Open heart surgery in the elderly patient

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Open heart surgery in the elderly patient

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Open heart surgery in the elderly patient

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit Maastricht,
op gezag van de Rector Magnificus,
Prof. dr. A.C. Nieuwenhuijzen Kruseman,
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen
op vrijdag 7 juli 2000 om 16.00 uur

door

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CHAPTER 1

Introduction

Open heart surgery in elderly patients was in the past associated with a high mortality rate. Keon et al reported in a retrospective study covering 3 decades a drop in mortality from 28% in 1970 to 12% in 1980 to 5% in 1990 in patients aged 70 years or over. In comparison to the younger patient with cardiac surgery the mortality decreased from 7% to 4% in the last 30 years¹. Factors explaining this spectacular improvement include: 1) improved anaesthesiological and surgical techniques and skills, 2) improved postoperative care, and 3) better selection of candidates, using a risk profile.

Because of lower mortality rates and the increased capacity to perform open heart surgery, the number of elderly patients operated upon has gradually increased during the last decade. Several studies indicated a 4–6 times increase of elderly patients operated over a 7–13 year period (1981–1987, and 1979–1992)^{2,3}. Also at our institution, where cardiac surgery started in 1986, the percentage of elderly patients being operated have increased more than 3 fold since the first year. However as shown in figure 1, during the last 5 years no further increase has been observed, with approximately 10% of all patients undergoing open heart surgery being 75 years or older.

This increase is expected to continue when we realize that demographic developments according to the Eurostat forecasting model⁴ indicate that the percentage of people aged 65 and older will increase from 15.2% in 1995 to 19.2–19.5% in 2020, and that people aged 80 and older will increase from 3.8% in 1995 to 4.9–5.5% in 2020.

There are because of ethical difficulties no randomized studies that compare the benefit of cardiac surgery versus conservative treatment in elderly patients. Ko et al⁵ studied retrospectively 65 octogenarians that had bypass surgery (n=36) or were treated conservatively (n=29). The surgically treated patients had more severe coronary artery disease and anginal complaints. The mortality after 3 years was 22.6% in the surgical group, compared to 44.8% in the conservatively treated group, suggesting a benefit from bypass surgery.

In this regard it is important to know the general life expectancy in the elderly in the different age groups. Table 1 shows the situation in the Netherlands (CBS, 1995)^{6,7}

% procedures ≥ 75 years old

Academic Hospital Maastricht

Figure 1.1. Percentage of patients aged 75 years and older, undergoing open heart surgery.

Table 1.1. Life expectancy in different age and gender groups.

	65 y	75 y	85 y
male	14.2 y	8.5 y	4.7 y
female	18.8 y	11.3 y	5.8 y

Recent studies show that the longevity in elderly patients after open heart surgery is similar or even better than the theoretical life expectancy.⁸⁻¹⁴

Although current mortality rates are rather low^{3;15-17}, several studies indicate that there is a higher morbidity post surgery in elderly patients^{2;18-20}. That results in a longer duration of hospital stay, higher costs, and therefore a worse cost/benefit ratio.²¹ Not only mortality but also quality of life is important for determining the success of the operation.

Many studies suggest that there is a clear improvement of quality of life²² after open heart surgery in elderly patients.²³⁻²⁹ However most of these studies are retrospective and without a control group. Results are therefore not very reliable because these studies are done quite late after the operation in a selected group which is still alive at that time. Until now no prospective studies were done comparing quality of life in both elderly and younger patients before and after open heart surgery.³⁰

One of the greatest problems is the selection of elderly patients likely to benefit from open heart surgery. There are several factors that influence the risk of an operation.³¹⁻³⁵ These risk factors can be divided in cardiac factors, like poor LV function, manifest heart failure, concomitant severe mitral incompetence and the

need for emergency cardiac surgery. Among the known non-cardiac riskfactors are kidney function disturbances, chronic obstructive pulmonary disease, cerebrovascular disease,³⁶⁻⁴⁰ diabetes mellitus and advanced age.⁴¹⁻⁴⁹ In addition there are perioperative riskfactors like complexity of the operation,^{50,51} type of valve used,⁵²⁻⁶⁰ longer aortic cross clamp time, and the need for inotropic support. Also the amount and type of cardiac protection fluids used during the operation is important for outcome.⁶¹⁻⁶³ Some of these factors however are not known at the time of patient selection. This makes the preoperative riskfactors most important.

All patients operated nowadays are considered to be "vital", and are without serious concomitant disease resulting in a shortened life expectancy. However, because of the process of aging⁶⁴ the elderly patient has a higher incidence of riskfactors than the younger patient. In the elderly patient the decision to perform surgery is than often based on the inability to find a satisfactory conservative approach.⁶⁵ This explains why elderly patients referred for surgery are frequently more disabled and have more advanced cardiac disease than younger patients. The purpose of our study is to compare the results of open heart surgery in patients older than 75 years with younger patients. Short- and long-term results will be related to pre-operative findings. The outcome will include medical data (morbidity and mortality), quality of life data (prospectively assessed with validated questionnaires), and cost aspects (admission duration and readmissions). The purpose of our study is to investigate the possibility to divide patients in three categories: 1) patients in whom cardiac surgery is beneficial, 2) patients where cardiac surgery is of questionable benefit, 3) patients where cardiac surgery is not beneficial. If possible, such a ranking could help in future selection of patients for open heart surgery.

The first part of this thesis (chapter 2) will describe a review of the current literature concerning open heart surgery in elderly patients. The next chapter (3) describes the methods and patient population of the prospective study we performed in 600 patients. In chapter 4 the results of our study with coronary bypass surgery are discussed. Chapter 5 shows our results of valve surgery and combined valve and coronary surgery. Since atrial fibrillation is an important complication of open heart surgery, especially in elderly patients, having a high incidence resulting in prolongation of the admission duration, a separate chapter deals with this problem (chapter 6). In Chapter 7 differences are described in quality of life following open heart surgery in different age groups. The next chapter (8) deals about the incidence and consequences of mental confusion post cardiac surgery in the elderly. Chapter 9 compares the life expectancy in the first years following surgery of different age groups to that of the general population. The general discussion is in chapter 10. Finally in chapter 11 the results and conclusions of this thesis are described in a summary.

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CHAPTER 2

Review of the literature

The number of elderly patients that are undergoing open heart surgery has been increasing during the last decade. Most studies that have been performed in the past to evaluate the results of open heart surgery in elderly patients are retrospective, and mostly limited to mortality data and morbidity. The mortality figures in these studies show a wide range varying between 0% and 29%, depending on the type of operation, risk factors, age of patients studied, and institution. In a retrospective study performed at our institution in 1991 (Ter Woorst F.J., unpublished) in which 186 patients aged 75 years and older were studied, with either coronary bypass surgery, valvular surgery or combined valvular and coronary surgery, the surgical mortality (within one month following surgery) was only 2.3%. These patients were operated during a four year period, which equals 47 patients each year.

The majority of retrospective studies that have been performed include patients over a time period varying from 3 to 16 years (table 1-3). When calculating the number of old patients that are operated in one year in these studies, the number is surprisingly low in many studies, varying between three and 126 cases each year, with a median of 25 cases. The conclusions from these studies are that results are favorable in elderly patients. This could suggest that several centers have strong selection criteria for open heart surgery in the elderly, thereby limiting the number of patients that have been operated.

In table 2.1 studies are listed that included only coronary bypass surgery. Table 2.2 shows studies with valve surgery and/or combined valvular with coronary surgery. Table 2.3 lists the studies that included all types of open heart surgery in elderly patients.

Factors that influence operative mortality are related to the actual condition of the patient. Important factors are: decreased kidney function, low LVEF/congestive failure, advanced age, emergency procedures. In table 2.4 an overview is given of several studies with the riskfactors that were found. All prospective studies are included in that table. Many studies also mention perioperative riskfactors for mortality. These include a prolonged perfusion- or aortic cross clamp time, need for inotropic support, prolonged mechanical ventilation after surgery and IABP use. Since these riskfactors are of not much help in pre-operative selecting patients, they are not reviewed here.

Table 2.1. Coronary bypass surgery in elderly patients.

Year	Reference	Type	Nr Pat	Period	Age	Hosp mort	Long term mort	QL an	Comments
1992	Ko ³	retro	36	5y	80+	12%	22.6%/3y	no	Also conservative group studied
1988	Acinapura ⁴	retro	685	6y	70+	8%	15%/6y	no	Comparison with 3,142 younger pts
1994	Antona ⁵	retro	71	3y	75+	4.2%	-	no	Comparison with 71 matched younger pts
1992	Khan ⁶	prosp	663	8y	75+	7.5%	-	no	Comparison with 1,464 younger pts
1991	Ko ⁷	retro	100	4y	80+	12%	23%/2y	no	No control group
1995	Williams ⁸	retro	300	5y	80+	11%	23.8%/4.5y	no	No control group
1987	Naunheim ⁹	retro	23	6y	80+	22%	30%/1y	no	No control group
1995	Peterson ¹⁰	retro	24,461	4y	80+	11.5%	28.8%/3y	no	Data from Medicare insurance database
1989	Tsai ¹¹	retro	693	5y	70+	6.2%	10.8%/3y	no	Comparison septua- and octogenarians
1991	Tsai ¹²	retro	157	9y	80+	7.0%	29.9%/2.7y	yes	Only postoperative QL assessment
1991	Uttley ¹³	retro	25	7y	80+	0%	8%/1.3y	no	Survival compared with general population
1995	Cane ¹⁴	retro	121	9y	80+	9.1%	30.9%/2.3y	no	Comparison with matched population
1994	Curtis ¹⁵	retro	668	13y	70+	5.2%	-	no	Comparison septua- & octogenarians
1994	Hannan ¹⁶	retro	4,933	2y	75+	5.3%	-	no	Comparison in 30,972 pts of all ages
1994	He ¹⁷	retro	1,399	7.5y	70+	8.9%	-	no	Emphasis on influence of LIMA

(Year= Year of Publication, Type= Type of study (Retrospective or Prospective), Nr. Pat.=Number of Patients, Period= Time Period of Patient Inclusion, Age=Minimal Age of included patients, Hosp. mort.=Hospital Mortality, Long term mort.=Long term Mortality, QL an.=Quality of Life analysis performed).

Table 2.2. Valvular surgery in elderly patients.

