TITLE: **CHALLENGES IN POSTOPERATIVE CARDIAC CARE IN THE GERIATRIC PATIENT**

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The Changing Playing Field

In Western countries not only is the average age of the population rising, but the so is the age of patients undergoing cardiac surgery. Between 1935 and 2009, the proportion of the US population ≥ 65 yrs increased from 6% to 13%, and now 6% are > 75 yrs of age. The Society of Thoracic Surgeons (STS) National Database revealed that of the more than 660,000 patients who underwent cardiac surgical procedures between 1997-2000, nearly 10% were over the age of 80 yrs; more than 1,000 patients were older than 90 yrs and 5 were older than 100 yrs[1]. Numerous studies attest to the fact that cardiac surgery in octogenarians – especially coronary artery revascularization or isolated aortic valve surgery - can achieve improved NYHA functional class, long-term functional benefit and enhanced quality of life[2-5]. More than 80% of all surviving patients live at home, either alone or with their family[6]. However, there are considerable challenges. Variability in organ function and reserve is much greater in the elderly. Compared with their counterparts aged 60-69 yrs, octogenarians are more likely to have hypertension, present with class IV angina or congestive heart failure (CHF) and the perioperative course is more complicated and longer[7]. There is a 50% increased risk of re-exploration for bleeding bleeding[8]. One study showed an increase in mortality (9 vs. 3.4%) and stroke (5.7 vs. 2.6%), and a decreased median 5-yr survival (55% vs. 81%)[9]. Survival also falls off quite rapidly between 3 and 8 years – from 79% to 38% in one study on aortic valve surgery[6]. It has been suggested that there is a need for more proactive elective surgery in patients > 80 yrs, because they do not do well with emergency cardiac operations. A review of the STS database indicated that major preoperative risk factors in patients >90 yrs are emergent/salvage surgery, IABP placement, acute renal failure, peripheral vascular disease (PVD) or cerebrovascular disease and mitral regurgitation (MR). If these factors are excluded, the CABG-related mortality risk approaches that of younger patients[1].

The Pathophysiology of Aging

Cardiovascular:

Cardiovascular disease progressively increases with age and remains the leading cause of death in the United States. The coronary arteries become stiffer, thicker, and more prone to vasospasm even without pathological atherosclerosis, increasing the risk for myocardial ischemia and heart failure[10]. One mechanism appears to be an aged-related decrease in density of certain voltage-dependent, calcium activated potassium channels. This decreases basal (tonic) endothelial release of nitric oxide (NO) and increases the response to endothelial constrictor factors [10].

A hallmark of the aging left ventricle (LV) is progressive diastolic dysfunction, characterized by abnormal relaxation and prolonged isovolumic relaxation time (IVRT). Some of this may also be induced left atrial (LA) impairment resulting in a decreased atrio-ventricular pressure gradient [11]. These changes may be a consequence of an age-related decline in myocardial cellular energy production, with impaired resilience to ischemic stress. Oral Coenzyme Q10 (CoQ10) therapy for 2 weeks preoperatively in patients undergoing elective cardiac surgery has been associated with increased efficiency of mitochondrial energy production and post-operative cardiac function, decreased troponin I release and shortened hospital stay[12]. The mechanism is assumed to be the replacement of the defective components in the respiratory chain so that the effects of oxidative stress are constrained.

Myocardial aging is characterized by oxidative modification of cardiac proteins by non-enzymatic glycation that produces advanced glycation end-products (AGEs). Animal studies reveal that an accumulation of AGEs contributes to cardiac diastolic dysfunction and reduced stress tolerance in aged cardiac myocytes[13]. Pericardial levels of carboxymethyllysine (CML), an AGE that is marker of cardiac senescence, correlate inversely with LV ejection fraction (EF) and directly with poor outcomes after cardiac surgery such as adverse cardiac events, prolonged ventilation time and prolonged ICU length of stay (LOS) [14].

Arterial baroreflex control of heart rate (i.e. cardiovagal baroreflex sensitivity) diminishes with age as a consequence of impairment of the parasympathetic component, although the sympathetic component is well maintained [15]. As a consequence, the elderly have increased variability in blood pressure, impaired heart rate response to vasodilation and hypotension and increased risk of sudden cardiac death[16]. Apparent sensitivity to vasodilator drugs such as sodium nitroprusside increases with age, but this is mediated through the progressive decline in reflex, compensatory increases in heart rate [17].

The incidence of atrial fibrillation after cardiac surgery increases with age[18], and increases postoperative morbidity and ICU LOS and cost[19]. Persistent atrial fibrillation requires anticoagulation, which further increases the risk of delayed bleeding, pericardial tamponade and hemorrhagic stroke. Conduction disease is also more common, and the requirement for postoperative permanent pacemaker placement is increased from <3% to nearly 10%[20].

In the peripheral circulation, aging is characterized by progressive increase in vascular stiffness and decline in arterial compliance leads to elastic mismatch and increased wave reflections, which further amplifies cyclic stress on the vasculature [21]. The net effect is widening of the brachial pulse pressure (PP). Wide PP has a significant correlation not only with the risk of stroke but also stroke-related mortality[22]. Progressive vascular stiffness is likely related to a progressive decline in endothelial NO production or relaese [23]. Aging and lack of exercise is associated with elevated plasma low-density lipoprotein cholesterol (LDL-C), which further impairs endothelium-dependent dilation[24].

Another ominous correlate of wide PP is isolated systolic hypertension (ISH), which has a high prevalence of in the elderly. In a large prospective epidemiological study of patients undergoing CABG surgery, ISH was found in 30% of patients, and was associated with a 40% increase in risk of adverse outcomes such as LV dysfunction, neurologic injury, acute kidney injury (AKI) and all-cause mortality [25].

