Comparison of laparoscopic and mini incision open donor nephrectomy: single blind, randomised controlled clinical trial

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Research

Comparison of laparoscopic and mini incision open donor nephrectomy: single blind, randomised controlled clinical trial

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Editorial by Townell

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Abstract

Objectives To determine the best approach for live donor nephrectomy to minimise discomfort to the donor and to provide good graft function.
Design Single blind, randomised controlled trial.
Setting Two university medical centres, the Netherlands.
Participants 100 living kidney donors.
Interventions Participants were randomly assigned to either laparoscopic donor nephrectomy or to mini incision muscle splitting open donor nephrectomy.
Main outcome measures The primary outcome was physical fatigue using the multidimensional fatigue inventory 20 (MFI-20). Secondary outcomes were physical function using the SF-36, hospital stay after surgery, pain, operating times, recipient graft function, and graft survival.
Results Compared with mini incision open donor nephrectomy, laparoscopic donor nephrectomy resulted in longer skin to skin time (median 221 *v* 164 minutes, $P<0.001$), longer warm ischaemia time (6 *v* 3 minutes, $P<0.001$), less blood loss (100 *v* 240 ml, $P<0.001$), and a similar number of complications (intraoperatively 12% *v* 6%, $P=0.49$, postoperatively both 6%). After laparoscopic nephrectomy, donors required less morphine (16 *v* 25 mg, $P=0.005$) and shorter hospital stay (3 *v* 4 days, $P=0.003$). During one year's follow-up mean physical fatigue was less (difference −1.3, 95% confidence interval −2.4 to −0.1) and physical function was better (difference 6.2, 2.0 to 10.3) after laparoscopic nephrectomy. Function of the graft and graft survival rate of the recipient at one year censored for death did not differ (100% after laparoscopic nephrectomy and 98% after open nephrectomy).
Conclusions Laparoscopic donor nephrectomy results in a better quality of life compared with mini incision open donor nephrectomy but equal safety and graft function.

Introduction

Donation of a kidney from a live donor is the most realistic option to expand organ donation,[1] but harm to the donor and grafts need to be minimised. Using small incisions to remove kidneys improved the comfort of donors. In less than a decade, laparoscopic surgery has been widely adopted. Concurrently open donor nephrectomy has been refined to a muscle sparing mini incision without resection of the ribs, which has improved convalescence of the donors.[2–4] We carried out a prospective randomised trial to compare laparoscopic donor nephrectomy with mini incision open donor nephrectomy for fatigue and quality of life of the donors and for clinical outcomes.

Participants and methods

We recruited living kidney donors from the university medical centres in Rotterdam and Nijmegen. Screening of donors included examination by a nephrologist, renal ultrasonography, and magnetic resonance angiography or computed tomography-angiography to evaluate the arterial and venous anatomy of the kidneys (see bmj.com for exclusion criteria).

Randomisation and surgical procedures

The surgeon telephoned the study coordinator after informed consent had been confirmed, who opened the next numbered sealed opaque envelope provided by the trial statistician. Randomisation was carried out according to a computer generated list using a hidden block size of four. Only the surgical team were aware of the allocated procedure. At the end of the operation the donor's abdomen was covered with a standard pattern of dressings stained with one or two drops of blood to simulate real wound dressings.

The surgical procedures were carried out, as described previously, by one of four surgeons.[4] The trial coordinator in each centre attended the operations to document blood loss, operation time, use of instruments, and complications (defined as events

Table with data for additional dimensions is on bmj.com

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necessitating intraoperative or postoperative interventions or that prolonged hospital stay).

Postoperative data and quality of life

We calculated postoperative hospital stay with and without adjustment for time spent in hospital as a result of non-medical reasons. Donors were seen at the outpatient clinic at three weeks, three months, and one year postoperatively. They were asked to complete forms on pain and nausea preoperatively and at days 1, 3, 7, and 14 using a visual analogue scale from 0 (none) to 10 (severe).

Body image was assessed at one year postoperatively using the body image questionnaire,[5] which uses the body image scale to assess attitudes to bodily appearance (five questions, score 5-20) and the cosmetic scale to assess degree of satisfaction with the appearance of the scar (three questions, score 3-24). Higher scores indicate greater satisfaction.

