

Preoperative and Intraoperative Factors Associated With Long-Term Survival in Octogenarian Cardiac Surgery Patients

Simon L. Rohde, MD, Robert A. Baker, PhD, Phillip J. Tully, BHSc (Hons),
Scott Graham, MD, Hugh Cullen, MD, and John L. Knight, FRACS, MD

Department of Cardiac and Thoracic Surgery, Flinders Medical Centre, Flinders Private Hospital, Ashford Hospital, and the Flinders University of South Australia, Adelaide, South Australia, Australia

Background. The proportion of octogenarians undergoing cardiac surgery is increasing though few studies have examined the simultaneous impact of preoperative and intraoperative factors on long-term survival in this age group. This study aimed to describe the preoperative clinical and demographic characteristics associated with long-term mortality risk and determine whether intraoperative factors related to surgical and cardiopulmonary bypass techniques impacted upon these.

Methods. Octogenarians undergoing coronary artery bypass grafting (CABG) \pm concomitant valvular procedure between 1992 and 2005 from three institutions were included in this study. The survival data of 606 octogenarians (414 isolated CABG, 192 concomitant valve procedures) were analyzed with multivariable proportional hazard models.

Results. There were 271 deaths and 2,675 person years of survival for analysis, and median follow-up was 7.15 years (95% confidence interval 6.47 to 7.82 years).

Five-year survival for isolated CABG and concomitant valve procedures was 66.5% and 61.5%, respectively. An increase in mortality risk was attributable to older age, hypercholesterolemia, severely impaired left ventricular function, tobacco smoking history and high creatinine (≥ 0.15 mmol/L). Time spent on cardiopulmonary bypass was the only intraoperative risk factor associated with an increase in mortality risk (hazard ratio 1.01, 95% confidence interval: 1.00 to 1.02; $p < 0.001$).

Conclusions. This study showed that from the intraoperative parameters examined only time spent on cardiopulmonary bypass was associated with long-term survival. Surgeons may be assisted in patient selection by identifying the factors that influence long-term survival among octogenarians and development of a preoperative risk model specific for this age group.

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Cardiac revascularization and valve repair surgery for those aged 80 to 89 years old has increased in the past 20 years and this trend is anticipated to continue in the future [1, 2]. Describing the survival outcomes of octogenarians and the risk factors for early and late mortality after cardiac surgery has mounting importance for patients and surgeons alike. Octogenarians undergoing cardiac surgery typically have longer and more complicated recovery compared with their younger counterparts [2–4], and poorer survival is often attributed to a greater prevalence of complex comorbidity such as renal insufficiency, diabetes and left ventricular dysfunction [2, 5, 6]. Despite these studies, there is limited information regarding how intraoperative factors, including those related to perfusion may influence the long-term survival of octogenarians above and beyond traditional risk factors.

Compounding this information gap it cannot be assumed that the intraoperative risk factors for mortality identified in younger cardiac surgery cohorts will necessarily translate to octogenarians who may undergo substantially different perfusion protocols [3]. For example, Willcox and van Uden [3] commented in their qualitative review that little is known about the role of perfusion parameters on elderly patient survival and only selected studies have reported multiple intraoperative risk factors such as cardiopulmonary bypass (CPB) time and transfusion of red blood cells [4] or revascularization with the left internal mammary artery (LIMA) [5, 6]. Thus, describing the preoperative risk factors for survival among octogenarian cardiac surgery patients in conjunction with potential intraoperative and perfusion risk factors may assist cardiothoracic surgical teams in deciding both suitable octogenarian candidates for surgery and optimal surgical strategies. The aim of this analysis was therefore to determine the influence of preoperative and intraoperative factors on long-term survival among octogenarian cardiac surgery candidates in a series of consecutive patients from three centers.

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Address correspondence to Dr Baker, Cardiac Surgery Research, Level 6, Flinders Private Hospital, Adelaide, South Australia, 5042, Australia; e-mail: rob.baker@flinders.edu.au.

