The impact of a muscle pump activator on incisional wound healing compared to standard stockings and compression devices in kidney and kidney-pancreas transplant recipients: A randomized controlled trial

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Abstract

Introduction: We aimed to evaluate the impact of thrombo-embolic-deterrent + intermittent pneumatic compression (TED + IPC) vs. muscle pump activator (MPA) on incisional wound healing in kidney and simultaneous pancreas- kidney (SPK) transplant recipients.
Methods: We conducted a single-centre, randomized controlled trial in which 104 patients (kidney n=94; SPK n=10) were randomly assigned to wear TED + IPC (n= 52) or MPA (n=52) for the first six days following surgery. Patient demographics, postoperative outcomes, and incisional wound images were taken using a HIPAA-compliant application on postoperative days (POD) 3, 5, and 30, and assessed using the validated Southampton Wound Care Score.
Results: There were no demographic differences between the groups. The MPA group had a significant improvement in wound healing on POD 3 (p=0.04) that persisted until POD 5 (p=0.0003). At POD 30, both groups were similar in wound healing outcomes (p=0.51). Bayesian inferential analysis revealed that the use of TED + IPC following transplantation had inferior outcomes compared to the use of MPA with sequential moderate evidence. The rate of complex wound infections was significantly greater in the TED + IPC group compared to the MPA group (29% vs. 12%, respectively; p=0.03). Patients were more satisfied with the use of a MPA device than TED + IPC. No major complications were encountered in either group.

Conclusions: The use of a MPA device in the immediate postoperative period leads to a significant improvement in immediate and early wound healing, and decreased number of complex wound infections following kidney and SPK transplantation compared to standard TED + IPC therapy. Patients were more satisfied with the use of a MPA device than TED + IPC.

Introduction

Transplantation is the optimal mode of renal replacement therapy for patients suffering from end-stage renal disease. Wound infections contribute to postoperative morbidity after transplantation [1] and are attributable to both the mandatory immunosuppression as well as to patient comorbidities at the time of surgery. The incidence of overall infectious complications during the first year after renal transplantation has been reported to be as high as 49% [2] with wound infection rate as high as 27% [3, 4, 5]. In the case of simultaneous kidney and pancreas (SPK) transplantation, surgical site infections are higher (>75%) [6,7]. Various risk factors contribute to impaired wound healing following kidney or SPK transplantation including recipient age greater than 60 years, patient dialysis pre- transplantation, a body mass index >30kg/m^2, the need for post-operative plasmapheresis, use of thymoglobulin as induction therapy or its use in acute rejection, the use of mycophenolate mofetil- or sirolimus for maintenance immunosuppression and delayed graft function [10,11].

Enhancing blood flow to a surgical site is known to improve wound healing. Post-operative fluid overload is common in patients following renal or SPK transplantation as ensuring adequate vascular pre-load to the graft is paramount. Unfortunately, this often leads to significant edema which could compromise micro-capillary blood flow to the wound. Common practices to decrease edema include limb elevation, [12] activating the calf muscle pump which involves more accurately: requires reciprocating ankle plantar flexion and/or dorsiflexion [13] and mechanical devices such as compression stockings [14] or intermittent pneumatic compression (IPC) devices [15,16]. Unfortunately, these strategies may not be effective in some patients with comorbid conditions that limit limb movement or in patients with contraindications to adequate compression, such as skin infections and vascular insufficiency. In addition, current mechanical compression devices can be difficult to apply and uncomfortable, which decreases compliance. A method to increase blood flow involves transcutaneous direct muscular stimulation which utilizes electrical stimulation via electrodes applied to the skin to stimulate the calf muscle pump and promote lower limb venous blood flow, [17,18] [19]. However, because of the high voltage intensity required to stimulate the muscle and subsequent discomfort, these devices have not been widely adopted in routine clinical use. Geko™ device is an alternative to direct electrical muscle stimulation for activating the calf muscle pump. [20] It is a self-contained neuromuscular stimulation device that adheres to the skin over the common peroneal nerve and delivers a low-voltage stimulus at a frequency of 1 Hz, thereby activating the calf and foot musculature of the lower limb without the voltage-related discomfort. The MPA device has previously been shown

to increases superficial femoral vein blood flow and velocity [20], reduce leg edema[21], and improve chronic wound healing by enhancing transcutaneous oxygen tension (a predictor of tissue viability and ischemic wound healing) [22,23].

Promoting wound healing in the transplant population is challenging given the chronic immunosuppression and patient factors which contribute heavily to post-operative wound complications. The use of a muscle pump activator in enhancing wound healing in this population has never been evaluated. Herein, we report the outcomes of a randomized controlled trial testing whether the use of the MPA device compared to traditional stockings TED +IPC would enhance wound healing and surgical site infection rates following kidney and SPK transplantation.

Methods

Study design

This Study was single center, open labelled RCT. All patients undergoing renal and simultaneous kidney-pancreas transplant were recruited in the study. The Trial followed the CONSORT 2010 Guidelines (Fig 1). The Protocol was approved by the University of Western Ontario Research Ethics Board (Protocol number 103618).