Table 1 Surgical outcomes of living kidney donor and postoperative outcomes of donor and recipient. Values are numbers (percentages) unless stated otherwise

Variable	Laparoscopic donor nephrectomy (n=50)	Mini incision open donor nephrectomy (n=50)	P value
Donor			
Conversion to open donor nephrectomy	0	—	—
Median (range) time (min):			
Kidney removal	181 (107-307)	118 (61-201)	<0.001
Skin to skin	221 (135-354)	164 (92-298)	<0.001
In operating theatre	289.5 (180-420)	226 (157-365)	<0.001
Median (range) warm ischaemia time (min)	6 (2-14)	3 (1-6)	<0.001
Blood loss (ml)	100 (10-860)	240 (20-1800)	<0.001
Complications:			
Intraoperative	6 (12)	3 (6)	0.23
Postoperative	3 (6)	3 (6)	1.00
Median (range) resumption of normal diet (h)	19.5 (3-48)	24 (16-72)	0.01
Median (range) morphine requirement (mg)	16 (0-93)	25 (1-107)	0.005
Median (range) length of hospital stay (days):			
Unadjusted	3 (1-6)	4 (2-8)	0.003
Adjusted*	3 (1-6)	3 (2-8)	0.002
Median (range) serum creatinine level (μmol/l):			
Day 1	112 (75-158)	112.5 (68-183)	0.81
Day 2	118 (76-167)	117.5 (74-222)	0.99
Month 3	107 (76-157)	117 (79-191)	0.31
Year 1	107 (72-153)	114 (75-169)	0.17
Median (range) nausea†:			
Day 1	0 (0-9.2)	0 (0-7.7)	0.52
Day 3	0 (0-4.6)	0 (0-5.2)	0.24
Day 7	0 (0-3.2)	0 (0-8.0)	0.31
Day 14	0 (0-2.2)	0 (0-8.0)	0.14
Median (range) pain†:			
Day 1	2.7 (0-6.2)	3.5 (0-7.7)	0.04
Day 3	1.4 (0-6.6)	1.8 (0-7.8)	0.12
Day 7	0.4 (0-6.1)	1.7 (0-8.0)	0.03
Day 14	0 (0-4.8)	0.4 (0-8.0)	0.008
Median (range) body image questionnaire:			
Body image scale	20 (13-20)	20 (14-20)	0.40
Cosmetic scale	20 (7-24)	18 (12-24)	0.14
Recipient			
Acute rejection	9 (18)	15 (30)	0.24
Ureteral complications	6 (12)	10 (20)	0.41
Graft survival at one year‡	48 (100)	48 (98)	1.00
Patient survival at one year	48 (96)	49 (98)	1.00

*Adjusted for time spent in hospital for non-medical reasons.
†Measured on visual analogue scale from 0 (none) to 10 (severe).
‡Censored for death.

To assess health related quality of life and fatigue we administered the SF-36 and the multidimensional fatigue inventory 20 (MFI-20) preoperatively and at 1, 3, 6, and 12 months postoperatively. The SF-36 includes a scale measuring eight health concepts: physical function, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health.[6] Scores per dimension range from 0 to 100, with higher scores indicating better quality of life. We considered a five point difference between laparoscopic and open nephrectomy on a dimension as minimally clinically relevant.[6]

We determined levels of fatigue using the MFI-20,[7] which consists of 20 items divided into five scales: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. Scores per item ranged from 1 to 5: total score per scale from 4 (no fatigue) to 20 (exhausted).

Recipients

Renal transplantation was carried out using preperitoneal placement in the iliac fossa. During the year postoperatively we recorded survival rates of recipients and grafts, acute rejection rates, venous thrombosis, and ureteral complications.

Statistical analysis

The primary outcome was physical fatigue (MFI-20) and the secondary outcome was physical function (SF-36). Other secondary end points were postoperative hospital stay, pain, operating times, recipient graft function, and graft survival. (See bmj.com for power calculation.) We used the χ^2 test to compare categorical variables and the Mann-Whitney U test to compare continuous variables. Repeated measurement of analysis of covariance was used to compare repeated continuous variables. We adjusted repeated measures for baseline values, donor's sex, and age. We analysed data according to the intention to treat principle. P values less than 0.05 (two sided) were considered statistically significant.