Material and Methods

Study Design

Data were obtained retrospectively from a database of all patients undergoing on-pump cardiopulmonary artery bypass grafting (CABG), with or without aortic or mitral valve procedures, between January 1, 1992 and December 31, 2005 at three institutions in South Australia: Flinders Medical Centre, Flinders Private Hospital, and Ashford Private Hospital. There were $n = 606$ octogenarians operated on during the study period: 414 isolated CABG and 192 concomitant valve repair-replacement. This represented 6% of the total isolated CABG and concomitant valve procedures performed during this period. The Ethics Committee of the Australian Institute of Health and Welfare approved this study (approval number EC 355, dated 23/09/2004) and the Clinical Governance Committee of the Flinders Medical Centre waived the need for patient consent for this study to report these findings.

Anesthetic, Surgical, and Cardiopulmonary Bypass Technique

Anesthetic technique consisted of midazolam, pancuronium, and fentanyl for induction and maintenance with isoflurane or sevoflurane, nitrous oxide, and (or) propofol as required. Before aortic cannulation, heparin was given at a dose of 300 IU/kg to achieve a target activated clotting time of 400 seconds or greater before commencement of CPB.

After median sternotomy, and harvesting of arterial and (or) venous conduit, CPB was instituted using an ascending aortic and either a two-stage right atrial or bicaval cannulation. Cardiopulmonary bypass was performed utilizing roller pumps and the circuit included a hard shell membrane oxygenator, PVC or biopassive tubing (SMARxT; Cobe Cardiovascular, Arvada, CO), and a 40 micrometer arterial line filter. Routine CPB protocol included nonpulsatile flow (rate 1.8 to 2.4 Lpm/m²), alpha-stat pH management, gravity venous drainage, and systemic temperature management (28°C to 36°C). Myocardial protection was achieved by using intermittent antegrade hyperkalemic cardioplegia. The initial or induction dose of cardioplegia was given for 2 minutes (250 mL/minute), and then the maintenance dose was given approximately every 20 minutes as required through the procedure. Seventy-three cases were performed with electric fibrillation of the heart. Attempts were made at all procedures to revascularize all vessels deemed operable by the respective surgeons. The heart was arrested and the target coronary artery was opened, and distal anastomoses between the bypass graft and native coronary artery were performed under aortic cross-clamping followed by valve surgery if indicated. Proximal anastomoses were performed with partial aortic clamping. Gradual weaning from bypass started after completion of the proximal anastomoses. Cardiotomy suction was utilized only in valve procedures. Patients were rewarmed at rates not in excess of 1°C per minute and separated from CPB when nasopharyngeal temperatures exceeded 36.5°C. On completion of all anastomoses and weaning off CPB, protamine was given to return

the activating clotting time to preoperative levels. At the end of surgery patients were transferred to the intensive care unit and managed according to unit protocol.

Mortality Assessment

Long-term survival was ascertained from the National Death Index provided by the Australian Institute of Health and Welfare for use in epidemiologic studies and medical research. National Death Index data provided all cause mortality up to December 31, 2006 and this date was taken as the censor date for patient survival, enabling a minimum of 12-month follow-up.

Statistical Analysis

Statistical analyses were performed using SPSS 15.0 (SPSS Inc, Chicago, IL). The early mortality rates 30 days or less across the study period were evaluated for linear trend. Potential preoperative risk factors for long-term mortality were evaluated with the Mantel-Cox log-rank test for categorical variables and univariable Cox proportional hazard models for continuous variables to ascertain the association with survival. The risk factors examined were principally derived from previous survival research among octogenarian and nonoctogenarian series [2, 4-11], determined by prevalence in the sample and according to available data across the study period, and included the following: age (continuous variable), concomitant valvular procedure (versus isolated CABG), urgency of operation (elective versus emergency, urgent), congestive heart failure, renal disease, female sex, cerebrovascular disease, myocardial infarction less than 30 days preoperatively, reoperative procedure, hypercholesterolemia, diabetes mellitus (type I or type II vs none), peripheral vascular disease, history of tobacco smoking, left ventricular ejection fraction ([LVEF] normal [0.60] category versus impaired [0.31 to 0.59], severe [<0.30]), body mass index (normal vs underweight, overweight, obese, morbidly obese), minimum preoperative hemoglobin (Hb), and preoperative creatinine prior to institution of CPB (analyzed categorically as quintiles). The hospital institution was evaluated by an interaction term with year of operation. The prevalence of intraaortic balloon pump in the sample was low ($n = 7$, 1.2% of total) and thus this variable was not considered.

