#### REVIEW



# Incisional hernias post renal transplant: a systematic review and meta-analysis

B. M. Mac Curtain<sup>1,2</sup> · W. Qian<sup>2</sup> · H. C. Temperley<sup>3</sup> · A. O'Mahony<sup>4</sup> · Z. Q. Ng<sup>5</sup> · B. He<sup>6</sup>

Received: 20 July 2023 / Accepted: 29 August 2023 / Published online: 15 September 2023 © The Author(s), under exclusive licence to Springer-Verlag France SAS, part of Springer Nature 2023

#### Abstract

**Purpose** Incisional hernia (IH) post renal transplant (RT) is relatively uncommon and can be challenging to manage clinically due to the presence of the kidney graft and patient immunosuppression. This systematic review and meta-analysis synthesises the current literature in relation to IH rates, risk factors and outcomes post RT.

**Methods** PubMed, EMBASE, and Cochrane Central Registry of Controlled Trials (CENTRAL) were searched up to July 2023. The most up to date Preferred Reporting Items for Systematic Reviews and Meta Analyses guidelines were followed. Pertinent clinical information was synthesised. A meta-analysis of the pooled proportions of IH rates, the rates of patients requiring surgical repair and the rates of recurrence post RT are reported.

**Results** Twenty studies comprising 16,018 patients were included in this analysis. The pooled rate of IH occurrence post RT was 4% (CI 3–5%). The pooled rate of IH repair post RT was 61% (CI 14–100%). The pooled rate of IH recurrence after repair was 16% (CI 9–23%). Risk factors identified for IH development post RT are BMI, immunosuppression, age, smoking, incision type, reoperation, concurrent abdominal wall hernia, lymphocele formation and pulmonary disease.

Conclusions IH post RT is uncommon and the majority of IH post RT are repaired surgically on an elective basis.

Keywords Incisional hernia · Renal transplant · Kidney transplant · Urology

# Introduction

The occurrence of incisional hernia (IH) after abdominal surgery via midline laparotomy remains one of the most common postoperative complications. Existing data suggests an incidence ranging between 8 and 20% [1–6]. Renal transplant (RT) recipients, due to their immunosuppressive regimen, extended dialysis periods, and complex comorbidities, are believed to face an elevated risk of developing

B. M. Mac Curtain b.maccurtain1@nuigalway.ie

- <sup>1</sup> School of Medicine, University of Galway, Galway, Ireland
- <sup>2</sup> Dept. of Surgery, St John of God Subiaco Hospital, Subiaco, WA, Australia
- <sup>3</sup> St James' University Hospital, Dublin, Ireland
- <sup>4</sup> University Hospital Limerick, Limerick, Ireland
- <sup>5</sup> Dept. of General Surgery, Royal Perth Hospital, Perth, WA, Australia
- <sup>6</sup> Renal Surgery and Transplant Unit, Austin Health, Melbourne, VIC, Australia

wound complications after surgery [7–9]. Compared to midline abdominal procedures, the rates of IH in renal transplant recipients are documented as being lower, between 1 and 7% compared to rates between 8 and 20% for midline incisions [9]. Single-centre studies have estimated the incidence of IH after RT surgery to range from 3.28 to 7% [10, 11]. Furthermore, IH secondary to RT are considered complex hernias as they are lateral to the sheath of the rectus abdominis muscle [12]. To enhance our understanding of abdominal wall IH rates amongst hernia surgeons, it is essential to ascertain the precise IH rate following RT surgery and it's associated risk factors through an extensive examination of the available primary literature.

A prior review has examined the literature in relation to IH and RT up to 2016, however this previous study excluded robotic and laparoscopic cases. It excluded studies in which there were less than 200 patients included and there was also no meta-analysis performed [9]. Pancreas transplant and RT IH rates were analysed in combination prior to this review, however, RT was never meta-analysed in unison, to the best of the author's knowledge [13]. We believe this systematic review which incorporates additional studies pre and post

2016 coupled with a meta-analysis of the rates of IH makes this review an informative comprehensive resource.

# Methods

# **Registration and search strategy**

Our search was conducted in line with the most recent Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) recommendations [14]. Our study protocol was prospectively registered on PROSPERO under the following registration number: CRD42023441024. A search was conducted of PubMed, EMBASE and Cochrane Central Register of Controlled Trials using the search algorithms provided in the below up to the 1st July 2023.

# (incision\* hernia\* OR herniorrhaphy OR hernioplasty) AND (renal OR kidney) AND (transplant\*)

The complete breakdown of analysed studies can be viewed in the PRISMA diagram in Fig. 1. The bibliographies of included publications were also searched for any relevant studies.

# Inclusion criteria

- Patients aged 17 years old and above, due to differing rates of IH observed in a paediatric population [15].
- Study detailing rates of all IH post RT, plus or minus rates of repair.
- Open / robotic kidney transplants with any incision or method of closure.



**Fig. 1** PRISMA Statement for incisional hernias in rental transplantation

- Prospective or retrospective studies.
- English language or translation available.
- Primary closure of transplant site.
- IH repair with and without mesh devices were included.
- Primary or subsequent renal transplant.
- First / second RT (primary-first incision) or 3rd/4th RT (repeat previous incision)
- Follow up of at least 6 months after RT.

#### **Exclusion criteria**

- Rates of IH reported with no surgery type detailed in the context of publication primarily examining novel immunosuppression regimes rather than surgery effect.
- Simultaneous or previous nephrectomy or simultaneous transplant or auto transplant.
- Case reports or small case series (defined as < 10 patients) or conference abstracts or conference papers or consensus statements.
- Trans-vaginal transplantation.
- Studies published prior to 2000, due to a large improvement in graft rejection outcomes after this point [16].

## Identification of studies and outcomes of interest

Studies that meet the inclusion criteria were included. The following PICO elements were used as the basis for selecting studies [17]:

Population: patients undergoing RT.

*Intervention*: RT under open or robotic assisted means. *Comparison*: patients whom also underwent RT but did not develop an IH.

Outcome: development of IH post-RT.

Studies were independently reviewed by two separate authors (BMC, WQ) using Rayyan [18]. If there was any disagreement between authors a third author (ZQN) was used to mediate the discussion and consensus was reached.

