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REVIEW ARTICLE

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Cardiac Anesthesia and Surgery in Geriatric Patients: Epidemiology, Current Surgical Outcomes, and Future Directions

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ABSTRACT

The mean life expectancy of the population of the United States is projected to increase from 78.3 years at present to over 81 years in 2025, with a concomitant increase in the percentage of the population over the age of 75 years. Elderly patients are more likely to present with valvular and coronary artery disease than younger patients, and as better perioperative management contributes to improving post-operative outcomes and lower referral thresholds, very elderly patients form an increasingly large proportion of the cardiac surgical population. This article summarizes the impact of age-related pathophysiologic changes on patients' response to cardiac surgery and anesthesia, outlines useful perioperative strategies in this age group, and reviews the literature on outcomes after valvular and coronary in elderly patients.

Keywords: *surgery, elderly, anesthesia, cardiac anesthesia, octogenarians.*

BACKGROUND

In 2007, average life expectancy in the United States was 78.3 years and the *Census Bureau* estimated that this will increase to 81 years in 2025 (1).The number of people older than 65 years is projected to grow 50% from 35 to 71 million in the United States alone, eventually representing 19.6% of the overall population (2, 3). The prevalence of cardiovascular disease, which remains the leading cause of death in the West, and which is responsible for a third of all mortality or about 17.5 million deaths annually in the US, is higher in older individuals and appears to be increasing. An updated analysis of data from the National Health and Nutritional Examination Survey, found that those individuals who are 65 years or older are substantially more likely than younger patients to present with cardiovascular disease, cerebrovascular accidents, chronic lower respiratory tract disease, and diabetes (3-5). An increasing number of elderly patients are therefore likely to require cardiac anesthesia and surgery.

The definition of "geriatric", "aged", "elderly" and "advanced age" varies widely in the medical literature. Medicare, the state health insurance for older patients in the United States, sets its current eligibility threshold at 65 years of age, and in the car-

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diac surgical literature elderly patients have traditionally been defined as those aged 65 years and above.
Not only does this cut-off seem relatively low in the context of the increasing mean age of patients undergoing cardiac surgery, but there is also a trend towards evaluating patients based on the physical examination and comorbid conditions rather than just their chronological age (4). It has been suggested that older adults should be categorized as "young-old" (65-74 years), "mid-old" (75-84 years), and "oldest-old" (≥85 years) but for the purposes of this review article "elderly" patients refers to those aged 75 years and above (4, 6).

AGE-RELATED FUNCTIONAL DECLINE

A gradual diminution in functional capacity over time is one of the hallmarks of aging, and impacts on the choice of therapy and surgical planning in elderly patients undergoing cardiac surgery (7-9). Optimizing care in this increasing pool of older patients mandates that cardiovascular professionals become familiar with age-associated changes in organ physiology and their impact on treatment and recovery. Cardiovascular changes primarily lead to reduction of the cardiac functional reserve, with a consequent increase in the risk of congestive heart failure (10, 11).
A reduction in pulmonary reserve has implications for the postoperative stay, and a decline in renal function leads to an increased potential for the occurrence of renal insufficiency requiring postoperative dialysis (12, 13). Changes in gastrointestinal physiology increase the risk of mucosal damage (14). Loss of neurological and muscular skeletal function is particularly important predictors of post-operative morbidity and mortality (15-17). All these changes impair the ability of older patients to tolerate surgical procedures and increase their risk of mortality, and morbidity leading to an overall decline in functional status, higher frailty scores, and poorer quality of life. It is clear that becoming familiar with age-related physiologic changes is the cornerstone for cardiovascular care givers in achieving better tailored treatments when possible.

Cardiovascular function

Decrease in cardiac functional reserve (systolic or diastolic dysfunction) considerably limits both the capacity to develop any kind of physical activity and the ability to tolerate pathophysiologic stressors such as surgery and sepsis (18). Furthermore, most patients will have coexisting hypertension and marked atherosclerotic disease which increases the risk of coronary artery disease and secondary myocardial ischemia (19). The changes in ventricular compliance involve a significant reduction in early diastolic filling due to diastolic dysfunction (20-22).
There may be no baseline change in the ejection fraction or cardiac index, but during stress the increase in ejection fraction is blunted and older patients, even those with normal systolic function, are more prone to heart failure (23-25). In addition to these ventricular changes, the aging heart provides a 1% yearly decline in aerobic capacity due to a decrease in the maximum volume of oxygen usage (23).
Although heart rate remains constant with age, there is a decrease in maximal heart rate in response to stress (26).
This effect may be caused by a combination of decreased catecholamine responsiveness and an age-related decrease in the intrinsic sinus rate. In addition, the aging cardiac conduction system is characterized by increasing fibrosis, calcification, and a decrease in the number of sino-atrial pacemaker cells and of bundle branch fibers

