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# Compression Stockings Limit the Incidence of Postoperative Lymphocele in Kidney Transplantation

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**Abstract.** *Background: Lymphoceles account for considerable morbidity rates after kidney transplantation. As yet, there is no therapeutic strategy to prevent the formation of lymphoceles. The lower limb provides a large reservoir for lymphatic tissue. Prophylactic compression therapy limits tissue volume and edema formation and may therefore reduce postoperative lymph flow. Patients and Methods and Results: In a non-randomized prospective study using a historical control group prior to 2006 as comparison from our center (2004-2008: total n=126), we found that lymphoceles are significantly diminished on the ipsilateral lower limb of the operative side when patients wear class II compression stockings (n=69) for four weeks after transplantation compared to patients achieving standard antithrombotic therapy by compression class I stockings (n=57) for thrombosis prophylaxis until full mobilization (33% versus 15%, p-value<0.05). Furthermore, a significantly lower percentage of patients needed surgical treatment of the lymphoceles for obstructive complications after class II compression (4% versus 18%, p-value<0.01). These findings were independent of the recipients' demographics, the duration of the surgical procedure, and the operating surgeon. Conclusion: Further studies are needed to demonstrate the usefulness of compressing stockings for the reduction of lymphoceles after kidney transplantation. This approach would not only reduce post-transplantation morbidity, but also provide an easy and cost-effective treatment without side-effects.*

A lymphocele is a lymphatic collection around a transplanted kidney, occurring two weeks to six months after transplantation with its peak incidence at six weeks (1). The incidence of lymphoceles after kidney transplantation in men has been reported to be between 25 and 40% (2-4). Most lymphoceles are clinically silent, but the most common manifestation, amongst others, is impaired graft function in the presence of perigraft collection and unilateral leg edema (1, 3). About 20% of postoperative lymphoceles need surgical intervention (1, 4). Lymphoceles have to be monitored and patients needing intervention for the treatment of lymphocele need to be hospitalized with increased costs and risks.

The lower limb, with its extensive surface and volume, has a rich amount of lymphatic tissue draining lymph from the skin and muscles along the iliac arteries and veins. In breast cancer, lymphedema of the arm is common and is reported to be dependent on the initial volume of lymph in the tissues (5). Compression therapy limits tissue volume and edema and could therefore reduce postoperative lymph flow in the iliacal compartment after kidney transplantation.

After a review of the literature, there is no evidence as to how far lymphoceles, after kidney transplantation, can be reduced by compression stockings.

In our retrospective study, we have found positive effects of continuous wearing of compression stockings class for four weeks after kidney transplantation compared to standard antithrombotic therapies. Therefore a prospective randomized controlled trial is of urgent importance to lower postoperative incidence of lymphoceles after kidney transplantation and to gather clinical evidence.

## Patients and Methods

*Study population*. In a prospective manner, from 2006-2008, all kidney transplant patients at our University Medical Center wore class II compression stockets (n=69) on the site of surgery for 4 weeks. These patients were compared to a retrospective cohort (2004-2006) of n=57 patients achieving standard antithrombotic therapy by compression class I stockings until full mobilization. Patients of both cohorts received standardized clinical care and surgical procedures according to a clinical pathway. Allocation of the donor kidneys to the individual recipient was centrally directed by Eurotransplant delivering a computerized algorithm, mainly based on waiting time and a Human Leucocyte Antigen matching. Study entry was defined by the date of transplantation, and follow-up was terminated at a minimum of six months after transplantation. The observation period for the current study was limited to a maximum

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Table I. *Patient data overview. No differences were observed in the means of recipient or donor age, cold ischemic time, number of mismatches and the duration of surgery between the two patient groups.*

| Factor | No stocking (n=57) | Stocking (n=69) | *t*-Test *p*-value |
|---|---|---|---|
| Recipient age (yrs) | 51.51±1.77 | 55.66±1.52 | 0.076 |
| Donor age (yrs) | 50.29±20.21 | 49.94±1.96 | 0.905 |
| Cold ischemic time (h) | 14.20±1.00 | 14.22±0.77 | 0.986 |
| Number of mismatch (n) | 2.66±0.21 | 2.69±0.22 | 0.922 |
| Duration of surgery (min) | 191±10 | 173±6 | 0.129 |

of five years. We excluded two patients due to death during follow-up. A further 9 patients were excluded due to being lost to follow-up. The mean duration of follow-up was 2.2 years.

*Diagnosis of lymphocele and documentation of co-factors*. Cohorts were compared for incidence of lymphocele needing surgical intervention and overall incidence of lymphocele. Data was statistically compared for differences in surgeon, sex, donor and recipient age, cold ischemic time, duration of operation, immunosuppressive therapy, number of mismatches and other associated factors. A correlation of these factors with the incidence of lymphocele was performed.

