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Social Security Organization of Islamic Repoblic of Iran



Major Surgery in Kidney Transplant Recipients

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Major Surgeries

Major surgeries	
Cardiothoracic surgery	CABG; Valvular surgery
Intraabdominal surgery	Bariatric surgery; major intraabdominal surgeries
Urologic surgery	Radical cystectomy; Radical prostatectomy; Nephrectomy
Orthopedic surgery	Hip or knee replacement
Neurosurgery	Spinal fusion surgery
Gynecology surgery	Cesarean section; total abdominal hysterectomy



Preoperative Evaluation and Preparation



- •Elective surgery should preferably be done one year post-transplant, or at least six months post-transplant, and it should ideally be conducted at a transplant center.
- •No elective surgery should be performed during an episode of rejection due to high mortality.



- •One should assess physical activity, evaluate the functional state of the graft, and look for signs and symptoms of infection and rejection.
- •Other comorbidities such as diabetes, hypertension, and ischemic heart disease should also be looked for and their severity assessed.



Cardiovascular System



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Traditional Risk Factors	Nontraditional Risk Factors
Older age	Decreased kidney function
Male gender	CNI
Family history of CVD	Proteinuria
Diabetes	Anemia
Hypertension	C-reactive protein
Dyslipidemia	Oxidative stress
low HDL	Advanced glycation end products
high LDL	Inflammation
Physical inactivity	Homocysteine
Left ventricular	Uric acid
hypertrophy	Hyperparathyroidism
Menopause	Obesity
Tobacco use	Thrombogenic factors





Perioperative Management of Diabetes





Summary of Perioperative Use of Anti-Diabetic Medications

Metformin

The American Diabetes Association (ADA) proposes holding of metformin on the day of surgery whereas the Association of Anesthetists of Great Britain and Ireland (AAGBI) suggests to continue it with the rest of the oral anti-diabetic medications other than sulfonylureas and sodium–glucose transport inhibitors on the day of the procedure as it does not cause low blood sugars. It might be safe to restart 48 hours after the major procedure and making sure of the adequate functioning of the kidney

Sulfonylurea

The usual strategy to withhold it on the day of surgery remains plausible

Dipeptidyl peptidase 4 (DPP4) inhibitors

To continue or discontinue it perioperatively is unlikely to produce any significant complications and either strategy is acceptable

Sodium-glucose co-transporters 2 (SGLT2) inhibitors

At present, there is no agreement on the withholding of SGLT2 inhibitors before surgery but the general strategy is to stop them before 24–72 hours or even longer

Glucagon-like peptide 1 (GLP1) agonists

Gastrointestinal adverse effects may become limiting factors to their use. Therefore, either plan of going with or against it perioperatively is workable

Insulin

Perioperative insulin – based management in the form of basal-bolus is quite effective in attaining blood glucose target than intermittent bolus with rapid-acting insulin in type 2 diabetes. Insulin infusion is also an option and can be used in critical and critical situations. Degludec has a long half-life of more than 42 hours and current data are not enough to determine its effect perioperative blood sugars

Laboratory Evaluations

- CBC, Platelet count, WBC
- Serum creatinine
- Urine analysis; U/C (in urology and hip replacement surgeries)
- Electrolytes: Na⁺, K⁺, Ca²⁺, Mg²⁺
- PT, PTT, INR, CT, BT
- AST, ALT, Bilirubin
- Drug level: Tacrolimus, Cyclosporine, Sirolimus, Everolimus
- FBS; HbA_{1c} (in diabetic patients)



Perioperative Concerns for Transplant Recipients



Prevention of Surgical Site Infection



Decontaminate hands

Remove hair on table (with electric clippers if available)

Peri-Operative

At risk hosts

Even in clean cases

Antibiotics

Use prophylactically for clean-contaminated, contaminated or dirty surgery



Select according to guidelines based on operation and local resistance patterns

Administer IV within 60 minutes before incision

Repeat dose if operation longer than half life of antibiotic

Do not routinely continue beyond 24 hours

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Operation	Recommended antibiotic	Comments
Cardiothoracic surgery	Cefazolin for CABG; Vancomycin for	Continue prophylaxis for up to
	valvular surgery	72 hours.
	If patient has β-lactam allergy:	
	clindamycin or vancomycin	
Vascular surgery	Cefazolin	
	If patient has β-lactam allergy:	
	clindamycin or vancomycin	
Colon surgery	Oral: if available neomycin+	Combination of oral and
	metronidazole	parenteral prophylaxis may
	Parenteral: Cefazolin + metronidazole	result in lower wound
		infection
Hip or knee arthroplasty	Cefazolin	
	If patient has β-lactam allergy:	
	clindamycin or vancomycin	
Gynecology surgery	Cefazolin	Metronidazole monotherapy
		can be used.