Year	Reference	Type	Nr. Pat.	Period	Age	Hosp. mort.	Long term mort.	QL an.	Comments
1995	Adkins ¹⁸	retro	42	10y	80+	14.3%	21%/21m	no	All combined surgery
1989	Antunes ¹⁹	retro	213	5y	65+	7.0%	8.1%/1y	no	Hosp. mort. for 75+ pts = 9.1%
1993	Aranki ²⁰	retro	717	12y	70+	6.6%	-	no	Only Aortic valve surgery
1989	Levinson ²¹	retro	64	13y	80+	9.4%	17%/1y	no	Only aortic stenosis
1994	Logeais ²²	prosp	675	17y	75+	12.4%	-	no	Analysis from existing database
1986	Tsai ²³	retro	120	4y	70+	23.3%	30%/2y	no	Combined valve & CABG
1996	Chocron ²⁴	retro	95	4y	75+	11.5%	24.2%/2.2y	yes	Only postoperative QL assessment
1984	Craver ²⁵	retro	152	8y	70+	5.3%	24%/5y	no	Compared to 489 young AVR pts
1990	Deleuze ²⁶	retro	60	8y	80+	28%	35%/1y	no	LVEF<40% in 50% of pts
1993	Elayda ²⁷	retro	171	16y	80+	17.5%	39.2%/3.3y	no	AVR patients
1989	Fiore ²⁸	retro	25	8y	80+	20%	36%/3y	no	No control group
1989	Fremes ²⁹	retro	469	5y	70+	10%	-	no	Compared to 2040 younger pts
1996	Gehlöt ³⁰	retro	322	21y	80+	13.7%	39.8%/5y	no	Only Aortic valve replacement

(Year= Year of Publication, Type= Type of study (Retrospective or Prospective), Nr. Pat.=Number of Patients, Period= Time Period of Patient Inclusion, Age=Minimal Age of included patients, Hosp. mort.=Hospital Mortality, Long term mort.=Long term Mortality, QL an.=Quality of Life analysis performed).

Table 2.3. Studies including both coronary and valvular surgery in elderly patients.

Year	Reference	Type	Nr. Pat.	Period	Age	Hosp. mort.	Long term mort.	QL an	Comments
1990	Bashour ³¹	retro	80	3y	80+	12.5%	16.3%/1y	no	55% CABG, 45% valve or combined
1997	Bouche ³²	retro	329	4y	70+	9.4%	22.2%/5y	partial	Only functional status assessment
1995	Katz ³³	retro	628	4.5y	70+	6.4%	-	no	Comparison with 1787 young pts
1995	Kumar ³⁴	retro	68	2y	80+	14.7%	31.3%/6y	yes	Comparison 3 diff. years of surgery
1994	Shah ³⁵	retro	56	4y	79+	7%	12%/1y	no	No control group
1994	Subayi ³⁶	retro	100	2y	75+	6%	12%/2y	no	Compared with 100 younger pts
1986	Tsai ³⁷	retro	76	4.7y	80+	13.2%	23.7%/2y	no	No control group
1994	Tsai ³⁸	retro	15	10y	90+	13.3%	26.7%/2y	yes	Only postoperative QL assessment
1996	Chocron ³⁹	retro	146	9y	75+	7.5%	17.1%/3.4y	yes	Postoperative QL study using NHP
1995	Deiwick ⁴⁰	prosp	50	4y	80+	8.0%	17%/2y	no	No control group
1988	Edmunds ⁴¹	retro	100	11y	80+	29%	46%/3.4y	no	No control group
1991	Freeman ⁴²	retro	191	5y	80+	15.7%	28.3%/2y	no	Survival comp. to general population

(Year= Year of Publication, Type= Type of study (Retrospective or Prospective), Nr. Pat.=Number of Patients, Period= Time Period of Patient Inclusion, Age=Minimal Age of included patients, Hosp. mort.=Hospital Mortality, Long term mort.=Long term Mortality, QL an.=Quality of Life analysis performed).

Table 2.4. Preoperative Risk factors for cardiac surgery in the elderly in different studies.

Author/Year	Ref	Operation	Risk factors
Logeais/'94	22	AVR	Age, heart failure, no sinus rhythm, emergency surgery
Deiwick/'95	40	CABG+valve	Main stem disease, LVEF<45%, diabetes, combined surgery
Ko/'92,'91	7,3	CABG	LVEF<30, AP class 4, MV/AoV disease, re-operation
Bashour/'90	31	All, >80y	NYHA=4, MVR, pulmonary disease
Tsai/'91,	12	CABG	NYHA=4, LVEF<40, low cardiac output, IABP use
Deleuze/'90	26	AVR	Emergency O.R., low LVEF, poor kidney function
Freeman/'91	42	All, >80y	Heart failure, MVR, pre-op. Bundle branch block on ECG
Edmunds/'88	41	All, >80y	Old Infarction, Cachexia, Emergency O.R.
Naunheim/'87	9	CABG	Low cardiac output, Emergency O.R., IABP use
Adkins/'95	18	Valve+CABG	Aortic insufficiency
Cammack/'87	43	MVR	Posterior mitral annulus calcification
Elayda/'93	27	AVR	LVEF<45, hypertension, heart failure, angina, combined O.R.
Aranki/'93	20	AVR	Male gender, mechanical prosthesis, combined O.R., NYHA=4

Most studies concerning Quality of Life after open heart surgery are focusing on young patients, and discuss items as return to work. In a recent meta-analysis by Duits/Erdman¹ in which seventeen prospective Quality of life studies were reviewed in patients with coronary bypass surgery, only one study looked at patients older than 70 years. In that study by Chocron² it was found that an age above 70 years was associated with a lesser improvement of quality of life. These differences were present in the Energy, Sleep, and Social isolation section from the Nottingham Health Profile Questionnaire that was used for that study before and 3 months after surgery. In the other 16 studies from the meta-analysis no relation between age and Quality of Life is suggested. The major predicting factor in those studies associated with a worse Quality of Life after surgery is pre-operative anxiety and depression.

In a recent review article by Stemmer⁴⁴ it was found that although the incidence of chronic diseases is higher in elderly patients, only 20% of patients aged 65 years and older have major limitations of activities. Heart disease appeared to be the most common disease that causes these limitations, followed by arthritis, visual impairment, and other less frequent disorders. Correcting heart disease by means of open heart surgery will result in improvement of quality of life in these patients. The incidence of anatomically significant coronary artery disease in patients over 70 years is 60–70%, and the incidence of symptomatic coronary artery disease in that age group is 20%. Also the incidence of sudden death is twice as high compared to that of 50-year olds.

The postoperative morbidity is higher in elderly patients and can be 65%. The major age related complication was atrial arrhythmias (atrial fibrillation) which

occurred in up to 40% of the elderly patients. Renal failure and pulmonary complications also had a higher incidence compared to younger patients. The admission duration is longer in elderly patients, resulting in higher costs.

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CHAPTER 3

The Maastricht study: material and methods

In order to investigate the outcome of cardiac surgery in elderly patients in comparison to younger patients we designed a prospective observational study. During a period of 3¼ years, starting September 22nd 1993 until December 18th 1996 we included 200 patients who underwent open heart surgery, and were 75 years or older (Old group). Each of these patients were matched with two patients of less than 75 years (Young group), having the same operative procedure, and being of the same sex. During the inclusion period 290 patients older than 75 years have been operated, and 2499 patients younger than 75 years. Ninety elderly patients were not included because of logistic reasons, partially due to matching problems.

The data analyzed include medical data, information about admission duration and costs, and assessment of the quality of life. The follow up duration of all surviving patients was minimally one year. All patients were operated upon in the Academic Hospital of Maastricht (Department of cardio thoracic surgery).

The Academic Hospital Maastricht is the only Hospital in the province of Limburg that offers cardiac surgery. Being located in the most southern part of the Netherlands explains that the majority of patients from hospitals in the southern part of Limburg are operated upon in Maastricht (figure 3.1). The majority of the Old patient group came from Maastricht (35.5%), followed by Heerlen (33%) and Sittard (15.5%), which are the hospitals nearest to Maastricht. Only 2.5% of the patients were referred from hospitals above Weert. Most patients from the Young (control) group were selected from Maastricht (47.3%) for logistic reasons (table 3.1).

PATIENT POPULATION

Main categories: According to the surgical procedure each patient was entered in one of the following major categories: 1) coronary artery disease, 2) valvular disease, 3) combined coronary and valvular disease. The majority ($\pm 2/3$) of all patients had coronary surgery (table 3.2).

There were more female patients in the Old age group (53.5%). For that reason a similar percentage of female patients was taken in the Young group. The mean age was higher in female patients, which was most pronounced in the Young group (table 3.3). A detailed age histogram is shown in figure 3.2.

Figure 3.1. Maastricht and its geographic relation to the referring centre.

Timing of surgery: Operations were divided in three categories: 1) acute surgery (defined as surgery within 2 days after referral), 2) urgent surgery (defined as surgery within 2 weeks after referral, but during the same hospital admission), and 3) elective surgery (defined as surgery more than 2 weeks after referral, usually from a waiting list). No significant differences were seen in the incidence of acute surgery. However Old patients had a slightly higher incidence of urgent surgery (53.0% versus 43.5%, $P < 0.05$, table 3.4).

DATA COLLECTION

All patients were screened one day prior to surgery by the main investigator, who collected the results immediately in special data forms, to be used for computer analysis at a later stage.

Data recorded from the clinical history included: cardiac risk factors (smoking, hypercholesteremia, diabetes mellitus, hypertension), presence of an old or recent myocardial infarction (<2 months old), history of congestive heart failure,

Table 3.1. Referring hospitals.

	Age group			
	Young		Old	
	Count	%	Count	%
Maastricht	189	47.3%	71	35.5%
Heerlen	58	14.5%	66	33.0%
Sittard	81	20.3%	31	15.5%
Kerkrade	44	11.0%	12	6.0%
Roermond	12	3.0%	9	4.5%
Weert	5	1.3%	6	3.0%
Other	11	2.8%	5	2.5%
Total	400	100.0%	200	100.0%

Table 3.2. Type of surgery.

	Age group			
	Young		Old	
	Nb	%	Nb	%
CABG	262	65.5%	131	65.5%
klep	72	18.0%	36	18.0%
CABG+klep	66	16.5%	33	16.5%
Total	400	100.0%	200	100.0%

Table 3.3. Gender related differences in each age group.

Age group	Sex	Nb	Mean age	Std. Deviation	Std. Error Mean
Young	male	186	63.1	7.6675	.5622
	female	214	67.0 ^a	6.3449	.4337
Old	male	93	77.6	2.2118	.2293
	female	107	78.4 ^b	2.9363	.2839

^a P<.001, ^b P<.05

Figure 3.2. Distribution of age.

Table 3.4. Timing of surgery.

Age group	Acute (within 2 days)		Urgent (within 2weeks)		Elective (after 2 weeks)		Total	
	Nb	%	Nb	%	Nb	%	Nb	%
Young	17	4.3%	174	43.5%	209	52.3%	400	100.0%
Old	10	5.5%	106	53.0%	83	41.5%	200	100.0%

previous cardiac operations, history of non-cardiac atherosclerotic vascular disease (cerebral, peripheral, kidney), history of arrhythmias, hypertension, and chronic obstructive pulmonary disease. If an aortic stenosis was present a history of syncope was also recorded.