Our primary outcome of interest was to identify the incidence of IH after RT.

Secondary outcomes of interest were to analyse risk factors and the rate for surgical repair and patient and graft survival outcomes.

# **Data extraction**

Relevant metrics and information were extracted using a template on Google Sheets (Mountain View, California, United States). Three independent authors (WQ, AOM, and BMC) were involved in the data extraction. The template used allowed for data to be extracted in a consistent and uniform manner and was updated in real time, which

enabled all authors to track progress and verify consolidated information.

## **Study selection**

Prospective and retrospective studies were included in this systematic review and meta-analysis. No randomised trials have been completed on the topic to the best of the author's knowledge.

Both mesh and non-mesh IH repairs were reported and analysed separately in the meta-analysis where applicable. If studies did not specifically report using a robotic assisted method, an open approach was assumed. The robotic assisted rates of IH were meta-analysed separately. Contrary to previous systematic reviews on the topic, we did not exclude studies containing less than 200 patients, as study sample numbers may or may not correlate to transplant centre's experience. Phillips et al. analysed two differing approaches to open RT, these were meta-analysed separately due to a statistical difference being detected in IH between techniques (p = 0.04) [19].

#### **Risk of bias assessment**

Assessment of potential biases for non-randomised studies was assessed using a modified Newcastle–Ottawa scale risk of bias tool [20], with the results tabulated as in Table 1. This assessment tool grades each study as being 'satisfactory' or 'unsatisfactory' across various categories. We assigned stars to evaluate study quality: 7 stars—"very good", 5–6 stars "good", 3–4 stars "satisfactory" and 0–2 stars "unsatisfactory". The critical appraisal was completed by two reviewers independently (HT and BMC), where once again a third reviewer (WQ) was asked to arbitrate in cases of discrepancies in opinion.

#### **Statistical analysis**

We performed a proportional meta-analysis as part of this review [21]. Statistical analysis was run using Stata 17 (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC). The proportion of patients developing IH after RT and undergoing repair after IH was pooled using the "metaprop" function within Stata [22]. A p value <= 0.05 was considered statistically significant and 95% confidence intervals were employed. Heterogeny was reported using  $I^2$  [22]. It has been put forward that  $I^2$  values of 25%, 50%, 75% can be used to assess the degree of heterogeneity [23]. We considered there to be a notable degree of heterogeny if  $I^2$  was greater than 50%. A random effects model was used due to evidence of significant statistical heterogeneity as well evidence of study design heterogeneity [24].

Author	Selection				Comparabil- ity	Outcome			Quality
	Representa- tiveness of the exposed cohort	Sample size (<25=no star)	Open cases only included	Ascertain- ment of the exposure	The subjects in different outcome groups are comparable	Assessment of outcome	Less than 10% missing data?	Average Follow up period (> 12 months)	
Tzvetanov	*	*	*	*	*	*	*	/	7
Reyna- Sepúlveda	*	*	*	*	/	*	*	*	7
Gusukuma	*	*	*	*	*	/	*	*	7
Harbell	*	*	*	*	*	*	*	*	8
Kapoor	*	*	*	*	*	*	/	*	7
Costa	*	*	*	*	*	*	*	/	7
Cassese	*	*	*	*	/	*	*	*	7
Alhassan	*	*	*	*	*	/	*	*	7
Heng	*	*	*	*	*	*	/	*	7
Territo	*	*	*	*	*	*	*	*	8
Yildız	*	/	*	*	/	*	*	*	6
Phillips	*	*	*	*	*	*	*	*	8
Araújo	*	*	*	*	*	*	*	*	8
Ooms	*	*	*	*	*	*	*	/	7
Smith	*	*	*	*	*	*	*	*	8
Brockschmidt	*	/	*	*	*	*	/	*	6
Varga	*	*	*	*	*	*	*	*	8
Nanni	*	*	*	*	*	*	*	*	8
Singh	*	*	*	*	/	*	*	*	7
Birolini	**	*	*	**	ste	ate	*	1	7

Table 1 Newcastle Ottawa risk of bias assessment for non-randomised studies for included studies

Funnel plots were not generated as previously recommended for proportional meta-analysis [25]. Qualitative bias assessment was also conducted as proposed by Barker et al., as this is a proportional meta-analysis [21]. If missing data or conflicting data was found upon review of included papers authors were contacted for clarification.

# Results

# **Primary outcome**

## **Rates of IH**

Twenty studies (n = 16,018) were included in this meta-analysis and systematic review. We report demographical details in Table 2. Seventeen studies were retrospective and three were prospective. Year of publication ranges from 2001 to 2023. Five studies were conducted in the United States, three in Brazil and two Italy, one in Canada, Mexico, India, Switzerland, Saudi Arabia, Spain, Turkey, Netherlands, Germany, and Czech Republic, respectively. A pooled rate of IH post RT was 3% (CI 2–4%) for open and 4% (CI 3–5%) including robotic.  $I^2 = 93\%$  (p < 0.001) indicating high heterogeneity between studies. Individual rates of IH observed post-transplant can be observed in Table 3. There were too few studies present to formally statistically analyse robotic assisted cases in unison, in the context of IH (Fig. 2).

## Secondary outcomes

## **Risk factors**

Nine studies reported risk factors for IH development. On multivariate analysis Costa et al. found BMI (OR, 1.080; 95% CI, 1.012–1.152; p = 0.020, pulmonary diseases (OR, 2.415; 95% CI, 1.218–4.790; p = 0.012), lymphoceles (OR, 2.362; 95% CI, 1.157–4.882; p = 0.018), and length of stay (LOS) (OR, 1.013; 95% CI, 1.000–1.025; p = 0.044) to be associated with IH development [26].