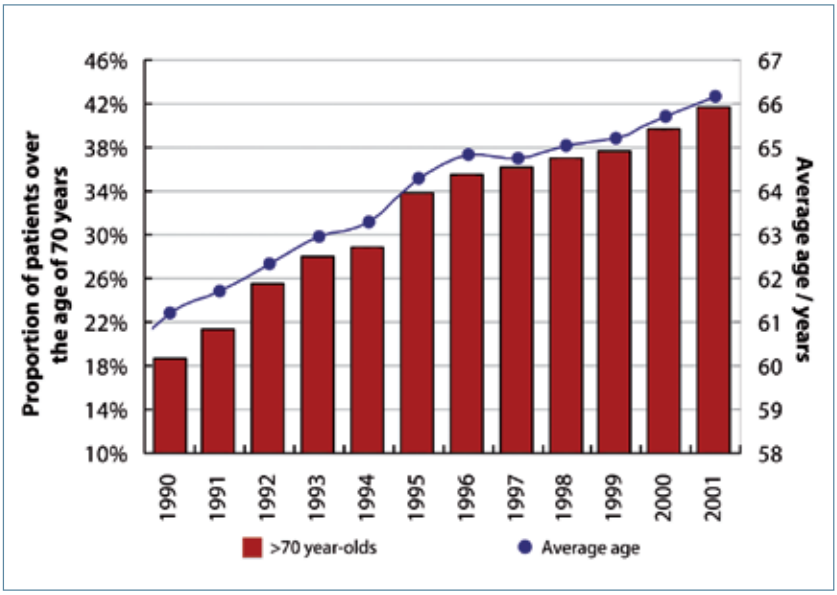

Figure 1 - *Proportion of patients over the age of 70 years referred for cardiac surgery in the United Kingdom during the last decade (The Society of Cardiothoracic Surgeons of Great Britain and Ireland, national Adult Cardiac Surgical Database report).*

(27). These factors may contribute to sick sinus syndrome, atrio-ventricular block, and intraventricular conduction delays; hence cardiac rhythm management devices are increasingly encountered in patients presenting for cardiac surgery, and may be required after valvular heart surgery (28).

Pulmonary function

Pulmonary changes are primarily due to multiple factors such as smoking, air pollution, heart failure, or skeletal system changes like kyphosis. Aging additionally affects the function and structure of the pulmonary system as well (29, 30). The most common finding is decreased lung compliance caused by a marked decrease in elastic recoil (31).

This progressive cease in elasticity decreases respiratory reserve and the area of alveolar gas exchange surfaces. These changes have mechanical, functional and anatomical consequences, and lead to an increase in residual volume and functional residual capacity both increase of 5-10 % and 1-3 % per decade, respectively.

The physiologic response to hypercapnia and hypoxia are dampened with age, probably due to a decline in sensitivity of these centers to chemical stimuli. Finally, there is decreased clearance of mucus from the airways due to diminished function or the lack of mucociliary structures, which in combination with age-related immune dysfunction, mean elderly patients are more at risk of respiratory tract infections (32). Recently, we conducted a retrospective analysis of 5798 patients undergoing all types of cardiac surgery in order to determine the predictors of respiratory failure following cardiac surgery (33, 34). Multivariate analysis revealed that age > 70 years was an independent predictor of respiratory failure (OR = 1.6).

Renal function

Several morphologic and histological changes occur in the renal system with age; including a decrease in cortical area and characteristic vascular changes (35-37). Although there are wide individual differences in the decline of the glomerular filtration rate (GFR) and renal plasma flow, GFR declines by 4 mL/min/year in individ-

uals older than 50 years of age compared to a decline of 1 mL/min/year in healthy younger individuals (38). As renal mass diminishes, renal blood flow decreases at a rate of approximately 10 % per decade with a resultant overall decrease in GFR. By the eighth decade, only 70 % of the nephrons are functioning and free of sclerotic changes, leading to a decreased filtration area and decreased permeability of glomerular basement membranes (39).

