Considerations for Renal Protection and Management: CPB

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Renal impairment is frequently a complication of CPB, often associated with unfavorable prognoses for patients. Depending on how renal failure is defined, incidence varies between 2.5% to 30% of all cardiac surgery patients [8]. In patients that develop acute kidney injury (AKI), the mortality rate can be as high as 60%, and about 1% of all routine coronary artery bypass grafting (CABG) patients require dialysis [3,12,16]. Moreover, renal impairment post-CPB has a complicated and multifaceted etiology. Even with the progress made in its management, post-CPB renal impairment persists. By identifying high-risk patients, using preoperative lab values, and improving protective and therapeutic measures, perfusionists can effectively detect and manage CPB related renal impairment.

Several models for examining high-risk patients developing renal failure post-CPB have been created [3,12,16]. The studies have pointed to several significant factors improving the ability to predict renal impairment. Possibly the most evident factor for developing post-CPB renal impairment is pre-existing renal dysfunction [11,13]. Renal dysfunction is often noted by elevated serum creatinine. Creatinine is a byproduct of creatine phosphate catabolism in muscle cells. Once filtered in the kidneys, creatine is minimally reabsorbed or secreted. Therefore, serum creatinine can approximate glomerular filtration rate (GFR) – predictive of renal failure. In patients with preoperative renal impairment, the incidence for post-CPB AKI was greater than 20% in addition to a greater than 50% mortality rate [11,13].

Advancing age is also considered a risk factor [9]. Older patients tend to have some degree of senile degeneration of nephrotic mass because of genomic changes that culminate with age [9]. Specifically, vascular endothelial growth factor gene expression decreases over time, increasing the risk of ischemic insult [9]. Furthermore, renal autoregulation is impaired significantly [3]. Renal autoregulation is a myogenic response the kidneys use to maintain GFR over a wide range of blood pressures (i.e., 70-180 mmHg). Patients greater than 70 years of age have a 2-fold increase in risk for renal autoregulation impairment, and those 80 years of age, a 4-fold increase in risk [3].

Another risk factor incurs before surgery when patients have angiograms done. The contrast dyes used for cardiac catheterization increase BUN levels preoperatively leading to azotemia [2,4]. Patients with azotemia are particularly vulnerable to developing post-CPB AKI [2,4]. Many times, surgery is postponed until BUN levels return to normal. Furthermore, contrast agents can also bind to calcium channels in the renal medulla and induce a vasoconstrictive response [2,4]. This potentially puts the patient at risk for upcoming surgery and/or exacerbates any medullary ischemia already present.

Other factors in a patient's chart that should be considered include a history of moderate to severe congestive heart failure (CHF), ejection fraction (EF) < 35%, previous surgeries (especially valvular), peripheral vascular disease, diabetes mellitus (DM), or a history of rheumatic fever [3,12,16]. Many of these factors indicate impaired circulation or cardiac function. Because of this, there is the possibility of decreased renal perfusion and pre-operative renal impairment.

After taking into consideration the patient's medical history and pre-

operative lab values, protecting the kidneys is the next priority. One important CPB factor affecting renal perfusion is hemodilution. Hemodilution lowers blood viscosity, increasing systemic blood flow, and perfusion [7,10]. Microcirculatory improvement reduces afterload (decreasing shear stress on the arterial side) and increases venous return resulting in an improved cardiac output [7]. This includes improved renal perfusion and urine output. Moreover, hemodilution lowers plasma oncotic pressure, thus maintaining GFR at low perfusion pressures. During CPB, this translates into an increased urine output and decreased creatinine and sodium clearance. By reducing urine osmolarity via hemodilution, renal tubule constitution is protected [7,8,10]. Hemodilution also generates less hemolysis when compared to blood prime [14].

Hemolysis results in hemoglobin release into the plasma [5]. If the level of filtered hemoglobin supersedes the transport maximum for reabsorption, hemoglobinuria may manifest [5]. Precipitate casts from the hemoglobin then form within the renal tubules, altering their ability to function and possibly leading to acute tubular necrosis [5,14]. Albeit, nephrotoxic levels of hemoglobin are rarely reached during CPB [5]. It could be considered, however, in high-risk patients to send cardiotomy suction to be processed (washed and concentrated) via cell saver before returning it to the extracorporeal circuit in an effort to prevent this from occurring.