Participants

Patients aged >18 years undergoing kidney or simultaneous kidney pancreas transplantation between Jan 1st, 2016 and 31st December 2017 were included in the study. The exclusion criteria were age younger than 18 years, history of deep vein thrombosis, history of leg amputation and patients with intra cardiac defibrillators. At the time of surgery, both groups of patients were placed on TED+IPC (Covidien and Flowtron Excel). On post-operative day 1, patients were randomly assigned to their assigned groups. The MPA device (Geko Plus, Perfuse Med, UK) was replaced daily as per the manufacturer's instructions to maintain battery performance. Both groups of patients were maintained on either TED+IPC or MPA for 6 days following surgery at which time the devices were removed. Incisional wound healing images were taken using a HIPAA (Health Insurance Portability and Accountability Act) compliant mobile app (MODICA, Clearwater Clinical Limited, Canada) on post-operative day 3, 5 and 30. We collected demographic and medical information on all patients and evaluated their wounds using the validated Southampton wound scoring system [24]. The questionnaire was used to assess patient satisfaction with the use of the devices on the 6th day post-transplant. There are six questions which relate to wound swelling, device comfort during the period, the intent to use the device in case of future surgeries, and devices' influence on patients' mobility and sleep are listed in Table 3.

Randomization

Before randomization, surgeons determined each patient's pre-operative frailty and functional status as well as proposed post-operative care including the need to go to ICU. The patients were randomized into the intervention arm (MPA) or control arm (TED +IPC) in a ratio of 1:1 using sealed, sequentially labelled randomization envelopes opened by the recipient co-ordinator.

Sample size estimation

Based on data from a previous pilot study at our institution which examined the impact of a muscle pump activator on incisional wound healing compared to standard stockings and compression devices in kidney and kidney-pancreas transplant recipients the sample size calculation was a priori performed with G*Power V.3.1.2. To detect a moderate effect size of 0.6 (mean difference of 3 units, SD 5) with a power of 80% and α set at 0.05, a minimum of 42 participants in each group were required. To account for attrition and the likelihood of increasing pediatric transplant practice at our institution, our accrual target was 50 participants in each of two study arms (MPA v/s TED+IPC).

Statistical analysis

The data was analyzed using the Statistical Package for the Social Sciences (SPSS, Version 23.0, IBM, USA). A Pearson's chi square correlation was run to assess the relationship of wound score between TED +IPC and MPA cohorts. The normalcy of distribution of demographics and patient characteristics with outlier detection were assessed by Shapiro-Wilk's test. P value of < 0.05 was considered to be significant. On Bayesian inferential analysis, there was evidence that MPA has superior outcomes compared to TED +IPC. The Null hypothesis "MPA leads to better wound scores compared to TED +IPC" was accepted with sequential Strong/Moderate evidence in favor of MPA, $H_0 > H_1$ at day 3 and day 5 post operatively.

Results

The demographic and outcomes characteristics in both cohorts are listed in Table 1. 104 patients were randomly assigned to wear TED+IPC kidney and kidney-pancreatic transplant recipients (TED+IPC, n= 52) and MPA device (MPA, n=52). Ninety-four patients underwent kidney transplantation and 10 underwent SPK transplantation. The median age of the groups were 49 and 51 years with a similar distribution of BMI (27.5 vs 25.8) in the TEC+IPC and MPA cohorts, respectively. On average, patients were hospitalised for 6.5 days kidney and kidney-pancreas 10 days post-transplant. There were no significant differences between the two groups with respect to age, gender, BMI, or length of hospital stay. In addition, all patients received maintenance immunosuppressive regimen consisting of prednisone, tacrolimus and mycophenolic acid. Levels were monitored closely in both groups and adjusted according to accepted practices (trough levels, lymphocyte counts under thymoglobulin therapy). Induction treatment was used and consisted of antithymocyte globulin (ATG 5-8mg/kg total) for the majority of the patients and Basiliximab (20 mg IV day 0 and 4) was given to low immunological risk kidney transplant recipients. Pre-operative antimicrobial prophylaxis was

standardised and consisted of cefazolin in kidney recipients and we added metronidazole in SPK recipients, which were all administered up to two days following transplantation. Our standard protocol following kidney/pancreas transplantation is to place two drains (one in the retroperitoneal space near the kidney (left) and another in the abdomen near the pancreas (right). In kidney transplant patients, we placed a single drain in the retroperitoneal space and majority of these drains was taken out on post-operative day 2 or 3 if output was less than 50 cc in 24 hours, otherwise they would be removed in clinic during follow up. Both cohorts of patients were treated equally throughout the process and had similar rates of early and late drain removal. In our fluid protocol included; 0.45% NS 30 ml/hr + previous hour urine output and 0.9% NS according to CVP protocol, if CVP < 5 rate is 250 ml/30 min and recheck CVP, 5-9 CVP rate is 100 ml/hr, >9 CVP 30 ml/hr. Routinely we are not used post-operative diuretic. Septra DS was given as prophylaxis for both UTIs and Pneumocystis pneumonia three times a week indefinitely. Antifungal prophylaxis was routinely used in kidney-pancreas transplantation for a period of 3 months.

