Sugammadex use in patients with end-stage renal disease: a historical cohort study

Utilisation de sugammadex chez les patients atteints d'insuffisance rénale terminale : une étude de cohorte historique

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Abstract

Purpose While sugammadex (SGX) is not approved for use in patients with end-stage renal disease (ESRD), its administration in this patient population has been reported. We designed the current study to review all instances of patients with ESRD receiving SGX and to describe their clinical outcomes.

Methods This is a historical cohort study of 219 patients with chronic kidney disease stage 5 who received SGX in one of three hospital locations within the same academic health system. Data were collected between 7 March 2016 and 1 August 2019 and included demographics, notable events from the anesthesia records, and postoperative complications. The primary outcome included any complication possibly related to SGX such as hypersensitivity reactions, need for reintubation, hypoxemia, pneumonia, and residual neuromuscular blockade. Secondary outcomes included any other complication not included in the primary outcome and/or patient mortality within 30 days after the procedure.

Results No patient experienced a hypersensitivity reaction. Three patients required reintubation while two patients developed hypoxemia that did not require reintubation. One patient developed hospital-acquired pneumonia. Fifty (23%) patients developed other

postoperative complications (different from our primary outcome) and nine patients (4%) died during the subsequent 30 postoperative days. None of the primary or secondary outcomes appeared to be related to SGX use. **Conclusions** We provide incremental evidence that SGX could be considered as an alternative neuromuscular blockade reversal agent in patients with ESRD.

Résumé

Objectif Bien que le sugammadex (SGX) ne compte pas parmi ses indications une utilisation chez les patients atteints d'insuffisance rénale terminale (IRT), son administration à cette population de patients est rapportée. Nous avons conçu cette étude afin de passer en revue tous les cas de patients atteints d'IRT ayant reçu du SGX et décrire leurs devenir cliniques.

Méthode Il s'agit d'une étude de cohorte historique portant sur 219 patients atteints d'insuffisance rénale chronique de stade 5 ayant reçu du SGX dans l'un de trois hôpitaux appartenant au même réseau de santé universitaire. Les données démographiques, les événements significatifs notés dans les dossiers anesthésiques et les complications postopératoires ont été colligés entre le 7 mars 2016 et le 1^{er} août 2019. Le critère d'évaluation principal incluait toute complication possiblement liée à l'utilisation de SGX telle qu'une réaction d'hypersensibilité, une réintubation, une hypoxémie, une pneumonie, et un bloc neuromusculaire résiduel. Les critères d'évaluation secondaires comprenaient toute autre complication non incluse dans notre critère d'évaluation principal et/ou la mortalité des patients dans les 30 jours suivant l'intervention.

Résultats Aucun patient n'a eu de réaction d'hypersensibilité. Trois patients ont dû être réintubés, et deux patients ont développé une hypoxémie qui n'a pas

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nécessité de réintubation. Un patient a contracté une pneumonie nosocomiale. Cinquante (23 %) patients ont souffert d'autres complications postopératoires (différentes de notre critère d'évaluation principal) et neuf patients (4 %) sont décédés au cours des 30 jours postopératoires subséquents. Aucun de nos critères d'évaluation primaire ou secondaires ne semblaient liés à l'utilisation de SGX.

Conclusion *Nous proposons des données probantes supplémentaires selon lesquelles le SGX pourrait être envisagé comme agent décurarisant alternatif chez les patients atteints d'IRT.*

Keywords neuromuscular blockade · sugammadex · end-stage renal disease · chronic kidney disease · patient safety

Sugammadex (SGX) is a modified cyclodextrin that antagonizes aminosteroidal neuromuscular blocking agents (NMBAs) through encapsulation.^{1,2} As the SGX-NMBA complex forms, NMBA is pulled into the plasma from its site of action at the neuromuscular junction because of a concentration gradient.^{3–5} The SGX-NMBA complex is hydrophilic and is excreted unchanged into the urine.^{4,6} As a result of this pharmacokinetic property, the United States Food and Drug Administration does not recommend using SGX as an NMBA antagonist in patients with a creatinine clearance $< 30 \text{ mL} \cdot \text{min}^{-1}$.⁷

Sugammadex antagonizes neuromuscular blockade faster than neostigmine and reduces the risk of postoperative residual neuromuscular blockade.^{8,9} It also has the novel ability to reverse deep levels of neuromuscular blockade (train-of-four count < 1) and $16 \text{ mg} \cdot \text{kg}^{-1}$ SGX can rapidly restore neuromuscular function after $1.2 \text{ mg} \cdot \text{kg}^{-1}$ rocuronium has been administered.⁹ As a result of this drug's novel applications and clinical efficacy, clinicians have expanded its use in various off-label scenarios such as in patients with significant renal impairment.^{2,5,10–16}

