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OPEN ACCESS

Journal of Surgery

Andacoglu O, et al. J Surg 5: 1344.

DOI: 10.29011/2575-9760.001344

Research Article

# Risk Factors for Incisional Hernia Recurrence and Surgical Site Infection in Solid Organ Transplant Population - Single Center Experience

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**Citation:** Andacoglu O, Cheema F, Özbek U, Sanchez L, Malcher F (2020) Risk Factors for Incisional Hernia Recurrence and Surgical Site Infection in Solid Organ Transplant Population - Single Center Experience. J Surg 5: 1344. DOI: 10.29011/2575-9760.001344

**Received Date:** 07 October, 2020; **Accepted Date:** 20 October, 2020; **Published Date:** 26 October, 2020

## Mini-Abstract

**Aim:** To investigate risk factors for recurrence and Surgical Site Infection (SSI) after Incisional Hernia (IH) repair following abdominal transplantation.

**Methods:** Retrospective review of IH repair patients following abdominal transplantation at Montefiore Medical Center. Primary outcomes were IH recurrence and SSI. We assessed 34 peri-operative factors with each outcome.

**Results:** We had 78 patients and 110 IH surgeries. 24 (35%) patients had recurrence, and 12 (15%) had SSI. Age, BMI, comorbidities, prior abdominal surgeries were similar between recurrence and no-recurrence groups ($p>0.05$). Basiliximab induction was more common in recurrence group compared to thymoglobulin (OR=8.13, CI=1.59-82.07, p=0.02). mTOR inhibitors, maintenance immunosuppressive regimens, re-do transplant, take back after transplant, mesh type (biologic vs. synthetic), laparoscopic vs. open approach, surgeon specialty, emergent repair were not associated with recurrence. Multiple hernia repair was the only factor remained significant at multivariable analysis (OR=16.26, 95%CI=4.14-103.97, $p<0.001$). None of the factors had association with SSI ($p>0.05$).

**Conclusion:** Multiple IH repair was the only factor found to be associated with hernia recurrence after abdominal organ transplantation. First recurrence is almost always associated with future failure therefore choosing personalized approaches at first repair is critical. Basiliximab could be associated with hernia recurrence. However, it is not an independent risk factor. Randomized studies with larger cohort are necessary to improve the power of these findings.

## Introduction

Incisional Hernia (IH) after abdominal organ transplantation is more common compared to general population following non-transplant laparotomy, with estimated incidence of 15% after kidney, and up to 34% after liver or pancreas transplantation, respectively [1-4]. Specific immunosuppressive medications (i.e. sirolimus, mycophenolate mofetil, steroids), repeat laparotomies, repeat transplant, pre-existing comorbidities (obesity, diabetes mellitus, age), bilateral subcostal incision with midline extension, advanced recipient's age (>60 years) are some of the factors identified in the literature for increased risk for hernia after transplant [5-9]. However there is less robust data regarding recurrence of incisional hernia following transplantation. Furthermore there is lack of consensus on the hernia management of post-transplant patients and the optimal surgical approach in transplant population.

### Aim

We aimed to evaluate 33 pre-defined variables available in our database for recurrence and Surgical Site Infection (SSI) after Incisional Hernia Repair (IHR) following abdominal organ transplantation.

### Methods

We performed a retrospective review of all patients who underwent incisional hernia repair after kidney, liver or combined

