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## Review Article

# Coronary Artery Bypass in Octogenarians<sup>☆</sup>

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### SUMMARY

Prevalence of coronary artery disease (CAD) has increased with the expansion of life span among the elderly population in the world. Hence, the issue of the coronary artery bypass in octogenarians has attracted more attention. Recent literature about the topic revealed nearly the same excellent results as those in the younger population under the newly developed operative techniques and improving concept in perioperative management and postoperative care. In this article, we review the current status of the procedure that was thought to be dangerous in the earlier era, including its risk factors, result, and benefit.

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## 1. Introduction

With the improvement of health-care system, life expectancy among the elderly population has increased. The population of octogenarians in European Union will increase by 57% during 2010–2030<sup>1</sup>. Coronary artery disease (CAD) is still the leading cause of morbidity and mortality in this population. The issue of the coronary artery bypass (CABG) in octogenarians has attracted more attention. In earlier series, longer hospital stays and increased morbidity and mortality were reported among octogenarians after CABG; recent reports stated the same results and survival benefits as those in the younger population<sup>2</sup>. In this article, we review the current status, including the risk factors, the result, and the benefit, of octogenarians accepting CABG.

## 2. Therapy choice

Although medical therapy alone was once the preferred approach in octogenarians with CAD, in the modern literature, revascularization is indicated to treat recurrent symptoms resistant to optimal medical therapy and also to improve survival<sup>3</sup>. In high-risk patients with multivessel disease, CABG has constituted the gold standard for revascularization since its introduction in 1962 and offers prolonged survival, as indicated in multiple studies<sup>4</sup>. Percutaneous coronary intervention (PCI), another method of

revascularization with less invasiveness since its introduction in 1977, has grown at a significant rate and contributed to a decline in the number of CABGs performed annually. According to ElBardissi's review<sup>5</sup>, the percentage of patients who underwent PCI prior to CABG increased by 37% during 2000–2009 (19% vs. 26%). However, the Synergy Between PCI With TAXUS and Cardiac Surgery (SYNTAX) clinical trial revealed that the rates of major adverse cardiac or cerebrovascular events at 12 months were significantly lower in patients with three-vessel or left main disease who underwent CABG than in those who underwent PCI<sup>6</sup>. CABG was associated with significantly higher survival rate (66.0% vs. 46.1%) and freedom from composite outcomes such as death, repeat revascularization, stroke, and acute myocardial infarction (AMI) at 3 years, as shown in Sheridan's series<sup>7</sup>. Hence, CABG plays an important role in the treatment of octogenarians with CAD. However, several complications such as stroke, bleeding, and systemic inflammation associated with the conventional CABG were blamed on the use of cardiopulmonary bypass (CPB); many surgeons started to use less traumatic alternatives such as off-pump coronary artery bypass (OPCAB), which was popularized in the early 1960s and abandoned on the arrival of CPB. Aging of the population with increased comorbidities and the desire to compete with less invasive PCI have urged surgeons to rehabilitate this challenging procedure.

## 3. Current status of CABG in octogenarians

The pooled estimate of 30-day mortality of CABG in octogenarians was 7.3% (6.3–8.2%) and 1-year survival rate was 86% (83–88%), similar to PCI [5.4% (4.4–6.4%) and 87% (84–91%)

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respectively) in a Mckellar's systematic review enrolling 65,376 patients aged over 80 years<sup>8</sup>. During the same period, the observed mortality rate of CABG in the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database analysis declined from 2.4% in 2000 to 1.9% in 2009. However, the trend in the proportion of octogenarians undergoing CABG increased from 1% in 1990 to 6% in 2005 in Maganti's series<sup>9</sup>, with the assumption that the risk profile including diabetes, dyslipidemia, hypertension, left main disease, chronic obstructive pulmonary disease (COPD), and peripheral artery disease (PAD) of patients undergoing isolated CABG is worsening. Therefore, CABG in octogenarians seemed to have a higher but acceptable mortality rate under the circumstance.

#### 4. Risk factors of mortality and morbidity

In LaPar's series including 1993 octogenarians undergoing CABG, the most common cause of mortality was cardiac in origin (47.6%), followed by pulmonary (17.1%), neurologic (10.5%), renal (5.7%), and infections (4.8%)<sup>10</sup>. Risk-adjusted odds ratios and multivariable logistic regression results in this series showed that the mortality was associated with female gender, preoperative atrial fibrillation (AF), presence of left main coronary artery occlusion of 50% or more, and degree of intraoperative blood transfusion. An increase in the odds of mortality was associated with performance of urgent/emergency operations and depressed ventricular function.

