

Off-pump coronary artery bypass grafting in octogenarians

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Abstract: Enhanced life expectancy has confronted cardiac surgery with a rapidly growing population of octogenarians needing coronary artery bypass grafting (CABG). Octogenarians are deemed a high-risk patient population with increased postoperative morbidity and mortality following conventional CABG using cardiopulmonary bypass (CPB). In such patients reducing the invasiveness of the surgical procedure by avoiding CPB may be tried in an attempt to improve outcomes. The increasing performance of off-pump coronary artery bypass (OPCAB) grafting within certain centers reflects surgeon preference to avoid the inherent risks of CPB and cardioplegic arrest including hemodilution, nonpulsatile arterial flow, global myocardial ischemia, atherosclerotic embolization from aortic manipulation, and systemic inflammatory response. Although OPCAB grafting is a well-established surgical myocardial revascularization strategy, its actual benefits in terms of morbidity and mortality remain questionable in the general population. In the higher risk octogenarian patients, however, there is a potential for more tangible clinical benefits when CPB is avoided. This review article provides an overview of the impact of OPCAB grafting on postoperative mortality and morbidity in octogenarians.

Keywords: Coronary artery bypass grafting (CABG); off-pump coronary artery bypass grafting; octogenarians; cardiopulmonary bypass (CPB)

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Introduction

The global elderly population is expanding rapidly, particularly as longevity is also on the rise. In the United States, the population aged 65 and over is projected to almost double from 43.1 million in 2012 to 83.7 million by 2050 (1). The most rapid growth in numbers is for those who are very old (≥ 85 years) (1). On a global scale, the population ≥ 85 years is projected to increase 151% between 2005 and 2030, compared to the increase of only 104% in the population aged ≥ 65 years and only 21% for the population under 65 (1).

Octogenarians tend to have higher rates of comorbid risk factors, which may result in more frequent and severe complications, and higher mortality rates (2). Specific cardiac risks in this patient group include aortic calcification, stiff vessels, diminished cardiovascular response to exercise, and intolerance of anemia. Additional age-

related changes affect performance and physiologic reserve of the pulmonary, renal, and nervous systems as well (3). Nevertheless, surgical outcomes in this age group have been encouraging (4-8).

The merits and indications of off-pump coronary artery bypass (OPCAB) grafting continue to be debated as the body of evidence examining this technique grows. The current best available evidence from meta-analyses suggests that compared with conventional coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB), OPCAB grafting significantly reduces stroke, renal failure, duration of ventilation, atrial fibrillation, transfusion requirements and postoperative length of stay (9-14). Conversely, some randomized controlled trials have been unable to show such benefits (15-21), or have questioned the long-term benefit of OPCAB grafting in terms of graft patency (16,18-21).

Irrespective of the ongoing debate about benefits of

OPCAB grafting in low and intermediate risk patients, there is abundant evidence to suggest that OPCAB grafting should be preferentially offered to high-risk patients including octogenarians as there is a potential for more tangible clinical benefits when CPB is avoided (22,23). This review article provides an overview of the impact of OPCAB grafting on postoperative mortality and morbidity in octogenarians.

Methods

Search methodology

English scientific literature was reviewed primarily by searching MEDLINE from 1966 to May 2016 using PubMed interface (24). The search strategy used was (“coronary artery bypass, off-pump”[MeSH Terms] OR (“coronary”[All Fields] AND “artery”[All Fields] AND “bypass”[All Fields] AND “off-pump”[All Fields]) OR “off-pump coronary artery bypass”[All Fields] OR (“off”[All Fields] AND “pump”[All Fields] AND “coronary”[All Fields] AND “artery”[All Fields] AND “bypass”[All Fields]) OR “off pump coronary artery bypass”[All Fields]) AND (“transplantation”[Subheading] OR “transplantation”[All Fields] OR “grafting”[All Fields] OR “transplantation”[MeSH Terms] OR “grafting”[All Fields]) AND (“aged, 80 and over”[MeSH Terms] OR “80 and over aged”[All Fields] OR “octogenarians”[All Fields]). The ‘related articles’ function was used to broaden the search and all abstracts, studies and citations scanned were reviewed. The reference lists of articles found through these searches were also reviewed for relevant articles. In addition, EMBASE, Cochrane Controlled Trials Register, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Science Citation Index, Current Contents, and International Network of Agencies for Health Technology Assessment databases were searched from the date of their inception to the last week of May 2016.

