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Development and implementation of an enhanced recovery after surgery protocol for renal transplantation

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Abstract

Background: Successful implementation of enhanced recovery after surgery (ERAS) in kidney transplantation requires multidisciplinary consultation, education and attention to protocol. This study discusses the process implementation pathway of the ERAS protocol and its outcome.

Methods: A standardized ERAS protocol was designed for the renal transplant recipient and implemented in July 2017. Data collected prospectively of recipients transplanted from July 2017 to December 2018 were compared to prospectively collected data of recipients who were transplanted prior to ERAS implementation from January 2016 to July 2017 from our renal database. The parameters of interest included length of stay, incidence of delayed graft function and readmission rate.

Results: There was no difference in the demographics and the incidence of delayed graft function across both groups, although subgroup analysis suggested a significantly lower incidence of delayed graft function with kidneys donated after circulatory death in the cohort that were managed by the ERAS protocol. The median length of stay for patients on the ERAS protocol was 5 days (range 3–16 days). This was 2 days shorter than the median length of stay for patients not on the ERAS protocol (7 days; range 5–14, $P < 0.001$). This statistically significant difference in length of stay was consistent across all donor subgroups (living donor, donor after cardiac death and donation after brainstem death). Seventy-nine percent of the patients on the ERAS protocol were discharged on post-operative day 4.

Conclusion: An ERAS protocol for renal transplant patients is feasible. Our data show that successful implementation of ERAS in kidney transplantation is possible and results in significant cost savings due to shorter length of stay.

Introduction

Kidney transplantation when possible is an excellent form of renal replacement therapy and gives the recipient both a better quality of life and survival advantage when compared to dialysis. It is the victim of its own success and the number of operations performed has increased dramatically worldwide.

However, with the increase in demand for the service in an era of limited resources, and escalating healthcare costs many programmes face a financial crunch. While successful transplantation costs approximately the same as dialysis in the first year, the maintenance cost of a successful renal transplant after the first year is about one-third of the annual cost of dialysis from the second year onwards.[1] Worldwide, in the last decade, it has become apparent that to keep health services afloat it is essential to save on cost without compromising quality. The enhanced recovery after surgery (ERAS) protocols aim to improve the patient journey through surgery and one of the useful by-products that comes of it is cost savings from a reduction in hospital stay. The cost of a renal transplant operation and post-operative stay contribute to about one-third of the first year costs of transplantation and, therefore, any intervention that shortens the length of stay after transplant will result in a cost saving.[1–3] The economic impact of ERAS protocols has been highlighted in colorectal surgery.[4,5] While implementation of ERAS was associated with a reduction in all health service utilization outcomes, only the reduction in primary length of stay was significant.[5]

ERAS is relatively new to renal transplantation and intuitively a shorter length of stay after transplantation without an increase in follow-up, readmission or complications will result in cost savings.

Factors that keep a patient in hospital following an uncomplicated renal transplant include the need for parenteral analgesia, intravenous fluids (to manage gut dysfunction and post-transplant diuresis), bed rest (due to lack of mobility), parenteral immunosuppression and most importantly patient and staff expectation. These factors often overlap and interact to delay return of function.[6,7]

The key elements of ERAS protocols in other surgical specialties include preoperative counselling, optimization of nutrition, carbohydrate loading, standardized analgesic and anaesthetic regimens and early mobilization.[8,9] Despite the significant body of evidence indicating that ERAS protocols lead to improved outcomes, they challenge traditional surgical doctrine, and as a result their implementation has been slow.[10,11] The ERAS society has established successfully validated and implemented guidelines for various intra-abdominal surgical operations.[10,12,13] However, the authors are not aware of any published ERAS guidelines for renal transplantation. This study describes the process adopted in implementing a successful ERAS protocol in kidney transplant recipients and the outcomes of the protocol that has resulted in significantly reduced patient stay with no increase in complications or surgery-related readmissions.

