

Incisional Hernia in Renal Transplant Recipients: A Systematic Review

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Abstract

Background

Incisional hernia follows midline laparotomy in 8 to 20% of cases but the rate following lateral incision is not well documented. This systematic review summarises incisional hernia rate after open renal transplant.

Method

We searched EMBASE, MEDLINE, and the Cochrane Library databases from January 2000 to November 2016 inclusive. The outcomes included in our analysis were the post-transplant incisional hernia rate, significant patient risk factors for incisional hernia, the definition of incisional hernia used, the method used to detect incisional hernia and the incision used for transplantation.

Results

Eight retrospective case series were identified, three describing renal transplant recipients and five describing incisional hernia repairs post renal transplant. All reported the incisional hernia rate post-renal transplant at the host institution. The hernia rate ranged from 1.1 to 7.0%, with a mean of 3.2%. Factors associated with incisional hernia were BMI >30, Age >50, cadaveric graft, and reoperation through the same incision.

Conclusion

Despite the significant co-morbidity of renal transplant recipients, the incisional hernia rate post-renal transplant is significantly lower than post midline laparotomy. The reasons for this are discussed. This demonstrates the importance of operative technique, local tissue quality and biomechanical factors in the formation of incisional hernia.

Background

Incisional hernia remains one of the most common postoperative complications following abdominal surgery. Current data suggests an incidence between 8 to 20% (1),(2),(3),(4),(5). Renal transplant recipients have a theoretically increased risk of developing wound complications postoperatively, given their immunosuppressive regime, prolonged periods of dialysis and often complex comorbidity (6),(7). However, the rates of incisional hernia in these patients are believed to be far lower than for midline abdominal operations. Single-centre studies have estimated the incidence of incisional hernia following renal transplant surgery to be between 3.2% (8) and 7% (9) at 4.5 years follow up. However, at the time of writing there is no published systematic review that reports the incisional hernia rate through a post renal transplant incision across several institutions. As academic hernia surgeons research abdominal wall dynamics and incisional hernia rates, the flank incisional hernia rate after renal transplant should be known with precision. Accordingly, via systematic review of the available primary literature we aimed to determine the incisional hernia rate following renal transplant and to assess the risk factors for hernia development in these patients.

Methods

Reporting

This systematic review was performed and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (10). Ethical permission is not required by our centre for systematic reviews of available primary literature.

Inclusion criteria for studies

We aimed to identify case series and observational studies reporting the incisional hernia rate following open renal transplant from January 2000 to November 2016 inclusive. Only studies reporting human patients and written in the English language were included.

Inclusion and exclusion criteria for participants

The target condition was incisional hernia following open renal transplant. Studies relating to nephrectomy, donor nephrectomy, non-renal transplantation, non-incisional hernia were excluded. Studies including augmented mesh closure post-transplant were excluded. So as to eliminate any learning curve or centres with limited experience, we excluded any study reporting less than 200 individual patients.

Search strategy and string

A surgical research trainee, NS, used the ProQuest search engine (ProQuest Dialog™, Ann Arbor, Michigan, USA) to search the EMBASE, MEDLINE, and the Cochrane Library databases from 1st January 2000 to 1st November 2016 inclusive. The search filters “human studies” and “written in English” were applied. Our search string combined three search terms using title and abstract keywords as well as subject (thesaurus) terms to identify articles for inclusion as follows:

- All titles, abstracts and subject terms containing the keywords “renal” OR “kidney”.
- All titles, abstracts and subject terms containing the keyword “transplant”.
- All titles, abstracts and subject terms containing the keywords “hernia” OR “incisional”.

Our complete search string is shown in Appendix 1

Citation management and Screening

After applying the search filters, ProQuest issued the search results in PDF format, which were then stored by NS. Two researchers, NS and TS, then independently screened the titles and abstracts of the citation results and categorised each as ‘clearly unsuitable’, ‘uncertain’ or ‘definitely possible’. Duplicate citations were removed. The independent screening results were then compared and any discrepancies resolved by face-to-face discussion. The full text of all the remaining ‘uncertain’ and ‘definitely possible’ citations were then retrieved and hand searched by NS and TS, and any paper

deemed ultimately unsuitable discarded. A senior member of the research team, SGP, was available for advice throughout the search. Ultimately, search results were discussed face-to-face and studies to be included in the review finalised.