The use of different types of medication was recorded, especially usage of nitrates, diuretics, betablocking agents including sotalol, calcium antagonists, platelet inhibitors, anticoagulants, digoxine, ACE inhibitors, anti-arrhythmic drugs, sedative drugs, alpha blocking drugs and lipid lowering drugs . Data about medication use were also recorded at discharge, and at one year after surgery.

The severity of anginal and dyspnea complaints was graded in functional classes between I-IV, according to the New York Heart Association (NYHA) scale. Data recorded from physical examination included Body Mass index, Body Surface area, systolic blood pressure, carotid pulsations and murmurs, pulmonary rales and stage of congestive failure (Killip class I-IV), and presence of leg varicosis.

Data obtained from cardiac catheterisation included: Number of coronaries diseased (1-3), presence and severity of left main coronary disease, subjective description about the severity of calcification of the coronary arteries (graded as normal, moderately calcified, and severely calcified), value for left ventricular end diastolic pressure.

One day prior to surgery an echocardiogram was made, from which data were obtained concerning Left ventricular (LV) ejection fraction, LV end-diastolic diameter, wall thickness and LV-mass index, e/a-ratio, presence and severity of mitral incompetence and right ventricular systolic pressure.

From a 12-lead Electrocardiogram data were obtained concerning Rhythm, AV-conduction, bundle branch block, left ventricular hypertrophy and presence of ischemia or infarction.

A blood sample was obtained to determine the Hemoglobin level, Creatinin, BUN, Sodium, Potassium, ALAT, ASAT, and Glucose level.

A chest X-ray was performed to measure the Heart/Thorax-ratio, and the presence and severity of pulmonary congestion and/or pleural fluid.

Pulmonary function tests measuring the Vital Capacity and Forced expiratory one second Volume were additionally performed in 91 (45.5%) Old patients and 203 (50.1%) Young patients.

QUALITY OF LIFE

Many tests have been developed in the past to measure various aspects of quality of life.¹⁻¹³ These aspects can be related to mood (anxiety, depression, sleep disorders), physical condition (immobility, exercise tolerance) and social functioning (restrictions in daily activities, work, contacts with people). Each of these tests measures a selected number of these aspects. Most of these tests are questionnaires that have to be filled out by the patients.

In order to cover both most of these aspects of quality of life, and to have a practical test with a limited number of questions, to be filled out in short time by each patient, we selected the following 2 questionnaires: 1) The Hospital Anxiety and Depression scale (H.A.D., after Zigmund and Snaith, 1983)^{14; 15} of which an official Dutch translation is available (*appendix 1*). This questionnaire has 14 multiple choice questions dealing with anxiety and depressive complaints. 2) The Nottingham Health Profile (N.H.P., after Hunt, McKenna, 1981)^{16; 17}, of which a Dutch translation exists since 1993 (*appendix 2*). This questionnaire has seven main items, consisting of: energy, pain, emotional reactions, sleep, social isolation, physical mobility and social functioning, with a total number of 45 questions, that can all be answered by filling out "yes" or "no".

Both questionnaires were filled out by the patient 1) one day before surgery, 2) two months after surgery, and 3) six months after surgery. The time that is needed to fill out these questionnaires varies between 5 and 15 minutes.

Several studies have shown that these questionnaires are suitable for serial comparison, and have been useful in showing changes of quality of life after surgery. Validation studies have also been performed of the Dutch version of these questionnaires.^{18; 19}

ANESTHESIA AND MYOCARDIAL PERFUSION DURING SURGERY

Standard anesthetic (lorazepam, fentanyl citrate, sufentanil citrate, alfentanil hydrochloride, midazolam hydrochloride, pancuronium bromide) and monitoring techniques (electrocardiogram, central venous/pulmonary and arterial pressure monitoring, urinary output, rectal and skin temperature monitoring) were used in both groups. Cefuroxim was used for antibiotic treatment, and the first dose was administered before sternotomy.

Before connecting the extra corporeal circuit for Cardio Pulmonary Bypass (CPB), heparin (300 IU/kg, Heparin Leo, Leo Pharmaceutical Products BV, Weesp, The Netherlands) was administered in order to achieve an activated coagulation time (ACT) > 480 s (Hemochron 400, International Technidyne Corp., New Jersey, USA).

The main components in the extra corporeal circuit consisted of a hollow fiber membrane oxygenator (Univox; Bentley/Baxter Inc., Irvine, CA, USA.), a venous reservoir (BMR-1900; Bentley/Baxter Inc.), a cardiotomy reservoir: William Harvey H4700; C.R.Bard Inc., Tewsbury, MA, USA.) and an arterial line filter: Sartorius; Sartorius AG, Göttingen, Germany.). The standard priming of the extra corporeal circuit was 1300 ml Haemaccel 3.5% (Behringwerke AG, Marburg, Germany), 200 ml Mannitol 20%, 100 ml Human-Albumin 20%, 50 ml NaHCO₃ 8.4%, 20 ml KCl 7.45% (B.Braun Medica BV, Uden, The Netherlands) and 6500 IU Heparin Leo. After institution of cardiopulmonary bypass at a flow rate of 2.4 L/min/m², and after reaching a blood temperature below 28 °C, the heart was topically cooled till fibrillation using cold saline 0.9% at 4 °C. The aorta was then cross clamped and a single dose of approximately 800 ml of St.Thomas I cardioplegic solution at 4 °C was infused into the aortic root in a period of 4 minutes (3-5 minutes) to provide myocardial preservation. Topic cooling was maintained during the infusion of the cardioplegic solution. Target flow rates of 2.4 L/min/m² were maintained at normothermia and correspondingly lower rates of 2.0 L/min/m² (1.8-2.2 L/min/m²) were maintained at moderate hypothermia of 28 °C, depending on the venous oxygen saturation and the arterial pressure. Pulsatile perfusion was used throughout the period of aorta cross clamping. In case the LAD was revascularized using the left internal mammary artery papaverine was locally applied to prevent spasm to the mammary artery following dissection. After completion of all the distal anastomoses, the aortic cross clamp was removed and the proximal anastomosis was performed with a partial occlusion clamp after spontaneous or electrical

defibrillation, while rewarming of the patient to 37 °C was continued. All pump blood was returned to the patient through the aortic cannula or intravenously via infusion bags without hemoconcentration.

Data was collected about bypass time, aortic cross clamping time, arterial blood pressure, central venous pressure, diastolic pulmonary artery pressure, circulatory arrest time, lowest temperature, lowest hematocrit during perfusion, cardioplegia, venous O² saturation, and the need for inotropic support, temporary pacing or intra-aortic balloon pumping (IABP) at the end of the procedure.

OPERATIVE PROCEDURE

The operative technique consisted of a standard median sternotomy, routine aortic and right atrial cannulation.

Data were collected on type of surgery, first or reoperation, use of intra-aortic balloon pump (IABP), quantity and type of grafts (arterial, venous), quality of vein grafts and native vessels, types of valve surgery (mechanical, biological, or reconstruction).

POSTOPERATIVE COURSE

Information was collected about mortality and morbidity. The last one included the need for inotropic support, use of IABP, duration of ventilatory support, occurrence of post operative arrhythmias especially atrial fibrillation or flutter. Data on complications were divided in cardiac complications (infarction, heart failure, conduction disturbances) and non-cardiac complications (e.g. bleeding, infections, renal failure, mental confusion, need for rethoracotomy).

FOLLOW-UP

During follow up an echocardiogram, a chest X-ray, and physical examination were repeated after six months by the principal investigator. Data about functional class (NYHA classification) were collected six months and one year after operation. The Quality of life questionnaires were sent by mail 2 and 6 month following surgery.

ADMISSION DURATION AND COSTS

Data are collected about the Pre-operative admission (Number of days in the coronary care unit and/or normal Department), the Post-operative admission (Number of days in the intensive care unit and the normal Department) and Readmissions (Number and days of readmissions because of cardiac causes, until one year after surgery).

STATISTICAL METHODS

The Unpaired *t*-test was used to demonstrate differences in Interval variables between both age groups. For Nominal variables Chi-square analysis of contingency was used. In case of Ordinal variables the Mann-Whitney rank-sum test was performed. To demonstrate changes in each treatment group after surgery the Paired *t*-test was used for Interval variables, McNemar's test for Nominal variables and Wilcoxon signed rank test for Ordinal variables. To analyze predictors of mortality Stepwise Logistic regression was performed. Survival analysis was done using the Kaplan-Meier method, with differences calculated using the Log rank test. Analyses were conducted using SPSS for Windows, release 8.0 (©SPSS Inc, Chicago, Illinois.)

APPENDIX 1

Dutch version of the questions used in the Hospital Anxiety and Depression scale^{14,15}

Naam:

Datum:

Dokters zijn er zich van bewust dat de emoties van angst en depressie bij de meeste ziektes een belangrijke rol spelen. Uw dokter zal beter in staat zijn om u te helpen indien hij weet hoe u zich voelt.

Deze vragenlijst dient als hulpmiddel voor uw dokter om te weten te komen hoe u zich voelt. Lees iedere vraag en onderstreep het antwoord dat het beste weergeeft hoe u zich gedurende de laatste week gevoeld heeft.

Denk niet te lang na over uw antwoord. Uw eerste reactie op elke vraag is waarschijnlijk meer betrouwbaar dan een lang doordacht antwoord.