In patients with reduced renal function, theoretical concerns include the effects of prolonged exposure to the SGX-NMBA complexes that remain within circulation. Cammu *et al.* have shown that standard convective and diffusive dialysis techniques can remove this complex.¹⁷ Nevertheless, neuromuscular blockade could recur if the circulating SGX-NMBA complex dissociates, allowing free NMBA to reach the neuromuscular junction. Additionally, delayed clearance of SGX-NMBA complex may increase the risk of hypersensitivity reactions.¹⁸ The use of neostigmine in patients with end-stage renal disease (ESRD) is also concerning as 50% of this drug is renally

cleared, a characteristic that prolongs exposure to its undesired muscarinic effects.¹⁹

Anecdotally, we were familiar with SGX being used to successfully antagonize neuromuscular blockade in patients with ESRD. As such, we designed the current study to review all instances of patients receiving SGX with ESRD within our institution's health system and to describe their clinical outcomes.

Methods

After obtaining Institutional Review Board approval (22 August 2019), electronic medical records of adult (age ≥ 18 yr) patients with chronic kidney disease stage 5 (CKD5) who underwent general anesthesia and received intraoperative SGX were identified and reviewed (Figure). The list of patients with CKD5 identified through hospital International Classification of Diseases (ICD)-9/ICD-10 codes was cross-referenced with patients receiving SGX via pharmacy data from 7 March 2016 (when SGX became available on our institution's formulary) until 1 August 2019. Subjects who signed a waiver to exclude their medical records from research studies were excluded. CKD5 was defined, as per the National Kidney Foundation,²⁰ as patients with glomerular filtration rate (GFR) $\leq 15 \text{ mL} \cdot \text{min}^{-1}$, with or without the need for renal replacement therapy (RRT) at the time of the procedure. Each medical record was reviewed for preoperative, intraoperative, and postoperative data up to 30 days after surgery. Patient demographics, perioperative data, and postoperative events were collected and managed using REDCap electronic data capture tools hosted at our institution.²¹

The primary outcome of the study was defined as complications that could be related to delayed clearance of SGX within 30 days following its administration. These complications included hypersensitivity reactions, the need for reintubation, hypoxemia, and pneumonia. Hypersensitivity reactions were defined as a constellation of clinical symptoms (rash, flushing, difficulty breathing, nausea, stomach discomfort, palpitations, tachycardia, hypotension, paresthesia, and visual disturbance) after administration of SGX. Need for reintubation was defined as any patient requiring endotracheal intubation within the next 30 postoperative days. Hypoxemia was defined as an oxygen saturation ($< 92\%$) for more than five minutes measured by pulse oximetry while in the recovery room, evidence of hypoxemia discussed in hospital progress notes and discharge summaries, or oxygen arterial pressure $\leq 75 \text{ mmHg}$ measured in an arterial blood gas analysis. Pneumonia was defined as clinical signs and symptoms suggestive of respiratory infection and confirmed by

laboratory or imaging studies (e.g., sputum culture and/or chest *x-ray*). Each electronic medical record of a patient who had any of these complications was examined to identify the cause and the possible association with SGX use. The secondary outcome was the identification by manual chart review of any other complication that could possibly be related to SGX administration and/or patient death up to 30 days after the procedure, independent of possible association with SGX.

Statistical analysis

An analysis was conducted using descriptive statistics. Continuous variables are presented using central tendency values, including mean (standard deviation [SD]) for normally distributed data and median [interquartile range (IQR)] for skewed distribution data. Categorical data are reported as frequencies and percentages (%).

Results

There were 543,142 general anesthesia cases performed throughout our health system at three distinct geographic locations (Scottsdale, AZ; Jacksonville, FL, USA; Rochester, MN, USA) during the period from 7 March 2016 to 1 August 2019. Sugammadex was used in 73,958 cases (7.3%), 565 of which also had a diagnosis of CKD5 listed in their medical record. After excluding patients who did not have CKD5 at the time of the surgery or were < 18 yr old, and one patient with an obvious charting error, 219 patients with CKD5 who received SGX were identified as our final study population (Figure).