Lastly, using a crystalloid prime rather than blood prime reduces the incidence of adverse homologous blood syndrome reactions [6]. Historically, homologous blood syndrome was blamed for intraoperative and postoperative bleeding diathesis in addition to post-CPB cerebral, pulmonary, and renal dysfunction [6]. It was thought to be a result of incompatibility from cross-reactions between multiple units of donor blood that mixed together in the extracorporeal circuit during priming [6]. However, now that blood prime is less frequently used, the incidence of homologous blood syndrome and associated renal dysfunction has reduced. Another relatively antiquated CPB protection consideration is the elimination of bubble oxygenation [15]. As membrane oxygenators and filters have become the standard of care, the incidence of emboli has gone down, including any ensuing renal impairment because of this.

Once protective measures have been deliberated, management strategies for patients on CPB that are presenting with renal impairment are considered more closely. Urine output for patients should be 1 cc/kg/hour [8]. This is the simplest indicator for renal function during CPB. It should be noted that variable perfusion pressures, hypothermic techniques, and mannitol in pump prime all commonly alter urine output, possibly making it an inaccurate predictor of renal perfusion [1,8].

Regardless, oliguria needs to be addressed immediately when present [8]. Technical problems should be ruled out first. Patency of the urinary catheter tubing, catheter tip obstruction with gel, or disconnected tubing are all possibilities [8]. Following this, CPB flow rates may need to be increased, ideally maintaining a mean pressure of 65 mmHg with vasodilators and pump flows at 30 to 50 mL/kg to maintain GFR [8]. Drugs that compromise renal function (e.g., phenylephrine, norepinephrine) should be eliminated if possible [8]. Hydration should be maintained by an infusion of a balanced electrolyte solution, ensuring appropriate intravascular volume [8]. If at this point the patient is still producing inadequate urine output, renal vasodilation and diuretic therapy should be considered.

To attenuate renal vascular resistance, dopaminergic agents such as dopamine, dopexamine, and fenoldopam are frequently used. Of the three, fenoldopam seems the most efficacious [17]. Dopamine stimulates both DA-1 and DA-2 receptors which have opposing effects on renal blood flow, sodium, and water secretion, making it difficult to predict how it will interact on a given patient [17]. Dopexamine is less receptor specific (i.e., active at DA-1, DA-2, and β_2 receptors) [17]. Fenoldopam is a specific DA-1 receptor agonist, having minimal effects on systemic blood pressure while increasing RBF, urine output, and decreasing renal vascular resistance [17].

Diuretics can also be given to maintain renal tubular flow [8]. Osmotic diuretics such as mannitol function by raising plasma and tubular fluid osmolarity. Mannitol is a pharmacologically in-

ert sugar with a low rate of metabolism in the body [17]. Mannitol is readily filtered with nominal reabsorption, limiting tubular water and electrolyte reabsorption, thus maintaining GFR and urine output [17]. However, if GFR is severely depressed and tubular necrosis supervenes, the kidney will be unable to form urine even with the osmotic load [17]. At this point, mannitol is contraindicated for because of its capability to cause plasma volume expansion which can lead to pulmonary edema and congestive heart failure [17].

If mannitol is no longer an option, high ceiling (loop) diuretics may be considered (e.g., bumetanide and furosemide) [17]. Loop diuretics function by inhibiting sodium reabsorption in the ascending limb of Henle, proximal convoluted tubule, and distal convoluted tubule, causing additional water and chloride excretions [8,17]. Furthermore, it is active in patients with relatively severe renal failure and has a rapid onset of 2-10 minutes with a duration of 1-2 hours, making it an excellent therapeutic choice in managing AKI [8,17]. While administering loop diuretics, electrolytes should be monitored closely as metabolic alkalosis may result [17].

Renal impairment persists as a complication of cardiovascular surgery and is a substantial contributor to post-CPB mortality. Geriatric patients with preexisting renal dysfunction may never recuperate kidney function following AKI, requiring a renal replacement therapy for the duration of their life. Recognizing vulnerable patients and being proactive along with aggressive intervention strategies vastly improves patient outcomes and is essential in addressing CPB induced renal impairment.

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