Results

From November 2001 until February 2004 we recruited 105 of 163 living kidney donors to the study (see bmj.com). In total the Rotterdam centre carried out 34 laparoscopic donor nephrectomies and 38 mini incision open donor nephrectomies and the Nijmegen centre carried out 16 laparoscopic nephrectomies and 12 open nephrectomies. (See bmj.com for the baseline characteristics of the donors and recipients.)

The procedures were carried out as planned without conversion to open or formal lumbotomy (table 1). In the laparoscopic group skin to skin time and warm ischaemia time were significantly longer and blood loss was less. Intraoperative complications occurred in six patients (12%) during laparoscopic nephrectomy: bleeding (n=3), a serosal lesion of the colon, a bladder lesion, and a small capsular tear of the spleen. The three (6%) complications during open nephrectomy involved bleeding.

Postoperative outcomes and recipients

Laparoscopic nephrectomy resulted in faster recovery (earlier resumption of a normal diet, less need for

intravenous morphine, and earlier discharge; table 1). During the first two weeks donors in the laparoscopic group experienced significantly less pain. Postoperative complications after laparoscopic nephrectomy were wound infections at the extraction site in two donors and a blood transfusion. Complications after open nephrectomy were a urinary tract infection, a minor pulmonary infiltrate, and an infected retroperitoneal haematoma. Donors in both groups had similar serum creatinine levels. Scores on the body image scale did not differ significantly between the groups.

One recipient (laparoscopic nephrectomy) died on the first postoperative day due to myocardial infarction. Two others (one in each group) died in the first year due to progressive infections related to an immunocompromised status. One recipient's graft (open nephrectomy) did not survive due to vascular rejection (table 1). Three recipients had ureteral complications after open nephrectomy leading to ureteral reconstructions. Serum creatinine levels in recipients of kidneys from donors in both groups decreased in parallel without any significant differences over time.

Quality of life and fatigue

At baseline donors in both groups had excellent health status.[8] Scores on the domains role physical and bodily pain were comparable at all time points (table 2). All other dimensions differed over time in favour of laparoscopic nephrectomy. Patients in the laparoscopic group had higher mean scores for physical function during follow-up (see bmj.com), indicating better quality of life (difference 6.2 points, 95% confidence interval 2.0 to 10.3). Similar patterns were found for the other dimensions (see bmj.com).

Physical fatigue scores were significantly lower for donors in the laparoscopic group, indicating less physical fatigue (see bmj.com): difference during one year's follow-up (−1.3, 95% confidence interval −2.4 to −0.1). Other dimensions of fatigue did not differ between the groups over time (see bmj.com).

Table 2 Quality of life of living kidney donors after laparoscopic nephrectomy or mini incision open nephrectomy

Dimension	Estimated difference (95% CI) (laparoscopic nephrectomy minus open nephrectomy)	P value
SF-36:		
Physical function	6.2 (2.0 to 10.3)	0.004
Role physical	7.7 (−2.1 to 17.5)	0.12
Bodily pain	4.1 (−0.3 to 8.5)	0.07
General health	7.2 (2.2 to 12.1)	0.005
Vitality	6.7 (1.1 to 12.2)	0.02
Social functioning	5.9 (0.5 to 11.4)	0.03
Role emotional	11.8 (4.1 to 19.5)	0.003
Mental health	5.6 (1.8 to 9.4)	0.005
Multidimensional fatigue inventory:		
General fatigue	−0.7 (−2.0 to 0.6)	0.31
Physical fatigue	−1.3 (−2.4 to -0.1)	0.03
Reduced activities	−0.8 (−2.0 to 0.3)	0.16
Reduced motivation	−1.0 (−2.1 to 0.1)	0.07
Mental fatigue	−0.2 (−1.7 to 0.3)	0.70

Positive differences on SF-36 dimensions indicate better quality of life after laparoscopic donor nephrectomy. Negative differences on multidimensional fatigue inventory dimensions indicate less fatigue after laparoscopic donor nephrectomy.