Immunosuppression Protocols

General names	Generic names	Brand names
Corticosteroids	Prednisone	
	Methylprednisolone	
Calcineurin inhibitors	Tacrolimus (or FK-506)	Prograf
	Cyclosporine (or cyclosporine A)	Sandimmune, Neoral, Gengraf, Eon, SangCya, generic cyclosporine
Antimetabolites	Azathioprine	Imuran
	Cyclophosphamide	Cytoxan, Neosar
	Mycophenolate mofetil	CellCept
	Mycophenolate sodium	Myfortic
TOR inhibitors (or rapamycin)	Sirolimus, Everolimus	Rapamune, Certican



Steroids

Surgery	Recommendations
Superficial	Daily dose only
Minor	Daily dose plus hydrocortisone (25 mg IV)
Moderate	Daily dose plus hydrocortisone (50–75 mg, taper 1–2 days)
Major	Daily dose plus hydrocortisone (100–150 mg, taper 1–2 days)
In suppressed patients (defined as equivalent mendations are surgery specific	to prednisone 20 mg/day for 3 weeks or more), recom-
Surgery	Recommendations
Minor	Morning dose only
Moderate	Morning dose plus IV 50 mg of hydrocortisone before incision; then IV 25 mg every 8 h for 24 h and then maintenance
Major	Morning dose plus IV 100 mg of hydrocortisone before induction; then IV 50 mg every 8 h for 24 h; Taper dose by half per day to maintenance level
Glucocorticoid dose adjustment based on sev	verity of illness or magnitude of stressor, as follows:
Surgery	Recommendations
Minor to moderate Major surgery, trauma, delivery, disease that requires intensive care, suspected adrenal crisis	Hydrocortisone, 25–75 mg/24 h (usually 1–2 days) Hydrocortisone 100 mg IV followed by continuous IV infusion of hydrocortisone 200 mg/24 h (alternatively 50 mg every 6 h IV/IM)



Calcineurin Inhibitors

- It is important to maintain immunosuppression (IS) at all times.
- The dose of IS drugs should not be altered and should be continued post-operatively to reduce the risk of rejection.
- •Oral immunosuppression is preferred.
- •Agents can be administered via a nasogastric tube, if suction is avoided.



•Oral CNI should be administered 4-6 hours before surgery to maintain blood level.

• The blood levels of patients receiving CNIs should be monitored daily during the perioperative period.







• It may be difficult to achieve full IS when gastrointestinal absorption is impaired, such as with surgical ileus, small bowel obstruction, or diarrhea.





- For patients unable to take oral cyclosporine, the intravenous dose should be equal to one-third of the oral dose.
- Intravenous administration should occur over at least two to six hours twice daily in a wellhydrated patient to avoid nephrotoxicity.



• If unable to swallow capsules, tacrolimus may be administered sublingually (decrease dose by 50%) by opening the immediaterelease capsules and placing the contents of the capsule(s) under the tongue, allowing contents to completely dissolve.



 If unable to swallow capsules, contents of immediate release tacrolimus capsule(s) may be mixed with water and flushed through a nasogastric tube; clamp nasogastric tube for 30 to 60 minutes after administration.







- For patients unable to take oral tacrolimus, the intravenous dose should be equal to onethird to one-fifth of the oral daily dose and should be given as a continuous 24-hour infusion.
- In order to convert back to oral tacrolimus, restart with previous dose 8-12 hours after holding infusion.



Mycophenolate

• Mycophenolate should be continued till the day of operation.

• If oral intake is not possible, withheld the drug, or if available use IV form with similar dose.



mTOR Inhibitors





Figure 2 Guidelines on using sirolimus in the case of minor elective, major (including cancer) and emergency surgery.

Anesthetic Considerations



Anesthetic Technique





Anesthesiologist factors

- Anticoagulation status
- Patient comorbidities
- Technical considerations
- Medical Association guidelines
- Complications
- Litigation

Surgeon factors

- Lack of reliability of neuraxial techniques
- Perceived delay
- Personal preference

Patient factors

- Concern of side effects
- Fear of spinal injury
- Increased age
- Surgeon attitude
- Personality traits
- Internet resources
- Curiosity

Choice of anesthetic technique

System factors

- Institutional culture
- Resource allocation
- Operating room time
- Cost



• If regional anesthesia is planned, bleeding risk should be ruled out by clotting studies and platelet count.