The elderly are at increased risk of developing hyperglycemia before the onset of end stage renal disease. This may be due to decreased in renin synthesis and impairment of renin release (40). Dysregulation of the renin-angiotensin system is characterized by decreased plasma renin activity under basal, stimulated, and suppressed conditions; renal vasoconstriction; increased angiotensin

II activity; increased renal nerve activity; increased endothelin; and decreased vasodilatory prostacyclins (41).

Renal dysfunction is particularly common after cardio-pulmonary bypass in the setting of prolonged perfusion time and transfusion of multiple blood products (12, 42).

Patients at the highest risk of post-operative renal failure include those with aneurysmal involvement of the renal arteries, renal dysfunction indicated by elevated creatinine, and those with congestive heart failure (41, 43). After retrospectively analyzing 6449 patients to determine the incidence and predictors of renal failure requiring dialysis in patients undergoing cardiac surgery, we observed an overall incidence of post-operative renal failure of 2.2 %.

Although multivariate analysis confirmed that age > 70 years was an independent risk factor for preoperative renal dysfunction (OR 1.6 95 % CI 1.2-2.3, P = 0.003), age was not found to be an independent predictor of post-operative renal dysfunction.

Gastrointestinal function

A variety of physiologic gastrointestinal changes are related to age, ranging from decreased basal gastric blood flow, to diminished blood flow and prostaglandin response to injury (44). The increased prevalence of atherosclerotic disease in older patients, who may be undergoing more complex reoperative procedures, potentially increases the risk of abdominal organ hypoperfusion and thromboembolic events, resulting in ischemic gastrointestinal complications.

Gastrointestinal hemorrhage has been reported in several studies to be the most frequent cause of post-cardiopulmonary bypass gastrointestinal complications with an incidence of 2 % following cardiac surgery (45). In contrast, in a more recent study, Mangi et al reported mesenteric ischemia as the dominant cause of post-operative gastrointestinal complications (46). Our data from 5188 consecutive patients showed that postoperative gastrointestinal complications after cardiac surgery occurred in 1.1 % of the patients, with the predominant etiology being intestinal ischemia (59 %) followed by gastrointestinal bleeding (41 %), and revealed that age over 65 was an independent predictor of this complication (OR 2.1, $p < 0.001$) (47).

Neurological function

Rudolph et al. recently published a key paper on the derivation and subsequent validation of a scoring system or rule to predict delirium after cardiac surgery (48). They enrolled 122 elderly (≥60 years of age) cardiac surgery patients that underwent a delirium assessment pre- and postoperatively beginning on postoperative day 2. Delirium, defined according to the confusion assessment method, occurred in 52 % of the patients and multivariate analysis identified 4 independent variables associated with delirium: previous stroke, MMSE scores, abnormal serum albumin, and the

geriatric Depression Scale scores. After assigning points to each variable they were able to accurately predict risk of postoperative delirium in cardiac surgery patients, further validating the scoring system in a sample of 109 patients.

Musculoskeletal function

Aging may influence negatively the physiological response to exercise and prolonged training, mainly due to the loss of muscular mass. Additionally cachexia, defined as a complex syndrome including weight loss, diminished muscle and adipose tissue, anorexia, and generalized weakness, is a significant problem in the elderly population (49). Although not exclusively limited to the elderly, there are several reasons why cachexia is more prevalent in geriatric patients, particularly its strong association with chronic diseases such as cancer, chronic obstructive pulmonary disease, heart failure, and renal insufficiency. In the context of cardiovascular disease, every physician is familiar with the classical "skin and bone" appearance with secondary heart failure. In a pioneer study on the role of wasting syndrome as an independent risk factor form mortality in chronic heart failure (CHF), Anker and coinvestigators showed that at least 16 % of patients with CHF present with cachexia defined as a weight loss of 7.5 % over 6 months.

When the cut-off point is risen to a 6 % weight loss, the prevalence of cachexia increases to 36 % with a consequent threefold increase in mortality rates (50, 51).

Aging and the Metabolic Syndrome

It is widely accepted that cardiovascular risk factors (hypertension, hyperlipidemia, obesity, diabetes mellitus, and impaired glucose tolerance) play a major role not only as a cause of cardiac surgical disease but also in the development of perioperative complications (52, 53).

In the United States the estimated rate of the metabolic syndrome in patients aged 60 to 70 years is 43.5 % (54).