Several recipient risk factors, known for the development of wound infections, including hypertension, diabetes mellitus, smoking and peripheral vascular disease were evaluated in both groups and found to be not significant between cohorts. Overall, 15 (29%) patients in the TED+IPC cohort and 7 (13%) in the MPA cohort developed superficial wound infections (p=0.03). There were 15 (22%) patients who developed superficial wound infections following kidney transplantation, (eleven patients in TED+IPC and four patients in MPA; p=0.04). In SPK transplant recipients, 6 patients (60%) developed superficial infections of which four were in the TED+IPC and two in the MPA cohorts (p=0.59). All superficial wound infections was managed conservatively with penicillin based antibiotics for 10 days and few cases managed by wound packing and drain insertion.

Incisional wound healing images were taken using the MODICA app and scored using the Southampton wound score system are listed in Table 2. On post-operative day 3, TED+IPC cohort had significant higher wound score in comparison to the MPA cohort (The Pearson chi-square 4.1, P = 0.04), Standard Deviation ±2.48 for TED + IPC group compared to MPA). By post-operative day 5, TED+IPC cohort still had significant higher wound score (≥ 2 in comparison to MPA cohort (The Pearson chi-square 6.88, P = 0.0003), Standard Deviation ±1.81 for TED+IPC group compared to MPA). At 30 days following transplant, MPA and TED+IPC cohorts had similar wound scores (The Pearson chi-square 6.20, P = 0.51), Standard Deviation ±1.84 for MPA compared to TED+IPC cohort). The likelihood of significant wound scores (>2 on Southampton wound score) were <1 for MPA group compared to TED+IPC group at day 3 and day 5 further proving the efficacy of MPA over TED+IPC . We did evaluate mobilization in both groups of patients and found that patients wearing the MPA device were more apt to mobilize early compared to the IPC+TED group, but there were no statistical differences with

the small numbers evaluated here. Regardless of mobilization, both groups of patients were maintained on their respective treatments until post-operative day 6.

Patient satisfaction

The answers from patients in both arms were recorded and presented as follows:
The first question asked of the patient was "How comfortable are the devices?" Of the 104 participants, 52 took part in the IPC+TED study while 52 were fitted with MPA device. When level of discomfort was evaluated in TED+IPC patients, 57% reported some level of discomfort, 29% reported no effect on comfort and 14% reported comfort. In contrast, the reports were skewed towards being more comfortable in the MPA arm with 13%, 23%, and 64%, being responses for discomfort, no effect on comfort, and comfortable, respectively. The Pearson Chi-square showed that there is a significant difference in comfortability between the two groups ($P<0.003$). In response to second question "What is the extent of the wound swelling?" When perception of wound swelling was evaluated, 52% of IPC+TED patients had an increase in wound swelling, 17% had no change, and 31% recorded a decrease in swelling while MPA device participants recorded 22%, 30%, and 48%, respectively for the same questions. This suggests that patients who wore the MPA device had the perception of improved wound edema compared to those patients who were on standard therapy. The Pearson Chi-square showed that there is a significant difference in the wound swelling between the two groups ($P<0.001$).
In response to third question "What was the device's influence on sleep patterns?" When asked about their sleep patterns, 49% of IPC+TED participants indicated no change in sleep patterns compared to 50% in the MPA arm. However, 31% reported a negative change in the IPC+TED compared to only 16% in the MPA group. Interestingly, 20% of patients reported that they had an easier time going to sleep in the IPC+TED group whereas this number was 34% in the MPA arm. The Pearson Chi-square showed that there is a significant difference in device's influence on sleep patterns between the two groups ($P<0.02$).

In response to fourth question "What is the device's mobility after surgery?" After undergoing surgery, 29% of patients fitted with IPC+TED reported no effect on mobility while 28% and 43% reported difficulty and improvement in mobility respectively. On the other hand, MPA device created a 10% mobility difficulty with 17% reporting no change effect and 73% reporting a free and improved mobility. This becomes increasingly important in-patient mobility after major surgery and could have a significant impact on patient convalescence and length of stay in hospital. The Pearson Chi-square showed that there is a significant difference in mobility after surgery between the two groups ($P<0.001$). The final question was "Would you want to use the same device if you had another surgery?" Interestingly, when asked about whether patients would like to use the same modality of treatment for another operation, only 57% of IPC+TED participants acknowledged that they would use it in comparison to MPA device whose participants gave it 83%.

Discussion

This is the first report of a randomized controlled trial evaluating the effect of a muscle pump activator on wound healing in transplant patients. We found that there was a significant improvement in wound healing and infection rates compared to standard TED+IPC, suggesting that this novel therapy may be an alternative strategy at improving patient outcomes in the perioperative period in this high wound complication risk group.