All patients underwent follow-up sonography at our hospital or by their nephrologist under the use of a standardized questionnaire to gather information on the incidence of lymphocele, their possible symptoms and whether surgical intervention was needed.

*Perioperative fluid management and immunosuppressive medication*. All patients, except those on continuous peritoneal dialysis, underwent a dialysis session immediately before transplantation, targeting 1-2 kg over the former dry weight. Perioperative hydration was initiated with intravenous saline 0.9% at a rate of 1-1.5 ml/kg/h and was subsequently altered according to urine output and fluid balance. Mannitol (20%; 250 ml) and a single bolus of *i.v.* furosemide (40-80 mg) were administered before opening of the arterial vessel clamp. No additional doses of diuretics were given over the first 24 h post operatively.

Immunosuppressive therapy was mainly based on a cyclosporine-containing triple-drug regimen (95% of all cases). Cyclosporin was given orally on the first post-operative day, and the initial dose (5 mg/kg bid) was adjusted according to a target trough level of between 180 and 250 ng/ml.

*Statistical analysis*. Numerical data are reported as mean±SD, and comparisons among groups were made using the two-sided Student's *t*-test. Differences in the distribution of categorical variables were tested with the chi-squared test. Significance was defined according to a $p$-value $<0.05$.

Logit analysis on the likelihood of association of the incidence of lymphoceles and lymphoceles requiring surgical intervention was performed.

Statistical analyses were carried out using the Stata Statistical Software for MS Windows (release 5.0; Stata Corp., College Station, TX, USA).

Table II. *Association of lymphocele. Logit estimates on the likelihood of association of the occurrence of lymphoceles and lymphoceles requiring surgical intervention were significant only for the factor of compression stockings (*). None of the other factors showed any significance.*

| | OR | CI | *p*-value |
|---|---|---|---|
| Lymphocele | | | |
| Stocking | 0.3382 | 0.135 0.845 | 0.020* |
| Recipient age | 1.007 | 0.969 1.046 | 0.741 |
| Gender | 1.728 | 0.654 4.561 | 0.270 |
| Donor age | 0.996 | 0.965 1.027 | 0.792 |
| Mismatch | 1.120 | 0.836 1.500 | 0.448 |
| Cold ischemic time | 0.949 | 0.865 1.041 | 0.268 |
| Duration of surgery | 1.000 | 0.994 1.007 | 0.957 |
| Cadaveric donor | 1.665 | 0.335 8.267 | 0.533 |
| Surgical intervention | | | |
| Stocking | 0.194 | 0.054 0.701 | 0.012 * |
| Recipient age | 1.030 | 0.975 1.089 | 0.289 |
| Gender | 1.323 | 0.382 4.586 | 0.659 |
| Donor age | 0.985 | 0.947 1.023 | 0.433 |
| Mismatch | 1.055 | 0.717 1.551 | 0.786 |
| Cold ischemic time | 0.961 | 0.853 1.082 | 0.510 |
| Duration of surgery | 0.995 | 0.984 1.006 | 0.372 |

OR: Odds ratio. CI: 95% Confidence Intervall.

## Results

No significant differences were observed in recipient age, donor age, cold ischemic time, mismatches and the duration of operation between the two cohorts (Table I).

The total incidence of lymphoceles was significantly lower in patients with class II compression stockings compared to those treated with standard therapy ($p$-value=0.028, Figure 1). The proportion of lymphoceles requiring surgical intervention was much lower after class II compression of the leg on the side of operation (3 out of 69 patients, which were 3 out of 11 lymphoceles (27%) compared to the control cohort, 10 out of 57 patients, 10 out of 19 lymphoceles (52%); $p$-value=0.023).

Logit analysis on the likelihood of association of the occurrence of lymphoceles (odds ratio=0.19; $p$-value=0.12) and lymphoceles requiring surgical intervention (odds ratio=0.34; $p$-value=0.020) was significant for the factor of compression stockings. None of the other factors showed any significance (Table II).

## Discussion

Lymphoceles are frequently seen after kidney transplantation in up to 40% of the cases contributing to considerable mortality after kidney transplantation (1-3, 6). Class II lower limb compression therapy during the early postoperative period improves lymph flow, lowers leg edema and might have influence on the incidence of lymphoceles.