Due to regression model constraints, only preoperative covariates p less than or equal to 0.20 were retained for further analysis to establish a baseline hazard model of risk factors and to avoid overfitting. Utilizing the mean of covariates method these covariates were entered into a proportional hazard model in block fashion at the first step (model 1). Given the particular interest in intraoperative covariates, these were forced into the regression model at the second step (model 2) regardless of univariable association and included the following: LIMA for revascularization, defibrillation, total time on CPB (minutes), maximum arterial outlet temperature (°C), minimum hematocrit value, minimum nasopharyngeal temperature (°C), and use of blood products intraoperatively (transfusion of red blood cells, frozen plasma), and total number of grafts.

Table 1. Descriptive Data of Medical and Surgical Variables Among Octogenarians and Univariable Association With Mortality

Descriptive Variables	N ^a	%	p Value ^b
Sex:			0.20
Male	374	61.7	
Female	232	38.3	
Median age, year, and interquartile range	81	80–84	<0.001
Year of operation and hospital institution interaction term	—	—	0.55
Renal disease	48	7.9	<0.001
Hypercholesterolemia	194	32.0	<0.001
Acute myocardial infarction ≤30 days	32	5.3	0.93
Congestive heart failure	63	10.4	0.35
Diabetes	91	15.0	0.42
Tobacco smoking history	271	44.7	0.02
Peripheral vascular disease	120	19.8	0.20
Cerebrovascular disease	102	16.8	0.40
Reoperation	24	4.0	0.11
Urgency of surgery:			0.09
Elective	532	87.8	
Urgent	61	10.1	
Emergency	13	2.1	
Left ventricular ejection fraction:			<0.001
Normal ≥0.60	401	66.2	
Impaired 0.31 to 0.59	147	24.3	
Severe ≤0.30	58	9.5	
Body mass index kg/m ² :			0.03
Underweight ≤18.5	16	2.6	
Normal 18.6 to 24.9	265	43.7	
Overweight 25 to 29.9	247	40.8	
Obese 30 to 39.9	65	10.7	
Morbidly obese ≥40	13	2.1	
Precardiopulmonary bypass creatinine:			<0.001
Creatinine ≤0.089 mmol/L	118	19.5	
Creatinine 0.09 to 0.10	79	13.0	
Creatinine 0.11 to 0.12	190	31.3	
Creatinine 0.13 to 0.14	104	17.2	
Creatinine ≥0.15	115	19.0	
Minimum preoperative Hb, mean and SD	8.7	2.0	0.09
Concomitant valve procedure	192	31.7	0.11
Intraoperative ^c :			
Time on CPB (minutes), M and SD	60.0	24.8	<0.001
Defibrillation	54	8.91	0.32
Number of grafts revascularized			0.78
1	104	17.2	
2	235	38.8	
3	216	35.6	
≥4	52	8.6	
LIMA	227	37.5	0.04
Maximum arterial temperature (°C), M and SD	37.9	0.6	0.77

Table 1. Continued

Descriptive Variables	N ^a	%	p Value ^b
Minimum hematocrit (mg/L), M and SD	22.8	3.5	0.12
Minimum nasopharyngeal temperature (°C), M and SD	32.8	2.5	0.02
Blood products intraoperatively	481	79.4	0.34

^a All data presented as N and % unless otherwise specified; ^b univariable Mantel-Cox log-rank test or univariable proportional hazard regression results; ^c intraoperative covariates forced into Cox proportional hazard models as shown in Table 2.

CPB = cardiopulmonary bypass; Hb = hemoglobin; LIMA = left internal mammary artery.