The search was performed in stages so as to achieve the search strategy with a high sensitivity (meaning that it has the highest likelihood of retrieving all relevant papers). Similar search terms were combined using the Boolean operator ‘OR’ to find all abstracts that contained information about a particular search term. These individual terms were then combined using the Boolean operator ‘AND’ to find papers that contained information on all the search terms. This is a well-recognized method

for performing sensitive searches and has been described in detail in the *British Medical Journal* (25).

Inclusion & exclusion criteria

All studies comparing OPCAB grafting with conventional CABG on CPB using cardioplegic arrest, recruiting octogenarian patients undergoing single or multiple vessel bypass, and reporting mortality or morbidity (organ dysfunction) as outcome of interest were included. Studies reporting on outcomes of hybrid (i.e., OPCAB grafting plus balloon angioplasty) procedures, robotically assisted surgery or using circulatory assist devices were excluded.

Data extraction and validation of the studies

The papers found by the search strategy were then appraised. The appraisal of each paper was performed in a structured format, using critical appraisal checklists. These are widely available in several formats and aid in assessing the paper for methodological and analytical soundness and help uncover any significant methodological flaws (26). The following information was extracted from each study: first author, year of publication, study population characteristics, number of patients operated on with each technique and key outcomes. The aforementioned search methodology and study selection strategy has been previously described (27).

Results

A total of 614 citations were retrieved and reviewed using the search strategy. After exclusion of case reports, review articles, case series, and editorials, 19 citations were selected for review of full text articles. Following exclusion of one article where the full text was in Japanese (28), 18 articles were deemed suitable and met the inclusion criteria listed above. All 18 studies were retrospective studies (2,29-45). Five studies (38,40,42-44) presented propensity-matched comparison of the 2 cohorts. One presented the analysis of the Nationwide Inpatient Sample database from 2005 to 2010 (39), whereas another reported data from the State of Virginia database for the period 2003 to 2008 (44). The remaining studies were from single centers. The detailed review process is outlined in *Figure 1* and study results in *Table 1*.

The selected studies suggested that rates of early mortality, new-onset renal failure, atrial fibrillation,

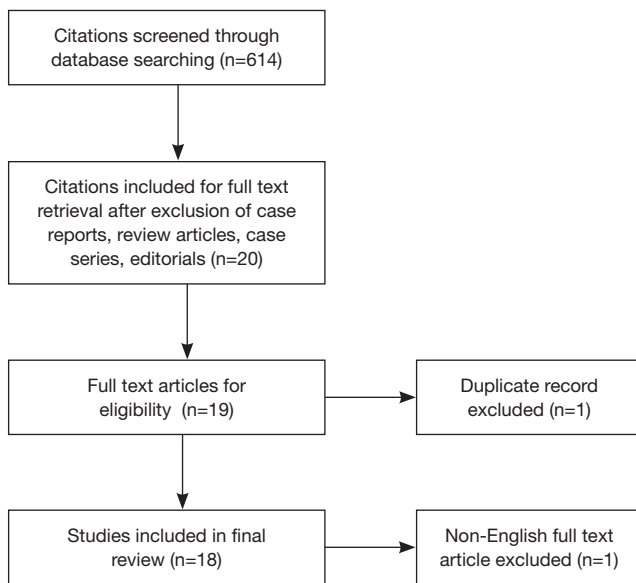


Figure 1 Flow chart depicting study selection for the review.

and myocardial infarction were comparable (*Table 1*). Respiratory failure and stroke rates were higher in octogenarians that had CABG with the aid of CPB (*Table 1*). There was wide variation in the number of grafts performed in each group amongst the selected studies with only four studies (34,35,38,40) reporting a similar number of grafts in both cohorts. Late survival (follow-up period ranging from 2–10 years) was reported by only 4 of the 18 studies (31,37,40,42) and was comparable. A meta-analysis of 16 of the 18 studies included in this review reported similar findings (46).

Discussion

Cardiac surgery in octogenarians has risen steadily since the 1980s. The octogenarians are now the fastest growing population in Western countries, and the number of octogenarians with coronary artery disease potentially eligible for surgery is expected to increase (47).