Accordingly, the impact of diabetes on the adverse outcome in cardiac patients, particularly in the geriatric population, is well recognized. However, most recent literature suggests that diabetes mellitus is not an independent risk factor for increased risk of wound infection, length of stay, or mortality after open-heart surgical procedures. It is rather the presence of perioperative hyperglycemia that affects biochemical and physiologic functions which in turn impacts surgical outcomes (55).

Furnary et al reported that the Portland CII Protocol based on insulin infusions is a safe and effective method of eliminating hyperglycemia, contributing to reduced postoperative mortality from 5.3 % to 2.5 % ($p < 0.001$) (56, 57).

DOES AGE REALLY MATTER?

Despite technological advancements, open-heart operations still carry a significant risk of mortality and morbidity and it is a reality that currently age still prevents many patients from being referred for cardiac surgery (58, 59).

Potential explanations include the elderly not being accurately represented in randomized trials and a resultant lack of clear data on criteria for referral, skepticism among physicians about postoperative quality of life, and the impact of preoperative mortality risk calculators on surgical decision-making.

More recent data suggests improving outcomes in terms of survival and quality of life in elderly patients undergoing cardiac surgery (60, 61). Although these studies may not be representative of the wider unselected elderly surgical population, the American College of Cardiology has re-clas-

sified age as a minor clinical predictor of increased perioperative cardiovascular risk in the latest update of the guidelines. The need for separate surgical type-based risk stratification models for hospital mortality is increasingly recognized as is the importance of including postoperative variables in risk stratification models (62).

Recently, Zingone and coauthors conducted a retrospective study on patients 80 years or older undergoing all types of cardiac surgery in order to determine the independent predictors of operative mortality.

After multivariate analysis, they created 2 different Cox proportional hazard models, including postoperative variables in the latter. Interestingly, when postoperative variables were included in the hazard model, age was no longer considered as a predictor of mortality, demonstrating that postoperative complications were stronger risk factors for hospital deaths than preoperative comorbidities and procedural variables confirming findings reported by our institution (59).

GENERAL CONSIDERATIONS AND PREOPERATIVE EVALUATION

Elderly patients classically present with age-specific comorbidities such as multiorgan functional decline, depression, alterations of mental status, cachexia, and absence of social or familiar support. These problems are seen with different grades of severity in this subpopulation and, as mentioned above, that is why chronological age by itself cannot be the only criterion for surgical planning and the biological age should be defined individually, based on comorbidities and performance status. Several publications have reported on the impact of comorbidities as a predictor of surgical outcome and survival in elderly patients (63, 64).

Concurrent comorbidities have an important prognostic impact and play a major role when trying to achieve an accurate assessment of geriatric patients. Ideally, every elderly patient should receive a comprehensive geriatric assessment (CGA) for different reasons including an accurate estimation of life expectancy, early identification of risk factors and predictors (dementia, delirium, malnutrition, or inadequate social support), and helps to create a warm and clear environment when consenting the patient to undergo surgery (65). Additionally, a correct CGA is crucial in classifying patients with functional limitations and may assist the surgeon in making the most appropriate surgical planning and decision for each patient.

PERIOPERATIVE MANAGEMENT AND SURGICAL RESULTS

Currently, admission to the hospital on the day of surgery has become standard for most elective surgery, including the geriatric population. Preoperative assessment of the patient is mandatory to assure there have been no interval changes (dehydration, fever, mental disturbance or other acute medical symptoms) from the time of the initial anesthetic evaluation (63, 66, 67). In addition, it is prudent to establish continuous arterial pressure recording before induction of anesthesia. The pulmonary artery catheter is inserted on an individual basis.

Anesthesia and endotracheal intubation should be induced, performed, and maintained with consideration of the pharmacokinetic and pharmacodynamic changes associated with aging with particular care to maintain hemodynamic stability. Transesophageal echo is a useful monitor of cardiac function, may confirm supplement preoperative diagnostic information

and to assist with the deairing of the cardiac chambers (6).
Furthermore, epiaortic echocardiography to detect any atherosclerotic lesions prior to manipulation or cannulation of the ascending aorta may help reduce embolic incidents particularly in elderly patients. An aggressive surgical approach after optimal perioperative preparation offers elderly patients prognostic and symptomatic benefit, particularly in coronary artery bypass and valvular heart surgery.