Multicollinearity statistics were deemed acceptable from examination of squared multiple correlations less than 0.90 and inspection of correlations between regression coefficients. Proportionality of hazards was inspected by covariate interactions with time, and examination of the baseline hazards function plot and log-minus-log plot of survival function.

Results

The descriptive and univariable predictors of long-term mortality among octogenarians are shown in Table 1. The risk factors retained for multivariable analysis can be observed in Table 2.

Short-Term Survival

There were 271 deaths (44.7% of sample) and 2,675 person years of survival for analysis, with a median follow-up of 7.15 years (95% confidence interval [CI] 6.47 to 7.82 years, standard error = 0.35). The intraoperative mortality rate among octogenarians was 1.8% (n = 11), and the total 30-day mortality rate inclusive of perioperative deaths was 5.1% (n = 31; 18 CABG, 13 concomitant valve). Analysis of 30-day mortality rates by year of operation was not significant; $\chi^2(13) = 8.45, p = 0.81$, indicating that early survival rates did not significantly change across the observation period.

Long-Term Survival: Preoperative Risk Factors

The Kaplan-Meier plot of actuarial survival is shown in Figure 1 for isolated CABG and concomitant valve procedures. Survival for isolated CABG patients at 1, 3, and 5 years was 91%, 77.8%, and 66.5%, respectively, and for valve-CABG patients at 1, 3, and 5 years was 86.2%, 74.4%, and 61.5%, respectively. By comparison, the expected survival for Australian males aged 80 to 84 is 7.9 years, while for females of the same age it is 9.7 years, and for males and females aged 85 years or greater the life expectancy is 5.6 and 6.9, respectively [12].

The baseline hazard model (model 1) comprised of preoperative clinical factors for long-term mortality is shown in Table 2. With regard to age, an 8% increased mortality risk was evident for every 1 year increase in age, and this translated to a 47% increase in mortality risk

Table 2. Multivariable Adjusted Hazard Model for Long-term Mortality in Octogenarians and Preoperative Risk Factors in Combination With Intraoperative Risk Factors