The mean (SD) age in our study was 61.5 (14.1) yr and 82 (37.4%) were female. Mean body mass index was 28.9 (6.8) $\text{kg}\cdot\text{m}^{-2}$. A total of 171 (78.1%) patients required routine renal replacement therapy (RRT) at the time of the procedure, 143 patients (83.6%) were on hemodialysis (HD), and 28 patients (16.4%) were on peritoneal dialysis. The mean (SD) dose of SGX was 217 (106) mg or 2.7 (1.2) $\text{mg}\cdot\text{kg}^{-1}$ (Table 1).

Eighteen (8.2%) of the 219 patients receiving SGX experienced 25 complications included in our primary outcome (Table 2) (Appendix 1). Thirteen (5.9%) patients developed hypoxemia, 3 (1.4%) developed pneumonia, and 9 (4.1%) required reintubation within 30 days of the surgical procedure. No patients experienced a hypersensitivity reaction.

Five of the eight patients developed hypoxemia not requiring reintubation that appeared unrelated to SGX. Three of these patients developed hypoxemia not requiring reintubation after discharge and presented to the emergency room on postoperative day 17, 18, and 26,

respectively. One patient developed hypoxemia secondary to septic shock after undergoing emergent bowel resection. One patient developed hypoxemia not requiring reintubation on postoperative day 9 due to a large pleural effusion. Two patients developed hypoxemia not requiring reintubation after receiving SGX and before being dialyzed (Table 3). The etiology of hypoxemia in these patients was thought to be pulmonary edema and prolonged apnea, respectively.

Two of three patients developed pneumonia that appeared unrelated to SGX. One of these patients developed airway hemorrhage from an aorto-esophageal fistula on postoperative day 4. One patient developed encephalopathy, septic shock, and aspirated on postoperative day 12. One patient developed hospital-acquired pneumonia three days after the procedure. While no evidence of aspiration was noted, adequate recovery from neuromuscular blockade was not confirmed as no quantitative monitor was utilized and residual weakness could be not excluded (Table 3).

Nine patients required reintubation that appeared to be unrelated to SGX in six patients. One patient developed hypoxemia after a tracheal stent became occluded. Two patients developed septic shock six and 14 days after the procedure, respectively. One patient developed hemorrhagic shock ten hours postoperatively. As previously mentioned, one patient had airway hemorrhage after a ligation of an aorto-esophageal fistula on postoperative day 4. One patient developed a myocardial infarction on postoperative day 22.

Three of the nine reintubations occurred before the patients were dialyzed. Although a careful chart review suggested that SGX was not implicated, this could not be definitively excluded (Table 3). One patient underwent a skin graft for a knee wound. The patient received 50 mg of rocuronium at induction. At the conclusion of the operation 88 min later, 2 $\text{mg}\cdot\text{kg}^{-1}$ of SGX were administered. In the postanesthesia care unit (PACU), the patient was reported to be unresponsive with an inadequate respiratory drive. Arterial gas analysis revealed hypercapnic respiratory failure and the patient needed to be reintubated 61 min after the initial extubation. A second patient underwent an inguinal hernia repair. After 40 mg of rocuronium at induction, 5.6 $\text{mg}\cdot\text{kg}^{-1}$ of SGX dose was administered 120 min later. After extubation, the patient was noted to be somnolent and developed hypoxemia requiring reintubation 64 min after the initial extubation. The anesthesia providers documented that this respiratory failure may have been due to “residual anesthesia.” In both cases, residual neuromuscular blockade could not be definitively excluded as a contributor to respiratory failure as no quantitative monitor was utilized to confirm adequate recovery. A third patient was reintubated after undergoing

TABLE 1 Demographics

Variable	Value
Age (yr)	61.5 (14.1)
Gender, female	82 (37.4%)
Body mass index (kg·m ⁻²)	28.9 (6.8)
Site	
Arizona	18 (8.2)
Florida	106 (48.4)
Minnesota	95 (43.4)
Race	
Asian	11 (5)
African American	38 (17.3)
Native Hawaiian	1 (0.5)
White	165 (75.3)
Other	2 (0.9)
Unknown	2 (0.9)
CKD etiology	
Diabetes	51 (23.3)
Glomerulonephritis	57 (26.0)
Hypertension/vascular disease	25 (11.4)
Multiple/combined	53 (24.4)
Structural disease/loss of renal mass	19 (8.7)
Unknown	14 (6.4)
Preoperative dialysis	
Yes	171 (78.1)
No	48 (21.9)
Type of dialysis	
Hemodialysis	143 (83.6)
Peritoneal dialysis	28 (16.4)
Type of procedure	
Abdominal surgery	49 (22.4)
Cardiothoracic surgery	22 (10.0)
ENT surgery	11 (5.0)
Neurosurgery	3 (1.4)
OB/GYN surgery	2 (0.9)
Ophthalmologic surgery	1 (0.5)
Orthopedic surgery	18 (8.2)
Plastic surgery	4 (1.8)
Transplant surgery	72 (32.9)
Kidney transplant	70 (31.9)
Urologic surgery	15 (6.9)
Vascular surgery	22 (10.0)

Values are n (%), mean (standard deviation), unless otherwise indicated.

