A Randomized, Double-Blind Comparison of Lactated Ringer's Solution and 0.9% NaCl During Renal Transplantation

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Normal saline (NS; 0.9% NaCl) is administered during kidney transplantation to avoid the risk of hyperkalemia associated with potassium-containing fluids. Recent evidence suggests that NS may be associated with adverse effects that are not seen with balanced-salt fluids, e.g., lactated Ringer's solution (LR). We hypothesized that NS is detrimental to renal function in kidney transplant recipients. Adults undergoing kidney transplantation were enrolled in a prospective, randomized, double-blind clinical trial of NS versus LR for intraoperative IV fluid therapy. The primary outcome measure was creatinine concentration on postoperative Day 3. The study was terminated for safety reasons after interim analysis of data from 51 patients. Forty-eight patients underwent living donor kidney transplants, and three patients underwent cadaveric donor transplants. Twenty-six patients received NS, and 25 patients received LR. There was no difference between groups in the primary outcome measure. Five (19%) patients in the NS group versus zero (0%) patients in the LR group had potassium concentrations >6 mEq/L and were treated for hyperkalemia ($P = 0.05$). Eight (31%) patients in the NS group versus zero (0%) patients in the LR group were treated for metabolic acidosis ($P = 0.004$). NS did not adversely affect renal function. LR was associated with less hyperkalemia and acidosis compared with NS. LR may be a safe choice for IV fluid therapy in patients undergoing kidney transplantation.

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Normal saline (NS) or potassium-free fluids are recommended for IV fluid therapy during kidney transplantation (1–4). A survey of U.S. kidney transplant centers revealed that NS and NS-based solutions are the preferred IV fluids for administration during kidney transplant surgery (5).

What is the basis for the use of NS in patients with renal failure, in particular in kidney transplant recipients? Theoretically, the administration of large volumes of potassium-containing fluids such as lactated Ringer's solution (LR) might cause hyperkalemia in patients with chronic renal failure and end-stage renal disease (ESRD). This concern was the most frequently cited reason for the use of NS during kidney transplantation in a one survey (5).

Evidence suggests that balanced salt-based solutions such as LR may offer clinical benefits over NS and NS-based solutions. Although controversial, the administration of large volumes of NS is associated with the development of hyperchloremic metabolic acidosis (6–9), which may theoretically cause hyperkalemia through an extracellular shift of potassium ions (10). Infusion of NS has also been associated with effects such as subjective mental changes and abdominal discomfort in healthy volunteers (8). The use of balanced salt-based solutions in elderly surgical patients may be associated with better splanchnic perfusion than NS-based solutions (9). Intriguing differences in indices of renal function have also been suggested in studies of patients treated with NS-based and balanced salt-based solutions (7,8,11,12).

Therefore, in view of these data and the predominant use of NS in kidney transplant recipients, we designed a randomized, blinded clinical trial to explore the effects of NS administration on graft function as reflected by the serum creatinine concentration on postoperative day (POD) 3. In addition, we aimed to

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Table 1. Demographic and Perioperative Variables

	NS (n = 26)	LR (n = 25)	P-value
Age, y	44 ± 13	44 ± 11	ns
Sex, No. (%) men	17 (65)	15 (60)	ns
Weight, kg	72 ± 14	75 ± 18	ns
Living donor, No. (%)	25 (96)	23 (92)	ns
Patients requiring preoperative hemodialysis, No. (%)	18 (69)	13 (52)	ns
Volume of study fluid, L	6.1 ± 1.2	5.6 ± 1.4	ns
Operating room time, h	5.6 ± 1.1	5.6 ± 1.3	ns
Warm ischemia time, min	34 ± 13	34 ± 9	ns
Patients receiving intraoperative dopamine, No. (%)	23 (85)	20 (80)	ns
Blood loss, mL	309 ± 162	310 ± 190	ns
Patients transfused, No. (%)	3 (11)	2 (8)	ns
Baseline serum creatinine, mg/dL	7.0 ± 2.7	8.0 ± 2.6	ns
Baseline serum potassium, mEq/L	4.2 ± 0.7	4.5 ± 0.5	ns
Peak intraoperative serum potassium, mEq/L	5.1 ± 1.1	5.1 ± 0.6	ns
End of surgery serum potassium, mEq/L	4.5 ± 0.8	4.6 ± 0.6	ns
Baseline pH	7.39 ± 0.05	7.36 ± 0.08	ns
Lowest intraoperative pH	7.26 ± 0.08	7.33 ± 0.07	0.001
End of surgery pH	7.28 ± 0.07	7.37 ± 0.07	<0.0001
End of surgery serum chloride, mEq/L	111 ± 4	106 ± 4	<0.0001
Baseline serum bicarbonate, mEq/L	22 ± 5	22 ± 6	ns
Lowest intraoperative serum bicarbonate, mEq/L	16 ± 3	19 ± 4	0.004
End of surgery serum bicarbonate, mEq/L	18 ± 3	21 ± 4	0.007