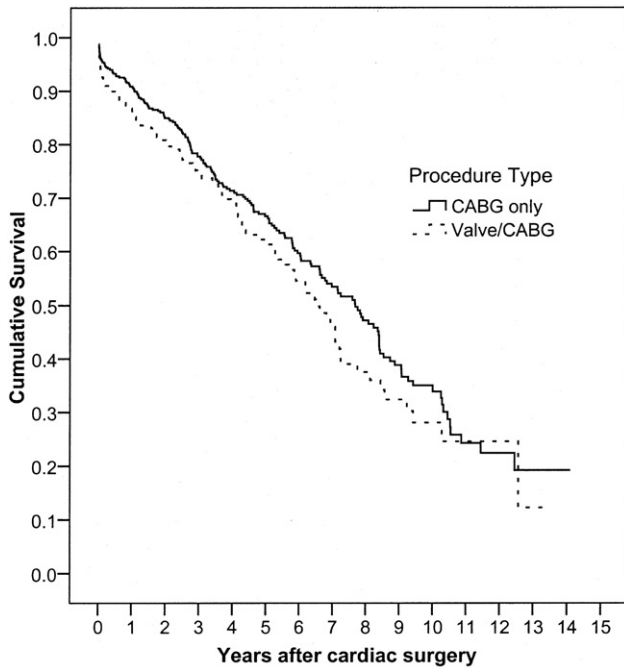
Covariates	Model 1				Model 2			
	Hazard Ratio ^a	95% CI Lower	95% CI Upper	p	Hazard Ratio ^b	95% CI Lower	95% CI Upper	p
Preoperative								
Reoperation	1.74	0.95	3.17	0.07	1.66	0.88	3.14	0.12
Concomitant valve procedure	1.17	0.90	1.52	0.26	0.81	0.51	1.28	0.36
Age	1.08	1.03	1.14	<0.01	1.09	1.03	1.15	<0.001
Female sex	1.12	0.83	1.51	0.46	1.09	0.78	1.52	0.62
Renal disease	1.55	0.96	2.51	0.07	1.46	0.88	2.40	0.14
Hypercholesterolemia	1.92	1.38	2.67	<0.001	1.92	1.37	2.69	<0.001
Urgency of surgery								
Elective (reference)	—	—	—	—	—	—	—	—
Urgent	1.22	0.79	1.91	0.37	1.16	0.73	1.84	0.54
Emergency	1.29	0.64	2.62	0.48	1.17	0.57	2.40	0.67
LVEF								
Normal ≥0.60 (reference)	—	—	—	—	—	—	—	—
Impaired 0.31 to 0.59	0.89	0.65	1.22	0.46	0.87	0.63	1.19	0.38
Severe ≤0.30	2.07	1.42	3.01	<0.001	1.92	1.30	2.84	0.001
Body mass index kg/m²								
Normal 18.6 to 24.9 (reference)	—	—	—	—	—	—	—	—
Underweight ≤18.5	1.91	0.94	3.87	0.07	1.66	0.79	3.49	0.18
Overweight 25 to 29.9	0.81	0.62	1.07	0.14	0.88	0.66	1.16	0.35
Obese 30 to 39.9	1.19	0.75	1.86	0.46	1.23	0.78	1.93	0.38
Morbidly obese ≥ 40	0.63	0.25	1.58	0.33	0.64	0.25	1.63	0.35
Tobacco smoking history	1.38	1.05	1.82	0.02	1.46	1.09	1.95	0.01
Minimum preoperative Hb	0.97	0.91	1.03	0.28	0.95	0.89	1.01	0.12
Peripheral vascular disease	1.25	0.93	1.67	0.14	1.28	0.95	1.71	0.10
Pre-CPB creatinine mmol/L:								
Creatinine ≤ 0.089 (reference)	—	—	—	—	—	—	—	—
Creatinine 0.09 to 0.10	0.60	0.35	1.02	0.06	0.58	0.34	0.99	0.05
Creatinine 0.11 to 0.12	1.27	0.87	1.87	0.22	1.15	0.77	1.71	0.49
Creatinine 0.13 to 0.14	1.24	0.81	1.89	0.32	1.09	0.71	1.67	0.69
Creatinine ≥0.15	1.81	1.18	2.80	0.01	1.66	1.06	2.60	0.03
Intraoperative								
Total grafts:								
1 (reference)	—	—	—	—	—	—	—	—
2	—	—	—	—	1.03	0.67	1.59	0.88
3	—	—	—	—	1.47	0.83	2.61	0.19
≥4	—	—	—	—	0.67	0.32	1.38	0.28
Time on CPB (minutes)	—	—	—	—	1.01	1.00	1.02	<0.001
LIMA	—	—	—	—	0.77	0.57	1.05	0.10
Defibrillation	—	—	—	—	1.31	0.85	2.02	0.23
Maximum arterial temperature (°C)	—	—	—	—	0.95	0.76	1.18	0.62
Minimum hematocrit mg/L	—	—	—	—	1.00	0.95	1.04	0.81
Minimum nasopharyngeal temperature (°C)	—	—	—	—	0.98	0.92	1.04	0.54
Blood products	—	—	—	—	0.87	0.60	1.24	0.43

^a Hazard ratio adjusted for preoperative covariates; ^b hazard ratio adjusted for all preoperative and intraoperative covariates.

CI = confidence interval; CPB = cardiopulmonary bypass; LVEF = left ventricular ejection fraction; Hb = hemoglobin; LIMA = left internal mammary artery.

for an increase in age by 5 years. There were several variables associated with approximately a twofold increased risk of mortality among octogenarians; severely

impaired LVEF, hypercholesterolemia, highest quintile of creatinine, while tobacco smoking history was also associated with mortality risk.