Coronary Artery Bypass Grafting

Studies have historically shown high operative mortality in very elderly cardiac surgical patients. In-hospital mortality rates of over 10 % were reported in octogenarians undergoing CABG or isolated aortic valve replacement during the 1980's, (68, 69) with one study reporting early mortality as high as 24 % (70).
Recent studies suggest results are improving: octogenarians who underwent isolated CABG experienced mortality rates of 5-10 % (71-74). We described an operative mortality of 1.9 % our for coronary artery bypass grafting in a large cohort of octogenarians (75). This overall low mortality occurred despite the prevalence of diabetes, peripheral vascular disease, severely depressed EF, left main stem disease, previous stroke, renal dysfunction and chronic obstructive pulmonary disease in our patient population, and indicates that patient selection was not the primary reason for our low mortality.

Aortic Valve Replacement

Calcified aortic stenosis is the most common structural cardiac disease in the elderly, with an estimated disease prevalence of 20 % (76).
Despite published series noting a trend towards a better in-hospital mortality and quality of life, physicians remain reluctant to recommend open AVR for patients greater than 80 years of age, instead pursuing medical treatment providing minimal symptomatic relief and diminishing survival (77).
It is well recognized that AVR should be the procedure of choice as it carries a low operative mortality and morbidity, even in very elderly patients, and provides excellent long-term outcomes. Thourani and

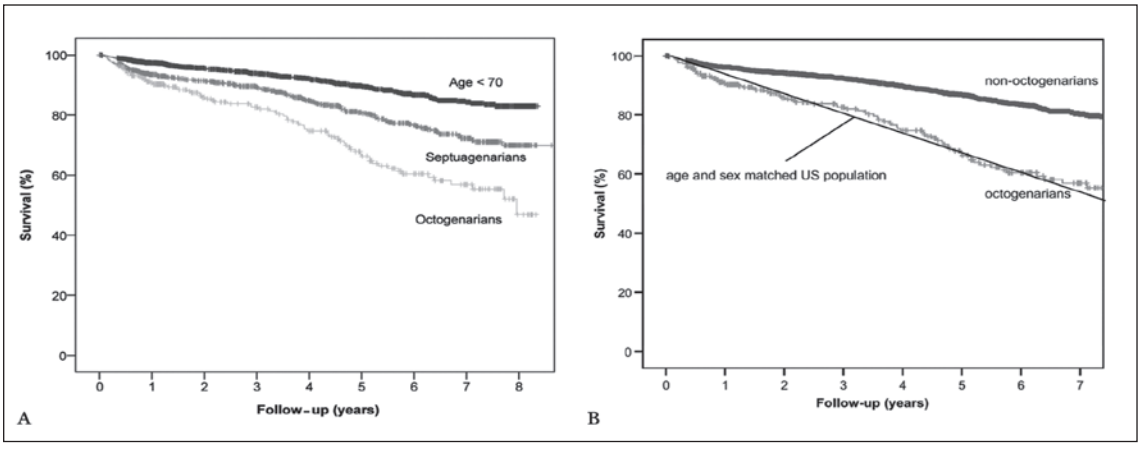

Figure 2 - *Unadjusted (A) Kaplan-Meier survival curves after coronary artery bypass grafting surgery for octogenarians compared to non-octogenarians and (B) for octogenarians after coronary artery bypass grafting compared to the survival of an age and gender matched US population.*

colleagues evaluated 515 patients (88 octogenarians) undergoing isolated AVR over a 10-year period: they did not observe significant differences in surgical outcomes and concluded that selecting octogenarians for cardiac surgery should be left at the surgeon's discretion after interviewing and examining the patient (78). Percutaneous valve therapy may offer a useful alternative in the elderly or debilitated patient.

Rankin et al reviewed 409,100 cardiac surgical procedures performed between 1994 and 2003 (67). Of these patients, 216,245 patients had isolated aortic valve replacement, with unadjusted mortality of 5.7%.

Nineteen variables independently influenced operative mortality.

The most significant of which were emergency surgery (OR, 2.11), followed by advanced age (OR, 1.88), and re-operation (OR, 1.16). Brown and co investigators explored the last 10 years of isolated AVR in the Society of Thoracic Surgery Database with regard to the patient characteristics and operative outcomes (79).

They showed that despite gradual increases in patient age and overall risk profile, morbidity and mortality of isolated AVR has fallen. In summary, we believe that clinicians should redouble their efforts to emphasize earlier surgical indication to avoid urgent and emergency surgery in elderly patients.

