

# **The Effect Of Epidural Anesthesia On Early Graft Function In Renal Transplantation**

Thesis Submitted for partial fulfilment of M.D. degree in anesthesiology

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# List Of Abbreviations

AAA	Abdominal aortic aneurysm
ABC	Adenosine triphosphate [ATP]–binding cassette
ABGs	Arterial blood gases
ABP	Arterial blood pressure
ACE	Angiotensin converting enzyme
AKI	Acute kidney injury
aPTT	Activated partial thromboplastin time
ASRA	American Society of Regional Anesthesia and Pain Medicine
AV	Arteriovenous
AVP	Arginine vasopressin
bpm	Beat per minute
Ca	Calcium
CAD	Coronary artery disease
CGRP	Calcitonin gene-related peptide
CrCl	Creatinine clearance
CRF	Chronic renal failure
CRR <sup>∞</sup>	Creatinine reduction ratio on post-transplant day <sup>∞</sup>
CSE	Combined spinal epidural
CSEA	Combined spinal epidural anesthesia
CSF	Cerebrospinal fluid
CT	Computed tomography
CVA	Cerebrovascular accident
CVP	Central venous pressure
DCD	Donation following cardiac death
DDGF	Dialysis-delayed graft function
DDS	The Deceased Donor Score
DGF	Delayed graft function
DU	Doppler ultrasound
EA	Epidural anesthesia
EAA	Epidural analgesia and anesthesia
ECD	Expanded Criteria Donor for Kidney Transplantation
ECG	Electrocardiogram
eGFR	Estimated glomerular filtration rate
ERBF	Estimated renal blood flow
ERPF	Estimated renal plasma flow

ESRD	End stage renal disease
F	Female
GA	General anesthesia
GFR	Glomerular filtration rate
Hb	Hemoglobin
HCO <sup>+</sup>	Bicarbonate
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
HR	Heart rate
ICP	Intracranial pressure
ICU	Intensive care unit
IGF	Immediate graft function
IL- <sup>1</sup>	Interleukin- <sup>1</sup>
IV	Intravenous
IV-PCA	Intravenous patient controlled analgesia
K	Potassium
kDa	Kilo Dalton
Kg	Kilo gram
KIM- <sup>1</sup>	Kidney Injury Molecule <sup>1</sup>
LA	Local anesthetic
M	Male
MAC	Minimum alveolar concentration
MAP	Mean arterial pressure
MASTER	The Multicentre Australian Study of Epidural Anaesthesia
Mg	Magnesium
MRI	Magnetic resonance imaging
Na	Sodium
NDDGF	Non-dialysis delayed graft function
NGAL	Neutrophil Gelatinase-Associated Lipocalin
NK <sup>1</sup> , NK <sup>2</sup>	Neurokini- <sup>1</sup> and - <sup>2</sup>
NSAIDs	Non steroidal anti-inflammatory drugs
N <sub>0</sub>	Number
P	Probability of event to occur (p value)
PAI- <sup>1</sup>	Plasminogen activator inhibitor
PaO <sup>2</sup>	Arterial oxygen tension
PCEA	Patient controlled epidural analgesia
PENIA	Particle-enhanced nephelometric immunoassay
PETIA	Particle-enhanced turbidimetric immunoassay
PI	Pulsatility index
PMI	Postoperative myocardial ischemia

PRA	Peak panel reactive anti-HLA antibodies
RBF	Renal blood flow
RCTs	Radomised controlled trials
RI	Resistivity index
SBP	Systolic blood pressure
SCr	Serum creatinine
SD	Standard deviation
SGF	Slow graft function
SPSS	Statistical package of the social science
TEA	Thoracic epidural anesthesia
TEE	Transeosophageal echocardiography
TNF	Tumor necrosis factor
UOP	Urine output
USRDS	US Renal Database System
VAS	Visual analogue scale
Yr	Year

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## **Introduction And Aim Of The Work**

The appropriate anesthesia for renal transplantation requires minimal toxicity for the patients and for the transplanted organ, as well as sufficient pain relief and maintenance of vital functions. <sup>(1)</sup>

General anesthesia is the most popular technique for renal transplantation. Although epidural anesthesia is used for major lower abdominal surgery, the most common limiting factor in the choice of regional anesthesia is anticipated long duration of surgery. The use of regional anesthesia in chronic renal failure patients is still controversial but promising. <sup>(2)</sup>

The duration of transplant surgery is usually the major determinant of anesthetic technique. With shorter operative times, renal transplants can be performed by using continuous epidural anesthesia. <sup>(3)</sup>

Some clinical studies suggest that postoperative morbidity and possibly mortality may be reduced when neuroaxial blockade is used either alone or in combination with general anesthesia in some settings. <sup>(4)</sup>

Neuroaxial blocks may reduce the incidence of venous thrombosis and pulmonary embolism, cardiac complications in high-risk patients, <sup>(5)</sup> bleeding, pneumonia and respiratory depression especially in patients with chronic lung disease. <sup>(6)</sup> Neuroaxial blocks may also allow earlier return of gastrointestinal functions following surgery. <sup>(7)</sup>