Conventional CABG with the aid of CPB and cardioplegic arrest has, for many years, been regarded the “gold standard” in coronary revascularization (43). However, during the last 10 to 15 years, OPCAB has emerged as a valid alternative. This status of OPCAB is based on the perception that avoiding injurious effects of the CPB improves outcomes and possibly decreases resource utilization and costs (48). High-risk patients including the octogenarians are particularly vulnerable to

organ dysfunction due to the deleterious effects of CPB (49). There is convincing evidence from observational studies, propensity score analyses, and randomized controlled trials, that OPCAB is associated with risk reduction for stroke and acute kidney injury as well as reduction in transfusion and inotrope requirements, ventilation time, intensive care unit and hospital stays (9,13). Hence, there is a logical argument to offer OPCAB surgery preferentially to octogenarians because decline of neurocognitive functions, delirium, stroke, increased length of stay, and renal failure are common complications more frequently encountered in this patient population (45,50).

Acute postoperative neurological events considerably affect the outcome of cardiac surgery in octogenarians (50). There is also a direct relationship between acute postoperative neurological events and operative mortality. Neurological events also increase the tendency to develop respiratory complications, and prolong hospital stay by slowing patient recovery and ambulation (50,51). Despite multifactorial pathogenesis of cerebral injury and cognitive dysfunction after cardiac surgery, there is increasing evidence that diffuse ischemic cerebral injury is caused by multiple microemboli arising from the ascending aorta, the heart chambers, or the bypass circuit (52). Elimination of CPB and adoption of the aortic “no touch” technique, which avoids intraoperative atheromatous embolization from the atherosclerotic aorta into the cerebral circulation, are associated with improved neurologic outcomes (53). The current best available evidence albeit from retrospective studies confirms the beneficial impact of OPCAB in improving neurological outcomes in octogenarians (*Table 1*).

Postoperative pulmonary dysfunction is a significant cause of morbidity after CPB-assisted surgery (53). The occurrence of pulmonary derangement after cardiac surgery is thought to be multifactorial. In addition, to disruption of chest wall mechanics, it is well recognized that CPB induced inflammatory response produces increased pulmonary endothelial permeability, parenchymal damage, and changes in the composition of alveolar surfactant (54,55). It can be hypothesized that avoiding CPB should reduce postoperative pulmonary dysfunction due to absence of the CPB-induced systemic inflammatory response. This benefit is more likely to be seen in the octogenarian population and is confirmed by the current best available evidence (46).

Currently, the evidence comparing impact of OPCAB on postoperative complications in octogenarians fails to show an impressive advantage of avoiding CPB other than reduction in respiratory failure and stroke

Table 1 Current best available evidence comparing impact of off-pump and on-pump coronary artery bypass grafting on outcomes in octogenarians