Ik voel me gespannen

- ☐ Meestal
- ☐ Vaak
- ☐ Af en toe, soms
- ☐ Helemaal niet

Ik geniet nog steeds van de dingen waar ik vroeger van genoot

- ☐ Zeker zo veel
- ☐ Niet zo veel als vroeger
- ☐ Weinig
- ☐ Haast helemaal niet

Ik krijg een soort angstgevoel alsof er elk moment iets vreselijks zal gebeuren

- ☐ Heel zeker en vrij erg
- ☐ Ja, maar niet zo erg
- ☐ Een beetje, maar ik maak me er geen zorgen over
- ☐ Helemaal niet

Ik kan lachen en de dingen van de vrolijke kant zien

- ☐ Net zoveel als vroeger
- ☐ Niet zo goed als vroeger
- ☐ Beslist niet zoveel als vroeger
- ☐ Helemaal niet

Ik maak me vaak ongerust

- ☐ Heel erg vaak
- ☐ Vaak
- ☐ Af en toe maar niet te vaak
- ☐ Alleen soms

Ik voel me opgewekt:

- ☐ Helemaal niet
- ☐ Niet vaak
- ☐ Soms
- ☐ Meestal

Ik kan rustig zitten en me ontspannen

- ☐ Zeker
- ☐ Meestal
- ☐ Niet vaak
- ☐ Helemaal niet

Ik voel alsof alles moeizamer gaat

- ☐ Bijna altijd
- ☐ Heel vaak
- ☐ Soms
- ☐ Helemaal niet

Ik krijg een soort benauwd, gespannen gevoel in mijn maag

- ☐ Helemaal niet
- ☐ Soms
- ☐ Vrij vaak
- ☐ Heel vaak

Ik heb geen interesse meer in mijn uiterlijk:

- ☐ Zeker
- ☐ Niet meer zoveel als ik zou moeten
- ☐ Waarschijnlijk niet zoveel
- ☐ Evenveel interesse als vroeger

Ik heb helemaal geen rust en voel dat ik iets te doen moet hebben

- ☐ Heel erg
- ☐ Tamelijk veel
- ☐ Niet erg veel
- ☐ Helemaal niet

Ik verheug me van tevoren al op dingen

- ☐ Net zoveel als vroeger
- ☐ Een beetje minder dan vroeger
- ☐ Zeker minder dan vroeger
- ☐ Bijna nooit

Ik krijg plotseling gevoelens van panische angst

- ☐ Zeer vaak
- ☐ Tamelijk vaak
- ☐ Niet erg vaak
- ☐ Helemaal niet

Ik kan van een goed boek genieten, of van een radio of televisieprogramma

- ☐ Vaak
 - ☐ Soms
 - ☐ Niet vaak
 - ☐ Heel zelden
-

APPENDIX 2

Dutch version of the Nottingham Health Profile questionnaire^{16,17}

Ja/Nee

1. Ik ben aldoor moe
2. Ik heb 's nachts pijn
3. Ik kan nergens meer tegen
4. Ik heb ondraaglijke pijn
5. Ik gebruik pillen om in slaap te komen
6. Ik ben vergeten hoe het is om ergens van te genieten
7. Ik voel me gespannen
8. Ik heb pijn wanneer ik van houding verander
9. Ik voel me eenzaam
10. Alleen binnenshuis kan ik wat lopen
11. Ik vind het moeilijk om te bukken
12. Alles kost me moeite
13. Ik word 's morgens erg vroeg wakker
14. Lopen is onmogelijk voor mij
15. Ik heb er moeite mee met mensen in contact te komen
16. De dagen slepen zich voort
17. Het kost me moeite om de trap op en af te gaan
18. Ik vind het moeilijk om iets te pakken
19. Ik heb pijn bij het lopen
20. Ik verlies tegenwoordig snel mijn geduld
21. Ik heb het gevoel dat niemand om me geeft
22. Ik lig het grootste deel van de nacht wakker
23. Ik heb het gevoel dat ik het niet meer in de hand heb
24. Staan doet mij pijn
25. Ik vind het moeilijk om mezelf aan te kleden
26. De fut is er snel uit
27. Ik vind het moeilijk om lang te staan (bijv. aan het aanrecht of bij de bushalte)
28. Ik heb altijd pijn
29. Ik kan moeilijk in slaap komen
30. Ik voel dat ik anderen tot last ben
31. Ik lig 's nachts te tobben
32. Het leven heeft weinig waarde voor mij
33. Ik slaap 's nachts slecht
34. Ik kan slecht met mensen opschieten
35. Ik heb hulp nodig om buiten te kunnen lopen (bijv. een wandelstok of iemand die me ondersteunt)
36. Ik heb pijn wanneer ik de trap op en af loop
37. Bij het opstaan ben ik al somber
38. Ik heb pijn bij het zitten

Welke activiteiten in uw dagelijks leven worden beïnvloed door uw gezondheid? Als een bepaalde activiteit niet op u van toepassing is, kruis dan het hokje onder nee aan.

Ja/Nee

1. Veroorzaakt Uw huidige gezondheid moeilijkheden met UW WERK (d.w.z. betaald werk)?
2. Veroorzaakt Uw huidige gezondheid moeilijkheden met UW HUISHOUDELIJKE WERKZAAMHEDEN (bijv. schoonmaken en koken, klusjes in en om het huis, enz.)?
3. Veroorzaakt Uw huidige gezondheid moeilijkheden met UW SOCIALE LEVEN (bijv. uitgaan, vrienden bezoeken, bezoek aan de sportclub)?
4. Veroorzaakt Uw huidige gezondheid moeilijkheden met UW HUISELIJK LEVEN (d.w.z. relaties met andere mensen in huis)?
5. Veroorzaakt uw huidige gezondheid moeilijkheden met UW SEXLEVEN?
6. Veroorzaakt Uw huidige gezondheid moeilijkheden met UW INTERESSES EN HOBBIES (bijv. sporten, knutselen en handenarbeid, cursussen volgen, doe-het-zelf activiteiten, enz.)?
7. Veroorzaakt Uw huidige gezondheid moeilijkheden met UW VAKANTIES (bijv. zomer- of wintervakantie, weekends weg, enz.)?

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CHAPTER 4

Coronary artery bypass surgery

INTRODUCTION

The benefits of coronary revascularisation for ischemic heart disease are well documented for the patient with coronary artery disease in general. With the improvement of surgical and anesthesiological techniques and myocardial protection, the outcome has improved over the last two decades with perioperative mortality now being below 5%. Because of these results, an increasing number of elderly patients are being operated upon. However, the effect of age on morbidity, operative mortality and quality of life after coronary bypass surgery remains controversial, and probably institution related¹⁻³. Knowledge of results is of importance because the elderly population is continuously increasing in Western societies, leading to an increasing demand for coronary revascularisation procedures.

To assess the differences in outcome of coronary bypass surgery we performed a prospective study, with two gender matched groups of 131 patients 75 years or older, and 262 patients younger than 75 years. None of these patients had concomitant valve surgery. The follow-up duration after surgery was minimally twelve months. All patients were operated over a 3-year period in the University Hospital of Maastricht, the Netherlands. Results were analyzed to determine risk factors for morbidity and mortality.

METHODS

From September 23, 1993 through November 21, 1996, 131 consecutive patients aged 75 years or older were included in our prospective study (Old group). During the same time 262 gender matched patients (50.4% male in both groups) younger than 75 years were included for comparison (Young group). In the Old group the mean age was 77.8 years with a range from 75 to 86 years. In the Young group the mean age was 65.0 years, with a range from 35 to 74 years. Women were relatively older than men, which was most pronounced in the Young group (mean age women 66.7 years, men 63.2 years, $P < 0.001$). In the Old group the mean age of women was 78.1 years, men 77.4 years, $P = \text{n.s.}$ (Figure 4.1)

Figure 4.1. Age and gender distribution of the patients studied.

Table 4.1. Timing of operation in different age groups.

		Time of operation ($P<.05$)			Total
		≤ 2 days after acceptation	≤ 2 weeks during admission	elective	
Age group	acute				
Young		16 6.1%	127 48.5%	119 45.4%	262 100.0%
Old	1 .8%	8 6.1%	81 61.8%	41 31.3%	131 100.0%

All patients were screened one day prior to surgery by the same investigator. Details about the variables that were recorded are described in chapter 3. In the Old group more patients were operated while being admitted to hospital for unstable angina (61.2% vs 48.5%, $P<0.05$, table 4.1). Except for differences in body mass index and area, no differences in physical examination were found.

ANESTHESIA AND MYOCARDIAL PERFUSION DURING SURGERY

A detailed description for the standard procedures of the anesthesia and myocardial perfusion is given in chapter 3. In table 4.3 the differences are described between both groups. Old patients had a significant lower hematocrit during surgery, and required more often temporary pacing at the end of surgery. No differences were found in cross clamp time, perfusion time, and hemodynamic measurements.

Table 4.2. Baseline characteristics of the patients studied

	Young (n=262)	Old (n=131)
Age (yrs)	65.0 ± 7.2	77.8 ± 2.3
Male	132 (50.4%)	66 (50.4%)
<i>Clinical History & Physical examination</i>		
Mean NYHA class (angina)	3.45 ± .7	3.67 ± .5***
Angina in rest, NYHA=4 (n)	146 (56%)	90 (69%)*
NYHA class 3-4 for dyspnea (n)	127 (48.4%)	66 (50.4%)
Previous Myocardial Infarction (n)	135 (51.5%)	77 (58.8%)
Recent Myocardial Infarction (<2months)	43 (16.4%)	24 (18.3%)
History of Congestive Heart Failure	27 (10.3%)	13 (9.9%)
Diabetes Mellitus (type 1 or 2)	52 (19.9%)	26 (19.9%)
Claudication (<500m walking distance)	25 (9.5%)	10 (7.6%)
Systemic Hypertension (treated with drugs)	88 (34%)	41 (31%)
Cerebrovascular Disease (TIA/CVA)	20 (7.6%)	14 (10.6%)
History of renal failure (Creat.>140μMol/l)	23 (8.8%)	14 (10.7%)
Hypercholesterolemia (≥6.5 mMol/l)	99 (37.9%)	32 (24.7%)**
Smoking	63 (24%)	18 (13.8%)**
Body mass index (g/m ²)	27.4 ± 4.2	25.7 ± 3.4***
Body surface area (m ²)	1.86 ± .18	1.79 ± .16***
Systolic blood pressure	136 ± 22.6	138 ± 21.4
Killip class 2 (n)	10 (3.8%)	7 (5.3%)
Re-operation	40 (15.2%)	15 (11.5%)
Anti-anginal triple medication	134 (51.1%)	71 (54.2%)
Intra-aortic Balloon pump pre-op	21 (8.0%)	8 (6.1%)
Preoperative stay on CCU (days)	1.07 (0-10)	1.73 (0-13)
<i>Cardiac measurements</i>		
LV Ejection Fraction pre-op (%)	54.9 ± 10.6	53.0 ± 9.9
LV Ejection Fraction <40% (n)	24 (9.2%)	12 (9.4%)
LV End-diastolic Diameter pre-op (mm)	49.2 ± 5.4	48.3 ± 5.6
Posterior wall enddiast wall thickness (mm)	9.5 ± 1.1	9.6 ± 1.0
LV-mass index pre-op (g/m ²)	112.3 ± 24.9	114.6 ± 20.9
e/a-ratio pre-op	.92 ± .34	.81 ± .35**
Mitral Insufficiency grade 3 (n)	12 (4.6%)	9 (7.1%)
Syst RV-press. pre-op (mmHg)	24.8 ± 5.8	26.2 ± 5.8*
Number of diseased coronaries (1-3)	2.62 ± .57	2.78 ± .5**
3 Vessel disease (n)	173 (66.3%)	107 (81.7%)**
Left Main stenosis >70% (n)	20 (7.7%)	18 (13.7%)*
Calcified coronary arteries (n)	65 (24.9%)	40 (30.5%)
LVEDP pre-cine (mmHg)	12.7 ± 7.4	15.7 ± 7.3*

Table 4.2. Continued.