organ (simultaneous kidney and pancreas, or simultaneous liver and kidney) transplantation at Montefiore Medical Center between 2009-2018. Medical records before 2013 were searched by ICD codes [10]. Electronic medical record after 2013 was filtered by searching patients who had liver, pancreas, or kidney transplant and subsequent hernia repair at any time after transplant. We assessed the relationship of **33 pre-defined risk factors** with each outcome**.** These included: Age at transplant, gender, prior organ transplantation (re-do transplant), transplant type (kidney, liver, Simultaneous Pancreas And Kidney [SPK] or Simultaneous Liver Kidney [SLK] [through separate incisions]), Body Mass Index (BMI) at the time of hernia repair and at the time of transplant, abdominal surgery prior to transplant, type of prior abdominal surgery (laparotomy versus laparoscopy), hernia repair prior to transplant, take back to operating room for transplant related complications or major abdominal surgery after transplant but before the hernia repair, number of incisional hernia repairs after transplant, laparoscopic versus open hernia repair, emergency hernia repair, mesh type (no mesh, biologic or synthetic), mesh explant, Length of Stay (LOS) after hernia repair. Immunosuppressive regimens were evaluated as single variable (tacrolimus/calcineurin inhibitors, steroid, Mycophenolate Mofetil [MMF]) as well as groups (Standard: combination of steroid, tacrolimus and MMF, non-standard/unknown). We compared outcomes based on induction agent (thymoglobulin versus basiliximab) and mTOR inhibitor usage. We also investigated outcomes based on surgeon specialty (transplant surgeon, non-specified general surgeon, plastic surgery/hernia specialist general surgeon). SSI was defined per CDC criteria and categorized as superficial, deep (muscle and fascia), and intraabdominal [5]. Overall patient demographics were summarized as median and minimum-maximum values or proportions.

## Statistics

The comparisons between the groups were performed with the use of Mann-Whitney U test for continuous measures and Pearson's chi-squared or Fisher's exact test for categorical measures as appropriate. Benjamini-Hochberg adjusted p values of less than 0.05 were considered to indicate statistical significance. Multivariable analysis was conducted using logistic regression to identify factors independently associated with the groups. Variables with significant adjusted p values in a univariable analysis were selected as candidates for the multivariable analysis. All statistical analyses were performed using R statistical package version 3.6.1 (R Development Core Team 2019).

## Results

We found 108 patients who underwent any hernia repair after abdominal organ transplantation at the institution. After excluding non-incisional hernias (i.e. inguinal), we had 78 transplant patients who had at least one Incisional Hernia (IH) repair. There were total of 110 IH surgeries performed. Of these, 22 (28%) patients had more than one IH repair (two patients did not have repeat repair despite recurrence on imaging). Table 1 summarizes all factors evaluated in this study. We compared all variables between recurrence (n=24) and no recurrence (n=54) groups. Overall recurrence rate was 35% (n=24), and SSI rate was 15% (n=12). Age, BMI, prior abdominal surgeries, prior transplant and other listed comorbidities were similar between recurrence and no recurrence groups ($p>0.05$). Type of transplant, take back or major abdominal operation after transplant, mesh type at first transplant (biologic vs. synthetic), type of IH repair (laparoscopic vs. open), emergent repair, time to hernia repair were similar between recurrence and no recurrence groups ($p>0.05$). Length of stay (LOS) after initial hernia repair was also similar between the groups. Post hernia SSI was higher in recurrence group compared to no recurrence (21% vs. 13%) however this did not reach statistical difference ($p>0.05$). Multiple hernia repair was strongly associated with recurrence (OR=66.91, CI=12.61-696.25, $p<0.001$) at univariate analysis. We also looked at induction agents. After eliminating patients with missing data, 89% of the patients in recurrence group (17 out of 19) had basiliximab induction and 11% had thymoglobulin induction whereas basiliximab use was 48% and thymoglobulin use was 51% in no recurrence group (OR=8.13, 95%CI=1.59-82.07, $p=0.02$). mTOR usage was not common, and it was not found to be associated with recurrence. Immunosuppressive agents as single variables or as groups (standard versus non-standard) were not found to be associated with recurrence ($p>0.05$). Majority of the hernia repairs were performed by transplant surgeon (vs. hernia specialist/plastic surgeon) and this was not associated with hernia recurrence ($p>0.05$). Among 34 parameters, only multiple hernia repair remained significant in multivariable analysis (OR=16.26, 95%CI=4.14-103.97, $p<0.001$) (Table 2). None of the factors evaluated had association with SSI ($p>0.05$).