The use of the MPA device in the immediate post-operative period lead to a significant improvement in wound healing at the 3 ($p=0.04$) and 5 day post-operatively ($p <0.0003$) in both kidney and kidney- pancreas transplant recipients compared to standard TED+IPC. Previous studies have reported the incidence of infectious complications after renal transplantation to be 49% [2] with wound infections comprising up to 27% of these cases [3, 4]. As expected, infection rates are higher in SPK transplants (75%). [6,7] Linhares et al. reported wound a higher prevalence of bacterial infections (71%) was observed after transplantation, of which 44% were by Gram-negative rods and 27% by Gram-positive cocci. [8]. In the current study, 15 (29%) patients in the TED+IPC cohort and 7 (13%) in the MPA cohort developed superficial wound infections ($p=0.03$). There were 15 (16%) patients who developed superficial wound infections following kidney transplantation, whereas in SPK transplant recipients, 6 patients (60%) developed superficial infections. Although these rates are slightly lower than what would be expected from the literature, they are quite significant in these populations. Although there was a reduction in wound infections observed in the SPK group, this was not significant, likely due to the low number of patients in this cohort. However, despite this, rates of superficial wound infections were found to be reduced considerably in the MPA group compared to the expected rate in the literature, suggesting that a larger trial would likely find significance. Given that recipient risk factors, including hypertension, diabetes mellitus, smoking and peripheral vascular disease, were evaluated in both groups and found to be not significant between the treatment cohorts, these findings are likely attributable to the use of the MPA device in the early perioperative period following transplantation. The shortcoming of this study is the relatively short follow-up of 30 days. It could help explain why so many of the known risk factors for wound complications, including drain placement and duration, fell out as statistically insignificant in our study. A larger, multi-center trial would be needed to further strengthen our findings.

Physiologically, electrical stimulation is believed to accelerate wound healing by imitating the natural electrical current that occurs in injured skin. Electrical field, along with chemotaxis and injury stimulation aids epithelial cell migration during wound healing. [25] Zhao et al [26] demonstrated that epithelial cells cultured in the presence of an electrical field demonstrate an increase in the distance of cell movement thus exhibiting rapid response towards wound healing. In a study by Xu et al [27] electrical stimulation was also shown to be an effective adjunctive therapy in reducing bacterial loads and clinical infections in diabetic ulcer.

Increased perfusion associated with electrical stimulation may also be associated with increased secretion of vascular endothelial growth factor (VEGF) [28]. In addition to increased skin perfusion, electrical stimulation therapy has been shown to improve venous flow, which can also positively contribute to wound healing through increasing capillary emptying [29] Whether the mechanism of positive action of the MPA device is via these pathways is unknown and requires further evaluation.

MPA is a self-powered neuromuscular stimulation device which stimulates the common peroneal nerve which in turn stimulates lower limb musculature to gently contract at a set frequency; this mechanism of action has been shown to increase femoral vein velocity and lower limb blood flow. [21] Increasing blood circulation has been shown to enhance transcutaneous oxygen tension (TCpO2), which is a predictor of tissue viability and ischemic wound healing. [30] There have been various studies demonstrating that the MPA device increases venous, arterial and microcirculatory blood flow in the lower limbs, reduces edema and increases TCpO2, thus creating favorable conditions for wound healing. In this regard, Clarke Moloney et al [31] demonstrated an increase in venous velocity using electrical stimulation as a treatment adjunct for venous ulceration. A meta-analysis by Gardner et al [32] reported a 13% net healing rate per week with electrical stimulation, equating to a 144% increase over the control population. The MPA device has been shown [33] to augment arterial flow, as well as microcirculation, whereas compression therapy generally has a beneficial effect on venous flow only, and may reduce arterial and microcirculatory flows. Where an ulcer has an arterial component to its aetiology, MPA device would be expected to be more efficacious than compression, by virtue of the augmentation of arterial inflow. Additionally, since healing any ulcer requires perfusion at the wound bed, the augmentation of microcirculatory flow brought about by the MPA device is expected to be beneficial for patients with chronic leg ulcers. Lower limb edema is commonly experienced by post- kidney transplant surgery patients. Numerous studies have investigated how motor electrical stimulation, achieved by stimulating lower limb muscle activity, affects blood and lymphatic flow both of which can reduce lower limb edema. Various studies have shown positive effects of motor electrical stimulation on increasing blood flow in human [34] and animal [35] models. In the surgical literature, Faghri et al [36] reported that electrically stimulated contractions activate the skeletal muscle pump, thereby promoting limb blood flow, and may be effective in reducing venous pooling and edema in arthroplasty patients. In addition, lymphatic flow has been shown to increase during muscular exercise, highlighting the notion that lymphatic flow can be externally influenced by muscle contraction [37]. In light of this, MPA demonstrated that the increase blood flow and velocity in the superficial femoral vein while providing a possible tolerable and safe method for lower limb and wound tissue edema treatment. In addition, we demonstrated that patients had much higher satisfaction scores wearing the MPA device compared to the IPC+TED, especially in terms of improved comfort, perception of decreased edema, improved post-operative sleep, and enhanced

early mobility. Patients, especially those recovering from surgeries, are delicate and require good handling to guarantee their comfort and reduce any chances of interfering with the recuperation process. To validate the MPA device's appropriateness and effectiveness, it is necessary that the device has to pass the comfort test and preferably outperform the control set and other available devices. However, MPA device had a cumulative positive comfort feedback of 64% against IPC+TED's 14%. Additionally, the discomfort percentage for MPA device was 13% against IPC+TED's 57%. In this regard, MPA device is designed to offer very high comfort levels of comfort to the patients.

