed to detect significant differences. The same applies for the incidence of lymphocele post kidney transplantation. These complications rarely occur and are often misclassified or missed as they often present asymptotically. [27] One of the surgical causes of lymphatic complications is the dissection of renal lymphatic tissue of the donor kidney either during the organ procurement surgery or during 'back table' work. [27] The surgeon performing the transplantation is often not the surgeon who procured the organ, which makes it hard to attribute this complication to the surgeon performing the transplantation and should not be used as a measure to quantify surgical skills.

The majority of the included studies were performed in low-volume hospitals. There is evidence that hospital volume may influence outcome in transplantation. Several studies have shown that higher hospital volume is associated with improved patient outcome and reduced postoperative complications. [13,28,29] This is possibly due to logistical advantage of centralizing specialized care. The whole medical care including nephrologists, surgeons, and OR-personal are more familiar with kidney transplant recipients. The medical process will be better organized, which will reduce human mistakes and medical errors.

Our study has several limitations. We included only nine articles due to the fact that a few studies have published on the learning curve in kidney transplantation. There was a lot of heterogeneity between the articles that were included. This heterogeneity was regarding the outcome and complications and the way surgeon were divided into different groups. We could not collect any information on the postoperative kidney function and the primary non function and delayed graft function rate. Another risk of bias is that more complex cases are assigned to experienced surgeons. One of the most important factor of surgical complications are patient characteristics. [1,30] Surgeries on more complex patients have therefor a higher risk of complications. Most studies included in this systematic review did not correct for case selection.

In conclusion, less experienced surgeons have a longer TOT and higher urological complications risk, possible due to the effect of the learning curve. The learning curve in kidney transplantation seems not to affect the risk of postoperative bleeding, lymphocele, infection and

vascular complication. Well performed studies are needed as risk of bias was high and quality of the reports are moderate.

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Authorship

L.O., J.N.M.IJ. and R.C.M. participated in the research design.
L.O., J.N.M.IJ. and R.C.M. participated in the writing of the article.
L.O. and R.C.M. participated in the extracting of data.
L.O. and R.C.M. participated in data analysis.

Author agreement

All authors have seen and approved the final version of the manuscript being submitted. They warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

Declaration of Competing Interest

The author declare that there is no financial or personal interest or belief that could affect their objectivity. The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.trre.2020.100564>.

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