Cassese et al. found previous abdominal surgery to be a risk factor for IH on univariate analysis (p=0.002) [27]. It was also found by Alhassan et al. that IH after RT are

Table 2 Study	y characteristic	s and patient de	mographics								
Autho	Year pub- lished	Country	Journal	Prospective/ Retrospective	Number of Patients	Inclusion Criteria	Exclusion Cri- teria	Age	Gender	BMI	Transplant type
Tzvetanov [32]	2019	USA	American Journal of Transplan- tation	Retrospective	239	> 18 years, BMI > 25	Severe iliac ath- erosclerosis	36 (median)	F 132 (55.2%) M 107 (44.8%)	41.4 (median)	69.4% liv- ing, 30.6% deceased
Reyna- Sepúlveda [33]	2017	Mexico	International journal of organ transplant	Prospective	55	All renal transplant recipients 2011–2015	I	49.5 (mean)	F 24 (43%) M31 (56%)	27 (mean)	Heterotopic cadaveric transplant
Gusukuma [51]	2014	Brazil	Transplanta- tion Pro- ceedings	Retrospective	3054	All renal transplants recipients 1998–2008 and were assisted after surgery by Brazil Uni- fied Health- care System	1	BMI < 30: 40.7 (mean), BMI30– 34.9: 46.6 (mean), BMI > 35: 46.5	F 1221 (40%) M 1833 (60%)	3 groups stratified according to BMI. Mean within these groups: 22.6 (<30), 31.9 (30–34.9), 36.8 (>35)	1

Table 2 (con	ntinued)										
Autho	Year pub- lished	Country	Journal	Prospective/ Retrospective	Number of Patients	Inclusion Criteria	Exclusion Cri- teria	Age	Gender	BMI	Transplant type
Harbell [52]	2012	NSA	Surgery	Prospective	150	<ul> <li>(1)</li> <li>CD4 + T-cell</li> <li>(CD4)</li> <li>CD4)</li> <li>CD4 + T-cell</li> <li>(CD4)</li> <li>counts &gt; 200</li> <li>cells per</li> <li>undetect-</li> <li>able plasma</li> <li>HIV-1 RNA</li> <li>levels (&lt; 50</li> <li>copies per</li> <li>millilitre) for</li> <li>kidney transplant recipients and (2)</li> <li>and secce</li> <li>op transplant recipients and (2)</li> <li>and secce</li> <li>corpies per</li> <li>multific (2)</li> <li>and secce</li> <li>corpies per</li> <li>multific (2)</li> <li>and secce</li> <li>corplatenty, and visceral</li> <li>Kaposi sarcoma</li> </ul>	1	1	1	1	Living and deceased donor
Kapoor [53]	2012	India	Clinical Queries, Nephrol- ogy	Retrospective	1990	Live donor renal transplant 1990–2011	I	1	1	I	Living
Costa [26]	2023	Switzerland	Transplanta- tion Pro- ceedings	Retrospective	737	Consecutive patients undergoing kidney trans- plant at a single centre between 1998 and 2018	1	No IH group: 49 (mean), IH group 55 (mean)	F 491 (66.6%) M 246 (33.4%)	26.8 (mean)	Living 289 (39.2%) Deceased 448 (60.8%)

Table 2 (cont	tinued)										
Autho	Year pub- lished	Country	Journal	Prospective/ Retrospective	Number of Patients	Inclusion Criteria	Exclusion Cri- teria	Age	Gender	BMI	Transplant type
Cassese [27]	2022	Italy	International Journal of Urology and Neph- rology	Retrospective	1546	Consecutive patients undergoing kidney trans- plant at a single centre between 2011 and 2020	1	58.5 (mean)	F 58% M 42%	26 (mean)	Deceased
Alhassan [28]	2021	Saudi Arabia	Cureus	Retrospective	287	Consecutive patients undergoing kidney trans- plant at a single centre bet ween 2015 and 2020, Age > 18	Passed away < 1 month post transplant surgery	45.5 (mean)	F 119 (41.5%) M168 (58.5%)	BMI < 30 152 (54.9%), BMI > = 30 125 (45.1%)	Living 223 (77.7%) Deceased 64 (22.3%)
Heng [29]	2018	USA	Experimen- tal and Clinical Transplan- tation	Retrospective	893	Consecutive patients undergoing kidney trans- plant at a single centre between 2007 and 2011	Missing data for height or weight at time of transplant, less than 2 weight measurements pre-transplant	Never been obese group 46.7 (mean), Obese group 53.6 (mean)	F 372 (41.7%) M 521 (58.3%)	Never been obese group: 25 (mean), obese group 34 (mean)	Living 661 (74.2%), Deceased 231 (25.8%)
Territo [38]	2018	Spain	BJU Interna- tional	Prospective	83	Patients with underwent robotic assisted kidney transplant at eight differ- ent European centres with 1 year mini- mal follow up	1	43 (median)	F 30 (36.1%) M 53 (63.9%)	25.3 (median)	Living
Yildız [54]	2017	Turkey	Annals of Transplan- tation	Retrospective	24	Patients under- went kidney transplant at a single cen- tre between 2015 and 2017	1	43 (mean) ]	F 11 (45.8%) M 13 (54.2%)	29 (mean)	Living 13( 54.2%) Deceased 11 (45.8%)

2 (cont	inued)										
	Year pub- lished	Country	Journal	Prospective/ Retrospective	Number of Patients	Inclusion Criteria	Exclusion Cri- teria	Age	Gender	BMI	Transplant type
[61]	2017	USA	Surgical Techniques in Urology	Retrospective	71	Consecutive patients undergoing kidney trans- plant at a single centre bet ween 2011 and 2014	Intraperitoneal transplants or simultaneous native nephrec- tomy	Anterior rec- tus sheath approach (ARS) 55.1 (mean), Conven- tional approach (CON) 53.9 (mean)	F 25 (35.2%) M 46 (64.8%)	BMI 30–34.9: 39 (54.9%), BMI > = 35: 32 (44.1%)	I
[55]	2016	Brazil	Transplanta- tion Pro- ceedings	Retrospective	147	> 18 years old, Kidney trans- plantation between 2008 and 2014 at a single centre	Surgery at another hospital	37 (mean)	F 46.9% M 53.1%	I	Living 26 (19.2%) Deceased 121 (73.6%)
[0]	2016	Netherlands	Surgery	Retrospective	1564	Consecutive patients undergoing kidney trans- plant at a single centre between 2002 and 2012	1	51 (mean)	F 560 (35.8%) M 1004 (64.2%)	25.7 (mean)	Living 1022 (65%) Deceased 542 (35%)
Ξ	2014	USA	Surgical Endoscopy	Retrospective	3460 (2247 kidney only)	All patients who under- went primary liver, kidney, or pancreas transplantation between 2000 and 2011	Incisional hernias at any site other than the transplant inci- sion, port-site hernias, stoma hernias, internal hernias, and umbilical hernias	50.9 (mean)	F 888 (39.5%) M 1359 (60.5%)	27.8 (mean)	1