The MPA device recorded higher mobility rates which cumulated to 73% by adding the "somewhat easy" and "very easy" responses in relation to IPC+TED's 43%. With discomfort patients accounting for 10%, this indicates that most of them could move easily without any negative effect from the device. The "very difficult" group accounted for 3% which quite a small number. The positive feedbacks realized in relation to effect on sleep pattern and future use in case of requirements (83% against 17%) indicate a high acceptability ration from the patients. Various studies support this outcome by showing both improvement in blood flow and a high patient satisfaction rate. [21,23]

Conclusion

The use of a MPA device in the immediate post-operative period leads to an improvement in wound healing as early as 3 days following kidney or kidney and pancreas transplantation compared to standard TED+IPC use. In addition, we report, for the first time, that the use of a MPA leads to a significant reduction in wound infection rates in transplant patients who are at high risk for wound complications. Patients were more satisfied with the use of MPA device than TED+IPC. These findings should be evaluated in larger, multi-center studies.

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Figures and Tables

Fig. 1. CONSORT diagram for the trial (protocol #103618).

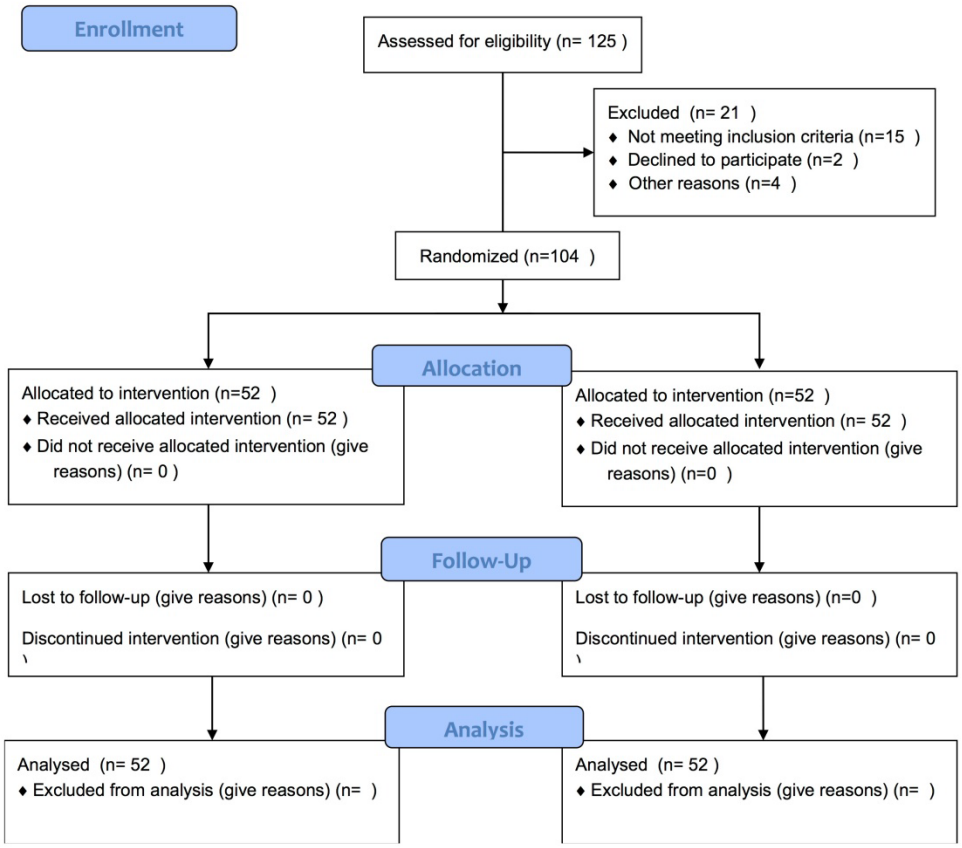
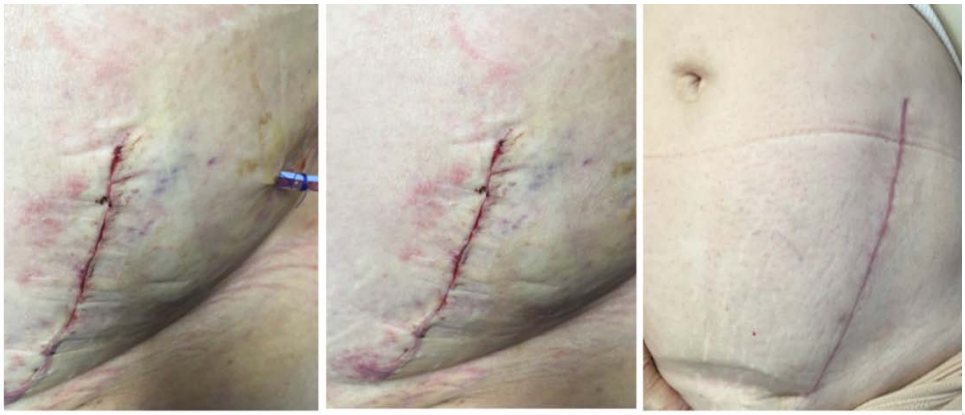
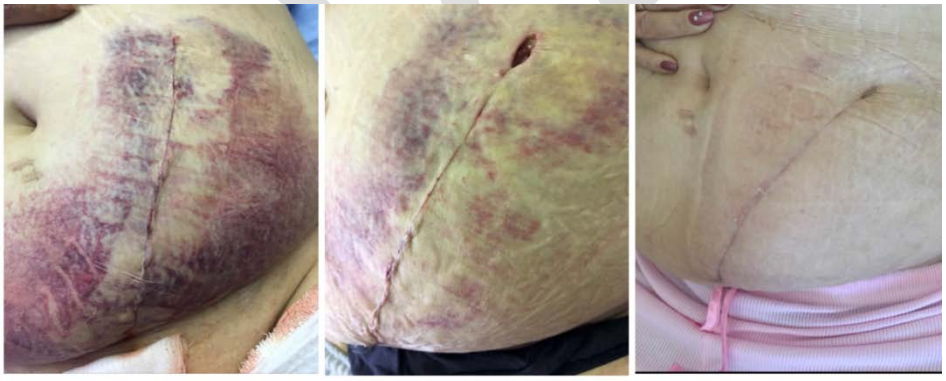