Several kinds of morbidities were mentioned. Postoperative AF (16.2%) and low cardiac output syndrome (9.5%) constituted the major morbidities in Nicolini's series. Other morbidities included major ventricular arrhythmia episodes (9.5%), perioperative myocardial infarction (1.7%), respiratory failure requiring prolonged mechanical ventilation, acute renal failure (9.5%), subcutaneous presternal wound infection (2.1%), and re-sternotomy due to bleeding (1.7%). Incidences of stroke and transient ischemic attacks were only 0.4% and 0.8%, respectively<sup>11</sup>.

#### 5. Could OPCAB offer better results?

Revival of OPCAB was initiated in the mid-1990s and has currently been adopted worldwide for the avoidance of the inherent risks of CPB and cardioplegic arrest. The less invasive nature of OPCAB makes it an attractive option in such a relatively high-risk group of octogenarians. According to the STS National Adult Cardiac Surgery Database, more than 163,000 isolated CABGs were performed in 2009, of which OPCAB accounted for just over 34,000 (20.8%)<sup>12</sup>. Concerns regarding higher incidence of incomplete revascularization, recurrent angina, and graft occlusion have prevented OPCAB from being universally adopted<sup>13</sup>. In Singhal's series, there was no statistically significant difference in mortality, stroke, renal dysfunction, AF, re-exploration for bleeding, deep sternal wound infection, or pulmonary complications. However, use of inotropes and blood transfusion requirements were less in the OPCAB group<sup>14</sup>.

In Saleha's series, 343 octogenarians were stratified into two groups accepting conventional CABG and OPCAB under the same preoperative patient characteristics, including logistic EuroSCORE. Postoperatively, the in-hospital mortality was 6.5% in the conventional CABG group compared to 4.7% in the OPCAB group ( $p = 0.55$ ). Postoperative complications such as stroke, renal failure, AF, re-sternotomy for bleeding, and deep sternal wound infections showed no statistically significant difference between the two groups. However, less use of inotropes, shorter mechanical ventilation, and shorter intensive care unit (ICU) stay were associated with the OPCAB group<sup>15</sup>. LaPar's series also revealed similar results, except

that prolonged ventilation and postoperative AF were more common in the conventional CABG group<sup>10</sup>.

#### 6. Strategies to improve the outcome

With continued refinements in preoperative preparation, surgical technique, cardiac anesthesia, and postoperative management, CABG could be performed in octogenarians with acceptable results. In Maganti's series, a decline in operative mortality among octogenarians undergoing CABG from 7.1% to 3.2% between 1990 and 2005 was noted, along with a decreased incidence of postoperative complications such as stroke, low cardiac output, and use of intra-aortic balloon pump (IABP). However, an increased prevalence of risk factors such as diabetes, dyslipidemia, hypertension, and left main disease in this population during the same period could not alter the improving operative results<sup>9</sup>. Although some preexisting risk factors could not be modified or corrected in time, several strategies could still be used to improve the outcome.

##### 6.1. Preoperative preparation

Urgent or emergent procedures constituted a significant predictor of hospital mortality following CABG<sup>16</sup>. All preoperative management must be taken to optimize the octogenarians and then to convert an urgent or emergent situation to a more elective predicament. Aggressive preoperative medication, including the use of intravenous nitroglycerin or heparin (or both) and inotropes use, mechanical ventilator support, and, if absolutely necessary, the IABP, should also be considered. Although the preoperative use of the IABP is a significant predictor of perioperative mortality, it likely reflects the severity of the patient's underlying cardiac disease, rather than any inherent risk in using the device. Imamaki stated that in high-risk patients such as those with marked left main disease and left ventricular dysfunction, the outcomes of OPCAB using elective IABP were similar to those of OPCAB in low-risk patients<sup>17</sup>. The use of elective IABP in OPCAB for octogenarians could afford better results than conventional CABG, and the catheter could be removed in early postoperative period for the prevention of complications.

##### 6.2. Stroke prevention

Perioperative stroke occurred in 6% of patients undergoing CABG and resulted in a six-fold higher mortality. Two common causes are embolization (atheroma, air, calcified debris) and hypotension resulting in inadequate perfusion of the central nervous system. Preoperative evaluation of the ascending aorta and carotid arteries, and intraoperative assessment of the proximal aorta using transesophageal or epiaortic echocardiography enable the surgeon to avoid cannulation or direct manipulation of heavily diseased portions of the aorta where atheromas may dislodge or where plaque disruption may cause aortic dissection. OPCAB was also expected to reduce neurologic complications on the basis of the assumption that CPB caused the decrease in embolization. However, it has not abolished the risk of postoperative stroke seen for conventional CABG in recent series report.