Data are mean ± SD unless otherwise stated.
NS = 0.9% NaCl (normal saline) group; LR = lactated Ringer's solution group.

determine the safety of the administration of LR to patients undergoing kidney transplantation through secondary end-points, including the serum potassium concentration and acid-base balance.

Methods

The study was approved by the IRB of the Columbia Presbyterian Hospital of the New York Presbyterian Hospital. After written, informed consent was obtained, eligible patients undergoing kidney transplantation were randomized in a prospective, double-blind fashion to receive either NS (Table 1) or LR (Table 1) for intraoperative fluid replacement during surgery for kidney transplantation. Randomization was achieved by computer generation of random number lists, in blocks of four, and a closed envelope technique. Separate randomization lists were compiled for the two surgeons who performed all kidney transplant operations. Exclusion criteria were age <18 yr old, a religious or ethical prohibition from the receipt of blood or blood products, or serum potassium level >5.5 mEq/L before surgery.

General anesthesia was induced with a combination of IV midazolam (2–5 mg), fentanyl (1–3 μg/kg), and propofol (1–3 mg/kg). Anesthesia was maintained using isoflurane in air/oxygen and fentanyl, with muscle relaxation achieved using IV intermediate-acting nondepolarizing neuromuscular blockers. Standard monitoring, according to the recommendations of the American Society of Anesthesiologists, was used. It is routine at our institution to insert a radial arterial cannula after the induction of anesthesia for monitoring of systemic arterial blood pressure and for blood sampling during surgery. Additional monitoring (e.g., central venous pressure monitoring) was at the discretion of the physician caring for the patient.

For living donor transplantation, the left kidney was procured from living donors via a laparoscopic approach unless otherwise indicated. The donor kidney was flushed with ice cold LR before transfer to the operating room for implantation into the recipient. Kidneys harvested from cadaveric donors were preserved with either Euro-Collins or University of Wisconsin solution for the duration of transfer to our center. The donor kidney was implanted in the right or left retroperitoneal space of the recipient with vascular anastomoses to the right or left external or internal iliac artery and vein. A dopamine infusion was commenced at 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (this infusion was discontinued on arrival to the postanesthesia care unit). Ureteroneocystostomy was performed by the established Leadbetter-Politano (13) or Lich-Gregoir technique (14).

Preoperative and postoperative immunosuppressive therapy was administered according to institutional guidelines. Briefly, all patients received triple therapy comprising tapering-dose steroids, a calcineurin inhibitor, and either mycophenolate mofetil or sirolimus. The clinician caring for the patient determined the precise combination and dose of medications.

Our goal was to conduct a clinical effectiveness study, which means that we wanted to assess the impact of the interventions in actual clinical practice. Hence, we did not impose an algorithm for the administration of study fluid, blood, or blood products. Study fluid was used for all intraoperative fluid replacement with the exception of blood or blood products that were administered if clinically indicated (as determined by the physician caring for the patient). The investigational pharmacy completely covered each bag of study fluid with opaque tape to ensure blinding of all study personnel and clinicians to the fluid type.

Clinicians titrated the administration of study fluid to whatever clinical end-points they routinely used. At the end of surgery, after application of the surgical dressing, study fluid was discontinued. Postoperative IV fluid therapy was the same for all patients and was administered according to the following institutional protocol. Urine output was replaced (milliliter for milliliter) with an IV infusion of dextrose 5%/0.45% NaCl + 20 mEq/L of sodium bicarbonate/L. For diabetic patients, fluid replacement routinely consisted of alternating liters of dextrose 5%/0.45% NaCl and 0.45% NaCl + 20 mEq/L of sodium bicarbonate. All patients received an additional 50 mL/h of either of these two solutions when appropriate.