Data extraction

NS and TS both extracted data from all included studies. Extracted data were recorded into a data extraction sheet (Microsoft Excel for Mac 2011 Version 14.4.7, Microsoft Corporation, Washington, USA) designed specifically for the systematic review. Extracted data were categorised according to: study design; primary outcome and secondary outcomes. The Methodological Index of Nonrandomized Studies (MINORS) (11) was used to evaluate methodologic quality and potential bias of selected articles. Both NS and TS scored the articles independently.

For study design, we recorded; the study type, the number of patients included, the patient demographics (age, gender, body mass index), the method of data collection (prospective versus retrospective), country of publication, year of publication, length of follow-up, statistically significant risk factors for hernia development, and the methodological quality of the study as assessed by MINORS (11) criteria.

Clinical outcome

For our primary outcome, we recorded the rate of incisional hernia formation and the time to hernia formation if reported. We also recorded definitions for incisional hernia

occurrence if reported and the method used for hernia detection (eg. Clinical examination, USS or CT scanning). Our secondary outcomes were any risk factors for incisional hernia reported as statistically significant by the authors. We recorded the p-values for these and the statistical methods used to show significance. Where possible, we also included postoperative complication rates following transplantation. Postoperative complications were grouped into intra-operative, early post-operative, and late post-operative. Early complications were defined as those occurring within 30 days of surgery and late complications as those thereafter.

Data synthesis, analysis and reporting

For data that were obviously heterogeneous by visual inspection, we used basic statistical methods and narrative to describe our findings. Tables were used to display results according to our data collection categories. We anticipated a significant amount of heterogeneity in terms of the variables recorded and the follow up period. However, we reported all available data to avoid selection and reporting bias. If possible we intended to combine studies and perform univariate and multivariate analysis to identify predictor variables for incisional hernia following renal transplantation.

Results

Study Selection

A total of 961 potential articles were identified from the initial literature search. 754 articles remained after the language, date and human trial filters were applied. Using

the inclusion criteria described above, 724 were eliminated after title and abstract review. The full text of 30 articles was obtained of which 23 were rejected. The references of the full text articles were interrogated and one additional suitable study was included. Thus eight articles were included for final analysis (Figure 1).

All eight studies were retrospective case series. Three described unselected renal transplant patients and five described incisional hernia repair following renal transplantation. These five papers were included as they reported the incisional hernia rates for the entire unselected population of renal transplants recipients at the host institution.