Fig. 2. Muscle pump activator (MPA) group patient post-kidney transplantation. Wound images take at ***(a)*** 3***; (b***) 5; and ***(c)*** 30 postoperative days (POD) show serial improvement in wound scores.



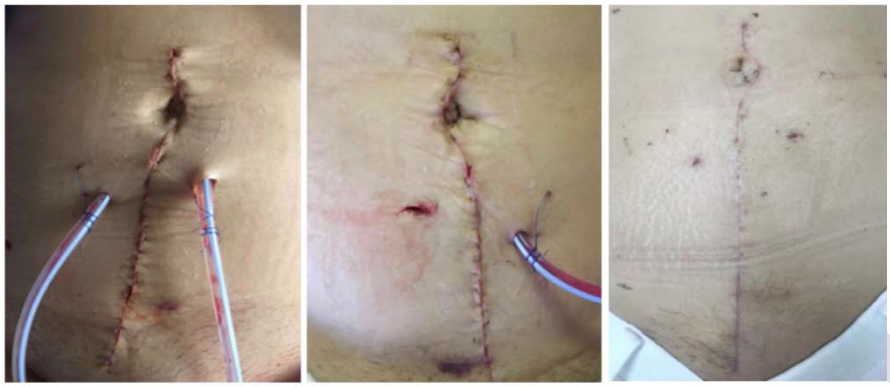
a.3rd POD **b. 5th POD** **c. 30th POD**

Fig. 3. Thrombo-embolic-deterrent + intermittent pneumatic compression (TED + IPC) group patient post-kidney transplantation. Wound images take at ***(a)*** 3; ***(b)*** 5; and ***(c)*** 30 postoperative days (POD) show interval improvement in wound scores.



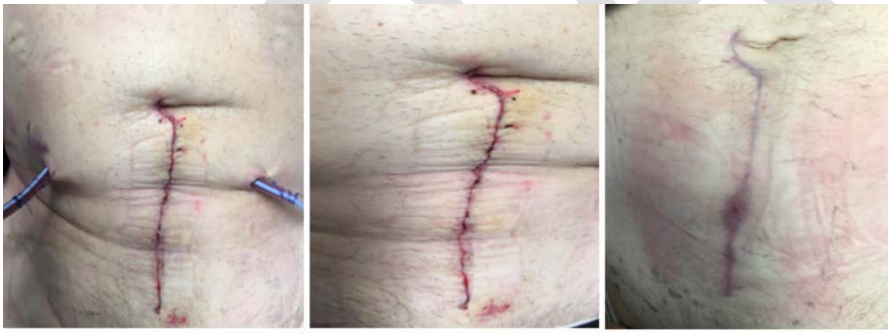
a.3rd POD **b. 5th POD** **c. 30th POD**

Fig. 4. Muscle pump activator (MPA) group patient post-kidney transplantation. Wound images take at ***(a)*** 3; ***(b)*** 5; and ***(c)*** 30 postoperative days (POD) show serial improvement in wound scores.



a.3rd POD **b. 5th POD** **c. 30th POD**

Fig. 5. Thrombo-embolic-deterrent + intermittent pneumatic compression (TED + IPC) group patient post-kidney-pancreas transplantation. Wound images take at ***(a)*** 3; ***(b)*** 5; and ***(c)*** 30 postoperative days (POD) show interval improvement in wound scores.



a.3rd POD **b. 5th POD** **c. 30th POD**

Fig. 6. At postoperative day (POD) 3, the thrombo-embolic-deterrent + intermittent pneumatic compression (TED + IPC) cohort had significantly higher wound score difference in comparison to the muscle pump activator (MPA) cohort (Pearson Chi-square 4.1; p=0.04; standard deviation [SD] ± 2.48 for TED + IPC group compared to MPA). Day 3 H0>H1 null hypothesis MPA leads to better wound scores compared to TED + IPC. Bayesian inferential analysis: strong evidence in favour of MPA.

