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Anesthesia for Pancreas Transplantation

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Abstract

As the frequency of pancreas transplants increase worldwide, clinicians are faced with providing care to recipients who may present with multiple comorbidities related to their underlying diabetes. This review summarizes the perioperative management of pancreas transplant recipients from the viewpoint of the anesthesiologist. Preoperative evaluation, intraoperative care and postoperative pain control are all discussed.

Keywords: Pancreas; Transplant; Anesthesia; Intraoperative care; Diabetes; Preoperative evaluation

Introduction

Pancreas transplant is indicated for patients with Type 1, as well as, select patients with Type 2 diabetes. Over 26,000 pancreas transplants were performed in the United States between 1988- 2012. Of these, over 19,000 were simultaneous kidney-pancreas transplants and 7400 were pancreas alone [1]. Additionally, over 3000 patients are currently waiting for a pancreas in the United States alone. Advances in immunosuppressant and surgical technique have greatly improved outcomes for these delicate surgeries. As a member of the surgical team, it is imperative for anesthesiologists to have a sound understanding of the perioperative management of these patients to maximize graft survivability.

Preoperative Evaluation

A transplant anesthesiologist should evaluate all patients prior to their approval for pancreas transplantation. The assessment of each candidate should always include a thorough evaluation for end organ disease associated with diabetes. Additionally, an evaluation of other preexisting comorbidities, a comprehensive airway exam, and evaluation of vascular access sites should also be performed during this initial exam.

Diabetes affects roughly 24 million Americans; with the majority (90%) suffering from type 2 diabetes and it is thought that 1 in 3 Americans born within the last decade will develop diabetes during their lifetime [2]. Type 1 diabetes, previously called insulin- dependent diabetes, results from a destruction of pancreatic beta cells resulting in the loss of insulin production. Environmental, genetic, and autoimmune causes have all been suggested as potential etiologies. Typically presenting in adolescence as weight loss, polydipsia, polyphagia, and polyuria; these patients may also present emergently with ketoacidosis and hyperglycemia. Therapy is aimed at restoring euglycemic with exogenously administered insulin. Type 2 diabetes, formerly known as non-insulin dependent diabetes, is associated with insulin resistance in the peripheral tissues often followed by beta cell dysfunction in the later stages. While often a disease of older adults, there is a growing percentage of adolescents and young adults being diagnosed [3]. These patients typically present insidiously and diagnosis can be made using guidelines established by the American Diabetes Association (ADA) [4]. Often patients with type 2 diabetes are managed initially with lifestyle changes and oral hypoglycemics, however many will progress to requiring insulin to manage their hyperglycemia.

An exam of the chronic diabetic should include a detailed evaluation of the cardiovascular system. Patients are predisposed to accelerated atherosclerosis due to oxidative stress, low grade inflammation, and endothelial dysfunction resulting from the effects of chronic hyperglycemia on intracellular metabolism [5]. Women may be at slightly greater risk than males when adjusted for age [6]. Since these patients are also at risk for silent ischemia, risk stratification should be assessed based on cardiac risk factors and functional status. The ADA suggests that the transition to higher cardiovascular risk may occur after age 40 and aggressive testing should be explored in these patients [7-9].

Poorly controlled diabetics may suffer from autonomic dysfunction. Cardiac and peripheral manifestations of this syndrome can increase the mortality and morbidity associated with surgery [10-13]. Loss of sympathetic tone can result in profound hypotension following induction of anesthesia, as well as, a predilection to intraoperative hypothermia. Additionally, these patients may not be responsive to atropine or ephedrine [14]. The diagnosis may be difficult to make, but may be detected with tests evaluating cardiovascular reflexes, such as heart rate variability and orthostatic hypotension.

Chronic renal insufficiency and renovascular disease are also common comorbidities associated with long standing diabetes that has been inadequately managed and typically presents as persistent proteinuria and a decreasing glomerular filtration rate. Several factors have been shown to increase the risk of disease progression [15-20]. The pathological process appears to begin with glomerular hypertrophy and hyper filtration progressing to inflammation of the glomeruli and tubulointerstitial regions, finally resulting in the loss of renal cell numbers and the accumulation of extracellular matrix [21]. Progression to renal failure can be slowed with proper management of hyperglycemia, as well as, renoprotective strategies using ace-inhibitors and angiotensin receptor antagonists [22].

Chronic glycosalation of intimal vascular tissue and accelerated atherosclerosis increases the risk the development of micro and macrovascular disease clinically presenting as retinopathy, systemic

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hypertension, stroke, and peripheral vascular disease [23,24]. Tight glycemic control and management of blood pressure can significantly slow the progression of these complications.