Methods

As a preamble to the development of the protocol, it was recognized that reperfusion injury is an unavoidable consequence of deceased donor kidney transplantation.[14] The degree of injury to a large part relates to the effects of the cytokine storm in the process of brainstem death or tissue hypoxia in donation after circulatory death and live donation. It manifests as a period of acute tubular necrosis (ATN) following transplantation.[15] Fluid loading does not alter the course of established ATN.[16] Fluid overloaded patients have a poorer microcirculation in end organs secondary to interstitial oedema that exacerbates ATN in the transplanted kidney, impairs wound healing as well as prolongs ileus and delays return of gut function.[17,18] CVP measurement is often inaccurate and is a poor marker of filling status in most cases.[19,20] Patients undergoing transplantation often have prolonged starvation before surgery and dehydration in preparation for transplantation because of preoperative dialysis.[21]

There was a preconceived notion that discharge on post-operative day 4 was too early both in the minds of healthcare professionals caring for the patient and the patient themselves. There were valid anxieties around whether patients would be able to know their drugs and manage themselves.

ERAS protocol for renal transplant patients

Following institutional review, an ERAS protocol was developed and implemented in the renal transplant unit at Adelaide from July 2017. The protocol was constructed to be delivered across three phases including preoperative work up, and perioperative and post-operative periods. The key steps unique to the protocol are described in Table 1. The graded exercise and recovery plan used in our recipients are described in Table 2.

Data analysis

Variables of interest to assess the impact of the implementation of the ERAS protocol were length of stay, rates of delayed graft function and post-operative complications, and readmission rates. The outcome variables of interest were measured before protocol development and

Table 1 Elements of the ERAS protocol for kidney transplant

Preoperative	Perioperative	Post-operative
Oral and written information at the time of listing Smoking cessation Maintenance of weight and blood pressure Use of incentive spirometer	Carbohydrate loading and oral fluids till 4 h before surgery TED stockings Prophylactic antibiotics Intraoperative insertion of transversus abdominis plane catheter with continuous infusion of 0.2% levobupivacaine for 48 h at 5 mL/h Fentanyl patient-controlled analgesia with early wean in 24–36 h Judicious use of metarminol to keep mean arterial pressure >75 mmHg at the time of reperfusion – not chase a CVP target Goal-directed fluid therapy with the aim to not go up on dry weight by >3 kg achieved by replacing volume for volume of urine output with crystalloid and up to 1300 mL for average weight patient of oral fluids – step away from chasing a CVP target Early institution of oral feeds after recovery rather than waiting for ileus to resolve	Goal-directed fluid therapy Early mobilization – nurse monitored Incentive spirometer Early removal of drains and catheter Change to casual clothes from hospital clothes on day 4 to enable a mindset change in recipient Education regarding drugs and doses, and outpatient review protocol Post-discharge outpatient clinic review with surgeons and physicians in 24 h with subsequent visits tailored to patient needs

CVP, central venous pressure; ERAS, enhanced recovery after surgery; TED, thromboembolism deterrent.

Table 2 Graded exercise and recovery plan in kidney transplant recipients on the ERAS protocol

POD 1	POD 2	POD 3	POD 4
Stop calf compression Prophylactic heparin Maintain weight gain to within 3–5 kg of dry weight Immunosuppression Carbohydrate drinks Light diet chewing gum till on general diet Sit out of bed for all meals Hourly coughing and deep breathing Remove Foley catheter if anuric Continue TAP elastomeric device 20 m first walk 40 m second walk Sit out in chair for at least 4 h	General diet Remove TAP catheter Immunosuppression Hourly deep breathing exercises Stop PCA and oral analgesia 60 m first walk 60 m second walk At least 6 h in chair	General diet Immunosuppression Hourly deep breathing exercises 60 m first walk 60 m second walk 60 m third walk 60 m fourth walk At least 6 h in chair	General diet Immunosuppression Hourly deep breathing exercises 100 m first walk 100 m second walk 100 m third walk 100 m fourth walk Post-transplant education + review plan All drains removed Foleys connected to leg bag if polyuric Discharge if safe

ERAS, enhanced recovery after surgery; PCA, patient controlled analgesia; POD, post-operative day; TAP, transversus abdominis plane.

implementation (January 2016 to June 2017) and after ERAS protocol implementation (July 2017 to December 2018). The two groups were then compared to analyse the impact of implementation of the ERAS protocol in the renal transplant unit.