Proposed mechanisms include amelioration of the hypercoagulable state associated with surgery, sympathectomy-mediated increase in tissue blood flow, improved

oxygenation from decreased splinting, enhanced peristalsis, and suppression of neuroendocrine stress response to surgery, which may result in less myocardial ischemia and reduced morbidity and mortality in patients with coronary artery disease. Reduction of parenteral opioid requirements may decrease the incidence of atelectasis, hypoventilation and aspiration pneumonia.<sup>(4)</sup>

Postoperative epidural analgesia may also significantly reduce the time until extubation and reduce the need for mechanical ventilation after major abdominal or thoracic surgery.<sup>(4)</sup>

A randomized controlled study comparing combined spinal epidural versus general anesthesia for recipients of renal transplant surgery was done and published in June 2000 concluded that the chance of hypotension, bradycardia and acidemia was comparable using either general anesthesia or combined anesthesia in renal transplant patients. The results also support the benefit of using combined anesthesia in renal transplantation surgery.<sup>(11)</sup>

## ***AIM OF THE WORK***

The aim of this study is to determine how the anesthetic technique influences the outcome in patients; early after renal transplantation in terms of; intraoperative hemodynamic changes, blood gas changes, and early postoperative renal allograft function.

# **Renal Transplantation**

Improvement in the success of solid organ transplantation over the past decades is remarkable and well documented. Refinement of perioperative care and improved post-transplant patient management over recent years have resulted in dramatic improvement in 1-year and 5-year graft survivals. These changes have led to a significant increase in the number of medical centers performing solid organ transplantation and increased public awareness<sup>(1)</sup>

The success of organ transplantation is based on a highly specialized team approach, including the cooperation of procurement organizations, transplant coordinators, nurses, and physicians from many specialties. This chapter reviews anesthetic considerations for kidney transplantation in adult recipients.

## ***History***

Organ transplantation has a long history, in 1906, Mathieu Jaboulay carried out the first attempts at human kidney transplantation. Jaboulay used pig and goat kidneys anastomosed to blood vessels of the arm of patients with chronic renal failure, which functioned for approximately 1 hour. In 1911, Hammond and Sutton of Philadelphia performed the first human-to-human kidney transplant with transient success.<sup>(2)</sup>

Alexis Carrel improved the methods of vascular anastomosis and introduced cooling as a method of organ preservation .

The first wholly successful human transplant took place on December 23, 1954, in Boston, Joseph Murray performed a kidney transplant between identical twin brothers. Although this and subsequent twin transplants did little to solve the problem of rejection,

these procedures contributed to proving the value of the surgical procedure and to the solution of many technical problems.<sup>(12)</sup>

In 1963, the introduction of azathioprine and steroid combination therapy produced encouraging results and became the mainstay of immunosuppression until the introduction of cyclosporine in 1983. Cyclosporine, in turn, substantially improved outcomes of cadaver kidney transplants. Further innovations include anti-T-cell antibodies, both monoclonal and polyclonal, and other agents (eg, tacrolimus, mycophenolate, sirolimus).<sup>(13)</sup>

### ***Living Kidney Donor***

A major concern surrounding living organ donation is the potential for great harm to be inflicted on entirely healthy individuals who undergo major surgery for purely altruistic reasons. The ethical and psychological aspects of living organ donation continue to be widely examined and discussed. In addition, the quality of life after organ donation and the financial impact on the donor are of great concern.<sup>(14)</sup>

Organ donation from living donors has significant advantages over deceased organ donation. In contrast to deceased donors, living donors are always hemodynamically stable, and the procedure can be planned on an elective basis. In addition, the cold ischemia time of the organ can be minimized compared with that associated with deceased donors. Perhaps the most important advantage of living donor transplantation is the significant reduction in time spent on the waiting list to receive an organ from a deceased donor.<sup>(15)</sup>

Renal transplantation with organs from living donors has rapidly been increasing in recent years. In the past, donor nephrectomy was done by the traditional approach through a subcostal lateral incision, by minimal incision nephrectomy, or by the

laparoscopic approach. Laparoscopic live donor nephrectomy now has almost completely replaced the traditional open approach via subcostal lateral flank incision. <sup>(15)</sup>

Donor nephrectomy is a low risk procedure, and the type of complication (e.g., reoperation, ileus, readmission to the hospital) depends on the surgical technique. <sup>(16)</sup>

To maintain good diuresis and to optimize graft function during donor nephrectomy, fluid administration is generous (10 to 20 mL/kg/hr), even though blood loss is minimal in most cases. The preferred type of fluid in this setting is unknown because no human trial has yet addressed this issue. In the absence of enough scientific data, most centers use isotonic crystalloids. The anesthetic technique in these healthy patients is not different from that used for other laparoscopic procedures. <sup>(17)</sup>

## ***Contraindications To Solid Organ Transplantation***

For all transplant candidates, the number of absolute and relative contraindications has diminished in recent years. Overall, candidates for kidney transplantation are increasingly older and have more complex medical problems. Active infection is an absolute contraindication until it has been resolved. Evidence of malignancy is not a contraindication per se. Hepatocellular carcinoma with underlying cirrhosis is considered an indication for liver transplantation as long as the tumor burden does not exceed established guidelines. <sup>(18)</sup>

Similarly, selected patients are reconsidered for renal transplantation after successful treatment of malignancy and no evidence of recurrence. Relative contraindications, such as noncompliance or a history of drug abuse, exist, but vary among centers. <sup>(19)</sup>