Numbers at risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CABG	414	379	323	151	195	152	123	93	73	53	31	15	10	3	1
CABG/valve	192	163	141	104	84	67	51	34	25	15	8	4	2	1	-

Fig 1. Kaplan-Meier actuarial survival graph for $n = 414$ octogenarian patients who underwent isolated coronary artery bypass graft surgery (CABG) (solid line), and $n = 192$ octogenarian patients who underwent concomitant valve repair-replacement with CABG (broken line).

Long-Term Survival: Intraoperative Risk Factors

Inspection of the intraoperative risk factors presented in Table 1 showed that time on CPB, LIMA use, and minimum nasopharyngeal temperature were associated with mortality in univariable analysis. In the multivariable analysis depicted in Table 2 (model 2), however, adjustment for other risk factors showed that only CPB time remained associated with greater mortality risk (hazard ratio 1.01, 95% CI: 1.00 to 1.02; $p < 0.001$). With regard to bypass time, a 1% increased mortality risk was evident for every 1 minute increase in bypass time, and this translated to a 10.4% increase in mortality risk for an increase in bypass time of 10 minutes. The mortality risk attributable to preoperative risk factors evident in model 1 was not attenuated for age, hypercholesterolemia, severely impaired LVEF, smoking, and the highest creatinine quintile as observed in model 2.

Comment

With regard to the study aim, the main finding was that only longer CPB time was found to significantly influence long-term survival beyond established preoperative clinical risk factors demonstrated here, including age, hyper-

cholesterolemia, severe LVEF, smoking history, and elevated creatinine. This supported Rady and colleague's [4] findings with short-term mortality among patients greater than 75 years old. A potential explanation is that longer CPB times are due to different perfusion intervention strategies for patients or simply the complexity of the operations among the elderly. For example, longer CPB times may reflect more revascularized grafts and technically complex valve procedures as extended CPB time correlates with total procedure time. However, our results have demonstrated increased bypass time to be significant independent of other factors, including type of procedure, number of grafts, use of LIMA, decreased Hb, and poor renal function.

Internal mammary artery grafts were used for revascularization in 37.5% of patients supporting the claim that uptake in the elderly has been disproportionate with LIMA's more commonly employed in younger patients [7]. The results with respect to the LIMA did not confirm favorable survival among octogenarians but suggested a trend toward lower mortality risk. Given that the number of grafts was also not associated with survival a potential explanation is that the variance attributable to total graft number was confounded by the significant effect found for time spent on CPB, which is a general marker of operative complexity.

These results suggested that other than total CPB time the remaining CPB-related and intraoperative risk factors did not significantly influence the risk of all-cause mortality in the long term after adjustment. Such intraoperative risk factors may reflect acute intraoperative risk and are perhaps associated with early morbidity. For example, intraoperative red blood cell transfusion is associated with low-output heart failure [13], while CPB temperature management may be related to stroke [14]. Octogenarians have been reported to present for CABG with lower hematocrit than nonoctogenarians, and increased age is associated with greater need for transfusion and packed red blood cells [8]. Hematocrit levels and requirement for intraoperative blood products bore no significant influence on long-term survival in this sample, though were recently implicated in long-term survival after cardiac surgery in adults [15, 16].

The findings with respect to traditional risk factors supported work elsewhere suggesting that many risk factors for late death among octogenarians are noncardiac comorbidities [5-7, 17, 18]. Specifically, age was a risk factor for mortality supporting other studies elsewhere that reported short-term mortality [8, 19] and late mortality [17, 20]. However, this result is not universal as, for example, Kamiya and colleagues [21] found that increasing age affected neither prognosis nor quality of life among octogenarians receiving CABG or percutaneous coronary intervention. Of the indicators of renal insufficiency, low creatinine was associated with a reduced mortality risk whereas the highest quintile of creatinine was associated with an increased mortality risk. This parallels the findings of de Vincentiis and colleagues [22] who showed that preoperative renal insufficiency (creatinine > 2.00 mg/dL) was a predictor of

hospital mortality in octogenarians undergoing aortic valve replacement and further supports the impact of poor renal function as a predictor of short-term [23] and long-term [24] mortality. The results with regard to LVEF support previous series on operative mortality [25] and late mortality [26, 27] as it is well documented that a severely impaired left ventricle portends greater mortality risk after cardiac surgery as does congestive cardiac failure [7].