Data for the study were obtained from a prospectively maintained departmental database. This database was maintained by the registrars and fellows in the unit with periodical consultant review for accuracy. The study included all adult patients who underwent isolated renal transplant during the time period. Patients who underwent additional transplants (dual kidney/pancreas/liver) and paediatric transplants were excluded. A total of 200 consecutive patients who met the inclusion criteria and underwent renal transplantation at the Royal Adelaide Hospital from January 2016 to December 2018 (3 years) were included in the analysis. The first group comprised of 100 consecutive patients who underwent renal transplantation from January 2016 to June 2017 prior to the development of the ERAS protocol. The second group comprised of 100 consecutive patients who underwent renal transplantation under the ERAS protocol from July 2017 to December 2018. The study design was approved by the institutional ethical review board and informed consent for data sharing was obtained from patients included in the study. Measures of length of stay, complications and infections were obtained from the renal transplant database. Important independent factors, including patient demographics and comorbid diseases, were also obtained from the renal transplant database. Demographic factors obtained were age at transplant and gender. Comorbid factors noted were the presence or absence of hypertension, diabetes, cardiac disease and duration of pre-transplant dialysis. Differences between the two groups were tested with Mann–Whitney, chi-squared test, *t*-test, and one-way analysis of variance, where appropriate.

Results

Table 3 demonstrates the patient characteristics in the two patient cohorts. No significant differences were found in the baseline characteristics of patients in the two groups.

Table 3 Baseline data of renal transplant patients included in the two groups

	Patients on ERAS *n* = 100	Patients not on ERAS *n* = 100	*P*-value
Age (years), mean (SD)	51.4 (14.2)	53.1 (14.3)	0.409
Sex, *n* (%)			
Male	54 (54)	64 (64)	0.152
Female	46 (46)	36 (36)	0.152
Comorbidities, *n* (%)			
Diabetes	32 (32)	31 (31)	0.865
Hypertension	72 (72)	69 (69)	0.762
Previous transplant, *n* (%)	12 (12)	13 (13)	0.698
Previous intra-abdominal surgery, *n* (%)	7 (7)	6 (6)	0.575
Length of pre-transplant dialysis (months), mean (SD)	18.8 (7.2)	19.2 (6.5)	0.311
Donor details, *n* (%)			
Living donor	19 (19)	22 (22)	0.601
DCD	25 (25)	16 (16)	0.116
BDD	56 (56)	62 (62)	0.391
Delayed graft function, *n* (%)	31 (31)	36 (36)	0.456
Living donor	2 (10.5)	1 (4.5)	0.476
DCD	10 (40)	13 (81.3)	0.009*
BDD	19 (33.9)	22 (35.5)	0.861
Total ischaemic time (h), mean (SD)	9.6 (4.5)	10.7 (6.4)	0.171
Living donor	4.7 (2.5)	3.7 (0.5)	0.092
DCD	10.5 (3.9)	14.1 (5.5)	0.022*
BDD	10.9 (4.2)	12.4 (6.0)	0.147
Length of hospitalization (days), median (range)	5 (3–16)	7 (5–14)	<0.001*
Living donor	4 (3–13)	7.5 (6–9)	<0.001*
DCD	5 (3–11)	8 (5–10)	<0.001*
BDD	5 (3–16)	7 (6–14)	<0.001*
Readmissions, *n* (%)	11 (11)	9 (9)	0.544
Complications, *n* (%)			
Overall	12 (12)	11 (11)	0.769
Clavien 1 and 2	4 (4)	5 (5)	0.542
Clavien >2	8 (8)	6 (6)	0.326
1-year patient survival, *n* (%)	98 (98)	97 (97)	NA
1-year graft survival, *n* (%)†	96 (98)	94 (97)	NA

*Statistically significant. †Patients who died in the first year following transplantation were excluded from the analysis. BDD, brain dead donor; DCD, donor after cardiac death; ERAS, enhanced recovery after surgery.