##### 6.3. Intraoperative management

In Rhode's series analyzing the long-term survival of 606 octogenarians accepting cardiac surgery, the mortality was associated with CPB time, internal mammary artery (IMA) use, and minimum nasopharyngeal temperature in univariable analysis. However, in the multivariable analysis after adjustment for other risk factors, only CPB time remained associated with greater mortality risk<sup>18</sup>.

This is compatible with the viewpoint that the OPCAB and the more IMA use, better operative results could still be expected under the worsened comorbidities of the patient.

The superiorities of IMA as a bypass graft over the commonly used saphenous vein are based upon several structural and physiological differences. IMA exhibits better size match with the grafted native vessel, and possesses no valves and fewer endothelial fenestrations. Physiological differences include the higher flow reserve and shear stress of the IMA, higher nitric oxide and prostacyclin production, relaxation response to thrombin, low vasoconstrictor sensitivity and high vasodilator sensitivity, and fewer fibroblast growth factor receptors. Each of these differences establishes the plausibility of a protective effect of IMA use on short-term mortality. Multicenter studies also revealed long-term survival after CABG using the IMA, even in the advanced age and high-risk groups<sup>19</sup>. In Yanagawa's series revealing better results of CABG in the elderly with time, the percent of IMA uses were 63.4%, 78.6%, and 88.6% in the three time periods 1990–1996, 1997–2003, and 2004–2010 respectively<sup>20</sup>; the trend of IMA use reaches the mainstream consensus progressively even in the octogenarians. However, octogenarians are more likely to develop sternal dehiscence because of osteoporosis of the sternum and higher prevalence of diabetes mellitus. Use of bilateral IMA should be avoided. In Savage's series including 120,793 diabetic patients, the crude deep sternal wound infection rate in the group using bilateral IMA is higher than in the group using single IMA (2.8% vs. 1.7%,  $p = 0.0005$ ). But the crude mortality rates were similar (1.7% vs. 2.3%,  $p = NS$ )<sup>21</sup>.

#### 6.4. Postoperative care

##### 6.4.1. Ventilator use

Octogenarians are more likely to require prolonged mechanical ventilator use. The associated risk factors include borderline hemodynamics, postoperative bleeding, and stroke or decrease the level of consciousness. Prolonged ventilation increased the incidence of nosocomial infections followed by development of sepsis, impeding the patient's rehabilitation program and thus delaying their recovery. Firstly, delicate care should be taken to avoid injury to the phrenic nerve during the IMA harvest intraoperatively. As soon as the patients wake up from general anesthesia, respiratory muscles must be exercised. Pulmonary hygiene and physiotherapy must be aggressive with early and progressive ambulation. Unlike the younger population, octogenarians have much less functional reserve; therefore, a successful first attempt at extubation and mobilization, decreasing the risks of ventilator-associated pneumonia and often improving hemodynamics, could ensure the best possible outcome<sup>22</sup>. After extubation, aggressive pulmonary care is important, including frequent incentive spirometry, coughing, and deep breathing to help maintain the functional residual capacity. In contrast, in patients requiring prolonged ventilator use, tracheostomy should be considered, owning the advantages of decreased airway resistance, absence of oral–labial ulceration, easier oral hygiene or bronchopulmonary toilet, and airway security improvement. Tracheostomy can also lead to less sedative use and less time in heavy sedation, enhanced patient's mobility, and early oral feeding. These maneuvers could allow the octogenarians to wean from the ventilator earlier<sup>23</sup>.

##### 6.4.2. Acute renal insufficiency

In octogenarians accepting CABG, acute renal insufficiency (ARI) is a more frequent complication than in the younger population. Other risk factors of ARI include preoperative renal insufficiency, advanced age, history of congestive heart failure, diabetes mellitus, recent exposure to nephrotoxic agents, IABP, emergency operation,