Blood was sampled at baseline (after insertion of the intraarterial cannula) and every 30 min for the duration of surgery for measurement of serum potassium concentration and acid-base balance (i-STAT® Portable Clinical Analyzer, i-STAT Corp, East Windsor, NJ). The clinician caring for the patient was informed if serum potassium concentration exceeded 6.5 mEq/L but was otherwise blinded to study measurements. The clinician caring for the patient could draw blood samples to measure serum potassium concentration and acid-base variables at any time, independently of the study protocol. The treatment for hyperkalemia, metabolic acidosis, and any other metabolic derangements was at the discretion of the clinician.

The primary outcome measure was the serum creatinine concentration on POD 3. This time-point was chosen because this is the minimum postoperative length of stay after kidney transplantation at our institution. Secondary outcomes included postoperative urine output, creatinine clearance, and requirement for dialysis, along with the incidence of biopsy-proven rejection and graft loss. Other secondary outcomes included intraoperative acid-base balance, intraoperative potassium concentration, blood loss and transfusion requirements, and postoperative hospital length of stay.

Data are presented as mean ± SD for continuous variables and as percentages for categorical variables. All data were tested for normality using the method of Kolmogorov-Smirnov. Differences in continuous variables between the two groups were tested using *t*-tests or Mann-Whitney tests as appropriate. Differences between categorical variables were tested using Fisher's exact test. A P value ≤ 0.05 (two-tailed) was considered to be significant.

Sample size was calculated to ensure sufficient statistical power to detect expected differences between fluids with respect to the primary outcome. A sample size of 100 in each group was calculated to have at least 80% power to detect a difference in the mean postoperative serum creatinine of 0.3 mg/dL given a common standard deviation of 0.6 mg/dL using a two-group *t*-test with a 0.05 two-sided significance. A planned interim safety analysis was conducted after 50 patients had been studied. This analysis of safety data revealed statistically significant differences in safety related end-points (serum potassium concentrations and acid-base balance) in favor of the experimental therapy (LR). Therefore, it was decided to stop study enrollment at this time.

Results

Fifty-four patients were enrolled and randomized to receive either NS or LR. Three patients were excluded after randomization because of a preoperative serum potassium level >5.5 mEq/L. There were 25 patients in the LR group and 26 patients in the NS group. All 51 patients were included in the final analysis. Of note, a separate analysis of the data, which excluded the cadaveric transplant recipients, revealed no difference in overall study results. The study groups were similar with regard to demographic factors (Table 1). Both groups received similar volumes of study fluid during surgery, and no patient received colloid during surgery (Table 1). Seven units of packed red blood cells were administered in the NS group versus 3 U in the LR group.

Serum creatinine on POD 3 was 2.3 ± 1.8 mg/dL in the NS group and 2.1 ± 1.7 mg/dL in the LR group ($P = 0.7$). Graft loss occurred in two patients in the NS group and in one patient in the LR group. Episodes of biopsy-proven rejection occurred in four patients who received NS and in two patients who received LR. Serum creatinine was similar in both groups at all other time-points, and there were no significant differences in any other markers of renal function (Table 2). Median (range) postoperative length of stay was 6.3 (3–27) days in the NS group and 5.3 (3–13) days in the LR group ($P = 0.6$).

Peak intraoperative potassium concentration was 5.1 ± 0.6 mEq/L in the NS group and 5.1 ± 1.1 mEq/L in the LR group. The serum potassium concentration exceeded 6.0 mEq/L in 5 of 26 (19%) patients in the NS group and in no patients in the LR group ($P = 0.05$)

Table 2. Postoperative Renal Function

	NS (n = 26)	LR (n = 25)
4-h urine output, L	1.6 ± 1.6	2.1 ± 1.5
24-h creatinine clearance, mL/min	81 ± 41	94 ± 30
Postoperative Day 3 serum creatinine, mg/dL	2.3 ± 1.8	2.1 ± 1.7
1-wk serum creatinine, mg/dL	1.9 ± 1.2	1.6 ± 1.3
6-mo serum creatinine, mg/dL	1.5 ± 0.6	1.5 ± 0.4
Patients requiring dialysis, No. (%)	2 (8)	1 (4)

Data are mean ± SD unless otherwise stated.
NS = 0.9% NaCl (normal saline) group; LR = lactated Ringer's solution group.