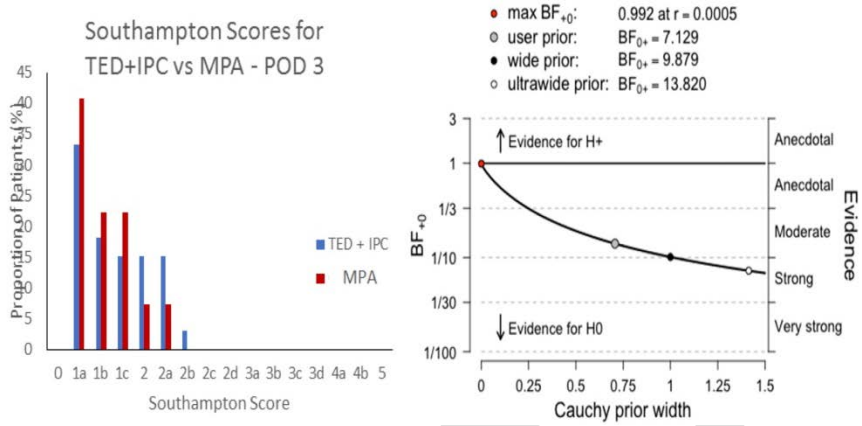


Fig. 7. At postoperative day (POD) 5, the thrombo-embolic-deterrent + intermittent pneumatic compression (TED + IPC) cohort had significantly higher wound score (≥2) in comparison to the muscle pump activator (MPA) cohort (Pearson Chi-square 6.88; p=0.0003; standard deviation [SD] ± 1.81 for TED + IPC group compared to MPA). Day 5 H0>H1 null hypothesis MPA leads to better wound scores compared to TED + IPC. Bayesian inferential analysis: moderate evidence in favour of MPA.

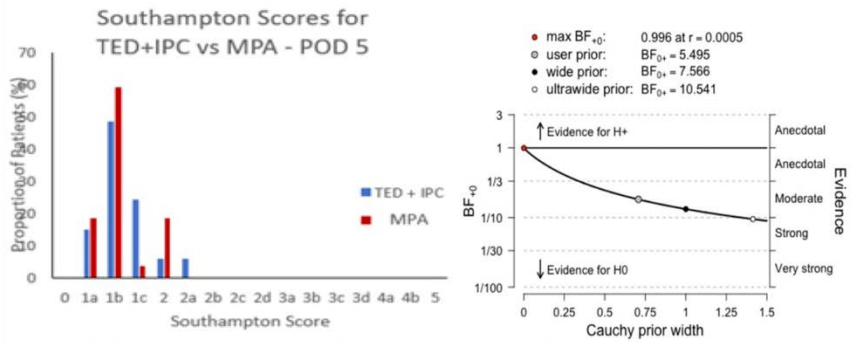


Fig. 8. At postoperative day (POD) 30, the muscle pump activator (MPA) cohort had equivalent wound score in comparison to thrombo-embolic-deterrent + intermittent pneumatic compression (TED + IPC) cohort (Pearson Chi-square 6.20; p=0.51; standard deviation [SD] ± 1.84 for MPA compared to TED + IPC). Day 30 H0>H1 null hypothesis MPA leads to better wound scores compared to TED + IPC. Bayesian inferential analysis: equivalent evidence for either group.

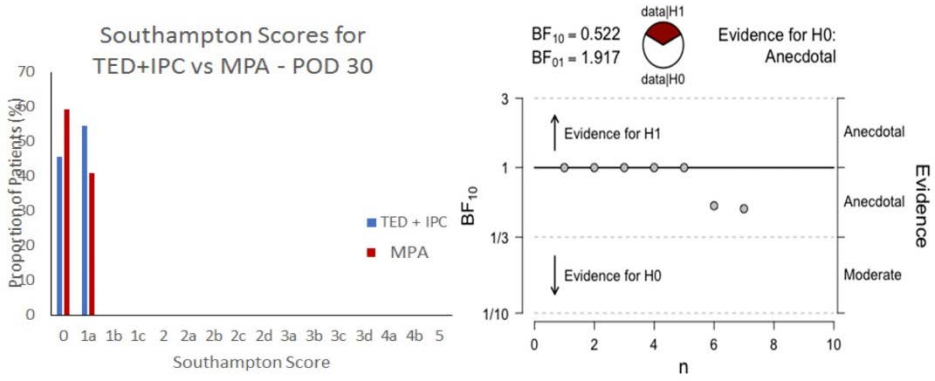


Fig. 9. At postoperative day (POD) 3, the muscle pump activator (MPA) cohort had significantly lower wound score in comparison to thrombo-embolic-deterrent + intermittent pneumatic compression (TED + IPC) cohort (p=0.04). At POD 5, the MPA cohort had significantly lower wound score in comparison to TED + IPC cohort (p=0.0003). At POD 30, there was no significant difference between both groups (p=0.051). Null hypothesis MPA leads to better wound scores compared to TED + IPC. Bayesian inferential analysis: overall moderate in favour of MPA.