What is already known on this topic

Both laparoscopic donor nephrectomy and minimally invasive open donor nephrectomy provide better outcomes than conventional open donor nephrectomy

What this study adds

Compared with mini incision open donor nephrectomy, laparoscopic donor nephrectomy was associated with faster recovery, less fatigue, and better quality of life of the donor but equal safety

Discussion

Laparoscopic donor nephrectomy results in faster recovery, less fatigue, and better quality of life of the donor compared with mini incision open donor nephrectomy but equal safety and graft function.

Three randomised trials compared hand assisted laparoscopic donor nephrectomy with mini incision open donor nephrectomy without blinding.[8–10] Open donor nephrectomy has been proposed as an acceptable alternative to laparoscopic surgery,[11] particularly if complications are expected.

We did not exclude donors for laparoscopic nephrectomy because of factors such as high body mass index. Unlike traditional lumbotomy, the open approach used a small incision and preserved continuity of abdominal wall muscles resulting in fewer complications, fast recovery,[12 13] and cosmetic outcomes equivalent to laparoscopic nephrectomy. Despite modification of the open technique, laparoscopic nephrectomy was superior for recovery, fatigue, and quality of life. The use of blood stained wound dressings blinded donors and medical staff in the immediate postoperative phase. The difference in variables measured after the operation, such as pain scores and length of hospital stay, was significantly in favour of laparoscopic nephrectomy, despite blinding.

Retrospective studies have shown an improved quality of life after laparoscopic surgery compared with open surgery.[14 15] In our study laparoscopic surgery led to a better quality of life of donors. Conversions from laparoscopic to open techniques often obscure the effect of the operation on quality of life. As donors are healthy individuals the benefits they achieve from laparoscopic surgery resemble the actual benefits for patients undergoing laparoscopic operations.

Extensive experience in laparoscopic surgery is necessary before implementation of a kidney donation programme using laparoscopic techniques. Complications, although rare, did occur in our study. Furthermore, the operation time was about an hour longer for laparoscopic nephrectomy. Retroperitoneoscopic donor nephrectomy may combine the advantage of a shorter operation time and a lower chance of complications from lesions of intraperitoneal organs.[16] Laparoscopic donor nephrectomy may be advocated for donation programmes using living kidney donors.

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Competing interest: None declared.

Ethical approval: This study was approved by the medical ethics committees of the university medical centres at Rotterdam and Nijmegen.