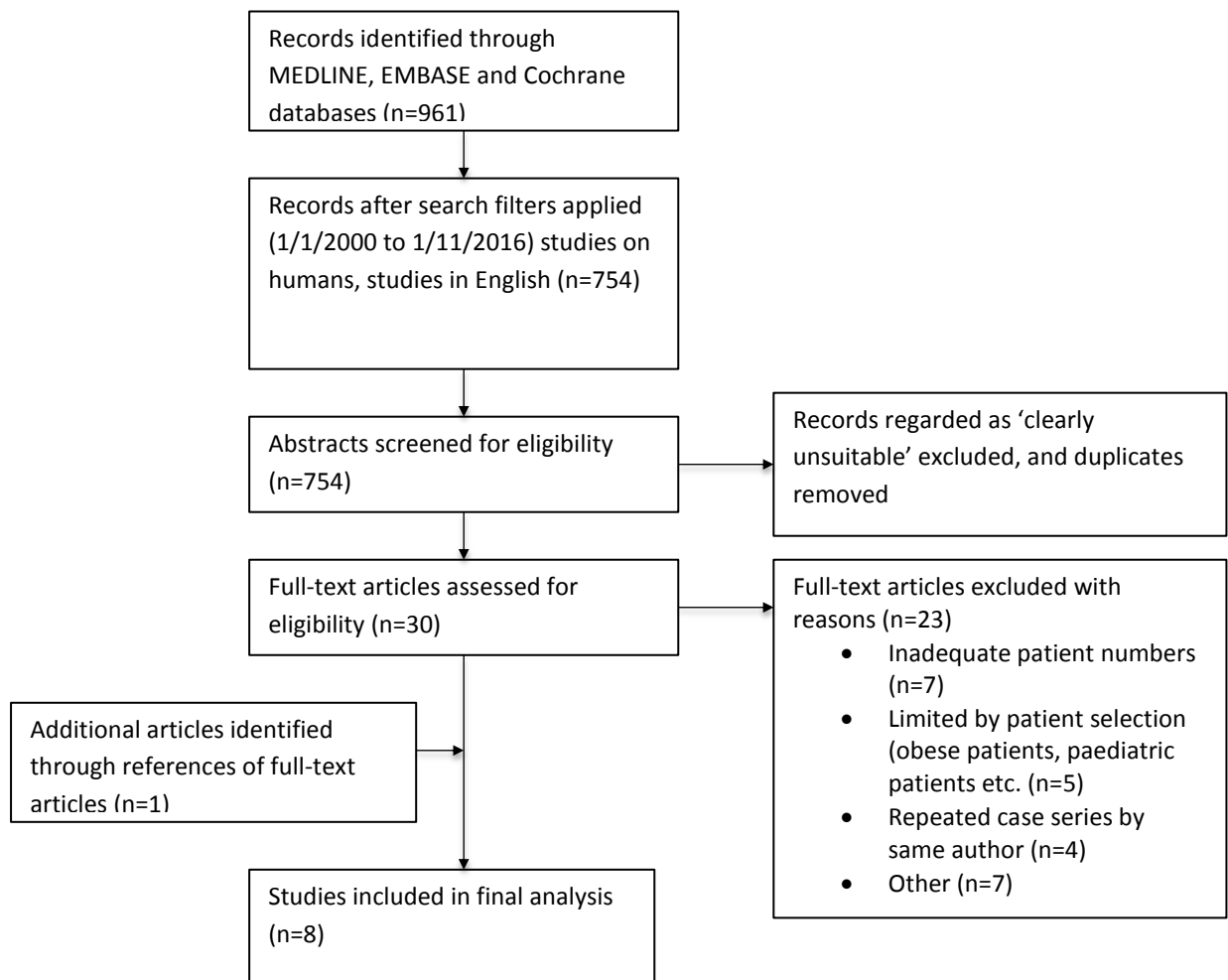
Study design and Study Quality

A total of 12,035 renal transplant recipients were reported by the eight studies. The number of patients included in each individual study ranged from 371 to 2499 with a mean of 1504. Three studies were carried out in Brazil (12),(13),(7) and two were carried out in the USA (14),(15). In seven studies the data were collected retrospectively from patient medical record review. In the remaining study, data were entered into a prospectively collected database but analysed retrospectively(9). Study quality, as assessed by the MINORS criteria, ranged from 6 to 10 (out of a total of 16) with a mean score of 7.3. Five of the studies only had a MINORS score of 6(6),(12),(13),(15),(16). The two most recent studies had the highest scores of 10 (8),(9). Based on MINORS criteria, six studies were limited by their inadequate description of follow up(6),(12),(13),(14),(15),(16), five by their inability to account for loss to follow up(6),(12),(13),(15),(16), the patients from all eight studies were

assessed by the primary surgical team in the outpatient clinic, subjecting the outcomes to reporting bias.

Where specified, the mean or median age of patients ranged from 31 to 54 years, with a mean age of 45 years for the studies overall. In the seven studies where gender was specified, there was a higher proportion of males, with a mean value of 62 percent of patients being male. Five of the seven studies that specified donor type, had a higher preponderance of cadaveric donors, with a range of 51 to 89 percent of donors cadaveric, whereas two studies reported predominantly live donors, with 65 (6) and 98 percent live donors (8). The mean percentage of cadaveric donors was 51 percent. BMI was specified in only two studies, and was 25.7 (8) and 27.8 (9) respectively.