Pulmonary:

Aging induces progressive changes in pulmonary function that compromise the elderly patient's reserve. With loss of elastin, the lungs become more compliant but alveolar static elastic recoil becomes more impaired and closing capacity (the volume at which expiratory airway closure occurs) increases. This in turn increases air trapping, the diaphragm flattens, and work of breathing increases. The chest wall becomes more calcified and less compliant, and respiratory muscle performance is less efficient. The net effect is an increased work of breathing. These changes are not reflected by arterial blood gases, but there is progressive compromise to pulmonary reserve when it is challenged by heart failure, sepsis, pneumonia or airway obstruction[26]. The decline in lung function with age – using serial measurement of FEV_1 - may be greater when endogenous cortisol levels are low[27].

Elderly patients are at increased risk of aspiration of oropharyngeal or gastric contents, and thereby at increased risk to postoperative and ventilator-associated pneumonia (VAP). The etiology is multifactorial. Saliva – which can eliminate Gram-negative bacilli – is often diminished by medications or poor oral hygiene. Oropharyngeal colonisation with pathogenic organisms ensues. Cerebrovascular disease causes dysphagia and increased aspiration risk. Subclinical aspiration can occur in the setting of silent cerebral infarction affecting the basal ganglia, which impairs dopamine metabolism and decreases substance P in the glossopharyngeal and sensory vagal nerves, impairing the cough reflex[28].

There is a strong positive correlation between age and the increase in extravascular lung water (EVLW) content after CPB. Oxygenation (PaO_2) is decreased and intrapulmonary shunt fraction (Qs/Qt) is increased[29]. This defect usually normalizes within five hours but if there are additional complications (prolonged CPB, blood transfusion, etc) it may expose the lungs to more long-standing injury and even ARDS.

Neurologic:

The risk of perioperative stroke increases progressively with age. This is largely due to progression of atherosclerosis, which is exacerbated by cigarette smoking, hypertension and diabetes. Involvement of extracerebral vessels predisposing to embolic stroke, while intracerebral lesions predispose to ischemic stroke. There is also progression of intracerebral small vessel disease, which results in cerebral white matter lesions and lacunar infarcts that are associated with cognitive decline and dementia[30]. Postoperative cognitive decline is more likely in these patients, and may be exacerbated by microembolization during surgical mainipulation and CPB, or by low flow / pressure ischemia.

Postoperative delirium may occur in up to 44% of elderly patients; pre-existing dementia is clearly the most important risk factor for its development. It is characterized by a fluctuating acute confusional state, loss of attention and cognitive skills, disorientation and even hallucinations. The impact on outcome is very negative, with increased hospital LOS, post-discharge institutionalization and 6 month mortality[31].

Renal:

Age induces a progressive decrease in kidney size and blood flow, and loss of glomerular function[32]. The glomerular filtration rate (GFR), which is about 125 mL/min in a young healthy adult, declines to about 80 mL/min in a sixty-year old, and 60 mL/min in an eighty-year old (age-related GFR may be approximated by [140-age]). However, serum creatinine (SCr) does not exceed normal laboratory values until the GFR is less than 50 mL/min. Thus, an octogenarian may have a normal SCr, but his / her renal reserve is less than half that of a young patient.

Although body fluid homeostasis is maintained until an advanced age, the ability to respond rapidly and appropriately to acute illness or surgical trauma becomes progressively impaired. Mechanisms controlling thirst, urinary concentrating ability, and free water excretion become impaired, which explains why sick older patients are so quick to develop hypernatremia or hyponatremia in the postoperative period. Potassium homeostasis is also impaired, and elderly patients are at greater risk of drug-induced hyperkalemia[33].

These changes are multifactorial, and are exacerbated by chronic illnesses that involve the kidney and cause glomerulosclerosis, including hypertension, diabetes, and atherosclerotic disease[34]. Compared with young patients, the renal vasoconstrictor response is more sensitive to physiologic and pathologic stimuli, including mental stress and intravascular hypovolemia, whether it is absolute or relative (e.g. CHF). It may reflect a decrease in endogenous vasodilator prostaglandins. Renal hemodynamic and humoral adaptation to adrenergic activation and elevated blood pressure is impaired, and in elderly patients with ISH, almost completely lost [35]

Hepatic:

Liver function and reserve is quite well preserved with age. However, in animal models demonstrate that cellular regeneration after injury is impaired, probably due to the aging antioxidant enzyme system, and post-necrotic restoration of liver function is delayed.[36].

A Check-list of Postoperative Complications in Elderly Patients after Cardiac Surgery:

- ❑ Increased requirement for inotropic support after CPB[37]
- ❑ Increased risk of bleeding and re-operation for exploration[8]
- ❑ Increased risk of perioperative stroke{van Dijk, 2008 #49}
- ❑ Increased risk of cardiac arrhythmias, especially atrial fibrillation[18]
- ❑ Increased risk of conduction disorders, temporary and permanent pacing [20].
- ❑ Increased risk of aspiration, pneumonia and postoperative respiratory failure[28].
- ❑ Increased risk of AKI and dialysis-dependent ARF – however, the outcome in the elderly requiring dialysis due to ARF post-cardiac surgery is comparable with the outcome in a younger population[38].
- ❑ Increased risk of postoperative delirium[39].
- ❑ Prolonged ICU and hospital LOS, increased requirement for prolonged rehabilitation and postoperative institutionalization.

A representative case (or two) will be presented.

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