prolonged duration of and decrease in urine output during CPB, and need for deep hypothermic circulatory arrest. It increases short- and long-term mortality, incidence of postoperative complications such as respiratory infections, sepsis, gastrointestinal bleeding, and hospital lengths of stay. In Swaminathan's series, the incidence of acute renal failure after CABG was noted to increase significantly from 1.1% to 4.1%, with the proportion of acute renal failure cases requiring hemodialysis decreasing from 15.8% to 8.7%<sup>24</sup>. OPCAB method or decrease in CPB time intraoperatively seemed to decrease the incidence of ARI. In ARI management, first the cause should be categorized as either nonoliguric or oliguric type. Nonoliguric renal failure is associated with a more easily negotiated balance between volume overload and electrolyte homeostasis. In this situation, it is paramount to avoid further insults to the kidney, including avoidance of nephrotoxic medication while awaiting renal function recovery. In oliguric renal failure, high-dose diuretics are often used to convert the nonoliguric phase with the hope of minimizing the impact of fluid retention and volume overload, resulting in pulmonary congestion, tissue edema, and then worsening of the heart function. Renal replacement therapy often becomes necessary as a result of hypervolemia, hyperkalemia, and metabolic acidosis. Correction of electrolytes can be achieved with either intermittent hemodialysis or continuous venovenous hemodialysis, frequently used in unstable hemodynamic status. However, renal replacement therapy is not benign. In Wijey-sundera's series, the incidence of renal replacement therapy in octogenarians was over 4%, 2–3 times that seen in a typical population of open heart surgery patients viewed as a whole, and was associated with a mortality of over 60%<sup>25</sup>.

##### 6.4.3. Delirium

Besides stroke, another common neurologic sequela is the postoperative delirium, a transient but global impairment in cognitive function, which occurs in up to 80% of the ICU population. In Miyazaki's series, the risk factors for postoperative delirium in patients after OPCAB included carotid artery stenosis >50%, age over 75 years, creatinine >1.3 mg/dL, a history of hypertension, a past history of AF, and smoking<sup>26</sup>. Delirium is associated with a significant increase in mortality and length of stay. The key steps in the management of delirium are to recognize and abolish all evident causes, and provide supportive care such as protecting the patient's airway, maintaining hydration and nutrition, transferring out of ICU when possible to restore the sleep–wake cycle, and encouraging family members to provide reassurance and encouragement. In pharmacological management, haloperidol is a more appropriate drug for the management of delirium in octogenarians because of its short-acting effect and safety margin. Since delirium may take weeks or months to resolve, patients must be taken care of in supervised settings. Close clinical follow-up after discharge is needed, especially because of the poor long-term prognosis associated with delirium.

##### 6.4.4. Wound complication

Incidence of wound complications, such as sternal dehiscence, superficial and deep sternal wound infections, or mediastinitis ranging from 0.3% to 8%, is commonly seen in the octogenarians. These result in increases in morbidity and mortality from 10% to 40%, health-care costs, and the length of hospital stay. Host factors, intraoperative variables, and postoperative complications all constitute the risk factors. Host factors include old age, diabetes, chronic renal insufficiency, obesity, osteoporosis (especially in women), and poor nutritional status, nearly compatible with the octogenarians. Intraoperative variables include emergent operations, prolonged CPB time, and bilateral IMA use, especially in diabetics. Postoperative complications include mediastinal

bleeding, prolonged ventilation, and poor glucose control. Use of OPCAB to avoid complications is more commonly seen in conventional CABG, and postoperative respiratory fast-track weaning seems to decrease the incidence of complication. Treatment modalities include early antibiotic therapy and timely debridement such as complete sternectomy with myocutaneous flap closure or a secondary closure with a wound vacuum device. Mediastinitis may produce long-term adverse effects on cardiac, pulmonary, and renal functions, which already have limited reserve in the elderly population. This has been shown to result in a 2–4-fold increased risk of death from 1 to 10 years after the initial cardiac operation. More aggressive treatment involving the plastic surgeons earlier at the time of first debridement seems to be the preferred management<sup>27</sup>.

#### 6.4.5. Atrial fibrillation

AF occurs in 16–40% of patients undergoing CABG<sup>28</sup>. It causes thromboembolic events and is responsible for increased risk of mortality, stroke, and congestive heart failure, and increased hospital stay and cost. Age, the major risk factor in most studies, increases the prevalence of AF by 44% in every 10 years.  $\beta$ -Blockers have been shown to be efficacious in reducing the risk of post-CABG AF, and is a class I indication in the American Heart Association (AHA)/American College of Cardiology (ACC)/European Society of Cardiology 2006 guidelines for the management of AF and in the ACC/AHA 2004 guidelines for CABG. Amiodarone is another proven preoperative therapy to reduce the risk of post-CABG AF. OPCAB used intraoperatively also seems to decrease the incidence in some series, although some controversies still exist. Postoperative management includes more commonly used rhythm control strategy with amiodarone, sotalol, or other antiarrhythmic medications, and rate control strategy with a  $\beta$ -blocker and/or digoxin. Combination use with warfarin for prophylaxis of thromboembolic events is also used in some centers. Lack of definitive data on the most effective therapies resulted in these variations. In Al-Khatib's series, after the development of post-CABG AF, 30-day mortality was higher than in patients without AF (1.5% vs. 0.7%,  $p = 0.01$ ), but 3-year mortality was similar (6.9% vs. 4.9%,  $p = 0.41$ )<sup>29</sup>.