	Young (n=262)	Old (n=131)
Chest X-ray (Redistribution/congestion)	9 (3.5%)	8 (6.1%)
Chest X-ray (Heart/Thorax ratio)	51.3 ± 4.9	51.8 ± 5.2
<i>Laboratory data</i>		
Sodium (mMol/l)	139.7 ± 2.4	139.9 ± 2.7
Potassium (mMol/l)	4.42 ± .41	4.38 ± .42
Creatinin pre-op (μMol/l)	98.7 ± 48	102.3 ± 40
Creatinin >200μMol/l (n)	6 (2.3%)	3 (2.3%)
BUN pre-op (mMol/l)	6.8 ± 3.0	7.7 ± 3.1**
Hemoglobin pre-op (mMol/l)	8.6 ± .9	8.1 ± .8***
<i>Pulmonary function</i>		
Vital capacity (l)	3.57 ± .98	2.90 ± .89***
Vital capacity % / norm	101.1 ± 15.6	99.5 ± 19.7
FEV1 (l)	2.6 ± .79	1.96 ± .56***
FEV1 % / Vital capacity	73.3 ± 10.2	69.9 ± 13.1

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

SURGICAL PROCEDURE

The operative technique consisted of a standard median sternotomy, routine aortic and right atrial cannulation. In 77% of all cases one venous graft was used for making the anastomosis (table 4.4). In the Young group in 13.3% no venous grafts were used (4.7% in Old group) because of complete arterial revascularisation ($P=0.006$). The use of two or three different venous grafts was more frequent in the Old group. Also the number of anastomoses was higher in the Old group with a mean total number of 3.95 ± 1.2 compared to 3.6 ± 1.3 in the Young group ($P=0.01$). In 97% of all cases in both groups with venous grafts the Saphena Magna vein was used, and in the remaining 3% the Saphena Parva vein. The quality of the vein grafts was subjectively judged by the surgeon and divided in three groups (good, moderate, poor). Although there was a tendency for more moderate and poor quality grafts in the Old group (22.4% vs 18.6%), this difference was statistically not significant (table 4.5). The quality of the native coronary vessels was also judged subjectively, showing again no statistical difference between both groups (table 4.6). Moderate and Poor quality coronaries were present in 47.9% of the Young group and 52.3% of the Old group. The Left internal mammary artery was used in 233 (89%) Young patients and 100 (76%) Old patients ($P=0.001$). The Right internal mammary artery only was used in 16 (6.1%) Young patients and 3 (2.3%) Old patients ($P=n.s.$). The Gastro-epiploic artery was exclusively used in Young patients in 12 (4.6%) cases ($P=0.013$). No prosthetic vein grafts were used in this study.

Table 4.3. Perioperative data of the patients studied

	Young (n=262)	Old (n=131)
Lowest Temperature (°C)	23.9 ± 4.6	23.4 ± 4.5
Cardioplegic solution (ml)	789 ± 358	828 ± 299
Bypass time (minutes)	86 ± 36	93 ± 34
Aortic Crossclamp time (minutes)	53.5 ± 23.7	56.1 ± 21.1
Total duration of surgery (minutes)	188 ± 59	189 ± 58
Mean arterial bloodpressure (mmHg)	73.5 ± 6.6	72.8 ± 5.1
Lowest bloodpressure during surgery (mmHg)	45.6 ± 10.0	44.0 ± 9.3
Lowest hematocrit during surgery (%)	22.1 ± 3.4	20.9 ± 2.9**
Venous O ₂ saturation at end of perfusion (%)	76.6 ± 7.8	78.6 ± 7.8*
Central venous pressure at end of surgery (mmHg)	9.0 ± 3.3	8.7 ± 3.5
Diastolic AP-pressure at end of surgery (mmHg)	15.2 ± 4.3	15.2 ± 4.5
Inotropic support needed at end of surgery (n)	60 (23.0%)	39 (29.8%)
Pacing required at end of surgery (n)	74 (28%)	60 (46%)**
IABP required at end of surgery (n)	24 (9.2%)	10 (7.6%)
Surgery without extracorporeal circulation (n)	2 (0.76%)	1 (0.76%)

* $P < 0.05$, ** $P < 0.01$ **Table 4.4.** Number of venous grafts used.

Age group	0	1	2	3	Total
Young	36 13.7%	201 76.7%	24 9.2%	1 .4%	262 100.0%
Old	6 4.6%	102 77.9%	20 15.3%	3 2.3%	131 100.0%

Table 4.5. Quality of venous grafts used.

Age group	good	moderate	poor	Total
Young	184 81.4%	37 16.4%	5 2.2%	226 100.0%
Old	97 77.6%	24 19.2%	4 3.2%	125 100.0%

Table 4.6. Quality of native coronary arteries.

Age group	good	moderate	poor	Total
Young	136 52.1%	99 37.9%	26 10.0%	261 100.0%
Old	62 47.7%	49 37.7%	19 14.6%	130 100.0%

Figure 4.2. Survival after bypass surgery in both age groups.

RESULTS

The overall *operative* mortality (defined as mortality within 30 days following surgery or during the same hospital admission) was 3.1%. There were 8 (3.1%) death in the Young group and 4 (3.1%) in the Old group. The *late* mortality (defined as mortality after discharge from hospital) was 5.9% being 15 in the Young group and 7.9% being 10 in the Old group ($P=n.s.$). The mean follow up duration of the hospital survivors was 28 ± 12.9 months. The calculated actuarial survival rate with the life table method, including hospital mortality, for 1 and 4 years is 95% / 86% in the Young and 95% / 81% in the Old group. Causes of death in the Young group were myocardial infarction, sudden death, heart failure, bleeding, septic shock, pulmonary embolism, malignancy and cerebrovascular accident, in the Old group myocardial infarction, sudden death, respiratory failure, septic shock and cerebrovascular accident. Sudden death was the most common cause of cardiac mortality after discharge, both in the Old and Young group.

Survival analysis showed no difference in survival between both groups within three years. After three years a somewhat higher mortality was seen in the Old age group, which was statistically not significant. This can be due to the lower normal life expectancy of elderly people.

To analyze predictors for one year mortality 15 pre-operative variables, that could be possible predictors, as suggested by other studies⁴⁻⁶, were entered into a

Table 4.7. Causes of early and late mortality.

		Time of death					Total
		during surgery	within 1 week	within 2 weeks	within 1 month	late mortality	
Myocardial Infarction	Young		1				1
	Old			1			1
Sudden death	Young					6	6
	Old					4	4
Heart failure	Young		1	1		3	5
	Old					1	1
Bleeding	Young	1					1
	Old						
Respiratory	Young						
	Old				2	1	3
Septic Shock	Young				3		3
	Old				1		1
Pulm. embolism	Young					1	1
	Old						
Malignancy	Young					4	4
	Old					2	2
Cerebrovascular	Young				1	1	2
Accident	Old					2	2

stepwise logistic regression model. Of these variables 4 remained in the final model, being of predictive value. The age of the patient was of no predictive value for outcome. Cardiac predictors of mortality (table 4.8) were a history of severe heart-failure requiring preoperative hospital admission, and persistent ischemia (ST-depression or elevation) on a pre-operative ECG. Non-cardiac predictors were the presence of a carotid murmur, a pre-operative Creatinin value of more than 200 $\mu\text{Mol/l}$, and severe COPD with a forced expiratory one-second volume of less than one liter. Factors that did not influence operative and 1 year mortality in the logistic regression model include: moderate COPD, diabetes, smoking, re-operation, emergency surgery, obesity, gender, LIMA use, intra-aortic balloonpump use, peripheral vascular disease and hypertension.

The only age specific predictor for mortality in elderly patients we found was a history of a myocardial infarction (table 4.9).

MORBIDITY

The mean admission duration on the intensive care unit was 2.95 ± 7.4 days in the Old group and 2.32 ± 4.2 days in the Young group ($P=\text{n.s.}$). The total postoperative admission duration however was three days (median) longer in the Old group, being 15.1 ± 10 (median 12) days versus 11.8 ± 9 (median 9) days ($P=0.001$). Except for a higher incidence in the Old group of atrial fibrilla-

Table 4.8. Results of logistic regression in all age groups for predicting one year mortality.

Variable	Parameter estimate (B)	Standard error	Wald χ^2	P value	R	Odds ratio
Severe COPD (FEV1<1)	3.3812	1.7269	3.8336	.0502	.1411	29.4048
Creatinin>200 μ Mol/l	2.3739	1.1842	4.0188	.0450	.1480	10.7391
Ischemia on ECG	2.3126	1.1430	4.0933	.0431	.1507	10.1007
Carotid murmur	1.8780	1.0086	3.4671	.0626	.1262	6.5403
History pumpfailure	1.5840	.9846	2.5883	.1077	.0799	4.8745

Table 4.9. Univariate Pre-operative Predictors of 1-year mortality.

	Young (n=262)	Old (n=131)
Pre-operative Creatinin >140 μ Mol/l	4/22 (18.2%)*	2/13 (15.4%)
Previous Myocardial infarction	9/135 (6.7%)	7/77 (9.1%)**
Diabetes Mellitus	4/52 (7.7%)	2/26 (7.7%)
LVEF <53%	8/103 (7.8%)	6/71 (8.5%)
Re-operation	3/40 (7.5%)	1/15 (6.7%)
Pre-operative Heart-failure	6/27(22.2%***	1/13 (7.7%)
Congestion on chest X-ray	2/9 (22.2%)*	1/8 (12.5%)
One-sided carotid murmur	4/13 (30.8%***	1/7 (14.3%)
Ischemia on pre-operative ECG	11/95 (11.6%)**	5/73 (6.8%)
Emergency surgery	1/16 (6.3%)	0/9 (0%)

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

tion and congestive heartfailure (especially moderate heartfailure, Killip 2), and a higher need for temporary pacing, there were no differences in the occurrence of postoperative complications (table 4.10).

FOLLOW-UP AFTER DISCHARGE FROM HOSPITAL

The follow-up duration of the surviving patients in this study varied from 1-4 years. After six and twelve months patients were asked about anginal and dyspnea complaints (graded in NYHA class I-IV) and quality of life using questionnaires. These questionnaires were filled out by 236/253 (93.2%) of the Young patients and 117/128 (91.4%) of the Old surviving patients. 155 out of 214 (72.4%) Young patients and 88 out of 114 (77.2%) Old patients being in preoperative NYHA class III or IV for anginal complaints improved to NYHA class I after six months ($P<0.001$, figure 3). However in the time period between six and twelve months following surgery there was a slight increase of complaints in both groups ($P<0.01$). The same pattern was seen for dyspnea complaints, where the mean NYHA class decreased from 2.32 to 1.94 in the

Table 4.10. Incidence of postoperative complications.