Mitral Valve Repair

Mitral regurgitation is the second commonest valvular heart lesion in elderly patients in industrialized countries (58). Although the optimal timing of intervention in elderly asymptomatic patients with mitral regurgitation is controversial, the ACC/AHA guidelines recommend surgical intervention in symptomatic patients who present with severe MR (80).

In a recent study conducted for the European Society of Cardiology, Mirabel et al found that mitral valve repair was denied in 49% of patients with severe symptomatic MR, with older age one of the main reasons cited (58).

A potential explanation is that the feasibility and efficacy of mitral valve repair in octogenarians remains controversial, as many surgeons prefer replacement in the interest in performing expeditious surgery, especially if more complex pathology or comorbidities are present.

We collected data on 79 consecutive octogenarians undergoing mitral valve repair with or without concomitant CABG or tricuspid repair from 1/2002 to 12/2008 in our institution. The mean age of patients was 83 ± 5 years).

Operative mortality rate was 5% and 2 of the 4 deaths occurred in patients undergoing reoperation for ischemic MR. Overall 90-day mortality for survivors of the initial hospitalization was 5% (n = 4). Major postoperative morbidities included mechanical ventilation > 72 hours (n = 12, 15%) and renal failure requiring dialysis (n = 5, 6%).

No patient experienced a postoperative stroke or required re-operation. Postoperative transthoracic echocardiography showed none-trace MR in 97%. No patient required mitral re-repair. Actuarial survival at 1- and 3-years was 86% and 77% respectively, with an unadjusted survival superior to 60% at 5 years, similar to that of an age-matched population.

Therefore, based on our own experience, mitral valve repair in a reference center provides excellent results in most octogenarians, with low operative mortality and postoperative morbidity, and good mid-term results.

We can conclude that cardiac surgical procedures can be performed safely and with therapeutic benefit in elderly patients, regardless of age in those carefully selected candidates (81).

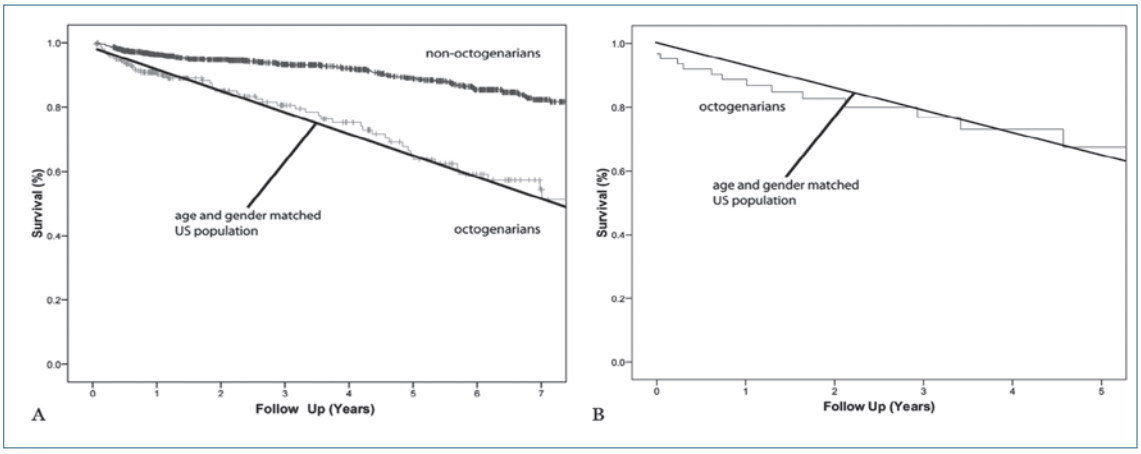

Figure 3 - *Unadjusted (A) Kaplan-Meier survival curves for octogenarians after aortic valve replacement (A) and mitral valve repair (B) compared to the survival of an age and gender matched US population.*

LONG-TERM OUTCOME

Our own experience with octogenarians undergoing AVR suggested that outcome and long-term survival can be similar to that of gender and age matched population. Previous publications on survival after AVR in elderly patients have traditionally reported one, three, and five year survivals ranging from 83-89 %, 79-80 %, and 61-63 % respectively. Our results in octogenarians are similar: after a mean follow up of 4.0±2.5 years, 1 and 5-year survival rates were 90.7±1.8 % and 66.3±3.6 % for octogenarians vs. 96.2±0.4 % and 86.8±0.8 % for younger patients. Among predictors of late death in octogenarians markers for late post-operative comorbidities with a strong negative impact on life expectancy including extensive aortic calcification, concomitant CABG, and previous renal failure or stroke were most significant. Congestive heart failure at the time of surgery was a strong independent predictor of late mortality, underlining the need for early, elective intervention in octogenarians identified as surgical candidates, and close follow-up of those who

The institutional results in octogenarians undergoing CABG are similar to those achieved with those octogenarians who underwent AVR, and highlighted that currently long-term survival and quality of life in these particular patient population can match that of octogenarians in the general population.