(Figs. 1, A and B). All five patients in the NS group with serum potassium concentrations larger than 6 mEq/L were treated for hyperkalemia. The serum potassium concentrations of the patients treated for hyperkalemia were 6.2 mEq/L, 6.6 mEq/L, 7.1 mEq/L, 7.2 mEq/L, and 7.7 mEq/L.

Patients randomized to receive NS exhibited more metabolic acidosis during surgery than patients who were randomized to receive LR (Table 2). Eight (31%) patients in the NS group received sodium bicarbonate for the treatment of metabolic acidosis in comparison to no patients in the LR group (P = 0.004). Within-group analysis of the NS group revealed that mean ± SD lowest intraoperative blood pH in the patients who were treated for metabolic acidosis was 7.20 ± 0.09 versus 7.28 ± 0.06 in patients who were not treated for metabolic acidosis (P = 0.01). The mean ± SD lowest intraoperative blood pH in the LR group was 7.33 ± 0.07. Serum chloride concentration at the end of surgery was 111 ± 4 mEq/L in the NS group versus 106 ± 4 in the LR group ($P < 0.0001$).

Of note, cumulative postoperative urine output was larger (Fig. 2A) and postoperative serum creatinine was lower (Fig. 2B) in patients in the NS group who received treatment for acidosis compared with patients who received no treatment for acidosis. The serum chloride concentration in patients who received bicarbonate was 113 ± 4 mEq/L versus 110 ± 4 mEq/L in patients who did not receive bicarbonate (P = 0.1).

Urine flow rate (range) in the first 4 h after revascularization of the donor kidney was 400 ± 370 (130–1050) mL/h in patients treated for hyperkalemia and 370 ± 410 (0–1520) mL/h in NS-treated patients with no hyperkalemia (P = 0.9). One patient received treatment for both hyperkalemia and metabolic acidosis. One patient in the NS group who received a transfusion of packed red blood cells was treated for hyperkalemia, and no patients who received blood transfusions were treated for metabolic acidosis.

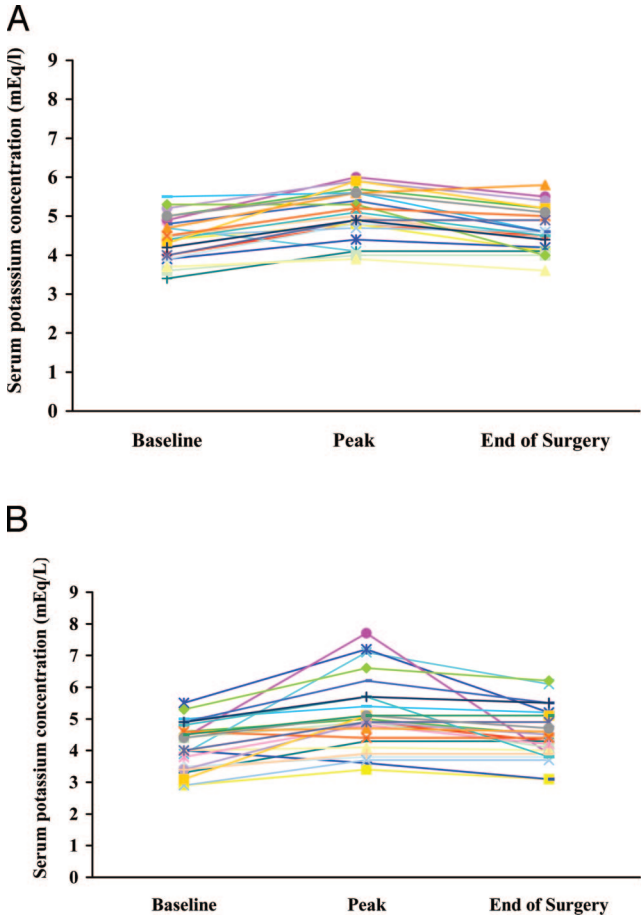

Figure 1. Perioperative potassium concentrations in (A) LR- and (B) NS-treated patients. NS = 0.9% NaCl; LR = lactated Ringer's solution

Discussion

This is the first study that has compared the effects of NS and LR as IV fluid therapy in kidney transplant recipients. There was no significant difference between groups in the primary outcome measure of the serum creatinine on POD 3. The study was terminated because of concerns for patient safety. However, our results strongly suggest that the administration of large volumes of LR to patients undergoing kidney transplantation is safe and that LR may be superior to NS for IV fluid therapy in this setting. These results have important implications for patient management because more than 10,000 kidney transplants are performed annually in the United States, with many thousands more conducted world wide each year (15).