Table 2 (con	tinued)										
Autho	Year pub- lished	Country	Journal	Prospective/ Retrospective	Number of Patients	Inclusion Criteria	Exclusion Cri- teria	Age	Gender	BMI	Transplant type
Brock- schmidt [56]	2014	Germany	Transplanta- tion pro- ceedings	Retrospective		April 2008 to July 2011, 11 consecutive living-donor kidney recipi- ents under- went MAKT performed by senior surgeon Matched with a historical group of living-donor kidney trans- plantations between 2000 and 2007	1	40.1 (mean)	1	24.8 (mean)	Living
Varga [31]	2012	Czech Republic	Transplanta- tion	Retrospective	1067	Consecutive patients undergo- ing kidney transplant at single centre between 2005 and 2010	1	54 (median)	F 372 (35%) 695 M (65%)	I	Deceased 952 (89%) Living 115 (11%)
Nanni [30]	2005	Italy	Transplanta- tion pro- ceedings	Retrospective	100	100 consecu- tive kidney transplant patients (50 of each incision), included dur- ing follow up at single cen- tre outpatient clinic	1	45.5 (mean)	F 30 (30%) M 70 (70%)	1	1

Iable z (conu	(nənu										
Autho	Year pub- lished	Country	Journal	Prospective/ Retrospective	Number of Patients	Inclusion Criteria	Exclusion Cri- teria	Age	Gender	BMI	Transplant type
Singh [57]	2005	Canada	Transplant proceed- ings	Retrospective	89	Kidney transplants performed at a single centre between 1999 and 2002, divided by BMI (obese vs non-obese)	Recipients of multiple organs	Obese group (BMI > 30): 48 (mean) Non-obese group (BMI < 30): 43.5 (mean)	F 32 (47.06%) M 66 (52.94%)	Obese group: 34.1 (mean), Non-obese group 23.6 (mean)	1
Birolini [34]	2001	Brazil	Hernia: the journal of hernias and abdomi- nal wall surgery	Retrospective	1685	Consecutive patients undergoing kidney trans- plant at a single centre between 1996 and 1999	Alternative surgi- cal method	48.8 (mean)	F3 (37.5%) M5 (62.5%)	22.8 (mean)	1

Hernia (2024) 28:301–319

less common than IH after liver transplant (OR 0.24 CI 0.08–0.73, p = 0.013) [28]. Heng et al. found that BMI > 30 was also associated with IH development after RT (p < 0.01) [29]. An anterior rectus sheath approach was found to reduce IH after RT (p = 0.04) [19].

On multivariate analysis BMI > 30 (HR 2.9, CI 1.6–5.2, p < 0.001), female sex (HR 2.6, CI 1.4–4.7, p = 0.002), concurrent abdominal wall hernia (HR 2.3, CI 1.2-4.3, p = 0.009), smoking status (HR 2.2, CI 1.1-4.1, p = 0.019), multiple operative explorations (HR 2, CI 1.1–3.7, p=0.26) and duration of surgery (HR 1.007, CI 1.001-1.012, p = 0.014) were linked to IH formation [10]. Smith et al. reported surgical site infection (HR 28.8, CI 15.59-53.03, BMI>25 (HR 1.8, CI 1.12–2.81), withholding calcineurin inhibitor (HR 2.3; CI 1.37-3.94) and withholding MMF (mycophenolate mofetil) (HR 2.5, CI 1.43-4.27) were linked with IH after RT [11]. The use of a "hockey stick" incision increased risk for IH in comparison with an oblique incision (p < 0.05) [30]. Varga et al. reported BMI > 30, age > 50 years old, re-operation and the use of MMF associated with IH [31]

#### Management and outcomes of IH

Eight studies (n=9140) were included in this meta-analysis. The pooled rate of IH repair post RT was 61% (CI 14–100%). There was significant heterogeneity observed between studies with I<sup>2</sup>=99.5% (p<0.001). In two studies, all patients (n=23) whom were found to develop an IH were repaired [32, 33]. Costa et al. reported 2 patients required emergency repair, with 38 being repaired electively [26]. Ooms et al. reported 26 total repairs with 9 done as an emergency case [10]. Pooled rates of IH repair in included studies can be seen below in Fig. 3. Birolini reported 5 patients were lost to follow up who developed an IH and as such these patients were left out of the meta-analysis [34].

Four studies reported mesh repair anatomical position metrics. Cassese et al reported 30% of patient meshes were placed intraperitoneal, 53.8% retromuscularly and (Fig. 4) 25% in a pre-peritoneal location [27]. Further studies reported the use of sublay mesh repair in 85 and 100% of cases [31, 34]. A bridging technique was used in 55% of cases by Ooms et al. [10].

Five studies (n = 6599) reported one or more recurrences of IH post RT after repair. A pooled rate of 16% (CI 9–23%) is observed.

Out of 37 repairs using a mesh, 16 patients experienced medical complications, 3 surgical site infections, 2 haematomas requiring surgical intervention and 3 hernia recurrences [26]. Cassese et al. also reported 14 (14%) patients experiencing 1 hernia recurrence with 2 patients experiencing 2 recurrences out of a total of 83 repairs using a mix of mesh and non-mesh techniques, while 4 patients developed