| Variable | Recurrent (N=24) | Non-recurrent (N=54) | Adjusted p value |
|---|---|---|---|
| **Female, %** | 38% | 39% | 1.0000 |
| **Age at tx (years)** | 55.5 (32 - 79) | 55 (19 - 70) | 0.9813 |
| **Prior transplant, %** | 4% | 19% | 0.4725 |
| **Transplant type, %** | | | 0.6804 |
| **Kidney** | 63% | 46% | |
| **Liver** | 33% | 44% | |
| **SLK** | 4% | 2% | |
| **SPK** | 0% | 7% | |
| **BMI at IHR (kg/m$^{2)}$** | 29.78 (20.55 - 49.8) | 29.1 (17 - 51) | 0.7866 |
| **Abdominal surgery prior to tx, %** | 58% | 59% | 1.0000 |
| **Pre-tx surgery type (laparoscopy vs. laparotomy) %** | 13% | 15% | 0.6164 |
| **Prior hernia repair, %** | 21% | 13% | 0.9803 |
| **Post-tx take-back or major abdominal surgery, %** | 42% | 48% | 0.9907 |
| **Multiple prior hernia repairs, %** | 92% | 13% | **<0.0001*** |
| **Emergency hernia repair, %** | 42% | 15% | 0.1114 |
| **Mesh used, %** | 96% | 94% | 1.0000 |
| **Type of mesh (biologic) %** | 54% | 35% | 0.6804 |
| **Mesh explanted, %** | 13% | 2% | 0.3401 |
| **Time to hernia repair, months** | 12 (0 - 168) | 25 (0 - 228) | 0.3378 |
| **# IHR** | 2 (1 - 5) | 1 (1 - 1) | **<0.0001*** |
| **SSI, any %** | 20% | 13% | 0.9813 |
| **Hypertension, %** | 75% | 81% | 0.9813 |
| **Diabetes, %** | 33% | 46% | 0.7866 |
| **Smoking, any %** | 25% | 21% | 1.0000 |
| **Malignancy history, %** | 29% | 15% | 0.6164 |
| **CKD III or higher, %** | 67% | 44% | 0.3942 |
| **Length of stay (days)** | 5 (0 - 42) | 5 (0 - 62) | 0.9803 |
| **IHR type laparoscopic** | 17% | 19% | 1.0000 |
| **Simulect induction, %** | 89% | 49% | **0.0242*** |
| **Standard maintenance regimen, %** | 35% | 43% | 0.9813 |
| **Steroids** | 52% | 72% | 0.4725 |
| **Calcineurin inhibitors** | 96% | 94% | 1.0000 |
| **MMF** | 65% | 64% | 1.0000 |
| **mTOR inhibitors** | 13% | 20.0% | 0.9813 |
| **Transplant surgeons, %** | 83% | 74% | 1.0000 |

**Table 1:** All variables examined in this study and comparison of recurrent and non-recurrent groups. BMI: Body Mass Index; Tx: Transplant; SPK: Simultaneous Pancreas-Kidney; SLK: Simultaneous Liver-Kidney; CKD: Chronic Kidney Disease; IHR: Incisional Hernia Repair; SSI: Surgical Site Infection; MMF: My-Cophenolate Mofetil. (*significant p values).

| Variable | OR | 95% CI | p value |
|---|---|---|---|
| **Number of hernia repairs** | 16.26 | (4.14, 103.97) | **0.0006*** |
| **Induction type (simulect vs thymoglobulin)** | 6.3 | (1.10, 57.04) | **0.06*** |