CKD = chronic kidney disease; ENT = ears, nose, and throat or otolaryngology; OB/GYN = obstetrics and gynecology.

a kidney transplant that required significant volume administration intraoperatively. After extubation, the patient developed hypoxemia and had to be reintubated

212 min after extubation. Chest radiograph was consistent with pulmonary edema. A quantitative neuromuscular monitor was utilized in this patient and although the anesthesia record documented train-of-four count of 4 at the conclusion of the operation, adequate recovery could not be verified as the train-of-four ratio from this quantitative monitor was not linked into the electronic medical record.

Fifty (23%) patients developed our secondary outcome of any postoperative complication within the first 30 days following surgery. The most common included bleeding (5%), need for transfusion of red blood cells (4.5%), pulmonary edema (3.2%), and arrhythmias (1.8%) (Appendix 2). Finally, nine patients (4.1%) died within 30 days of their operation (Appendix 3).

Discussion

In the current study, we found 18 of 219 patients (8.2%) with CKD5 and SGX administration that required reintubation, developed hypoxemia, or pneumonia within the first 30 postoperative days. No patients experienced a hypersensitivity reaction. A careful review determined that complications related to neuromuscular blockade management could not be excluded in six of the 18 patients; however, the authors felt it to be unlikely. These results suggest that SGX can be used as an agent for reversing aminosteroidal-induced neuromuscular blockade in patients with CKD5.

The efficacy and safety profile of SGX in CKD patients has been evaluated in several small studies.^{2,10,11,17} Panhuizen *et al.* showed a complete, rapid, and well-tolerated reversal of deep rocuronium blockade in patients with both normal renal function ($n = 35$) and ESRD ($n = 35$).² While train-of-four ratio (TOFR) recovery from SGX is slower in patients with CKD when compared with patients with normal renal function [median recovery to TOFR 0.9 was 3.1 (95% CI, 2.4 to 4.6) vs 1.9 (95% CI, 1.6 to 2.8) min, respectively; $P = 0.0002$], reversal still occurs faster than with neostigmine. De Souza *et al.* also evaluated the efficacy and safety of SGX in 20 patients undergoing kidney transplants who had CKD stages 4 and 5, compared with 20 patients without renal failure and concluded that although the mean (SD) recovery was slower in the CKD population [5.6 (3.6) min vs 2.7 (1.3) min; $P = 0.003$], SGX was still effective and safe, reporting zero complications.¹⁰ While we cannot comment on the speed of reversal in our study, our results suggest a similar safety profile of SGX.

Sugammadex-induced hypersensitivity reactions have been reported and the concern has been raised about this being increased in patients with delayed renal clearance.^{11,18,22–25} Nevertheless, a large retrospective

TABLE 2 Complications within 30 days after surgery

Variables	Values
Primary outcome complication at 30 days	18 (8.2%)
Hypersensitivity reactions	0 (0%)
Need for reintubation	9 (4.1%)
Hypoxemia	13 (5.9%)
Pneumonia	3 (1.4%)
Mortality	8 (3.7%)
SGX-related mortality	0 (0%)
Any complication at 30 days	
Yes	50 (22.8%)
No	169 (77.2%)

SGX = sugammadex.

review from Japan of 15,479 patients found an extremely low (0.039%) incidence of anaphylaxis possibly related to SGX use.¹⁸ Similarly, Adams *et al.* conducted a retrospective observational study to evaluate SGX safety in 158 surgical patients with ESRD requiring RRT, and the results showed no cases of anaphylaxis.¹¹ Our results are consistent with these previous efforts.