Table 3 Operation	vincision type, here	nia incidence, diagi	nosis method, hernia	repair, mesh used,	incisional hernia rej	pair outcomes, follo	w up duration, risk	factors	
Author	Operation/Inci- sion type	Hernia Occur- rence rate	How was it diagnosed	Hernia repair	Mesh used	Mesh location	Outcomes relat- ing to repair	Follow up dura- tion	Risk factors
Tzvetanov	Robotic Transab- dominal with Gel port	21 (8.8%)	1	Yes—21 (100%) (Laparoscopi- cally)	. 1	1	. 1	25.9 months (Median)	1
Reyna-Sepúlveda	Open	2 (4%)	I	Yes—2 (100% at 6 months)	Yes	I	I	3 months and 12 months	I
Gusukuma	Open	46 (1.5%)	I	I	I	1	I	6 months	I
Harbell	Open	2 (1%)	I	I	I	1	1	30 months	I
Kapoor	Open	17 (1.6%)	I	I	I	I	I	6 months	I
Costa	Open—Para- rectus hockey stick incision	47 (6.4%)	Clinical and radiological	Yes-38 (81%) (2 emergency repair)	Yes—37 (97%) (Polypropylene mesh)	Onlay, sublay and intraperito- neal positions used, numbers not specified	Post repair complications: medical—16 (42%), surgical site infec- tion—3 (8%), haematoma –2 (5%)(required surgical revi- sion), recur- rence—3 (8%)	96 months (median)	Multivariate analysis—BMI (OR, 1.080; 95% CI, 1.012–1.152; P=.020, pul- monary diseases (OR, 2.415; 95% CI, 1.218–4.790; P=.012, lym- phoceles (OR, 2.362; 95% CI, 1.157–4.882; P=.018), and Length of stay (LOS) (OR, 1.013; 95% CI, 1.013; 95% CI, 1.000–1.025; P=.044)
Cassese	Open—Gibson incision	93 (6%)	Radiological (computerised tomography)	Yes—83 10 refused surgery due to lack of symp- toms	Yes—16 no mesh (16.1%), 25 resorbable mesh (25.3%) 58 non-resorb- able mesh (58.6%)	Intraperito- neal—23 (30.2%), Retro- muscular—41 (53.8%), Pre- peritoneal (19 (25%)	One recur- rence—14 (14.4%), Two recurrences—2 (2.4%), Surgical site infection—4 (4%), Chronic pain—3 (3%)	67.5 months (median)	Univariate analysis risk factor for recurrence– Pre- vious abdominal surgery other than kidney transplant p=0.002
Albassan	Open	5 (1.7%)	1	1	1	1	1	> 24 months	When compared to IH rate post liver transplant, kidney transplant is protective (OR 0.24 CI 0.08– 0.73 p=0.013)

🙆 Springer

Table 3 (continue	(pe								
Author	Operation/Inci- sion type	Hernia Occur- rence rate	How was it diagnosed	Hernia repair	Mesh used	Mesh location	Outcomes relat- ing to repair	Follow up dura- tion	Risk factors
Heng	Open	15 (1.7%)	I	1	1	I	1	> 12 months	Significantly higher rates of IH in obese group (BMI > 30) p < 0.01
Territo	Robotic assisted kidney trans- plantation -described by Menon et al. [58]	0	1	I	1	1	1	> 12 months	· 1
Yildız	Open—oblique incision Left or Right lower quadrant, continuous technique	0	Clinical and radiological (ultrasound)	1	1	1	1	7.58 months (mean)	I
Phillips	Open—40 Anterior rectus sheath approach (ARS), 31 conventional (CON)	7 (9.9%). 1 ARS, 6 CON	1	1	1	1	1	12 months	ARS approach significantly reduced inci- sional hernia rate p=0.04
Araújo	Open	6 (4.5%)	I	I	1	I	1	24 months	I

Table 3 (continu	(pa								
Author	Operation/Inci- sion type	Hernia Occur- rence rate	How was it diagnosed	Hernia repair	Mesh used	Mesh location	Outcomes relat- ing to repair	Follow up dura- tion	Risk factors
Ooms	Open—semilu- nar supraingui- nal incision	50 (3.2%)	Clinical and radiological	Yes-26 (52%) 9 underwent emergency repair due to small bowel incarceration	Yes—poly- propylene mesh—15 (57.7%), poly- ester mesh—4 (15.4%), pol- yglactin mesh –1 (3.8%), No mesh—6 (23.1%)	Bridging technique—11 (55%), Non- bridging technique –7 (35%), Not documented—2 (5%)	6 (23%) had recurrence	59 months (median)	Multivariate analy- sis—BMI > 30 (HR 2.9, CI 1.6- 5.2, $p < 0.001$ ), Female (HR 2.6, CI 1.4-4.7, p = 0.002), Concurrent abdominal wall hernia (HR 2.3, CI 1.2-4.3, p = 0.009), Smoking (HR 2.2, CI 1.1-4.1, p = 0.019), Mul- tiple explorations (HR 2, CI 1.1- 3.7, $p = 0.26$ ), Duration of sur- gery (HR 1.007, CI 1.001-1.012,
Smith	Open (Assumed)	1 year: 56 (2.5%) 5 years: 110 (4.9%) 10 years: 157 (7%)	I	1	I	I	I	54 months (median)	p=0.014) SSI (Hazard ratio(HR)) was 28.8 for kidney (CI) 15.59– 53.03, BMI over 25 HR 1.8 (CI 1.12–2.81), withholding cal- cineurin inhibitor (HR 2.3; CI 1.37–3.94), with- holding MMF HR 2.5 (CI
Brockschmidt	Minimal access kidney trans- plantation (MAKT)	0	Radiological (Ultrasound)	I	I	I	I	12 months	(/7. <del>1</del> -c+.1

Table 3 (continue	(pc								
Author	Operation/Inci- sion type	Hernia Occur- rence rate	How was it diagnosed	Hernia repair	Mesh used	Mesh location	Outcomes relat- ing to repair	Follow up dura- tion	Risk factors
Varga	Open-Oblique incision	28 (2.6%)	. 1	Yes—Suture 8 (28.6%), Mesh 20 (71.4%)	Yes—20 (71%)	Onlay—17 (85%), Inlay—3 (15%)	Hernia recur- rence post repair: 4 (20%), 3 onlay, 1 inlay	34.5 months post repair (median)	BMI> 30, > 50 y/o, re-opera- tion and use of mycophe- nolate mofetil associated with incisional hernia, in accordance with literature
Nanni	Open—Hockey stick 50, oblique 50	Hockey stick 8 (16%) oblique 2 (4%) overall 10 (10%)	Clinical	1	1	1	I	54 months (mean)	Hockey stick inci- sion more risk in comparison with oblique incision (p < 0.05)
Singh	Open (assumed)	3 (4.11%)		I	Ι	I	I	Minimum 7 months	I
Birolini	Open—left external pararec- tal infraumbili- cal	(%1.1) 91	1	Yes— repaired—11 (57.9%), lost to follow up—5 (26.3%), poor clinical condi- tion/surgical candidate—3 (15.8%)	Yes—Poly- propylene mesh—8 (72.7%)	Onlay	No recurrence. 1 developed left inguinal her- nia—repaired with Lichten- stein technique	12–36 months	1

 $\underline{\textcircled{O}}$  Springer

**Fig. 2** Forest plot displaying the pooled proportion of patients post renal transplant developing an incisional hernia over their respective follow up periods, ES = Odds ratio



surgical site infection and 3 developed chronic pain [27]. Varga et al. reported a recurrence rate of 20%, or 4 patients in total [31]. Birolini et al. reported no recurrence in patients repaired using mesh repair [34]. No graft loss was reported with the occurrence of an IH.