However, there is a marked difference when we compare long-term outcomes to the younger patients undergoing the same surgical procedures. Besides the granted difference in age and biological long-term survival, previous studies have pointed out that during the last decade survival in octogenarians undergoing CABG can reached up to 87 % at 1 year, 78 % at 3 years, and 66 % at 5 years. Our institutional experience and analysis revealed that after a mean follow-up time of 3.6 ± 2.5 years, 1- and 5-year survival rates were 90.3 ± 2.1 % and 63.8 ± 4.8 % for octogenarians versus 96.3 ± 0.6 % and 88.8 ± 1.3 % in younger patients ($p < 0.001$), suggesting that the common comorbidities in the elderly group may preclude any benefit on long-term survival due to a better surgical outcome and perioperative management.

FUTURE DIRECTIONS

Additional clinical research in cardiac geriatric anesthesia (preoperative optimization of the patient, brain protection, improvements in surgical and perfusion techniques, prevention of complications, new discoveries in organ protections) will further contribute to improve surgical outcome, and age alone should not therefore be a precluding factor for any indicated cardiac surgery.

The term "frailty" was defined as a state of multisystem impairment and increased vulnerability to adverse outcomes. However, how best to generalize its use is debated. The principle is to assess "deficits" such as symptoms, signs, diseases, disabilities or abnormal laboratory, radiographic or electrocardiographic findings, which relate deficit accumulation to the individual risk of death.

The more deficits a patient presents with, the more likely that person is to be frail, independently of age. Therefore, when expressed as an index, frailty is often expressed as a ratio of deficits present to the total number of deficits considered. It is well known that the frailty index is strongly associated with the risk of death, institutionalization and worsening health status, especially when an increasing number of variables are included in the scoring system. The standardization and reproducibility of the findings in relation to the frailty index is of interest because none of the reported systems or calculators considered the same deficits (82). This finding suggests that frailty involves a complex network of biological variables and may be measured in many ways.

In order to encourage and propose a more widespread evaluation and application of frailty indexes, several geriatricians have attempted to refine the term and validate an applicable index with potential to be posterior generalized to any medical field.

In a very recent publication by Ensrud and colleagues, the authors conducted a prospective multi-center study to compare the validity of a simple three-variable frailty index (weight loss, inability to rise from a chair, and poor energy) with a more complex and specific skills-required one such as the *Cardiovascular Health Study* index (83). After the analysis, they concluded that parsimonious scores are able to provide an operational definition of frailty that predicts falls, disability, fracture, and long-term mortality as accurately as the more complicated index. Therefore, simple indexes may provide a useful phenotype of frailty to identify high-risk older patients in any clinical practice, suggesting that the generalization of their applicability must be expedited, particularly in the setting of achieving a tailored surgical planning.

Furthermore, Fillit and Butler recently published a special article on what they called "*The Frailty Identity Crisis*" and discussed about the psychological changes associated with frailty, especially in light of an upcoming surgical procedure or intervention (84). As a result of a longer life-expectancy, maximizing functional independence and quality of life during the years of frailty has become the main goal of the current geriatric medicine. The authors proposed that a better understanding, assessment and recognition of physical frailty can assist individuals to anticipate and manage associated social and psychological changes, transforming passive acceptance into an adaptive and robust response to frailty and consequently enabling predisposition to receive an appropriate care.

CONCLUSION

Advanced age is still viewed as a relative contraindication to cardiac surgery. The significant improvement in operative out-

comes in very elderly patients, combined with the increasing recognition that more sophisticated markers of frailty than age in isolation predict adverse results after surgery, mean that this view point is changing.

Very elderly patients therefore continue to make up a growing proportion of the cardiac surgical population: a clear understanding of the impact of age on perioperative management and outcomes will be increasingly important to clinicians involved in their care.

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