#### 6.4.6. Low cardiac output syndrome

The incidence of low cardiac output syndrome after CABG is 3–14%, and is associated with a 10–17-fold increase in mortality and markedly increased morbidity. The risk factors include left ventricular ejection fraction <20%, emergent operation, and female gender<sup>30</sup>. Its management includes the establishment of the meticulous monitor system including central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) measurement, and even echocardiography performance, for early detection of perioperative cardiovascular dysfunction and assessment of the mechanisms leading to it. In case of preload deficiency, volume supplement should be given cautiously in octogenarians under the guidance of CVP and PCWP. Pharmacological management for myocardial dysfunction include dobutamine and epinephrine, both improve stroke volume and increase heart rate, while PCWP is moderately decreased. Milrinone decreases PCWP and systemic vascular resistance while increasing the stroke volume, and causes less tachycardia than dobutamine, which may increase myocardial oxygen consumption. Norepinephrine should be used in case of low blood pressure due to vasoplegia to maintain an adequate perfusion pressure. Volemia should be repeatedly assessed to ensure that the patient is not hypovolemic while under vasopressors. If the pharmacological management could not improve the cardiac output, mechanical support such as IABP should be considered in case of heart dysfunction with suspected coronary hypoperfusion, and even the extracorporeal membrane oxygenation, an elegant

solution as a bridge to recovery or decision making, should be considered earlier rather than later, prior to the development of end organ dysfunction<sup>31</sup>.

#### 6.4.7. Rehabilitation

Cardiac rehabilitation programs are integral components of the postoperative care. Baseline patient assessment, nutritional counseling, risk factor management (lipids, hypertension, weight, diabetes, and smoking), psychosocial management, physical activity counseling, and exercise training constituted the core elements in the cardiac rehabilitation program recommended by the AHA and the American Association of Cardiovascular and Pulmonary Rehabilitation<sup>32</sup>. A structured exercise program can produce substantial physiological benefits, including the increase of aerobic capacity, muscle strength, and functional performance, and then reduce the later mortality. Resistance exercise after appropriate screening could improve muscular strength and endurance, and then improve the patient's flexibility and balance, resulting in the decrease of fall risks that are common in the octogenarians<sup>33</sup>. A structured inpatient physiotherapy-supervised walking program, with or without musculoskeletal and respiratory exercise, could also improve post-CABG walking capacity at discharge. Organized cardiac rehabilitation program could increase functional capacity, modify disease-related risk factors, detect signs and symptoms of disease before they become serious complications, and improve quality of life.

## 7. Long-term results and benefits

In Filsoufi's series enrolling 2985 patients after CABG, age >80 years was not a predictor of hospital mortality in multivariate logistic regression analysis. The length of stay was significantly higher in octogenarians compared with nonoctogenarians ( $16 \pm 24$  days vs.  $10 \pm 13$  days,  $p < 0.001$ ). Five-year survival was  $63 \pm 4\%$  in octogenarians and was similar to that of an age- and sex-matched general US population<sup>34</sup>. In Nicolini's series, the actuarial 1- and 5-year survivals were 91.9% and 83.5%, respectively. The mean New York Heart Association functional class for survivors improved from  $2.13 \pm 1$  to  $1.8 \pm 0.8$  ( $p = 0.0078$ ), and the functional status derived from Physical Component Summary score questionnaire significantly improved after surgery<sup>11</sup>.

In summary, CABG could meet the demand in upcoming demographic explosion of octogenarians in the world by offering the same results and survival benefits as in case of the younger population under continued refinements in surgical technique, improving concept in preoperative evaluation and postoperative care, and organized cardiac rehabilitation program. Although OPCAB seemed not to have the predominance over conventional CABG, decrease in common morbidities still makes OPCAB an acceptable alternative to conventional CABG for myocardial revascularization in octogenarians.

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