First author, journal, year of publication (Ref)	Study population characteristics	Number		Key outcomes
		OPCAB	ONCAB	
Ricci <i>et al.</i> , <i>Ann Thorac Surg</i> , 2000 (29)	Octogenarians	97	172	Increased reoperations in OPCAB cohort (16.5% vs. 4.7%; P=0.002); trend towards higher graft-patient ratio in ONCAB cohort (3.3 vs. 1.8; P= NS); higher freedom from reoperation in OPCAB cohort (85.6% vs. 75%; P=0.04); higher rate of stroke in ONCAB cohort (0% vs. 9.3%; P<0.0005); trend towards higher 30-day and risk-adjusted mortality rates in the OPCAB cohort (10.3% vs. 5.2% & 2.8% vs. 1.8%; P= NS); slightly reduced length of stay in the OPCAB cohort (9.1 vs. 10.8 days; P= NS)
Yokoyama <i>et al.</i> , <i>Ann Thorac Surg</i> , 2000 (30)	High-risk patient groups including 80 years of age or older; ventricular dysfunction EF \leq 0.25), prior neurologic event or renal failure, COPD, & reoperation	28	58	Less mortality in the OPCAB cohort (0.4% vs. 2.7%; P= NS); decreased renal complications (3.6% vs. 15.5%; P= NS); decreased neurologic events in the OPCAB cohort (7.1% vs. 13.8%; P= NS)
Demaria <i>et al.</i> , <i>Circulation</i> , 2002 (31)	Octogenarians	62	63	Lower operative mortality in the OPCAB cohort (4.8% vs. 15.9%; P=0.04); lower stroke rate in the OPCAB cohort (0% vs. 6.3%; P=0.04); lower transfusion rate in OPCAB cohort (72.6% vs. 92.1%; P<0.01); similar postoperative MI rate (14.5% vs. 11.3%; P= NS); stroke & mortality 4 times more often in ONCAB patients (or =4.171)
Hoff <i>et al.</i> , <i>Ann Thorac Surg</i> , 2002 (32)	Octogenarians	60	169	Similar mortality (0% vs. 4.7%; P= NS); lower perioperative stroke in OPCAB cohort (0% vs. 7.4%; P=0.04); lower incidence of prolonged ventilation (1.7% vs. 11.8%; P=0.02); lower transfusion rate in OPCAB cohort (33% vs. 70.4%; P<0.001); shorter hospital stay for the OPCAB group (6.3 vs. 11.5 days; P<0.001); lower hospital cost in the OPCAB group (\$9,363 vs. \$12,312; P<0.001)
Shimokawa <i>et al.</i> , <i>Jpn J Thorac Cardiovasc Surg</i> , 2003 (33)	Octogenarians	25	18	Fewer distal anastomoses in the OPCAB cohort (2.0 \pm 1.0 vs. 2.8 \pm 0.5; P<0.01); shorter postoperative ventilation in OPCAB cohort (13.4 \pm 17.2 vs. 45.2 \pm 52.8 hours; P<0.05); Less transfusion in the OPCAB cohort (16% vs. 89%; P<0.01); shorter mean hospital and ICU stay in OPCAB group (P<0.05); similar incidence of major postoperative complications
Lin <i>et al.</i> , <i>ANZ J Surg</i> , 2003 (34)	Octogenarians	17	12	Similar number of distal anastomoses; similar incidence of major complications; significantly shorter ventilation time, ICU stay & hospital stay in the OPCAB cohort
D'Alfonso <i>et al.</i> , <i>Ital Heart J</i> , 2004 (35)	Octogenarians	73	41	Fewer deaths in OPCAB group (6.8% vs. 14.6%; P=0.05); similar rates of stroke and major cardiac events; fewer minor neurological events in OPCAB cohort (2.8% vs. 12.2%; P=0.04); similar late mortality & actuarial survival at 24 months; similar linearized rate of neurological events
Nagpal <i>et al.</i> , <i>Can J Cardiol</i> , 2006 (2)	Octogenarians	131	105	Similar in-hospital mortality, postoperative MI & new onset renal dysfunction; lower incidence of postoperative neurological events in OPCAB cohort (1.5% vs. 7.6%; P=0.05); decreased incidence of prolonged intubation (5.3% vs. 13.3%; P=0.04)

Table 1 (continued)

Table 1 (continued)

First author, journal, year of publication (Ref)	Study population characteristics	Number		Key outcomes
		OPCAB	ONCAB	
Serrão <i>et al.</i> , <i>Rev Port Cardiol</i> , 2010 (37)	Octogenarians	65	36	Less complete revascularization in OPCAB cohort (43.1% vs. 83.3%; P=0.0001); shorter mean hospital stay (9.3±5.4 vs. 11.5±7.3 days; P=0.09); similar in-hospital mortality; similar late survival & cardiovascular mortality at 6-year follow-up
Saleh <i>et al.</i> , <i>Interact Cardiovasc Thorac Surg</i> , 2011 (38)	Octogenarians	107	107	Trend towards lower in-hospital mortality in OPCAB group (4.7% vs. 6.5%; P=0.55); similar postoperative complications; shorter duration of mechanical ventilation & hospital stay in OPCAB group; less use of inotropes in OPCAB group
LaPar <i>et al.</i> , <i>J Thorac Cardiovasc Surg</i> , 2011 (39)	Octogenarians	1,589	404	Higher blood transfusion rates in ONCAB cohort (2.0±1.7 vs. 1.6±1.9 units; P=0.05); more postoperative atrial fibrillation in ONCAB cohort (28.4% vs. 21.5%; P=0.003); more prolonged ventilation in ONCAB group (14.7% vs. 11.4%; P=0.05); more major complications in ONCAB group (20.1% vs. 15.6%; P=0.04); similar postoperative stroke rate (2.6% vs. 1.7%; P=0.21); similar renal failure rate (8.1% vs. 6.2%; P=0.12); similar postoperative length of stay (P=0.41); similar operative mortality (P=0.53); similar hospital costs (P=0.43)
Sarin <i>et al.</i> , <i>Innovations (Phila)</i> , 2011 (40)	Octogenarians	540	397	Fewer distal anastomoses in OPCAB group [2.7±1.0 (median 3) vs. 3.4±0.9 (median 3); P<0.001]; similar length of postoperative stay (P=0.3); similar in-hospital mortality (5.4% vs. 5.3%; P=0.81); improved observed in-hospital mortality in OPCAB group (15/540, 2.8% vs. 37/397, 9.3%; P=0.007); similar ten-year survival (28.8% vs. 26.3%; P=0.22)
Lee <i>et al.</i> , <i>Cardiology</i> , 2013 (41)	Octogenarians	49	48	Shorter length of hospital stay in OPCAB group (17±19 vs. 8±4 days; P<0.01); shorter duration of inotropic requirement in OPCAB group (47±70 vs. 18±39 h; P<0.04); shorter duration of ventilator support in OPCAB group (51±54 vs. 16±27 h; P<0.01); less incidence of tracheostomy (16% vs. 3%; P<0.02); similar in-hospital mortality (3.2% vs. 2.7%); similar stroke rate (3 per group); similar 5-year survival (57% vs. 67%, P=0.50, NS)
Vasques <i>et al.</i> , <i>Heart Vessels</i> , 2013 (42)	Octogenarians	56	56	Lower postoperative stroke rate in OPCAB cohort (0%, 95% CI: 0–0 vs. 3.6%, 95% CI: 0–10.0; P=0.50); similar other outcome endpoints
Raja <i>et al.</i> , <i>Innovations (Phila)</i> , 2013 (43)	Octogenarians	217	73	Lower number of distal anastomoses in OPCAB cohort (mean difference, 0.2; 95% CI, 0.02–0.4; P=0.03); similar in-hospital mortality (6.0% vs. 11.0%; P=0.08); similar stroke rate (2.8% vs. 2.8%; P=1.0); similar other major complications; similar length of hospital stay
Cavaliaro <i>et al.</i> , <i>Eur J Cardiothorac Surg</i> , 2014 (44)	Octogenarians	6,865	15,479	Reduced risk of stroke in OPCAB group; reduced incidence of postoperative respiratory failure in OPCAB group; similar other major complications; similar length of hospital stay