Figure 1. Selection of articles for review as per PRISMA guidelines



Author	Year Published	Country	Journal	Study Type	Incision Used	Prospective/Retrospective Study	No. of Patients	Age (mean)	Male/Female (%)	BMI (mean)	Cadaveric/Live Donor (%)	Method (MIN)
Ooms(8)	2016	Netherlands	Surgery	Transplant Recipient Case Series	Semi-lunaire supra-inguinal	Retrospective	1564	51	64/36	25.7	35/65	10
Smith(9)	2015	USA	Surgical Endoscopy	Transplant Recipient Case Series	Not documented	Retrospective	2247	51	61/39	27.8	-	10
Humar(14)	2001	USA	Transplantation	Transplant Recipient Case Series	Hockey-stick	Retrospective	2013	43	61/39	-	51/49	8
Birolini(12)	2001	Brazil	Hernia	Incisional Hernia Case Series	Extended Pararectal	Retrospective	1685	-	-	-	-	6
Mazzuchi(13)	2001	Brazil	Journal of Urology	Incisional Hernia Case Series	Extended Inguinal	Retrospective	371	40	54/46	-	64/36	6
Mahdavi(6)	2004	Iran	Urology Journal	Incisional Hernia Case Series	Paramedian	Retrospective	589	31	66/34	-	2/98	6
Li(15)	2005	USA	Hernia	Incisional Hernia Case Series	Not documented	Retrospective	2499	-	-	-	64/36	6
Varga(16)	2011	Czech Republic	Annals of Transplantation	Incisional Hernia Case Series	Oblique	Retrospective	1067	54	65/35	-	89/11	6

Table 1. Study design and patient demographics.

Author	Number of patients with incisional hernia	Incisional hernia rate (%)	Time for hernia development (weeks)	Definition of incisional hernia described? (Yes/No)	Length of follow up (months)	Method used to detect incisional hernia
Ooms(8)	50	3.2	68	No	59	Clinical Examination +/- imaging if in doubt
Smith(9)	157	7.0	-	No	55	Clinical Examination
Humar(14)	73	3.6	55.6	No	60	Not stated
Birolini(12)	19	1.1	-	No	-	Not stated
Mazzucchi(13)	14	3.8	8.6	No	-	Clinical Examination
Mahdavi(6)	16	3.0	6.8	No	-	Not stated
Li(15)	41	1.6	-	No	-	Not stated
Varga(16)	20	2.6	76	No	-	Not stated

Table 2. Incisional hernia formation rate post renal transplant

Author	Reported risk factors for incisional hernia	Univariate Multivariate Analysis	P value
Ooms(8)	Female BMI >30 Smoking History Concurrent abdominal wall hernia Left-sided implantation Duration of surgery Multiple explorations of iliac fossa	Univariate analysis	0.006 <0.001 0.032 0.007 0.046 0.02 0.001
	Female Smoking History BMI>30, Multiple exploration of iliac fossa, Duration of operation, Concurrent abdominal wall hernia	Multivariate analysis	0.002 0.019 <0.001 0.026 0.014 0.009
Smith(9)	BMI>25, Surgical site infection Delayed graft function, Absence of MMF inhibitor Absence of calcineurin inhibitor	Univariate analysis	0.02 <0.001 0.003 0.001 0.002
	Surgical Site Infection, Absence of MMF,	Multivariate analysis	<0.001 <0.001
Humar(14)	BMI >30 Age>50 years, Re-operation through same incision, MMF vs Azathioprine	Multivariate analysis	0.0003 0.01 0.0001 0.0004

Table 3. Significant risk factors for development of incisional hernia in renal transplant recipients

Incisional Hernia

The mean rate of incisional hernia across all studies was 3.2% (390/12035), ranging from 1.1% (19/1685) (12) to 7% (157/2247) (9) for the individual studies. Length of follow up was only reported in three out of eight studies (8),(9),(14). Two studies reported 10-year incisional hernia rates, which were 7% (9) and 4.4% (8). The average (mean or median) time taken for hernia to develop was recorded in five studies and ranged from 6.8 weeks to 76 weeks (Table 2), with a mean of 43 weeks. Six studies described the incision used for renal transplantation; three studies used an oblique incision described separately as either an oblique incision(16), an extended inguinal(13), or a semi-lunaire supra-inguinal incision(8). The remaining three studies used a non-midline longitudinal incision described as pararectal(12), paramedian(6) and hockey stick(14). None of the studies defined incisional hernia. Five studies did not mention how incisional hernia was detected. Two studies(9),(13) used clinical examination to detect incisional hernia and one study(8) adopted US or CT imaging where the clinical diagnosis of incisional hernia was in doubt.