Postoperative complications	Young (n=262)	Old (n=131)
Inotropic support > 1 day	22 (8.4%)	15 (11.4%)
Intra aortic ballon pump > 1day	15 (5.7%)	4 (3.1%)
Mechanical ventilation > 1 day	42 (16.0%)	28 (21.4%)
Atrial fibrillation	92 (35.1%)	83 (63.4%)**
Ventricular tachycardia/fibrillation	6 (2.3%)	5 (3.8%)
Myocardial infarction	33 (12.6%)	22 (16.8%)
Congestive heart failure (Killip 2-4)	81 (30.9%)	56 (42.7%)*
AV-conduction disturbances requiring pacing	20 (7.6%)	19 (14.5%)*
Excessive blood loss (transfusion/rethoracotomy)	40 (15.2%)	20 (15.3%)
Respiratory infection	16 (6.1%)	13 (9.9%)
Mediastinitis	6 (2.3%)	6 (4.6%)
Acute Tubular Necrosis	13 (5.0%)	7 (5.3%)
Cerebrovascular accidents	6 (2.3%)	5 (3.8%)
Mental confusion	29 (11.1%)	22 (16.9%)
Rethoracotomy performed	24 (9.2%)	11 (8.4%)

* $P \leq 0.05$, ** $P < 0.001$

Young group and from 2.45 to 1.97 in the Old group ($P=0.001$), again followed by a small increase after 12 months ($P<0.01$).

The mean number of anti-anginal drugs used (max. 3, being betablocker, nitrate and calcium-antagonist), decreased from 2.40 pre-operatively to 0.38 one year after surgery in the Young group and from 2.48 to 0.36 in the Old group ($P<0.001$). 185 (70.9%) Young and 93 (71.0%) Old patients did not use any anti-anginal medication six months following surgery. Platelet inhibiting drugs were used in 77.2% of the Young and 75% of the Old patients ($P=n.s.$). The use of diuretics was more frequent in the Old group (44.2% versus 27.8%, $P=0.002$), and the use of lipid lowering drugs was more frequent in the Young group (29% versus 15%, $P=0.003$).

44 (17.3%) Young and 11 (8.7%) Old patients had a readmission to hospital within one year for cardiac reasons or surgery related reasons ($P<0.05$). The mean duration of these readmissions was longer in the Young group being 18.6 ± 18.7 days, versus 9.6 ± 7.0 days ($P=0.014$).

6-7 Months following surgery a routine echocardiogram was performed in 229 (91%) Young and 111 (88%) Old surviving patients. In contrast to the preoperatively performed echocardiogram a significantly higher Left ventricular mass index was found in the Old group ($116.2 \pm 19.6 \text{ g/m}^2$ versus $110.3 \pm 25.1 \text{ g/m}^2$, $P<0.016$), due to an increase of LV-mass in the Old group and a decrease in the Young group. The ascending aorta diameter increased in both groups signifi-

Changes in Anginal Complaints

Figure 4.3. Incidence of anginal complaints before and 6 and 12 months after coronary bypass surgery.

Physical Mobility

Figure 4.4. Changes in physical mobility before and after surgery.

cantly, from 35.1 to 35.5 ± 3.3 mm in the Young ($P < 0.05$), and from 34.9 to 35.9 ± 3.2 mm in the Old group ($P < 0.001$). Also a significant increase in e/a-ratio (0.93 to 1.01, $P < 0.001$, Young group, and 0.81 to 0.93, $P < 0.001$, Old group), and left atrial size (45.6 to 46.5 mm, $P < 0.001$) was found. A Chest X-ray that was repeated the same day as the echocardiogram, showed a significant decrease of the heart/thorax ratio compared to the pre-operative Chest X-ray (51.3 to $48.9 \pm 5\%$ in the Young, and 51.9 to $50.8 \pm 5\%$ in the Old, $P < 0.001$).

QUALITY OF LIFE

Both questionnaires were returned by 236 (94%) Young and 116 (92%) Old surviving patients. Items of the Nottingham Health Profile (NHP) were expressed in a 0-100 scale, in which 100 means that all items were present for that variable. The maximal range in the Hospital Anxiety and Depression scale was 0-21. Old patients had a significantly worse score for Physical Mobility (NHP) pre-operatively (35.8 ± 27 , Old, versus 29.0 ± 27 , Young, $P = 0.01$). Despite the improvement in mobility following surgery, the difference between the groups was still present after two ($P = 0.019$) and six ($P = 0.001$) months. All other variables showed no differences between the two groups (table 11). Two months following surgery a significant improvement was measured in all items from both scales. The amount of improvement was similar in both groups. No further improvement in quality of life was seen in the time period between two and six months following surgery.

Table 4.11. Results of Hospital Anxiety and Depressions scale and Nottingham Health Profile.

	Pre-op		2 months		6 months	
	Young	Old	Young	Old	Young	Old
Anxiety	8.6	8.3	5.2	5.1	6	5.3
Depression	6.5	6.8	5	5.5	5.3	4.9
Energy	46.3	44	24.4	29	24	26
Pain	25.9	26	15.1	14	13	17
Emotional Reactions	30.7	26.5	14.2	15.6	16.8	16.3
Sleep	43.2	44	34.9	31.6	32.6	32.7
Social Isolation	9.5	10.5	5.9	7.7	8.8	6.4
Physical Mobility	29	35.8	16.7	23.1	15.5	24.4

DISCUSSION

During the last 3 decades a dramatic decrease in operative mortality for CABG has been reported in patients older than 70 years, going down from 28% in 1970 to 5% in 1990⁷. In our study we found in our institution an even lower mortality of 3.1% in patients 75 years and older. Despite the fact that Old patients had significantly more often angina in rest, used more anti-anginal medication before surgery, had more severe coronary artery disease and left main disease, and were pre-operatively hemodynamically more compromised with higher right ventricular pressures and more often mitral incompetence, the mortality rate was not different compared to the younger group (3.0%). This is in contrast to several other studies that reported a higher mortality rate in the elderly^{2; 8-11}. The strongest pre-operative cardiac predictors for mortality were persistent ischemia on the last pre-operative ECG, and a history of severe cardiac dyspnea. A strong non-cardiac predictor was severe COPD with a forced expiratory one second volume of less than one liter. Also a serum creatinin of more than 200 $\mu\text{Mol/l}$ ^{14; 12} and the presence of an one sided carotid murmur had an important predictive value. Several authors suggest that patients with a carotid murmur should have preoperative carotid screening and carotid endarterectomy in selected cases¹³⁻¹⁷. We could not confirm that emergency surgery was a predictor for mortality⁵, but only 6.4% of our population had emergency surgery.¹² Equivalent to the study of Jacob et al¹⁸ we also did not see that a moderate diminished lungfunction was a predictor for mortality. However in severe COPD we also found a longer mean admission duration, irrespective of age (25 ± 26 days versus 12.6 ± 7 days, $P < 0.001$).

The median postoperative admission duration was four days longer in the Old group. This was mainly due to a 35% higher incidence of postoperative heart failure, a 78% higher incidence of postoperative atrial fibrillation and a 93% higher incidence of temporary AV-conduction disturbances requiring temporary pacing. This longer admission duration is consistent with other studies, that also not surprisingly demonstrated that this was accompanied with higher costs^{19; 20}. Despite the fact that the initial admission duration was longer, the number and duration of readmissions was lower in the Old group in the first year following surgery. The number of patients that were in NYHA class I after 1 year was similar in both groups (68% Old, 66% Young).

By using the Dutch version of the Nottingham Health Profile^{21; 22} and the Hospital Anxiety and Depression scale^{23; 24} repeatedly we could demonstrate a significant improvement of Quality of life in the first two months following surgery, which was equal in both groups. This improvement also remained present after six months.

In conclusion we can state, that coronary bypass surgery in patients older than 75 years has the same prognosis, and gives the same improvement of quality of life as in younger patients. Only the direct postoperative morbidity was greater in the older age group, leading to a longer admission duration. We can conclude that advanced age on its self should not be a contraindication for coronary bypass surgery.

Following discharge sudden death was the most important cause for cardiovascular mortality, both in the Young and Old group. As shown very few patients received β -blocking and lipid lowering agents following surgery. Since coronary artery disease is a progressive disease those drugs should probably be continued after coronary bypass surgery to slow progression of the disease and to protect the patient against sudden death from a new ischemic episode.

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CHAPTER 5

Valvular surgery

INTRODUCTION

The upper age limit for cardiac surgery has constantly been extended since the 1980's, with the most pronounced extension observed in surgery of the aortic valve, especially in calcified aortic stenosis. Only limited data exists on the effect of different types of valve surgery on the final outcome in elderly patients, regarding morbidity, mortality and quality of life.

To assess differences in outcome of valvular surgery we performed a prospective study with 69 patients of 75 years and older in comparison to 138 younger patients. These patients underwent valve surgery with or without concomitant coronary artery bypass surgery.

METHODS AND PATIENTS

From October 1, 1993 through November 11, 1996, 69 consecutive patients aged 75 years and older were included in our prospective study (Old group). In the same time period 138 gender and procedure matched patients younger than 75 years were included for comparison (Young group). Since there were more women operated in the Old group ($n=42$, 61%), an equal proportion of women were included in the control group. Male patients were relatively younger than female patients, especially in the Young group (median age 63.5 ± 8.0 vs 69.0 ± 6.3 , $P<0.001$ [Young], and 77.6 ± 2.4 vs 78.1 ± 3.5 [Old], $P=n.s.$, figure 5.1).

One day before surgery data from each patient were recorded concerning clinical history (cardiac and non-cardiac), risk factors and physical examination. Additional data were collected from an 12 lead electrocardiogram, a chest X-ray, laboratory findings, cardiac catheterisation, an echocardiogram, and pulmonary function testing.

Quality of life assessment was also done one day before surgery, and repeated 2 and 6 months later. This was done by using the Dutch version of the hospital anxiety and depression scale (HAD)¹⁻⁵ and the Nottingham Health profile (NHP)⁶⁻⁸.

Figure 5.1. Age distribution in valvular surgery.

Table 5.1. Time of operation.

Age group	≤ 2 days after acceptation	≤ 2 weeks during admission	elective	Total
Young	1 .7%	47 34.1%	90 65.2%	138 100.0%
Old	2 2.9%	25 36.2%	42 60.9%	69 100.0%

Most patients in both groups had elective surgery (table 5.1), with no significant differences between both groups.

Old patients had a higher incidence of diabetes mellitus (type 2), a lower incidence of treated systemic hypertension, a lower smoking incidence, a smaller body surface area, and a larger wall thickness on echocardiography (table 5.2). No differences were present in severity of complaints, severity of valvular or coronary disease, and stage of heart failure.