# Discussion

The incision used for RT may vary between surgeons, with a Gibson incision most common [35]. The Gibson incision is a curvilinear incision in the lower quadrant of the abdomen 2-3 cm medial to the anterior superior iliac spine, extending inferiorly and medially, ending 1 cm above the pubic symphysis. The external oblique muscle and external oblique aponeurosis is incised. Then, the internal oblique muscle, transversus abdominis and transversalis fascia are subsequently divided to the confluence where the rectus sheath and obliques meet. Inferiorly, the rectus muscle is preserved and retracted, medially. The peritoneum is mobilised and iliac vessels are exposed for RT [36]. In contrast, the hockeystick incision is made along the para-rectus line, extending cranially towards the subcostal margin and caudally towards the midline ending superior to the pubic symphysis. This incision is often used for small paediatric recipients. The kidney graft is usually placed extraperitoneally. The incised abdominal wall layers are usually closed in layers, namely the transversus abdominus and internal obliques as one layer and the external oblique as the other [35].

From this systematic review and meta-analysis, the incidence of IH after RT was relatively low at 4%. However, it can cause catastrophic results if it occurs, and has previously been reported to lead to kidney incarceration and loss of graft [12]. As such, it is of paramount importance to have a strategy for prevention, prompt diagnosis and adequate management of IH after RT.

Previous studies have shown that hockey-stick incisions may be associated with a higher rates of IH [13, 30, 37]. However the method of closure and type of incision was not found to be statistically significant in renal and pancreas transplant cohorts when meta-analysed [13]. Of note, there is a large discrepancy between our 2 reported robotic assisted cases with one reporting an IH rate of 0% and the other reporting an IH rate of 9%, which is at the higher range observed in this review [32, 38]. This may be potentially explained by a median difference in BMI of 16.1.

Within this meta-analysis we reported mixed results detailing BMI as associated with IH formation after RT, which has also been linked with further adverse outcomes after RT [39]. Additional modifiable risk factors such as incision type, surgical approach, surgical site infection, smoking status and pulmonary disease were reported. These



Fig. 3 Forest plot displaying rates of repaired incisional hernia post renal transplant, ES: Odds ratio

factors should be considered by treating teams when trying to ensure optimal long term patient outcomes. Perhaps in patients whom many risk factors are present, the surgical approach or prehabilitation should be tailored to reduce exposure to known IH risk factors.

Non-modifiable risk factors such as female gender, previous reoperation and reoperation were also reported. Patients with additional risk factors within this patient cohort may benefit from additional monitoring for IH occurrence.

The use of MMF has been observed as a risk factor of IH formation after RT [31, 40], whilst withholding calcineurin inhibitors was found as a risk factor for IH in one study [11], suggesting a possible differing effect of immunosuppression on IH formation. Different calcineurin inhibitors also have differing effects on wound healing [41]. Other risk factors may have also contributed to this finding [42]. Calcineurin inhibitors have been previously shown to be associated with an increased risk of IH after RT when compared with MMF [43]. Only one included study mentioned the use of everolimus in patients with IH after RT, however, no further

analysis was reported [31]. This is a possible modifiable risk factor for IH formation that may warrant further study.

The treatment of IH after RT is complex with the renal graft in-situ. In our reported studies details regarding the exact presenting complaint of patients with an IH after RT are lacking. IH repair using mesh in RT patients has been cautioned due to the concerns of infection and the lack of consensus regarding the technique for IH repair and management [44]. However, it should be noted, the use of mesh repair has been reported as safe and effective in this cohort [8]. Various approaches by open, or laparoscopic surgery, with or without mesh placement have been described, with satisfactory outcomes [45-49]. Costa et al. report using an intraperitoneal, sublay or onlay mesh repair, however, the outcomes following each method of repair are not reported separately [26]. Cassese et al. report a mix of herniorrhaphy, intraperitoneal, pre-peritoneal and retro muscular approaches to repair utilised [27]. Further included studies also report varied approaches to repair indicating the lack of consensus in regard to IH repair after



Fig. 4 Forest plot displayed rates of IH recurrence post repair after RT, ES: Odds ratio

RT [10, 34]. The use of closed suction drains as part of the IH repair was also reported [31].

Our pooled IH repair rate after RT of 61% (CI 14–100%) and recurrence rate of 16% (CI 9–23%) is similar to a previously published review [44]. One patient (7%) in a series of repairs was noted to require mesh explanation due to infection [27]. Two (5%) re-operations after repair were required for haematoma evacuation [26]. No graft loss was reported as a result of an IH in the included studies.

There are a number of limitations to this review. The inherent issues with retrospective studies are valid [50]. As well as this the potential differing effect of incision type was not accounted for in this study which may have skewed results, however, as previously mentioned this has been analysed in a prior publication and was not shown to be statistically significant. This study was also underpowered to detect any difference between IH outcomes in robotic versus open RT. As well as this, the differing follow up times will have had an impact on the rates of IH in each study [5] as is demonstrated by Ooms et al. whom recorded the cumulative incidence of IH over time [10]. However, with prospective and retrospective studies included it was not possible to standardise follow up time.

To conclude, the pooled rate of IH post RT was 4%, the pooled rate of repair was 61% and the pooled rate of recurrence was 16%. A mix of mesh and non-mesh repairs in RT have been successfully employed, however, further randomised controlled trials are likely required in order to inform consensus regarding method of repair in relation to IH after RT.