1 Ingelfinger JR. Risks and benefits to the living donor. *N Engl J Med* 2005;353:447-9.
2 Srivastava A, Tripathi DM, Zaman W, Kumar A. Subcostal versus transcostal mini donor nephrectomy: is rib resection responsible for pain related donor morbidity. *J Urol* 2003;170:738-40.
3 Yang SL, Harkaway R, Badosa F, Ginsberg P, Greenstein MA. Minimal incision living donor nephrectomy: improvement in patient outcome. *Urology* 2002;59:673-7.
4 Kok NF, Alwayn IP, Lind MY, Tran KT, Weimar W, Ijzermans JN. Donor nephrectomy: mini-incision muscle-splitting open approach versus laparoscopy. *Transplantation* 2006;81:881-7.
5 Dunker MS, Bemelman WA, Slors JF, van Duijvendijk P, Gouma DJ. Functional outcome, quality of life, body image, and cosmesis in patients after laparoscopic-assisted and conventional restorative proctocolectomy: a comparative study. *Dis Colon Rectum* 2001;44:1800-7.
6 Ware JE, Snow KK, Kosinski M, Gandek B. *SF-36 health survey. Manual and interpretation guide*. Boston, MA: Health Institute, New England Medical Centre, 1993.
7 Smets EM, Garssen B, Cull A, de Haes JC. Application of the multidimensional fatigue inventory (MFI-20) in cancer patients receiving radiotherapy. *Br J Cancer* 1996;73:241-5.
8 Wolf JS Jr, Merion RM, Leichtman AB, Campbell DA Jr, Magee JC, Punch JD, et al. Randomized controlled trial of hand-assisted laparoscopic versus open surgical live donor nephrectomy. *Transplantation* 2001;72:284-90.
9 Simforoosh N, Basiri A, Tabibi A, Shakhssalim N, Hosseini Moghaddam SM. Comparison of laparoscopic and open donor nephrectomy: a randomized controlled trial. *Br J Urolog Int* 2005;95:851-5.
10 Oyen O, Andersen M, Mathisen L, Kvarstein G, Edwin B, Line PD, et al. Laparoscopic versus open living-donor nephrectomy: experiences from a prospective, randomized, single-center study focusing on donor safety. *Transplantation* 2005;79:1236-40.
11 Lewis GR, Brook NR, Waller JR, Bains JC, Veitch PS, Nicholson ML. A comparison of traditional open, minimal-incision donor nephrectomy and laparoscopic donor nephrectomy. *Transpl Int* 2004;17:589-95.
12 Berends FJ, den Hoed PT, Bonjer HJ, Kazemier G, van Riemsdijk I, Weimar W, et al. Technical considerations and pitfalls in laparoscopic live donor nephrectomy. *Surg Endosc* 2002;16:893-8.
13 Lind MY, Liem YS, Bemelman WA, Dooper PM, Hop WC, Weimar W, et al. Live donor nephrectomy and return to work: does the operative technique matter? *Surg Endosc* 2003;17:591-5.
14 Perry KT, Freedland SJ, Hu JC, Phelan MW, Kristo B, Gritsch AH, et al. Quality of life, pain and return to normal activities following laparoscopic donor nephrectomy versus open mini-incision donor nephrectomy. *J Urol* 2003;169:2018-21.
15 Buell JF, Lee L, Martin JE, Dake NA, Cavanaugh TM, Hanaway MJ, et al. Laparoscopic donor nephrectomy vs open live donor nephrectomy: a quality of life and functional study. *Clin Transplant* 2005;19:102-9.
16 Wadstrom J. Hand-assisted retroperitoneoscopic live donor nephrectomy: experience from the first 75 consecutive cases. *Transplantation* 2005;80:1060-6.

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Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder: observational follow-up study

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Abstract

Objective To study the association between prescribed antipsychotic drugs and outcome in schizophrenia or schizoaffective disorder in the community.
Design Prospective cohort study using national central registers.
Setting Community care in Finland.
Participants Nationwide cohort of 2230 consecutive adults hospitalised in Finland for the first time because of schizophrenia or schizoaffective disorder, January 1995 to December 2001.
Main outcome measures Rates of discontinuation of drugs (all causes), rates of rehospitalisation, and mortality associated with monotherapy with the 10 most commonly used antipsychotic drugs. Multivariate models and propensity score methods were used to adjust estimates of effectiveness.
Results Initial use of clozapine (adjusted relative risk 0.17, 95% confidence interval 0.10 to 0.29), perphenazine depot (0.24, 0.13 to 0.47), and olanzapine (0.35, 0.18 to 0.71) were associated with the lowest rates of discontinuation for any reason when compared with oral haloperidol. During an average follow-up of 3.6 years, 4640 cases of rehospitalisation were recorded. Current use of perphenazine depot (0.32, 0.22 to 0.49), olanzapine (0.54, 0.41 to 0.71), and clozapine (0.64, 0.48 to 0.85) were associated with the lowest risk of rehospitalisation. Use of haloperidol was associated with a poor outcome among women. Mortality was markedly raised in patients not taking antipsychotics (12.3, 6.0 to 24.1) and the risk of suicide was high (37.4, 5.1 to 276).
Conclusions The effectiveness of first and second generation antipsychotics varies greatly in the community. Patients treated with perphenazine depot, clozapine, or olanzapine have a substantially lower risk of rehospitalisation or discontinuation (for any reason) of their initial treatment than do patients treated with haloperidol. Excess mortality is seen mostly in patients not using antipsychotic drugs.

Introduction

Treatment algorithms for schizophrenia are currently based on outcome data from randomised controlled trials, but it is difficult to extrapolate data to wider community settings.[1] Most trials have a follow-up of a few

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