Risk Factors for Incisional Hernia

Three studies (8),(9),(14) analysed risk factors for hernia development using multivariate analysis. The reported significant risk factors for hernia development were Body Mass Index (BMI) >30 ($p<0.001$) (8),(14) surgical site infection (SSI) ($p<0.001$), absence of mycophenolate mofetil ($p<0.001$)(9), Age >50 years ($p=0.01$)(14), reoperation through the same incision ($p=0.0001$)(8),(14) mycophenolate mofetil compared to azathioprine immunosuppression ($p=0.0004$)(14), female sex

($p=0.002$)(8), concurrent abdominal wall hernia ($p=0.009$)(8), history of smoking ($p=0.019$)(8), and prolonged duration of surgery ($p=0.014$)(8),(Table 3). A weighted statistical analysis of the risk factors from all the studies for incisional hernia development was not possible because of the lack of the unacceptable heterogeneity of the reported data.

Post-operative complications

Post renal transplantation complication rates were reported poorly and could not be categorised as we had intended. Ooms et al.(8) reported a re-operation rate of 19% (301 of 1564 patients) having re-intervention for bleeding, urological complications, or transplanted kidney removal. Humar et al.(14) reported a post-operative wound infection rate of 4.8% (97 of 2013 transplant recipients), with a superficial wound infection rate of 3.8% (76 of 2013 transplant recipients) and a deep wound infection rate of 1.0% (21 of 2013 transplant recipients). Post transplant complications were not reported by any other series.

Discussion

Incisional hernia following abdominal surgery is reported at between 8 to 20%. A recent systematic review reported the overall midline incisional hernia rate at 12.8%, with an overall increase from 8% to 16% over the last thirty years (17). In this systematic review, we focus specifically on lateral hernias following renal transplantation, which has been relatively under-investigated. We found a mean

incisional hernia rate after renal transplant of 3.2%, a figure very significantly lower than that for midline laparotomy.

Much of the literature on incisional hernia has focused on comorbidities that may predispose a patient to herniogenesis. In our review, the included studies that performed univariable and multivariable analysis showed repeatedly that BMI >30, age >50, cadaveric graft and reoperation through the same incision predispose to incisional hernia. The use of mycophenolate mofetil (MMF) for post-transplant immunosuppression remains a contentious issue as Humar et al.(14) list MMF as a risk factor when compared to azathioprine, whereas Smith et al.(9) link absence of MMF to development of incisional hernia. In the literature, smoking(18), diabetes(19), previous wound infection(20), steroid use(21), and increased BMI(22) have all been shown to increase the probability of incisional hernia after intra-abdominal surgery. Consequently, renal transplant patients would be expected to be at higher risk of incisional hernia due to prolonged periods of dialysis prior to transplantation, immunosuppression post transplantation, and a higher prevalence of co-morbidities such as obesity, diabetes, chronic obstructive pulmonary disease, and hypertension(7),(23). However, despite increased comorbidity we found the opposite is true; incisional hernia is significantly less frequent than for midline laparotomy. It seems likely, therefore, that incisional hernia must have a higher dependency on factors specific to the abdominal incision rather than general patient comorbidity. These dependent factors could include; the location of the abdominal incision, the technique used to close the incision, the quality and strength of the abdominal wall tissue around the incision site, and the local biomechanical forces around the closed incision.