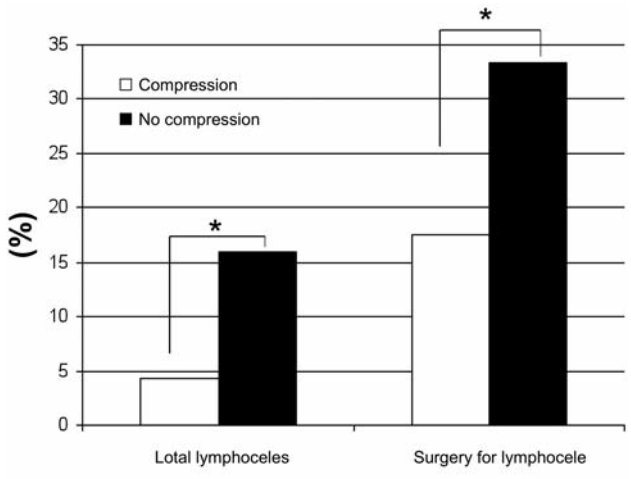


Figure 1. *Lymphoceles and required operative therapy after kidney transplantation. The total incidence of lymphoceles was significantly reduced in patients wearing compression stockings postoperatively (n=69) compared to patients without compression therapy (n=57). The percentage of lymphoceles requiring operative therapy after conventional treatment was significantly higher compared to that in patients with postoperative compression stocking treatment. *means p-value<0.05.*

In our analysis of 123 patients after kidney transplantation, we found a significantly lower incidence of lymphoceles needing surgical intervention after class II compression therapy, compared to standard therapy alone. No other factors collected in our database were significantly correlated with the incidence of lymphedema. This means that the wearing of class II compression stockings significantly reduced both the patient risk for lymphocele and the risk for another operative intervention due to lymphoceles after kidney transplantation. The intervention of compression stockings, simple and harmless, indeed resulted in lower morbidity and lower postoperative costs within our series.

Most lymphoceles originate from leakage of lymph from unligated iliac vessel lymphatic's of the recipient. The drainage route of the lower limb lymphatic vessels is along the iliac vessels. As a consequence, when the iliac vessels are mobilized for anastomosis, some lymphatic vessels are unavoidably divided (3). Ligation of the lymphatic vessels during preparation of either the graft or the site of transplantation and appropriate external drainage thereafter can reduce the incidence of lymphocele (7). The operative method in our hospital has not changed over the years. Ligation of lymphatic vessels during operations is performed cautiously as far as it is needed. More than 93% of the operations were performed by four surgeons without differences in the occurrence of lymphoceles. A total of eight patients were operated on by various other surgeons, former attendants of the Department, overall, without higher incidence of lymphocele compared to the other surgeons.

There is some evidence that the incidence of lymphocele has decreased since the introduction of low-steroid regimens for immunosuppression. However, there are controversies in the literature about this matter (8-11). Rejection episodes may also have a role in lymphocele formation. In a study by Lipay and colleagues, a high frequency of cellular rejection in patients with lymphocele was indicative of a possible cause-effect relationship (12). In another study on 115 patients, multivariate analysis of possible lymphocele risk factors showed that only rejection was accompanied by high risk of lymphocele formation. The authors concluded that allograft rejection was the most important contributing factor in lymphocele formation (13). However, in our study we could not confirm these findings. No association between immunosuppressive regimen or allograft rejection was found in our data. Lymphoceles were not significantly correlated to any of the other parameters within our cohort.

As yet, there are no data regarding the effect of compression therapy on the incidence of lymphocele after kidney transplantation. For lymph node dissection, however, a multicenter randomized controlled study has been started in 2007 in the Netherlands (PROTECT-study) on the prevention of lymphedema after inguinal lymph node dissection by therapeutic elastic compression hoses, which is still ongoing (Rooij, J.D.: NOD number: OND1324995; www.onderzoekinformatie.nl): "The objective of the study is to determine the efficacy of the use of elastic compression hoses to prevent lymphedema after inguinal lymph node dissection in cancer patients, and to explore the impact on body image and health-related quality of life".

Although the data of our study are promising, there are several limitations in this article. Firstly the study had to be performed in a retrospective manner by questionnaire. However, the fact that all patients are associated with our transplantation unit ensures, that lymphoceles needing surgical intervention are operated on in our Department. Furthermore, there is a close collaboration between the patients' nephrologists and the transplantation unit, which resulted in a high return of questionnaires of over 85%.

A prospective randomized controlled trial is warranted to ultimately prove the usefulness of class II compressing stockings as a therapeutic tool for the reduction of lymphocele after kidney transplantation. This approach would not only reduce post-transplantation morbidity but also would provide an easy and cost-effective treatment without side-effects.

## Conclusion

In our retrospective study we have shown that effective compression therapy of the lower limb can reduce the incidence of lymphocele and associated operative interventions.

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