ANESTHESIA AND MYOCARDIAL PERFUSION DURING SURGERY

Standard anesthetic and monitoring techniques were used in both groups (see chapter 3). Old patients had a significant shorter duration of the surgical procedure. This was accompanied with a tendency to a shorter (but not statistically significant) perfusion and crossclamp time (table 5.3).

Table 5.2. Baseline characteristics of the patients studied.

	Young (n=138)	Old (n=69)
Age (yrs)	64.8 ± 7.5	78.2 ± 3.1
Male	54 (39%)	27 (39%)
<i>Clinical History & Physical examination</i>		
Angina Pectoris NYHA=3 or 4 (n)	48 (34.8%)	28 (40.6%)
Dyspnea in rest, NYHA=4 (n)	36 (26.1%)	15 (21.7%)
Previous Myocardial Infarction	24 (17.4%)	11 (15.9%)
History of collapse (in aortic stenosis)	14 (16.7%)	14 (25.9%)
History of congestive Heart Failure	74 (53.6%)	40 (57.9%)
Diabetes Mellitus (type 1 or 2)	17 (12.3%)	11 (15.9%)*
Systemic Hypertension (treated with drugs)	46 (33.3%)	14 (20.3%)*
Cerebrovascular Disease (TIA/CVA)	14 (10.2%)	3 (4.3%)
History of renal failure (Creat.>140μMol/l)	15 (10.9%)	5 (7.2%)
Smoking	43 (31.1%)	11 (15.9%)*
Body mass index (g/m ²)	26.3 ± 4.5	25.7 ± 3.3
Body surface area (m ²)	1.79 ± .17	1.74 ± .13*
Systolic blood pressure	137 ± 25	138 ± 28
Killip class 2-4 (n)	14 (10.1%)	7 (10.1%)
Re-operation	26 (18.8%)	7 (10.1%)
AV-conduction disturbances	14 (10.3%)	9 (13%)
Atrial fibrillation	31 (22.5%)	20 (29%)
<i>Cardiac measurements</i>		
LV Ejection Fraction pre-op (%)	55.6 ± 13.1	55.5 ± 12.0
LV Ejection Fraction <40% (n)	22 (15.9%)	10 (14.5%)
LV End-diastolic Diameter pre-op (mm)	52.1 ± 7.5	50.2 ± 6.4
Posterior wall enddiast wall thickness (mm)	10.4 ± 1.4	11.2 ± 1.5***
LV-mass index pre-op (g/m ²)	143.6 ± 35.1	153.4 ± 33.9
Left atrial size (mm)	51.8 ± 8.7	53.0 ± 7.2
e/a-ratio pre-op	1.1 ± .65	1.1 ± .93
Mitral Insufficiency grade 3-4 (n)	48 (34.8%)	16 (23.2%)*
Syst RV-press. pre-op (mmHg)	36.6 ± 14.7	37.0 ± 13.8
3 Vessel disease (n)	34 (24.6%)	14 (20.3%)
Chest X-ray (Redistribution/congestion)	23 (16.6%)	13 (18.8%)
Chest X-ray (Heart/Thorax ratio)	54.0 ± 5.58	55.7 ± 6.69
<i>Laboratory data</i>		
Sodium (mMol/l)	139.9 ± 2.6	139.9 ± 3.0
Potassium (mMol/l)	4.37 ± .46	4.36 ± .56
Creatinin pre-op (μMol/l)	92.3 ± 21.9	97.0 ± 25.7
BUN pre-op (mMol/l)	7.14 ± 3.0	7.75 ± 3.7

Table 5.2. Continued.

	Young (n=138)	Old (n=69)
Hemoglobin pre-op (mMol/l)	8.37 ± 1.0	8.13 ± .9
<i>Pulmonary function</i>		
Vital capacity (l)	3.06 ± 1.12	2.65 ± .73
Vital capacity % / norm	95.2 ± 19.9	101.6 ± 19.9
FEV1 (l)	2.10 ± .85	1.95 ± .60
FEV1 % / Vital capacity	69.5 ± 14.6	74.1 ± 10.9

* $P<0.05$, *** $P<0.001$

Table 5.3. Perfusion data.

	Young (n=138)	Old (n=69)
Lowest Temperature (°C)	22.6 ± 3.6	22.5 ± 3.6
Cardioplegic solution (ml)	1263 ± 526	1255 ± 541
Bypass time (minutes)	136 ± 50	124 ± 49
Aortic Crossclamp time (minutes)	97.7 ± 37	87.9 ± 37
Total duration of surgery (minutes)	234 ± 84	197 ± 66***
Mean arterial bloodpressure (mmHg)	73.4 ± 5.3	73.6 ± 4.5
Lowest bloodpressure during surgery (mmHg)	41.8 ± 9.1	40.8 ± 9
Lowest hematocrit during surgery (%)	22.1 ± 3.0	21.7 ± 2.8
Venous O ₂ saturation at end of perfusion (%)	78.3 ± 7.3	77.4 ± 8.4
Central venous pressure at end of surgery (mmHg)	10.1 ± 3.4	10.5 ± 4.2
Diastolic AP-pressure at end of surgery (mmHg)	17.0 ± 4.6	17.7 ± 4.6
Inotropic support needed at end of surgery (n)	62 (45%)	25 (36.2%)
Pacing required at end of surgery (n)	79 (57%)	38 (55%)
IABP required at end of surgery (n)	8 (5.8%)	1 (1.4%)

*** $P<0.001$

SURGICAL PROCEDURE

The operative technique consisted of a standard median sternotomy, routine aortic and right atrial cannulation. Male patients more often had concomitant coronary bypass surgery (55.6%) than female patients (42.9%, table 5.4). Aortic valve surgery was performed in 93 Young patients and 56 Old patients. In Old patients more bioprostheses were implanted compared to Young patients (27 [48%] versus 10 [11%], $P<0.001$). Aortic incompetence without the presence of aortic stenosis as a reason for aortic valve surgery was present in only one Old patient and 5 Young patients. Combined aortic incompetence (grade 2-4) and stenosis (moderate or severe) was present in 33 Old and 50 Young patients. Pure aortic stenosis without hemodynamic important incompetence ($\leq$ grade 1) was

Table 5.4. Gender related differences in procedure.

type of surgery	Male		Female	
	valve	valve + CABG	valve	valve + CABG
Young	24 (44%)	30 (56%)	48 (57%)	36 (43%)
Old	12 (44%)	15 (56%)	24 (57%)	18 (43%)

present in 23 Old and 38 Young patients. A Bentall procedure was done in only 5 Young patients and not done in Old patients. The mean size of the aortic valve that was implanted was 23.3 ± 2.58 in the Young group and 22.6 ± 1.71 in the Old group ($P=n.s.$). A small sized (19) mechanic valve was used in 8 Young and 2 Old patients.

Mitral valve surgery was performed in 59 Young patients and 17 Old patients. A mitral valve reconstruction with a Carpentier ring was performed more often in the Old group (35% versus 20%, $P<0.05$). In only 3 cases a bioprosthesis was used (1 Old, 2 Young patients). All other patients received a mechanical prosthesis. Severe mitral incompetence, without the presence of significant mitral stenosis was the major indication for mitral valve surgery (12 Old and 37 Young patients). Moderate or severe mitral stenosis was present in 3 Old and 18 Young patients. Valve abnormalities due to endocarditis or a local tumor were present in one Old and 3 young patients. The mean size of the mitral valve that was implanted was 30.3 ± 2.43 in the Young group and 31.1 ± 2.21 in the Old group ($P=n.s.$). Calcification of the mitral annulus was present in 20 (33.9%) Young and 9 (56.3%) Old patients undergoing mitral valve replacement ($P<0.05$).

Combined Aortic and Mitral valve surgery was done in 15 Young and 5 Old patients.

Additional reconstructive surgery for correction of tricuspid incompetence was done in 15 Young and 5 Old patients.

The St. Jude, Carbomedics and ATS valve were the mechanical valves that were used. Only bileaflet mechanical valves were implanted. The Carpentier Edwards valve was the most used biological valve (Table 5). No homografts were implanted

RESULTS

The *Operative* mortality (defined as mortality within 30 days following surgery or during the same hospital admission) was 5.8% ($n=4$) in the Old group and 7.2% ($n=10$) in the Young group ($P=n.s.$). The *Late* mortality (defined as mortality after discharge from the initial admission from hospital and after 1 month following surgery) was 12.3% ($n=8$) in the Old group and 6.3% ($n=8$) in

Table 5.5. Type of valve prosthesis used in the patients studied

Type valve		Young		Old	
		Aorta	Mitral	Aorta	Mitral
Mechanical	St. Jude	29 (35%)	14 (31%)	16 (55%)	2 (20%)
	Carbomedics	44 (54%)	18 (40%)	10 (35%)	6 (60%)
	ATS	9 (11%)	13 (29%)	3 (10%)	2 (20%)
Biological	Carpentier Edwards	7 (70%)	1 (50%)	25 (93%)	1 (100%)
	Sorin	3 (30%)	1 (50%)	2 (7%)	0 (0%)

the Young group ($P=n.s.$). This is calculated with a median follow-up duration of 29 months (range 1.3 – 51 months). The actuarial *Total* survival rate (including hospital mortality) after 1 and 4 years, calculated with the Life table method is 94%/83% in the Old group and 95%/89% in the Young group. Despite a lower life expectancy in elderly people, no significant statistical differences in mortality could be demonstrated within 4 years following surgery.

The most frequent cause for early mortality in the Old group was Bleeding (table 5.6), and in the Young group Heart failure. The major cause for late mortality was a Cerebrovascular accident in the Old group and Sudden death in the Young group. 50% of the patients with sudden death had coronary artery disease and a previous myocardial infarction. Four of six Old patients that died because of a cerebrovascular accident were on coumarin treatment at that time.

Survival analysis with the Kaplan Meier method showed no difference in survival between both groups (figure 5.2).

Significant predictors of 1 year mortality in the Old age group were: a preoperative Creatinine value $>140\mu\text{Mol/l}$, a systolic R.V pressure preoperative of more than 45mmHg, postoperative bleeding requiring a rethoracotomy, and postoperative need for inotropic support longer than 4 days. All other riskfactors that were significant in the Young group appeared not to be significant in the Old group (table 5.7). Concomitant coronary surgery appeared not to be an extra risk factor for mortality in both groups. Also emergency surgery, the presence of severe lungfunction disturbances, a diminished Left ventricular ejection fraction, and carotid murmurs, which were all of predictive value in coronary bypass surgery, appeared not to be predictive in the elderly patient with valvular surgery. This may be the result of the low incidence of some of these variables in our study population.

Table 5.6. Time of dying and cause of death in both age groups.