Limitations

The results are presented with several limitations, including the retrospective design, examination of concomitant valve procedures, and also the sample size that was, however, comparable with other studies [7, 8, 18]. There was a potential unknown selection bias due to the lack of information on octogenarian patients considered for surgery but not operated on. The univariable selection of preoperative risk factors for multivariable hazard models may limit the conclusions drawn about potential risk factors. For example, the recent work by Billah and colleagues [28] suggested that along with the risk factors explored here, both New York Heart Association class and use of inotropes were important variables in determining preoperative mortality risk in cardiac surgery candidates. The final limitation of this report relates to the scope of perfusion-related data as continuous variables such as flow, pressure, and other parameters could not be analyzed with respect to mortality. Multicenter and international partnerships such as the Perfusion Downunder Collaboration and the International Consortium for Evidence Based Perfusion [29], through prospective multicenter registries, will be able to provide access to a broader range of perfusion and intraoperative data in the future.

Traditional risk factors increased the risk of mortality among octogenarians after cardiac surgery, and perfusion and intraoperative risk factors were not found to significantly influence mortality risk other than the total CPB time. In general there is limited information from large series documenting the role of intraoperative risk factors combined with preoperative variables in determining long-term survival in octogenarian cardiac surgery patients. As an increasing number of octogenarians are referred for cardiac surgery, closer examination of these factors will aid surgeons in deciding which patients are suitable for cardiac surgery and further inform suitable intraoperative management. Identification of a range of preoperative and intraoperative risk factors may allow optimization of patient characteristics before surgery that may translate to a survival benefit. Octogenarians can also be informed about the individual risks imposed by surgery and provide a clearer scope for long-term recovery.

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INVITED COMMENTARY

The selection of patients aged older than 80 years as candidates for cardiac operations remains a multifactorial issue. Not only are there the obvious cardiac pathology factors that dictate the technical feasibility of the operation, there are also numerous studies that have identified important comorbidities that contribute to operative mortality and postoperative morbidity. The increased mortality and morbidity for octogenarians, plus their limited life expectancy, has created an important third factor to be considered before offering cardiac procedures to someone older than 80, namely, the presence of symptoms. The diminished life expectancy of octogenarians makes prolongation of life relatively less important and improvement in quality of life relatively more important than it is in younger patients.

Unfortunately, the study by Rohde and colleagues [1] mentions nothing about the indications for operation, nor do they describe the quality of life for those who survived. Survival should not be the only benchmark used to assess operative results in patients over 80 years of age. In addition, there is no actual documentation of operative survival. A patient first needs to be a short-term survivor to become a long-term survivor.

Their study was directed at determining the effect of comorbid conditions and intraoperative factors on long-term survival, which they found lacking in previous studies. The authors were able to confirm important comorbidities identified in other studies, including increasing age, hypercholesterolemia, impaired left ventricular ejection fraction, and elevated creatinine. Only prolonged cardiopulmonary bypass time proved to be an intraoperative predictor, but the authors were missing important intraoperative data during the early years of the study.

Even if other intraoperative variables had been identified as predictors of poorer long-term survival, how can a surgeon use that information prospectively (ie, preoperatively) to assess operative risk and thus influence patient selection? Identifying intraoperative risk factors that one could alter might influence subsequent operative risk, but it would seem to be of limited value in preoperative patient selection.

As cardiac surgeons join the effort to define and improve quality of care, cardiac operations in octogenarians remain a fruitful field of investigation because the increased mortality and morbidity make the evaluation of new approaches easier to assess with smaller numbers of patients. Given the relatively higher expense for limited years of improved survival and quality of life, this cohort will certainly be a focus of attention in the growing debate to limit health care costs.

Cary W. Akins, MD

Cardiac Surgery Division

Cox 648

Massachusetts General Hospital

55 Fruit St

Boston, MA 02114

e-mail: cakins@partners.org

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