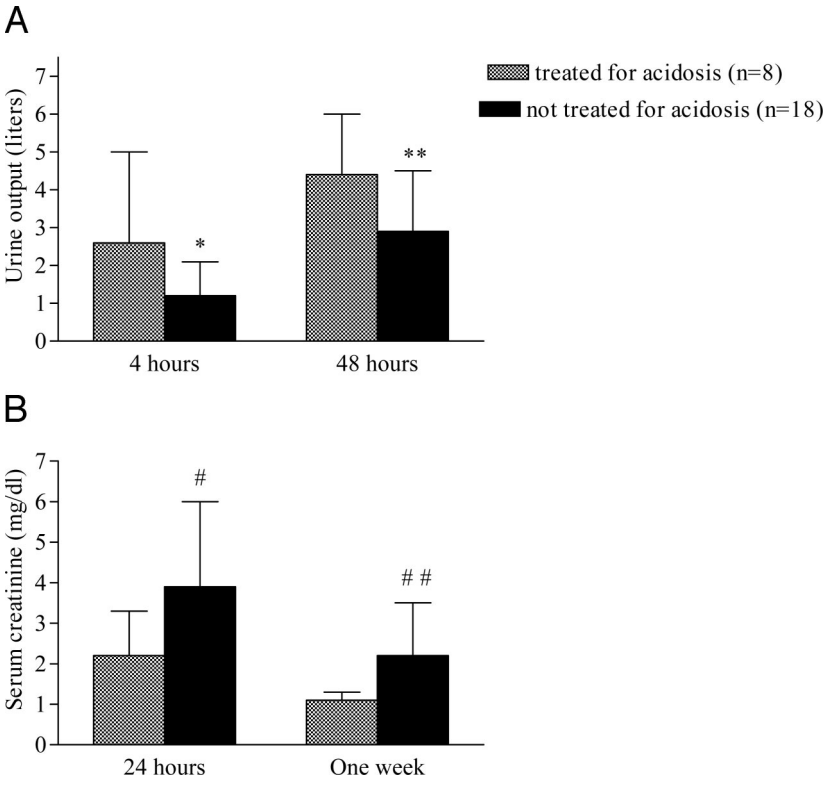

Figure 2. Postoperative urine output (A) and serum creatinine (B) in patients treated for acidosis and in patients not treated for acidosis in the NS group. NS = 0.9% NaCl. (A) *$P = 0.04$ vs patients treated for acidosis; **$P = 0.05$ vs patients treated for acidosis. (B) #$P = 0.0.008$ vs patients treated for acidosis; ##$P = 0.02$ vs patients treated for acidosis.

The development of metabolic acidosis in association with the administration of large volumes of NS is a well-recognized phenomenon (6,8,16,17). In our study, metabolic acidosis requiring treatment occurred only in patients who received NS. The mechanism for this metabolic derangement has been attributed to the dilution of bicarbonate by large volumes of buffer-free fluid (18). An alternative explanation is that the hyperchloremia caused by NS causes a decrease in the strong ion difference of the blood with consequent development of metabolic acidosis (19). Regardless of the mechanism by which it occurs, the acidosis may be of particular significance in patients with ERSD and those undergoing kidney transplantation. These patients may have preexisting abnormalities of acid-base balance. Therefore, the administration of large volumes of NS or NS-based fluid may cause worsening of acidosis, complicate interpretation of acid-base data, and, at worst, result in unnecessary interventions, particularly if the etiology goes unrecognized. The choice of balanced salt-based solutions such as LR rather than NS-based solutions for IV fluid therapy averts the risk of IV fluid-induced hyperchloremic metabolic acidosis.