**Table 2:** Multivariable analysis on risk factors for recurrence (*significant p value).

## Discussion

Transplant population has high incidence of hernia following transplantation up to 30%. Many risk factors for forming incisional hernia following abdominal transplantation are reported in the literature: Male sex, abdominal re-interventions, living-donor liver transplantation, postoperative respiratory complications, immunosuppressive therapy with the use of steroids, sirolimus or mycophenolte mofetil, prolonged stay in intensive care unit, acute rejection, severe post-transplantation ascites, viral hepatitis, obesity (BMI >25 kg/m$^2$) are some of these risk factors [5-9,11,12]. Herein we report that induction with basiliximab is associated with 6.30 times higher risk for hernia recurrence after organ transplantation, compared to thymoglobulin. However it was not an independent risk factor. We know that choice of induction agent is directly related to the organ transplant type and varies highly among transplant centers. For instance most of the liver transplant recipients do not receive thymoglobulin whereas choice of induction for kidney patients varies depending on the sensitization profile, co-morbidities and institutional habits. Furthermore incision type is also different for different organ type, however transplant type was not found to be associated with recurrence in our analysis although majority of recurrent hernia cases were kidney transplants. Given all, induction agents could have direct impact on hernia recurrence. Basiliximab is an IL-2 inhibitor and is not directly associated with wound repair mechanisms, therefore the relationship of basiliximab and hernia recurrence demonstrated in this report remains to be hypothetical until the possible interactions are proven at molecular level. We did not find association between maintenance regimens (standard versus non-standard) or mTOR inhibitors and recurrence. Yet, not only organ specific but also immunosupression specific comparison groups with larger cohorts are necessary to improve the power of our findings therefore results from this analysis should be interpreted cautiously.

The literature also suggests that repeat transplantation or repeat laparotomy, diabetes, bilateral subcostal incision with midline extension, advanced recipient's age (>60 years) are associated with higher hernia incidence after transplantation [6-9]. In our study, age at transplant and prior abdominal surgery or prior transplant rates were similar in recurrence and no recurrence groups. It is well demonstrated that laparoscopic approach in elective hernia repair in non transplant population is associated with less infection rates. Specifically in BMI > 30 groups, it is associated with more seromas and lower quality of life in long term. Recurrence rates after laparoscopic repair vary between 5-17% in non-transplant series [13-17]. There is increasing data about the use of laparoscopic approach in transplant population. Weiss et al. reported 54 laparoscopic incisional hernia repair after liver transplant. They used coated IPOM mesh. Their recurrence rate was 17%. BMI and sirolimus as immunosuppressive therapy were significantly associated with hernia recurrence [12]. Hernia recurrence occurred at a mean time of 19 (1-34) months post surgery in transplant group. They concluded that laparoscopic incisional hernia repair with intraperitoneal onlay mesh is a safe and feasible method to treat hernias after liver transplant and BMI and sirolimus as immunosuppressive therapy are risk factors for recurrence of hernia after laparoscopic hernia repair [12]. Yannam et al. reported laparoscopic hernia repair in renal and kidney pancreas transplant recipients. A total of 36 transplant patients were compared with 62 non-transplant patients. Mean follow up was 2.2 years in the transplant group and 3 years in the non-transplant group One patient in each group had a mesh infection requiring explant. Overall there were five (14%) recurrences in the transplant group and four (6%) in the non-transplant group (p>0.05) [18]. Fikatas et al. reported incidence of hernia after liver transplant up to 15% at a follow-up of 60 months. Recurrent hernia was observed in 12 of 77 patients (15.6%) at a median time of 7.9 months (4.8-46.8) after primary surgical repair. The recurrence rate after intraperitoneal onlay mesh implantation was lower compared to other mesh techniques (7.7% vs. 21.4%). They had variable mesh types and repair techniques but they did not compare recurrences depending on mesh type or surgical approach [11]. In our series, time to 1st hernia repair was longer in recurrence group (median 25 mo, range 0-228) compared to no recurrence group (median 12 months, range: 0-168) but this was not significant. We also did not see any association between recurrence and mesh type, surgical approach (laparoscopic versus open) or surgeon specialty. Rate of laparoscopic repair in our series was similar between recurrence and non-recurrence groups (17% vs. 19%, respectively). All laparoscopic cases were performed via intraperitoneal onlay mesh technique and there was significant missing data in terms of technique for the open approach therefore we were only able to compare laparoscopic versus open approach. The rate of transplant surgeons performing hernia repair was high in both groups and there was no statistical difference. Non-significance could be due to low number cases performed by hernia specialized surgeons, similarly low rates of laparoscopic repairs in the overall cohort. In other words, we cannot make a firm conclusion about the impact of surgical approach or of surgeon specialty. However, with these limited results, this indifference should be interpreted cautiously.