Additionally, patients should be questioned about gastroparesis, neuropathy, metabolic abnormalities, and hospitalizations. A complete blood count and metabolic panel should also be obtained. Measurement of hemoglobin A1C levels can provide insight into the degree of glucose control. Questions regarding their insulin regimen should also be elucidated.

An airway exam is essential during the initial visit. Type 1 diabetics have been shown to have a higher incidence of difficult intubation due to stiffness at the atlanto- occipital joint [25]. Obesity is a frequent comorbidity associated with type 2 diabetes and while, by itself, is not an independent risk factor for difficult intubation, these patients can have anatomic and physiologic features that make securing the airway difficult [26]. Mallampati score, neck extension, thyromental distance, and dentition should be carefully inspected.

Intraoperative Management

Pancreas transplantation is typically performed under general anesthesia. A balanced technique using protocol, midazolam, and narcotics is typically used for induction. In patients with severe heart disease, etomidate may be a safe alternative to protocol given its more stable cardiovascular profile. Patients with a difficult airway should be properly preoxygenated and intubated awake. Patients with decreased range of motion at the atlanto-occipital joint can be done asleep with the assistance of airway devices, such as a video assisted laryngoscope or fiberoptic bronchoscopy to minimize neck extension.

Since gastroparesis can occur with long standing diabetics, a rapid sequence intubation with cricoid pressure should be performed to minimize the risk of aspiration. Succinylcholine, a depolarizing neuromuscular blocking agent, is often used to accomplish this due to its rapid onset of action. While effective at rapid paralysis, succinylcholine has many significant adverse effects and caution should be used in patients with renal disease as they may be at risk for cardiac arrest resulting from hyperkalemia, although this has recently been challenged [27]. In patients with a contraindication to succinylcholine, rocuronium can be substituted if the airway appears straightforward.

Maintenance of anesthesia is best done by using a volatile anesthetic such as isoflurane or desflurane with intermittent narcotics [28]. Muscle paralysis should be employed to facilitate surgical exposure. This can be accomplished by maintaining a single twitch on train of four monitoring. Any nondepolarizing agent is sufficient, however, patients with significant renal disease, may benefit from the use of cis-atracurium due to its organ independent metabolism.

In addition to standard monitors, a central venous catheter and radial artery catheter should be placed to assist in monitoring of intravascular volume, administration of medications, and intraoperative blood sampling [28,29]. More advanced monitoring, such as transesophageal echocardiography and pulmonary artery catheters are rarely indicated. Intraoperative blood pressure and heart rate should be maintained at baseline values, and increased slightly prior to recirculation of the graft. This can usually be accomplished with liberal fluid resuscitation and intermittent vasopressor administration.

Following graft recirculation, pancreatic beta cells begin secreting insulin within 5 minutes, so careful attention to glucose levels is paramount [28,30]. Blood glucose levels should be assessed every 15 minutes for the first hour, then every 30 minutes thereafter for the duration of the surgical case. The goal of tight glucose control is to prevent hyperglycemia induced islet cell dysfunction and to rest the beta cells until reperfusion abnormalities have normalized [29,31-33]. An insulin infusion should be initiated and titrated to maintain a blood sugar in the range of 120-150 mg/dl. At our institution, the formula (blood glucose-60)×0.3 is used to determine the insulin infusion rate.

Following skin closure, neuromuscular blockade is reversed and the majority of patients are extubated in the operating room. Patients are then observed in the recovery area while electrolyes and pain control are optimized. Additionally, we obtain a chest X-ray to confirm proper line placement and a postoperative electrocardiogram. Typically most patients' pain is well managed using patient controlled analgesia with either morphine or hydromorphone. In patients with renal failure, hydromorphone is best suited as there is a risk of accumulation of the renally cleared morphine metabolites. The metabolite morphine-6-glucuronide has been associated with respiratory depression and obtundation [34] and morphine-3-glucuronide was initially felt to be neuroexcitatory, although recent evidence suggests this may be untrue [35,36]. Epidural anesthesia is typically avoided as many centers administer anticoagulation postoperatively to minimize the risk of vascular thrombosis [37]. Instead pain that is poorly controlled pain with narcotics may be ameloriated with transverses abdominis plane blocks [38]. These blocks when performed under ultrasound guidance appear to be safe in coagulopathic patients since they are placed within a fascial plane and away from major vascular or neurological structures. These blocks have a finite duration of action, however, and would need to be repeated if the pain persists. Transversus abdominis plane block using indwelling catheters have been described for various abdominal surgeries, however these have not been described for pancreas transplants.

Summary

Pancreas transplantation has the ability to restore euglycemia in patients suffering from type 1 and select patients with type 2 diabetes. Advances in surgical technique and immunosuppression have improved outcomes for patients receiving pancreas transplants. A sound knowledge of the pathophysiology associated with diabetes is fundamental to developing a safe perioperative plan and improving graft survivability.

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