The recurrence of neuromuscular blockade has been described via possible dissociation of SGX from NMBA in the plasma.¹¹ Sugammadex has a high association constant (K_a) with rocuronium (17,000–20,400 M^{-1}), and a low dissociation rate constant ($K_2 = 0.00216 \text{ min}^{-1}$).^{1,26} Such

pharmacokinetics suggest that even if dissociation occurs, a rapid re-association is likely because of its strong binding force, leaving little free rocuronium available for restoring neuromuscular blockade.^{1,11,27} There is no evidence that this pharmacology is significantly altered in ESRD patients and prior work has failed to show recurrence of neuromuscular blockade 48 hours after SGX administration.^{2,5,12} We did not identify any cases of neuromuscular blockade recurrence in our study, although universal quantitative monitoring was not utilized in our study population.

Pulmonary complications, including hypoxemia, the need for reintubation, and pneumonia, are frequently related to residual NMB.^{5,28} Our incidence of 5.9% was slightly higher than the reported incidence of 3.1% in patients with $GFR < 30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^2$.^{2,29} Moreover, the general incidence of any postoperative complication in CKD patients ranges from 15% to 64%.^{30,31} Our incidence of 22.8% is comparable with reported data of 23.5% of complications after 30 days of a major abdominal surgery in patients requiring hemodialysis.³² The overall reported mortality of CKD patients ranges from 1% in non-cardiac patients to up to 20% for cardiac patients.^{29,32–35} Our postoperative mortality of 4.1% was lower than previous descriptions of ESRD patients. While the present work cannot attribute reduced mortality to the use of SGX instead of neostigmine, SGX use has been associated with reductions in postoperative complications in patients with normal renal function.^{8,36}

TABLE 3 Patients with complications occurring after sugammadex administration and prior to next scheduled dialysis

Age (yr)	Sex	Procedure	NMBA	Total dose (mg)	Type of NM monitoring	SGX dose ($\text{mg} \cdot \text{kg}^{-1}$)	Brief description
51	F	Split-thickness skin graft	Roc	50	PNS	2.0	Reintubated 61 min after extubation because of hypercapnic respiratory failure
48	M	Inguinal hernia repair	Roc	40	PNS	5.6	Reintubated 64 min after extubation, anesthesia note suggests “residual anesthesia”
33	M	Kidney transplant	Roc	85	AMG	2.4	Reintubated 212 min after extubation because of pulmonary edema
63	M	A-V fistulogram	Roc	40	PNS	4.0	37 min after the procedure, the patient presented with hypoxemic respiratory failure due to pulmonary edema. Patient was treated with supplemental oxygen
69	M	Kidney transplant	Roc	100	PNS	2.0	Patient with history of OSA and central apnea. On POD #1, patient presented with hypoxemia due to several prolonged apneic episodes, requiring BiPAP
48	F	Laparoscopic sleeve gastrectomy	Roc	130	PNS	2.0	Hospital-acquired pneumonia POD #3, no signs of aspiration

AMG = acceleromyography; A-V = arteriovenous; BiPAP = bilevel positive airway pressure; NM = neuromuscular; NMBA = neuromuscular blocker agent; NMB = neuromuscular blockade; NRB = non-rebreather mask; OSA = obstructive sleep apnea; PMH = past medical history; PNS = peripheral nerve stimulation; POD = postoperative day; Roc = rocuronium; SGX = sugammadex.

CKD, Chronic Kidney Disease; SGX, Sugammadex; NMBA, Neuromuscular Blocker Agent

FIGURE Selection process of final study population. CKD = chronic kidney disease; NMBA = neuromuscular blocking agent; SGX = sugammadex.

This study was conducted at three distinct geographic locations within one health system. One site had a higher utilization of SGX in CKD5 patients per total number of anesthetics compared with the other two sites. Of note, this site frequently uses quantitative neuromuscular monitoring as a result of local interest and investigations related to NMBA and monitoring. Unfortunately, such objective measurements were not automatically transferred into the medical record at the time of the study, a shortcoming that has since been remedied. The authors agree with a recent consensus statement that recommends quantitative monitoring whenever a NMBA is administered.³⁶ This practice would significantly reduce the risk of residual blockade-related complications, especially in vulnerable populations such as CKD patients.

There are multiple limitations to our study. First, the use of SGX in CKD5 patients should be considered “off-

label”. In March 2016, SGX was introduced to our hospital formulary and became a frequently utilized NMBA antagonist, even in patients with CKD. Additionally, this retrospective review is subject to the limitations of any chart review and we indeed discovered one obvious charting error, in which the provider documented 1/10 of the normal dose of SGX, and had to be excluded from the final data analysis. Also, this study is limited by a relatively small sample size ($n = 219$), and we investigated infrequent outcomes such as reintubation. Nevertheless, to our knowledge, this study represents the largest cohort and longest follow-up of patients with CKD5 receiving SGX. Finally, the lack of a historical cohort for comparison limits the ability to assess the complication rate of CKD5 patients who received SGX compared with those who received conventional reversal with neostigmine.