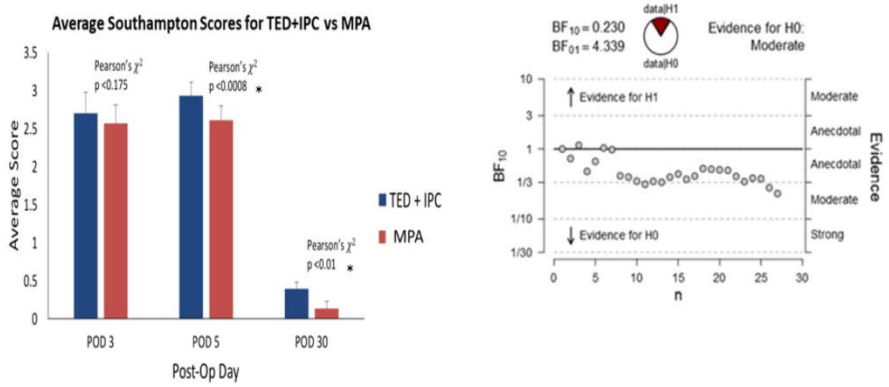


Table 1. Demographics and patient characteristics			
	Type of recipients		
	IPC + TED	**MPA**	**p**
Number of patients	52	52	–
Age, years (range)	49 (27–65)	51 (40–69)	0.98
Male: Female	34:18	30:22	0.89
BMI (kg/m^2)	27.5±4.2	25.8±4.6	0.26
Weight (kg)	89.2±6	86.6±5	0.69
Height (cm)	160.0±5.02	158.9±2.92	0.43
Superficial wound infection (%)	15 (29)	6 (12)	0.03
Kidney transplant	46	48	–
Length of stay (days)	6.9±1.5	6.6±1.4	0.85
DM	20	22	0.91
HTN	10	12	0.75
Smoking	8	10	0.78
Peripheral vascular disease	8	6	0.18
Induction immunosuppression			
Thymoglobulin	30	35	0.65
Basiliximab	16	13	0.71
Maintenance immunosuppression			
Tacrolimus/mycophenolic acid/prednisone	52	52	0.84
Superficial wound infection (%)	11 (24)	4 (8)	0.04
Kidney + pancreas transplant	6	4	–
Length of stay (days)	10.2±1.5	9.6±1.7	0.94
DM	5	4	0.99
HTN	3	2	0.45
Smoking	3	2	0.75
Peripheral vascular disease	2	1	0.24
Induction immunosuppression			
Thymoglobulin	6	4	0.99
Maintenance immunosuppression			
Tacrolimus/mycophenolic acid/prednisone	6	4	0.64
Superficial wound infection (%)	4 (67)	2 (50)	0.59

Data are presented as median ± standard deviation. BMI: body mass index; DM: diabetes mellitus; HTN: hypertension; MPA: muscle pump activator; TED + IPC: thrombo-embolic-deterrent + intermittent pneumatic compression.

Table 2. Southampton wound scoring system.[24]		
Southampton scoring system		
Grade	**Appearance**	**Assigned numerical score**
0	Normal healing	0
I - Normal healing with mild bruising or erythema		1
A	Some bruising	2
B	Considerable bruising	3
C	Mild erythema	4
II - Erythema plus other signs of inflammation		5
A	At one point	6
B	Around sutures	7
C	Along wound	8
D	Around wound	9
III - Clear or hemoserous discharge		10
A	At one point only (<2 cm)	11
B	Along wound (>2 cm)	12
C	Large volume	13
D	Prolonged (>3 days)	14
IV - Pus		15
A	At one point only (<2 cm)	16
B	Along wound (>2 cm)	17
V - Deep or severe wound infection with or without tissue breakdown; hematoma requiring aspiration		18

Table 3. Questionnaire to assess patient satisfaction with the use of the various devices *(participants asked to check one reply for each question)*	
To which random group were you placed?	IPC + TED stockings MPA device
How comfortable are the device?	Extremely comfortable Moderately comfortable Average Moderately uncomfortable Extremely uncomfortable
What is the extent of the wound swelling?	Extremely increased Slightly increased No change Slightly reduced Extremely decreased
What was the device's influence on sleep patterns?	Extremely positive Moderately positive No effect Moderately negative Extremely positive
What is the device's mobility after surgery?	Extremely difficult Moderately difficult No change Moderately easy Extremely easy
Would you want to use the same device if you had another surgery?	Yes No

MPA: muscle pump activator; TED + IPC: thrombo-embolic-deterrent + intermittent pneumatic compression.

Table 4. Likelihood of significant wound score >2 comparing MPA vs. TED+IPC cohort			
Likelihood of significant wound score >2	3 days	5 days	30 days
MPA vs. TED + IPC	0.18 (95% CI 0.06–0.27)	0.01 (95% CI 0.002–0.13)	NS

CI : confidence interval; MPA: muscle pump activator; NS: non-significant; TED + IPC: thrombo-embolic-deterrent + intermittent pneumatic compression.