Abnormalities of electrolyte balance are common in patients with renal failure. Indeed, hyperkalemia is an indication for the institution of renal replacement therapy. An important aspect of the management of patients with renal disease is to minimize the risk of the development of hyperkalemia. Therefore, potassium-containing fluids such as LR have been avoided in patients with renal failure. In our study, no patient who received LR required treatment for hyperkalemia. However, it cannot be concluded from our findings that hyperkalemia never occurs in patients who receive LR during kidney transplant surgery. Hyperkalemia may occur, for example, during the rapid infusion of large volumes of LR. However, our findings support our hypothesis that the risk of hyperkalemia may be more theoretical than real in patients undergoing uncomplicated kidney transplant surgery who are treated with potassium-containing, balanced salt-based solutions. The mechanism for the development of hyperkalemia in NS-treated patients is presumably through an extracellular shift of potassium caused by acute changes in blood hydrogen ion concentration, which occurs in association with hyperchloremic metabolic acidosis (10).

IV fluid composition may have an impact on renal function, although this point is controversial (20). A few small studies have suggested that the administration of NS may be detrimental to renal function (6,8,9,11,21,22). In our study, small differences in postoperative markers of renal function were observed, but these differences were not clinically relevant and did not achieve statistical significance. However, within-group analysis of data from the NS group revealed that postoperative urine output was larger in

patients who were treated with sodium bicarbonate for metabolic acidosis. In addition, serum creatinine was lower in these patients, and this effect was apparent at one week after surgery. The significance of this finding is unclear.

Previous studies have suggested that hyperchloremia may be the mechanism by which large-volume transfusion of NS may adversely affect kidney function (9,21,23). Our findings do not support this suggestion because the serum chloride concentrations did not differ between the patients who received bicarbonate and those who did not. It is possible that the larger urine output and lower serum creatinine concentration in patients who received sodium bicarbonate may be explained by the volume expanding properties of concentrated sodium bicarbonate. Alternatively, the differences in renal function may suggest that the deleterious effects of NS are mediated through metabolic acidosis and acidemia. Indeed, in two studies of surgical patients treated with large volumes of NS and, in many cases, sodium bicarbonate, NS-treated subjects did not exhibit inferior urine output and serum creatinine concentrations compared with patients who received LR (17,24).

The study is subject to a number of limitations. For logistical reasons only, 3 cadaveric donor kidney recipients were enrolled, with 48 of the 51 study patients undergoing living donor transplantation. Therefore, our results are strictly applicable only to patients undergoing living donor transplants. Notably, 43% of kidneys transplanted annually in the United States are from living donors (15). This study is also limited by the fact that it was a single-center investigation. Factors such as surgical technique and the duration of surgery may differ among institutions. However, outcomes after kidney transplantation at the Columbia Presbyterian Hospital of the New York Presbyterian Hospital are similar to outcomes in patients treated at other transplant centers in the United States (15).

Another possible criticism of the study design is the lack of an algorithm for study fluid administration and for the treatment of acidosis and hyperkalemia. We allowed the clinician attending each patient to determine the rate and volume of fluid administered as well as the decision to treat metabolic acidosis because this more accurately reflects day-to-day clinical practice. In addition, because this was a double-blind study, there was no possibility of bias on any clinician's part with regard to the decision to treat acidosis or hyperkalemia. Finally, it is possible that some patients may have received diuretics in the days after surgery, and this may have influenced postoperative urinary output. It seems unlikely that diuretic-induced changes in urine output would have masked an effect of NS on urine output.

Most patients undergoing kidney transplantation in the United States receive NS for IV fluid therapy during surgery because of the risk of hyperkalemia (5). This is the first study to compare the effects of NS and LR in patients with ESRD. Our findings demonstrate that NS is not detrimental to renal function in these patients. In addition, the administration of large volumes of LR to patients undergoing kidney transplantation seems safe and may be superior to NS for IV fluid therapy in these patients because it avoids the risk of metabolic acidosis and clinically significant hyperkalemia.