Funding This work did not receive funding from any source.

**Data availability** Further data is available upon reasonable request to the author's.

## Declarations

Conflict of interest The authors have no conflict of interest to declare.

Ethical approval, Human and animal rights and Informed consent As this study solely included published information regarding studies conducted solely with human participants, institutional ethical approval and informed consent was not required.

#### References

- Burger JW, Luijendijk RW, Hop WC, Halm JA, Verdaasdonk EG, Jeekel J (2004) Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia. Ann Surg 240(4):578–583
- van Ramshorst GH, Eker HH, Hop WC, Jeekel J, Lange JF (2012) Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study. Am J Surg 204(2):144–150
- Patel SV, Paskar DD, Nelson RL, Vedula SS, Steele SR (2017) Closure methods for laparotomy incisions for preventing incisional hernias and other wound complications. Cochrane Database Syst Rev 11(11):005661
- Borab ZM, Shakir S, Lanni MA, Tecce MG, MacDonald J, Hope WW et al (2017) Does prophylactic mesh placement in elective, midline laparotomy reduce the incidence of incisional hernia? A systematic review and meta-analysis. Surgery 161(4):1149–1163
- Fink C, Baumann P, Wente MN, Knebel P, Bruckner T, Ulrich A et al (2014) Incisional hernia rate 3 years after midline laparotomy. Br J Surg 101(2):51–54
- Mingoli A, Puggioni A, Sgarzini G, Luciani G, Corzani F, Ciccarone F et al (1999) Incidence of incisional hernia following emergency abdominal surgery. Ital J Gastroenterol Hepatol 31(6):449–453
- Szumilas K, Wilk A, Wiśniewski P, Gimpel A, Dziedziejko V, Kipp M et al (2023) Current status regarding immunosuppressive treatment in patients after renal transplantation. Int J Mol Sci 24(12):678
- Mahdavi R, Mehrabi M (2004) Incisional hernia after renal transplantation and its repair with propylene mesh. Urol J 1(4):259–262
- Simson N, Parker S, Stonier T, Halligan S, Windsor A (2018) Incisional hernia in renal transplant recipients: a systematic review. Am Surg 84(6):930–937
- Ooms LS, Verhelst J, Jeekel J, Ijzermans JN, Lange JF, Terkivatan T (2016) Incidence, risk factors, and treatment of incisional hernia after kidney transplantation: an analysis of 1564 consecutive patients. Surgery 159(5):1407–1411
- Smith CT, Katz MG, Foley D, Welch B, Leverson GE, Funk LM et al (2015) Incidence and risk factors of incisional hernia formation following abdominal organ transplantation. Surg Endosc 29(2):398–404
- Nawabi A, Marlor D, Camarata C, King CD, Nawabi P (2021) (2021) Incarceration of transplanted kidney through incisional hernia. J Surg Case Reports 6:34
- Shahrestani S, Tran HM, Pleass HC, Hawthorne WJ (2018) Optimal surgical management in kidney and pancreas transplantation to minimise wound complications: a systematic review and meta-analysis. Ann Med Surg 33:24–31
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. J Clin Epidemiol 134:178–189
- Tanaka K, Misawa T, Ashizuka S, Yoshizawa J, Akiba T, Ohki T (2018) Risk factors for incisional hernia in children. World J Surg 42(7):2265–2268
- Pilch NA, Bowman LJ, Taber DJ (2021) Immunosuppression trends in solid organ transplantation: the future of individualization, monitoring, and management. Pharmacotherapy 41(1):119–131
- Brown D (2020) A review of the PubMed PICO Tool: using evidence-based practice in health education. Health Promot Pract 21(4):496–498

- Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A (2016) Rayyan—a web and mobile app for systematic reviews. Syst Rev 5(1):210
- Phillips SH, Hill SK, Lipscomb LD, Africa JB (2017) Altering the approach: open minimally invasive renal transplant in obese patients through the anterior rectus sheath. Urology 105:192–196
- Wells G, Shea B, OConnell D, Peterson J, Welch V, Losos M, et al (2000) The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analysis. Methods 34:3
- 21. Barker TH, Migliavaca CB, Stein C, Colpani V, Falavigna M, Aromataris E et al (2021) Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. BMC Med Res Methodol 21(1):189
- Nyaga VN, Arbyn M, Aerts M (2014) Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health 72(1):39
- Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327(7414):557–560
- Borenstein M, Hedges LV, Higgins JP, Rothstein HR (2010) A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods 1(2):97–111
- Hunter JP, Saratzis A, Sutton AJ, Boucher RH, Sayers RD, Bown MJ (2014) In meta-analyses of proportion studies, funnel plots were found to be an inaccurate method of assessing publication bias. J Clin Epidemiol 67(8):897–903
- Costa L, Martin D, Zingg T, Venetz JP, Demartines N, Golshayan D et al (2023) Incidence, risk factors, and management of incisional hernias after kidney transplant: a 20-year single center experience. Transplant Proc 55(2):337–341
- Cassese G, Castaldi A, Al Taweel B, Le Quintrec M, Thuret R, Navarro F et al (2022) Incisional hernia repair after kidney transplantation in a tertiary high-volume center: outcomes from a 10-year retrospective cohort study. Int Urol Nephrol 54(3):525–531
- Alhassan AM, Alghunaim MN, Alqarni AA, Abdullah AM, Altoyan MK, Alharbi AS et al (2021) Incidence rate of incisional hernia post liver and kidney transplant at a tertiary center in Riyadh. Saudi Arabia Cureus 13(12):e20223
- 29. Heng AE, Aniort J, Pereira B, Fervenza F, Boirie Y, Prieto M (2019) Renal transplant in obese patients and impact of weight loss before surgery on surgical and medical outcomes: a singlecenter cohort study. Exp Clin Transplant 17(5):604–612
- Nanni G, Tondolo V, Citterio F, Romagnoli J, Borgetti M, Boldrini G et al (2005) Comparison of oblique versus hockey-stick surgical incision for kidney transplantation. Transplant Proc 37(6):2479–2481
- Varga M, Matia I, Kucera M, Oliverius M, Adamec M (2011) Polypropylene mesh repair of incisional hernia after kidney transplantation: single-center experience and review of the literature. Ann Transplant 16(3):121–125
- Tzvetanov IG, Spaggiari M, Tulla KA, Di Bella C, Okoye O, Di Cocco P et al (2020) Robotic kidney transplantation in the obese patient: 10-year experience from a single center. Am J Transplant 20(2):430–440
- 33. Reyna-Sepúlveda F, Ponce-Escobedo A, Guevara-Charles A, Escobedo-Villarreal M, Pérez-Rodríguez E, Muñoz-Maldonado G et al (2017) Outcomes and surgical complications in kidney transplantation. Int J Organ Transplant Med 8(2):78–84
- Birolini C, Mazzucchi E, Utiyama EM, Nahas W, Rodrigues AJ, Arap S et al (2001) Prosthetic repair of incisional hernia in kidney transplant patients: A technique with onlay polypropylene mesh. Hernia 5(1):31–35
- Farzad K, Saman N, Seyed AM (2013) Kidney Transplantation Techniques. In: Thomas R (ed) Current Issues and Future Direction in Kidney Transplantation. IntechOpen, Rijeka, p 7