Overall, rates of delayed graft function were similar between the two groups. Mean total ischaemic times were also similar across the two groups. However, subgroup analysis revealed significantly higher delayed graft function rates in the group of patients transplanted with donor after cardiac death (DCD) kidneys in the pre-ERAS group (80% versus 40%, $P = 0.009$). Not surprisingly, the mean total ischaemic times were also significantly higher in this subgroup of patients (14.1 versus 10.5 h, $P = 0.022$). Univariate regression analysis was performed using ischaemic times as covariates, delayed graft function as the dependent variable and age, sex, ERAS group and the type of donor kidney (living, DCD or brain dead donor). Only ischaemic times were found to be predictive of delayed graft function ($P < 0.0001$). More importantly, patients on the ERAS protocol were not found to be at an increased risk of delayed graft function ($P = 0.341$).

The median length of stay for patients on the ERAS protocol was 5 days (range 3–16). This was 2 days shorter than the median length of stay for patients not on the ERAS protocol (7 days; range 5–14, $P < 0.001$). This statistically significant difference in length of stay was consistent across all donor subgroups (living donor, DCD and brain dead donor). More importantly, 79% of the patients on the ERAS protocol were discharged on post-operative day 4.

The readmission rates were similar in the two groups (11% for patients on ERAS versus 9% for patients not on ERAS). The 1-year patient and graft survival were not significantly different in the two groups.

Discussion

Our experience in implementing the ERAS protocol for the perioperative managements of renal transplant patients has resulted in a significantly reduced length of hospitalization. The goal-directed fluid management component of the implemented ERAS protocol did not result in any significant increase in the rates of delayed graft function. The implementation of the ERAS protocol did not result in any increase in the 90-day complication rate in our study. Although a formal cost impact analysis has not been performed, the ERAS protocol achieved the objective of a protocol-driven day 4 discharge in 79% of patients enrolled under the ERAS pathway. As the readmission and complication rates did not change post implementation of ERAS, we believe that a protocol-driven shorter length of stay did contribute to significant cost savings following implementation of the ERAS protocol in renal transplantation.

Ours is the first Australian study that demonstrates a significant reduction in in-patient stay across all groups who received a kidney transplant. While data around ERAS in kidney transplantation is sparse and only just emerging, our data correlate well with the other published studies of Espino *et al.*[22] who described that the length of stay was shorter by 1 day among ERAS compared to a historic cohort. Ojogho *et al.*[23] described a median length of stay of 48 h in patients receiving living donor and deceased donor kidneys using an ERAS protocol in an abstract format.

Our experience has been different to that of Kruszyna *et al.*[24] in Poland who demonstrated a median hospital stay of 10 days (range 6–46), which is possibly related to their practice of managing patients with delayed graft function in the hospital as opposed to our practice of managing them in the community. However, they had a readmission rate of 8.9% that is similar to our data.

In 1998, Holtzman *et al.*[6] first demonstrated the effects of clinical pathways for renal transplantation on patient outcomes and length of stay. The authors concluded that the development and use of a clinical pathway for deceased donor renal transplant patients was associated with a significant decline in length of stay, complications and infections. More than a decade later, Seawright and Taylor[7] demonstrated that clinical pathways offer an opportunity for maximizing coordination of care among transplant team members, decreasing the length of stay for deceased donor renal transplant patients and minimizing exacerbations of costs for kidney transplant populations. While both these studies evaluated the effects of clinical pathways in the perioperative management of renal transplant recipients, it is important to note that these clinical pathways were not developed on the principles of the ERAS guidelines. These institution-based clinical pathways were developed based on the logistics prevalent in respective institutions and hence could not necessarily be implemented across other renal transplant units. We believe our protocol is easy to implement and adheres to the essential principles of ERAS.

Limitations

The study does have limitations inherent to its design. We have compared outcomes before and after implementation of a clinical pathway (ERAS protocol) and hence lacked contemporary controls for comparison of complication rates and rates of delayed graft function. A formal cost impact analysis was not performed for reasons outlined previously. Further multicentre trials will address whether the conclusions and cost savings are truly justified.

Conclusions

An ERAS protocol for renal transplant patients is feasible. Our data show that implementation of an ERAS protocol in a renal transplant unit resulted in reduction in post-operative length of stay with no increase in the overall complication and readmission rates, thereby reducing hospitalization costs. Goal-directed fluid therapy should be a significant component of an ERAS protocol in renal transplantation and our study demonstrates that this can be achieved safely with no significant increase in complication rates and/or rates of delayed graft function.

Conflicts of interest

None declared.

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