The studies included in our review used a variety of incisions for renal transplantation including para-medial incision, oblique incision, extended inguinal incision, para-rectal

incision, and hockey-stick incision. Previous systematic reviews of general surgical patients (non-transplant patients) have shown that paramedian and transverse abdominal incisions have statistically lower incisional hernia rates(24) when compared to midline incisions. Paramedian incisions are similar to hockey-stick and pararectal incisions as all use the semilunar ligament, at the lateral border of the rectus abdominis, to gain access to the abdominal cavity. The oblique and extended inguinal incisions are also similar and extend laterally parallel to the muscle fibres of the external oblique. A study comparing the incisional hernia rates for hockey stick versus oblique incisions has shown the oblique incision to have statistically lower herniation rates(25). Indeed, the evidence for transverse laparotomies demonstrating low complication rates at the wound site is well-known and the European guidelines recommend transverse incisions where possible as not only is the incisional hernia rate decreased but so is post-operative analgesia (26),(27).

Not all of our included studies reported their incision closure technique. The studies that did used a continuous non-absorbable suture to close the abdominal fascia. There is no mention of using the 'small bites' technique or closure with mesh augmentation. This is understandable as even though there is strong evidence showing the 'small bites' closure technique reduces incisional hernia rates in midline laparotomies there is no evidence that this is true for oblique or paramedical incisions. As for closure with mesh augmentation, even though European guidelines do state that mesh is advised for 'high-risk' closures(26), most transplant surgeons do not use mesh for primary closure due to the risk of infection in immunosuppressed patients. Transplant surgeons should be meticulous about their primary closure technique as flank hernias can be difficult to close, with some hernia specialists using bone anchors to the iliac crest to establish a strong repair(28),(29).

The quality and strength of the abdominal wall structures at the incision site must influence incisional hernia rates. Comorbidities will affect the health, quality and strength of abdominal wall structures (muscles and ligaments). However, we found that comorbidities are likely to play only a small part in herniogenesis, as transplant patients, assumed to have multiple comorbidities, exhibited a relatively low incisional hernia rate. Apart from anatomical incision site and method of wound closure, future research should also focus on the direction and strength of the abdominal wall biomechanical forces as well as tissue structure and orientation at the incision site. Research in these areas is still in its infancy. We know that a lower collagen I/III ratio reduces tissue tensile strength and predisposes to herniogenesis(30). Biomechanical studies of the linea alba and the rectus sheath show reduced tensile strength of scar tissue and anisotropy with increased strength in the transverse direction compared to longitudinal (31),(32). Abdominal wall compliance and strain have been found to be greater in the longitudinal direction(33). How these discoveries affect herniogenesis and surgical repair remains unclear and further research comprising histological and biomechanical analysis of abdominal wall structures is warranted.

Importantly our review also highlights a lack of a standardised definition for incisional hernia and no standardised method of incisional hernia diagnosis (only one study used imaging to aid diagnosis(8)). Both of these phenomena predispose to unstandardised data and variability in hernia diagnosis. In addition, most studies did not specify the length of follow up. Accordingly, it seems that a universally accepted definition of incisional hernia; a standardised test method to detect such hernia; and standardised assessment time-frame for diagnosis is required.

Conclusion

The reported incidence of incisional hernia following renal transplantation averages 3.2%, ranging from 1.1 to 7%, a rate significantly lower than that following midline laparotomy. As end-stage renal failure patients have multiple comorbidities(7),(23) we conclude that incisional hernia cannot be principally dependent on comorbidity but must be dependent on the local factors that influence biomechanics and wound healing at the incisional site. Lastly, our review found that a standardised definition of incisional hernia, diagnostic methods, and duration of follow-up is required in hernia research to reduce the variability of reported data.

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Appendix 1 – Search Strategy to identify initial papers

Search Strategy

Databases: Embase®, MEDLINE®

Set#	Searched for	Results
S1	ti,ab,su(renal* OR kidney*)	2332570*
S2	ti,ab,su(transplant*)	2690710*
S3	ti,ab,su(hernia* OR incisional*)	204353*
S4	s1 AND s2 AND s3	961°
S5	(s1 AND s2 AND s3) and pd(20000101-20161101) and human(yes) and la.exact("English")	754°

* Duplicates are removed from the search, but included in the result count.

° Duplicates are removed from the search and from the result count.