- Junjie Z, Zhenli G, Ke W (2011) The Transplantation Operation and Its Surgical Complications. In: Jorge O, Jason A (eds) Understanding the Complexities of Kidney Transplantation. IntechOpen, Rijeka, p 22
- Filocamo MT, Zanazzi M, Li Marzi V, Marzocco M, Guidoni L, Dattolo E et al (2007) The approach by midline incision for extraperitoneal kidney transplantation. Transplant Proc 39(10):3077–3080
- Territo A, Gausa L, Alcaraz A, Musquera M, Doumerc N, Decaestecker K et al (2018) European experience of robot-assisted kidney transplantation: minimum of 1-year follow-up. BJU Int 122(2):255–262
- Grosso G, Corona D, Mistretta A, Zerbo D, Sinagra N, Giaquinta A et al (2012) The role of obesity in kidney transplantation outcome. Transplant Proc 44(7):1864–1868
- Humar A, Ramcharan T, Denny R, Gillingham KJ, Payne WD, Matas AJ (2001) Are wound complications after a kidney transplant more common with modern immunosuppression? Transplantation 72(12):1920–1923
- Dean PG, Lund WJ, Larson TS, Prieto M, Nyberg SL, Ishitani MB et al (2004) Wound-healing complications after kidney transplantation: a prospective, randomized comparison of sirolimus and tacrolimus. Transplantation 77(10):1555–1561
- Knight RJ, Villa M, Laskey R, Benavides C, Schoenberg L, Welsh M et al (2007) Risk factors for impaired wound healing in sirolimus-treated renal transplant recipients. Clin Transplant 21(4):460–465
- 43. Girman P, Lipár K, Kočík M, Voska L, Kožnarová R, Marada T et al (2020) Sirolimus vs mycophenolate mofetil (MMF) in primary combined pancreas and kidney transplantation Results of a long-term prospective randomized study. Am J Transplant 20(3):779–787
- 44. Gioco R, Sanfilippo C, Veroux P, Corona D, Privitera F, Brolese A et al (2021) Abdominal wall complications after kidney transplantation: A clinical review. Clin Transplant 35(12):e14506
- Petro CC, Orenstein SB, Criss CN, Sanchez EQ, Rosen MJ, Woodside KJ et al (2015) Transversus abdominis muscle release for repair of complex incisional hernias in kidney transplant recipients. Am J Surg 210(2):334–339
- 46. Li EN, Silverman RP, Goldberg NH (2005) Incisional hernia repair in renal transplantation patients. Hernia 9(3):231–237
- Chang EI, Galvez MG, Padilla BE, Freise CE, Foster RD, Hoffman WY (2011) Ten-year retrospective analysis of incisional herniorrhaphy following renal transplantation. Arch Surg 146(1):21–25
- 48. Zolper EG, Black CK, Devulapalli C, Wang J, Mahan M, Kroemer AH et al (2020) Long term outcomes of abdominal wall

reconstruction using open component separation and biologic mesh in the liver, kidney, and small bowel transplant population. Hernia 24(3):469–479

- Yannam GR, Gutti TL, High R, Stevens RB, Thompson JS, Morris MC (2011) Experience of laparoscopic incisional hernia repair in kidney and/or pancreas transplant recipients. Am J Transplant 11(2):279–286
- Hess DR (2004) Retrospective studies and chart reviews. Respir Care 49(10):1171–1174
- Gusukuma LW, Harada KM, Baptista APM, Alencar MRP, de Sandes-Freitas TV, Tedesco-Silva H et al (2014) Outcomes in obese kidney transplant recipients. Transpl Proc 46(10):3416–3419
- Harbell J, Fung J, Nissen N, Olthoff K, Florman SS, Hanto DW et al (2012) Surgical complications in 275 HIV-infected liver and/ or kidney transplantation recipients. Surgery 152(3):376–381
- Kapoor R, Srivastava A, Srivastava A, Kumar SS (2012) Surgical complications of renal transplantation in patients with diabetes mellitus. Clin Queries 1(2):157–158
- Yildız I, Koca YS (2017) What kind of incision should be made to reduce the risk of incisional hernia in kidney transplantation? Ann Transplant 22:689–693
- 55. Araújo JC, Barbosa RW, Machado MF, Furtado PS, Pugas CM, Filho JS et al (2016) Clinical impact of surgical complications in kidney transplant recipients in a reference hospital in Salvador, Bahia. Brazil Transplant Proc 48(7):2301–2305
- Brockschmidt C, Kaltenmeier C, Köksal E, Mayer B, Henne-Bruns D, Wittau M (2014) The minimal-access kidney transplantation technique in living-donor transplantation: results from a retrospective analysis. Transplant Proc 46(5):1286–1289
- Singh D, Lawen J, Alkhudair W (2005) Does pretransplant obesity affect the outcome in kidney transplant recipients? Transplant Proc 37(2):717–720
- 58. Menon M, Sood A, Bhandari M, Kher V, Ghosh P, Abaza R et al (2014) Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta technique (IDEAL phase 2a). Eur Urol 65(5):991–1000

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.