CI, confidence interval; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; ICU, intensive care unit; MI, myocardial infarction; NS, not significant; ONCAB, on-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass.

rates. However, an argument for offering OPCAB to octogenarians preferentially could be based on the assumption that reduction of neurological derangements including stroke and respiratory complications results in a shorter postoperative period of intensive care unit stay and hospital stay along with lesser use of inotropes and blood product usage. Such findings although apparently insignificant, may translate into substantial savings in this group of patients with a higher-level of resource utilization perioperatively (56).

Survival, mortality, morbidity, complication rate, symptom recurrence, and need for re-interventions, well-recognized objective outcome measure, have long been used as benchmarks for successful cardiac surgery, including CABG. In addition to these benchmarks, acquired improvement by cardiac surgery in subjectively experienced health-related quality of life (HRQoL) has gained importance during the last decade in cardiac surgical research. If an increasing proportion of adult patients referred for CABG are elderly, octogenarians or even nonagenarians, the acquired HRQoL benefit from bypass surgery should be considered to be at least as important an outcome measure as potentially marginal improvement in life expectancy or longevity alone (57). It is extremely important that informed discussion of treatment options, potential for discharge to a nursing care facility, and quality of life expectations should precede a decision to undertake cardiac surgery in octogenarians (56).

The available evidence on the subject is fraught with limitations. Majority of the studies are prone to a degree of selection bias due to their retrospective, single center observational nature. The relatively long time period these studies cover and their retrospective nature may carry unidentified variables affecting outcomes that remain unaccounted for in the final analysis in all of these studies. Furthermore, size of the study populations in most studies published to date remains small predominantly as the population size for octogenarians remains relatively small when compared to the total volume of most surgical units. Last but not the least, there is a need for further studies with longer follow-up as majority of the studies report short-term or early outcomes.

Conclusions

The decision to offer surgery is complex in octogenarian patients and one must take into account multiple factors,

such as the lack of conformity between physiological age and chronological age, the quality of life, and the risk-benefit ratio. Furthermore, with consistent and careful application of modern techniques and clinical practices the risk of death from a cardiac operation in octogenarians can be reduced to that of younger patients. It is therefore not unreasonable to hypothesize that OPCAB, due to its less invasive nature compared to conventional CABG, appears an attractive option to reduce procedure-specific mortality and morbidity in the octogenarian patients. However, current retrospective studies with small numbers, examining the impact of OPCAB on early mortality and morbidity in octogenarians, have failed to prove overwhelming superiority of one technique over the other. At present it can be safely concluded that both on-pump and off-pump CABG are reasonable revascularization strategies in octogenarians. The decision to offer one or the other strategy preferentially must be guided predominantly by the patient's risk profile reiterating the importance of careful patient selection and individualized treatment decisions.

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Footnote

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