In conclusion, 18 of 219 (8.2%) patients with ESRD developed postoperative pneumonia, hypoxemia, or required reintubation after SGX administration. While the majority of these complications appeared unrelated to neuromuscular blockade management, we could not definitively exclude SGX as a contributing factor in six of the 18 patients. Nonetheless, we felt that it was unlikely that administering SGX to these patients with ESRD significantly contributed to their postoperative complications. We recommend the routine use of quantitative neuromuscular monitoring when NMBA are employed, an effective practice to reduce postoperative complications associated with NMB.³⁷ Prospective studies are needed to make recommendations about the clinical impact of SGX in ESRD. We provide incremental evidence that SGX could be considered as a neuromuscular blockade reversal agent in patients with ESRD.

Author contributions Stephania Paredes, Steven Porter, and J. Ross Renew contributed to all aspects of this manuscript, including study conception and design; acquisition, analysis, and interpretation of data; and drafting the article. Ivan Porter contributed to study conception, study design, and manuscript editing.

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Appendix continued

Patient	Need for reintubation (n = 9)	Hypoxemia (n = 13)	Pneumonia (n = 3)	Causes
Patient 8	X	X	X	Pneumonia
Patient 9			X	Aspiration pneumonia at postoperative day 12
Patient 10		X	X	Hospital-acquired pneumonia at postoperative day 3
Patient 11	X	X		Tracheal stent blockade
Patient 12	X			Septic shock
Patient 13	X			Septic shock
Patient 14	X			Hemorrhagic shock
Patient 15	X	X		Myocardial infarction
Patient 16	X	X		Hypercapnic respiratory failure
Patient 17	X	X		Residual anesthesia
Patient 18	X			Pulmonary edema

APPENDIX 1: List of patients experiencing primary outcome complication

Patient	Need for reintubation (n = 9)	Hypoxemia (n = 13)	Pneumonia (n = 3)	Causes
Patient 1		X		Volume overload
Patient 2		X		Volume overload
Patient 3		X		Volume overload
Patient 4		X		Septic shock
Patient 5		X		Pleural effusion
Patient 6		X		Pulmonary edema
Patient 7		X		Apneic episodes

APPENDIX 2: All complications after 30 days of follow-up

	n* (%)
Pulmonary complications	
Hypercapnic respiratory failure	3 (1.3)
Pulmonary edema	7 (3.2)
Prolonged apneic episodes	1 (0.5)
Occlusion of tracheal stent	1 (0.5)
Airway hemorrhage	1 (0.5)
Cardiovascular complications	
Myocardial infarction	2 (0.9)
Takotsubo cardiomyopathy	1 (0.5)
Arrhythmia	4 (1.8)
Acute heart failure decompensation	1 (0.5)
Endocarditis	1 (0.5)
Surgical complications	

Appendix continued

	<i>n</i> * (%)
Dehiscence of surgical site	2 (0.9)
Bleeding	11 (5)
Need for transfusion after procedure	10 (4.5)
Residual anesthesia	2 (0.9)
Transplant complications	
Kidney transplant rejection	2 (0.9)
Pancreas transplant rejection	1 (0.5)
Infections	
Pneumonia	2 (0.9)
Respiratory syncytial virus	1 (0.5)
Clostridium difficile infection	1 (0.5)
Urinary tract infection	2 (0.9)
Sepsis	2 (0.9)
Neurologic complications	
Encephalopathy	1 (0.5)
Stroke	1 (0.5)
Gastrointestinal complications	
Intestinal ischemia	1 (0.5)
Falls	1 (0.5)
Total deaths after 30 days	9 (4.1)

*Please note that 50 patients experienced one of these 70 complications with some patients experiencing more than one of these complications

APPENDIX 3: Causes of death at 30 days

Cause of death	<i>n</i> (%)
Septic shock	2 (0.9)
Gastrointestinal perforation	1 (0.5)
ESRD	2 (0.9)
Intestinal ischemia	1 (0.5)
Stroke	1 (0.5)
Aortoenteric fistula bleeding	1 (0.5)
Unknown cause*	1 (0.5)

ESRD = end-stage renal disease.

*Patient died at an outside hospital.

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