References

1. Belani KG, Palahniuk RJ. Kidney transplantation. Int Anesthesiol Clin 1991;29:17–39.
2. Alfrey EJ, Dafoe DC, Haddow GR. Liver/kidney transplantation. In: Jaffe RA, Samuels SI, eds. Anesthesiologist's manual of surgical procedures. Philadelphia: Lippincott Williams & Wilkins, 1999;487–92.
3. Grant IS. Intercurrent disease and anaesthesia. In: Aitkenhead AR, Smith G, eds. Textbook of anaesthesia. Edinburgh, Scotland: Churchill Livingston, 1994:645–76.
4. Yao FF. Kidney transplant. In: Yao FF, Artusio JF, eds. Anesthesiology: problem-oriented patient management. 3rd ed. Philadelphia: J.B. Lippincott, 1993:446–64.
5. O'Malley CMN, Frumento RJ, Bennett-Guerrero E. Intravenous fluid therapy in renal transplant recipients: results of a U.S. survey. Transplant Proc 2002;34:3142–5.
6. Scheingraber S, Rehm M, Sehmisch C, Finsterer U. Rapid saline infusion produces hyperchloremic acidosis in patients undergoing gynecologic surgery. Anesthesiology 1999;90:1265–70.
7. Reid F, Lobo DN, Williams RN, et al. (Ab)normal saline and physiological Hartmann's solution: a randomized double-blind crossover study. Clin Sci (Lond) 2003;104:17–24.
8. Williams EL, Hildebrand KL, McCormick SA, Bedel MJ. The effect of intravenous lactated Ringer's solution versus 0.9% sodium chloride solution on serum osmolality in human volunteers. Anesth Analg 1999;88:999–1003.
9. Wilkes NJ, Woolf R, Mutch M, et al. The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid-base and electrolyte status and gastric mucosal perfusion in elderly surgical patients. Anesth Analg 2001;93:811–6.
10. Halperin ML, Kamel KS. Potassium. Lancet 1998;352:135–40.
11. Gan TJ, Wright D, Robertson C, et al. Randomized comparison of the coagulation profile when hextend or 5% albumin is used for intraoperative fluid resuscitation. Anesthesiology 2001;95: A193.
12. Lang K, Boldt J, Suttner S, Haisch G. Colloids versus crystalloids and tissue oxygen tension in patients undergoing major abdominal surgery. Anesth Analg 2001;93:405–9.
13. Politano VA, Leadbetter WF. An operative technique for correction of vesicoureteral reflux. J Urol 1958;79:932–4.
14. Lich RJ, Howerton LW, Davis LA. Recurrent urosepsis in children. J Urol 1961;86:554–8.
15. 2003 Annual Report of the U.S. Scientific Registry of Transplant Recipients and the Organ Procurement and Transplantation Network: Transplant Data 1993–2002. Department of Health and Human Services, Health Resources and Services Administration, Office of Special Programs, Division of Transplantation, Rockville, MD; United Network for Organ Sharing, Richmond, VA; University Renal Research and Education Association, Ann Arbor, MI, 2003.
16. McFarlane C, Lee A. A comparison of Plasmalyte 148 and 0.9% saline for intra-operative fluid replacement. Anaesthesia 1994; 49:779–81.

17. Waters JH, Gottlieb A, Schoenwald P, et al. Normal saline versus lactated Ringer's solution for intraoperative fluid management in patients undergoing abdominal aortic aneurysm repair: an outcome study. Anesth Analg 2001;93:817–22.
18. Prough DS, White RT. Acidosis associated with perioperative saline administration: dilution or delusion? Anesthesiology 2000;93:1167–9.
19. Kellum JA. Determinants of blood pH in health and disease. Crit Care 2000;4:6–14.
20. Cittanova ML, Leblanc I, Legendre C, et al. Effect of hydroxyethylstarch in brain-dead kidney donors on renal function in kidney-transplant recipients. Lancet 1996;348:1620–2.
21. Gan TJ, Bennett-Guerrero E, Phillips-Bute B, et al. Hextend, a physiologically balanced plasma expander for large volume use in major surgery: a randomized phase III clinical trial—Hextend Study Group. Anesth Analg 1999;88:992–8.
22. Moretti E, Robertson K, Habib E-M, Gan T. Intraoperative colloid administration reduces postoperative nausea and vomiting and improves postoperative outcomes compared with crystalloid administration. Anesth Analg 2003;96:611–7.
23. Wilcox CS. Regulation of renal blood flow by plasma chloride. J Clin Invest 1983;71:726–35.
24. Boldt J, Haisch G, Suttner S, et al. Are lactated Ringer's solution and normal saline solution equal with regard to coagulation? Anesth Analg 2002;94:378–84.