Tastaldi et al. reviewed 40 liver transplant patients who had posterior component separation with Transversus Abdominis Release (TAR). There were 11 (25%) recurrences; 8 due to central mesh fractures. Seven recurrences have been repaired either laparoscopically or using an onlay. There were 5 SSIs (4 deep, 1 superficial) [19]. As stated above we utilized IPOM mesh in all laparoscopic cases however due to small sample size it is not possible to draw firm conclusions. Regarding mesh use, Gowda et al. compared Porcine Acellular Dermal Matrix (PADM), Human Derived Acellular Dermal Matrix (HADM) and synthetic mesh for IH repair after organ transplantation [20]. There were 27 patients with PADM, 34 patients with HADM and 26 with synthetic mesh. The rate of wound infection in those repaired with PADM, HADM, and synthetic mesh were 14.8%, 14.7%, and 65.4%, respectively. Rates of recurrence were 13.3%, 23.5%, and 76.9%, respectively. Rate of mesh removal was found to be 7.4%, 11.8%, and 69.2%, respectively. These complication rates were significantly lower in patients who received HADM or PADM compared with patients repaired with synthetic mesh ($P < 0.001$). They concluded that the use of PADM for incisional hernia repair after kidney and/or pancreas transplant significantly reduces the incidence of hernia recurrence, wound infection, and need for mesh removal compared to synthetic mesh and they stated longer follow-up in the PADM group is warranted [20]. Borab et al. reviewed 14 studies (2,114 patients), with 1,152 receiving prophylactic mesh placement [21]. Prophylactic mesh placement decreased the risk of incisional hernia overall when compared to primary suture closure (relative risk = 0.15; $P < .00001$) reflecting an 85% risk reduction, although immunosuppressed patients were excluded [21]. In our report, we did have: Synthetic mesh was used in 51 surgeries, biologic mesh was used in 40 surgeries (these included temporary closures of the initial transplant), and 8 primary hernia repairs without mesh. We carefully reviewed each operative notes individually and did not count intentional use of biologic mesh at the time of transplant as hernia repair (i.e. due to large graft and inability to close the abdomen safely for transplant related issues) and we specifically analyzed first actual hernia repair as the index case and the mesh used at that repair. We also compared recurrence rate for each mesh type following each repair. Based on these results, mesh type was not associated with recurrence in our series. Also mesh explant rates were similar in recurrence and no recurrence groups.

In our study, we did find multiple repair was the most significant risk factor for recurrent hernia. Similar to our findings Hollihan et al. reported that patients with multiple repairs were more likely to undergo subsequent reoperation, have a longer operative duration, develop SSI, and have a recurrence [22]. We demonstrated that if first hernia repair fails after the transplant, then the patient has 16 times higher risk to develop subsequent hernias, emphasizing the importance of first repair. Therefore we conclude that first repair should be the best and only repair. However the best approach for each case is variable and not well established. Larger and prospective randomized studies are necessary as to the management of incisional hernia after abdominal transplantation. We encourage involvement of abdominal wall specialists in hernia repairs after transplantation to ensure the best curative approach at first operation. Limitations of our study include: Small sample size, heterogeneous groups, retrospective nature of the review.

## Conclusion

We conclude that multiple IH repair is strongly associated with IH recurrence after abdominal organ transplantation. Basiliximab is also found to be associated with hernia recurrence in univariate analysis but is not an independent risk factor. mTOR inhibitors, standard vs. non standard immunosuppressive regimens, mesh type (biologic vs. synthetic) or surgical approach (laparoscopic vs. open) did not differ between recurrence and no recurrence groups. Once IH recurs, it is almost certain that IH repair will fail again therefore choosing personalized approaches and the most ideal approach at first the time of first repair is the most critical component in IH repair in transplant patients. While choice of induction agent may not be modifiable due to the inherent risks of transplant, pre-transplant hernia risk reduction strategies (i.e. weight loss), patient counseling about transplant specific medication risks, and even considering prophylactic mesh and collaboration with a hernia specialist should be taken into consideration to maximize the opportunity of a durable repair at first operation. Randomized studies with larger cohorts and more homogeneous groups are necessary to improve the power of these findings.

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