• Central neuraxial blockade is relatively contraindicated in the presence of clinical evidence of uremic platelet dysfunction or severe hypovolemia.



Interactions Between Immunosuppressive and Anesthetic Drugs



Anesthetic agent	Effect with immunosuppressive drugs
Isoflurane	↓ Clearance of oral CyA
Thiopental	Nil
Benzodiazepines	↑ Blood level of benzodiazepines
Propofol	Nil
Etomidate	Nil
Opioids	CyA \uparrow analgesic effect produced by fentanyl
Muscle relaxants	Prolonged neuromuscular blockade
Neostigmine	Caution in heart transplant patients
Local anesthetics	Bupivacaine and ropivacaine can be safely used

• Cyclosporine enhances the effects of muscle relaxant.

• Patients receiving cyclosporine need smaller dose of nondepolarizing muscle relaxant and the recovery time may be prolonged.

• Because CNIs may cause neurotoxicity and decrease seizure threshold, it seems prudent to avoid hyperventilation.



• Isoflurane appears to be the preferred inhalation agent.

• In order to avoid changes in therapeutic level of CNIs with isoflurane, patients should receive peroral drug form more than 4 hours preoperatively.



Anemia & Transfusion

•A hemoglobin level of 11 g/dL for transplant recipients presenting for surgery is a reasonable goal to minimize transfusions.

•Treatment options for PTA include nutritional supplementation, adjustment of immunosuppressant medication, and ESAs.





- Any potential units of packed red blood cells to be transfused should be leukocyte reduced, to reduce the chance of allo-immunization and CMV infection.
- Platelet units, cryoprecipitate, and FFP are apheresed and are considered leukoreduced.



Postoperative Care Management



Post Operation Pain Control





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ESRA-AZ POPM 2005

from N. Rawal

Opioids

Morphine	Conj. to M-3-G, M-6-G , active metabolite, resp depresion	Active metabolite has renal elimination, 40% conj occurs in kidney	Dose adjustment required
Meperidine (Pethidine)	Normeperidine, CNS toxicity	Active metabolite has renal elimination	Dose adjustment required
Fentanyl	↓ Plasma protein binding,↑ free drug	Clearance not altered	safe
Sufentanil	↓ Plasma protein binding,↑ free drug	Clearance not altered	safe
Alfentanil	↓ Initial vol of distribution,↑ free drug	Clearance not altered	safe
Remifentanil	No change	Clearance not altered	safe

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Stress Ulcer Prophylaxis

 Surgical stress, corticosteroids, and mycophenolate may contribute to GI ulcers.

• So, it is absolutely necessary to provide stress ulcer prophylaxis for transplanted patients.

• PPI or H₂ Blocker



VTE Prophylaxis

LMWH should not be administered during the first 4-12 hours after epidural or spinal anesthesia. Prevention of venous thromboembolism (VTE) after surgery

Undergoing surgery and bed rest after surgery increase the risk of VTE. Ways to help prevent VTE following surgery include



Early walking As soon as your doctor allows, get out of bed and walk several times a day.

BUCHER

Sequential compression devices (SCDs) Wear SCDs when sitting or lying down.

Enoxaparin

niection



You may receive blood-thinning medication after surgery. For some types of surgery, this medication may be continued briefly after you go hon

Wound Healing

• Immunosuppressive drugs, steroids, diabetes, and obesity are risk factors of delayed wound healing.

• Remove stiches 3-4 weeks after surgery.



Special Considerations



Cardiac Surgery

• In case of cardiopulmonary bypass, there is an increased chance of renal function during the first 48 hours.

 Invasive hemodynamic monitoring during surgery and in early post operation, and maintaining perfusion pressure >70 mmHg and HCT during bypass, help improving the prognosis.



Weight Loss Surgery

- Routine monitoring of drug levels may prevent adverse consequences of altered pharmacokinetics after BS.
- Nutritional consult, calcium supplement, and monitoring of urine or serum oxalate level is recommended.



Orthopedic and Spinal Surgeries

- Preoperative evaluation and management of MBD and osteoporosis.
- Thromboprophylaxis for one month post surgery or until complete mobility.
- •Pain control strategies.



Take Home Message

- Stable graft function
- Cardiac Consult
- •Blood glucose and hypertension control
- Evaluation of renal function; bleeding risk evaluation; drug level.
- Evaluation of MBD
- Prevention of surgical site infection
- Immunosuppression modifications



• Drug interactions

- •Anemia management
- Pain control strategies
- Stress ulcer prophylaxis
- VTE prophylaxis
- Wound healing risk factors