Cause of death		Time of death				Total
		within 1 week	within 2 weeks	within 1 month	Late mortality	
Myocardial infarction	Young	1			1	2
	Old					
Sudden death	Young			1	3	4
	Old					
Heart failure	Young	1	2	1	1	6
	Old	1			1	2
Bleeding	Young			2	1	4
	Old	2				2
Septic shock	Young			2		2
	Old				2	2
Cerebrovascular Accident	Young				2	2
	Old			1	5	6

Table 5.7. Univariate Predictors of 1-year mortality.

	Young (n=138)	Old (n=69)
<i>Pre-operative variables</i>		
Pre-operative Creatinin >140μMol/l	2/15 (13.3%)	4/5 (80%)*
FEV1 < 1 liter	11/36 (30.6%)*	2/19 (10.5%)
Previous Myocardial infarction	7/24 (29%)*	1/11 (9.1%)
Diabetes Mellitus	2/17 (11.8%)	2/11 (18.2%)
LVEF <53%	10/44 (22.7%)*	5/25 (20%)
Re-operation	5/26 (19.2%)	1/7 (14.3%)
RV Syst. pressure >45mmHg Pre-operative	5/30 (16.7%)	6/11 (55%)*
Additional coronary surgery	12/66 (18.2%)	6/33 (18.2%)
Mitral valve surgery	11/59 (18.6%)	4/17 (23.5%)
Emergency surgery	0/1 (0%)	0/2 (0%)
<i>Peri/Postoperative variables</i>		
Mechanical ventilation > 24 hours	12/33 (36%)*	4/20 (20%)
Acute tubular necrosis	9/18 (50%)*	2/11 (18.2%)
Postoperative AV-conduction disturbances	10/44 (22.7%)*	4/23 (17.4%)
Bleeding requiring rethoracotomy	6/20 (30%)*	2/5 (40%)*
Sternal dehiscence	3/6 (50%)*	0/0
Inotropics required at end of perfusion	15/62 (24%)*	5/25 (20%)
Inotropic support for ≥ 4 days	6/9 (66.7%)*	1/4 (25%)*
Postoperative infarction	6/16 (37.5%)*	1/8 (12.5%)
Bypass time >165 minutes	14/27 (52%)*	3/12 (25.0%)
Aortic cross clamp time > 110 minutes	12/45 (27%)*	3/14 (21.4%)
Lowest mean ABP. during perfusion <40mmHg	15/77 (19.5%)*	5/40 (12.5%)
Postoperative intensive care stay >6 days	7/13 (54%)*	1/9 (11.1%)
Postoperative admission duration >20 days	8/27 (30%)*	3/16 (18.8%)

* P<0.05, ** P<0.01, *** P<0.001

Figure 5.2. Survival analysis using Kaplan-Meier curves.

MORBIDITY

The median postoperative stay in the intensive care unit was two days in both groups. The median postoperative admission duration was 13 days (mean 17 ± 16 days) in the Young group and 14 days (mean 17 ± 12 days) in the Old group. Old patients had a higher incidence of postoperative atrial fibrillation and mental confusion (table 5.8).

Mental confusion occurred more frequently in elderly patients. The severity of symptoms varied from slight desorientation in time, place and person to symptoms of psychosis. From the group with mental confusion 8 (44.4%) Young and 11 (47.8%) Old patients had such severe symptoms that treatment with neuroleptic drugs was required. Symptoms of mental confusion were in all cases transient and had disappeared at the time of discharge. The incidence of Mental confusion was clearly lower in patients with mitral valve reconstruction (table 5.9). No statistical differences were seen between mechanical or biological valves, aortic or mitral valve position and additional coronary surgery. Risk factors for mental confusion in elderly people were: prolonged bypass time, aortic crossclamp time, together with increased use of cardioplegic solution and prolonged duration of surgery (table 5.10). These risk factors could not be demonstrated in the Young group.

Table 5.8. Postoperative Complications.

Complications	Young (n=138)	Old (n=69)
Inotropic support >1 day	21 (15.3%)	10 (14.5%)
Intra aortic balloon pump > 1 day	7 (5.1%)	1 (1.4%)
Mechanical ventilation >1 day	33 (23.9%)	20 (29.0%)
Atrial fibrillation	89 (64.5%)	54 (78.3%)*
Ventricular tachycardia/fibrillation	6 (4.3%)	1 (1.4%)
Myocardial infarction	16 (11.6%)	8 (11.6%)
Congestive heart failure (Killip 2-4)	61 (44.5%)	34 (49.3%)
Cardiogenic shock (Killip 4)	11 (8.0%)	2 (2.9%)
Pacing required	44 (32.1%)	23 (33.3%)
Permanent pacemaker implanted	6 (4.4%)	7 (10.1%)
Excessive blood loss (transfusion/rethoracotomy)	47 (34.3%)	17 (24.6%)
Rethoracotomy performed	22 (16.1%)	7 (10.1%)
Respiratory infection	25 (18.2%)	13 (18.8%)
Mediastinitis	5 (3.7%)	1 (1.4%)
Acute Tubular Necrosis	18 (13.2%)	11 (15.9%)
Cerebrovascular Accidents	5 (3.7%)	4 (5.8%)
Mental confusion	18 (13.1%)	23(33.3%)**

* $P<0.05$, ** $P<0.01$ **Table 5.9.** Incidence of Mental Confusion following surgery. †a bioprosthesis in mitral position was implanted in only 2 Young and 1 Old patient.

	Young (n=138)	Old (n=69)
Pure valve surgery	12 (16.7%)	11 (30.6%)
Combined valve + coronary surgery	6 (9.2%)	12 (36.4%)**
Aortic valve (mechanical)	11 (13.3%)	10 (34.5%)*
Aortic valve (biological)	2 (20.0%)	10 (37.0%)
Mitral valve (mechanical)†	7 (15.9%)	5 (50%)*
Mitral valve (reconstruction)	1 (8.3%)	1 (16.7%)

* $P<0.05$, ** $P<0.01$

FOLLOW-UP AFTER DISCHARGE FROM HOSPITAL

The follow-up duration of the surviving patients in this study was at least 12 months with a maximum of 51 months. The median follow-up duration was 28 months. After six and twelve months patients were asked about anginal and dyspnea complaints (graded in NYHA class I-IV). 67 out of 91 (73.6%) Young patients and 29 out of 41 (70.7%) Old patients who were in preoperative NYHA class III or IV improved to NYHA class I or II after six months ($P<0.001$). No changes were seen between 6 and 12 months following surgery

Table 5.10. Riskfactors for mental confusion in both age groups.

				Std.			
Age group				N	Mean	Deviation	Std. Error
Young	Bypass time	confusion	no	119	132.92	50.08	4.59
		present	yes	18	147.56	36.49	8.60
	Crossclamp time	confusion	no	119	96.62	37.14	3.40
		present	yes	18	105.11	37.26	8.78
	Duration of surgery	confusion	no	119	230.48	85.56	7.84
		present	yes	18	250.83	63.46	14.96
	LVEF pre-op	confusion	no	119	55.92	12.95	1.19
		present	yes	18	53.00	14.32	3.38
	Creatinin pre-op	confusion	no	119	91.78	22.65	2.08
		present	yes	18	96.00	16.60	3.91
	Syst.	confusion	no	119	35.79	13.46	1.23
	RV-pressure	present	yes	18	39.83	19.80	4.67
	Cardioplegic solution (ml)	confusion	no	119	1247.31	508.92	46.65
		present	yes	18	1350.00	647.39	152.59
Old	Bypass time	confusion	no	46	114.65	37.00	5.44*
		present	yes	23	142.13	62.76	13.09
	Crossclamp time	confusion	no	46	79.89	24.59	3.62**
		present	yes	23	103.83	49.93	10.41
	Duration of surgery	confusion	no	46	182.11	50.07	7.38**
		present	yes	23	225.52	82.82	17.27
	LVEF pre-op	confusion	no	46	55.33	11.34	1.67
		present	yes	23	55.78	13.45	2.80
	Creatinin pre-op	confusion	no	46	95.95	28.43	4.19
		present	yes	23	99.00	19.39	4.04
	Syst.	confusion	no	46	36.35	11.42	1.68
	RV-pressure	present	yes	23	38.39	13.49	2.81
	Cardioplegic solution (ml)	confusion	no	46	1143.48	411.58	60.68*
		present	yes	23	1478.26	693.94	144.70

* $P<0.05$, ** $P<0.01$

(figure 5.3). 46 out of 72 (63.9%) Young patients and 25 out of 39 (64.1%) Old patients that were on treatment with diuretics before surgery, continued using diuretics One year following surgery.

There were more Young patients (87.4%) than Old surviving patients (72.1%) on coumarin treatment one year after surgery ($P<0.05$).

Readmissions because of cardiac or procedure related problems up to one year after surgery were significantly more common in the Old group (19/64, 29.7%)

Figure 5.3. Changes in NYHA dyspnea class after surgery.

than in the Young group (13/125, 10.4%, $P<0.01$). The median admission duration of these readmissions was however not statistically different (Young=10 days, Old=8 days). The highest incidence of readmissions in the Old group was in patients that receiving a mechanical mitral valve (5/9, 55.6%) or undergoing mitral valve reconstruction (3/5, 60%).

6-7 months following surgery a routine echocardiogram and chest X-ray were performed in 118/120 (98%) Young and 52/61 (85%) Old surviving patients. Both groups showed a decrease in left ventricular mass index, systolic right ventricular pressures and the heart/chest ratio on the chest X-ray. The Young group also showed a significant decrease in Left ventricular end diastolic diameter and Left atrial dimension. No changes were seen regarding Left ventricular ejection fraction and e/a-ratio (table 5.11).

The results of valve surgery were echocardiographically graded in three categories: 1) good result of surgery (normal functioning valve), 2) moderate result of surgery (small paravalvular leakage or slightly increased gradient over valve), 3) poor result of surgery (important paravalvular leakage and/or high gradient over valve with hemodynamic impairment).

In case of aortic valve surgery moderate / poor results were found in 5 (6.0%) / 3 (3.6%) Young patients and 5 (11.4%) / 1 (2.3%) Old patients ($P=n.s.$).

In case of mitral valve surgery moderate / poor results were found in 4 (8.2%) / 4 (8.2%) Young patients and 3 (21.4%) / 1 (7.1%) Old patients ($P=n.s.$). Mitral valve reconstruction was disappointing in the Old age group. Only 25% of the Old group had good results, compared to 54.5% in the Young group ($P<0.01$).

Table 5.11. Echocardiographic and Chest X-ray changes before and six months following surgery.

	Young		Old	
	Before	After	Before	After
LV ejection fraction	56.1 ± 12.9	57.3 ± 11.3	56.4 ± 11.4	59.0 ± 10.2
LV enddiast. diam.	52.2 ± 7.2	49.6 ± 6.4***	49.9 ± 5.9	48.7 ± 6.2
LV mass index	144.4 ± 33.9	128.4 ± 29.9***	148.9 ± 32.6	133.7 ± 22.2***
e/a- ratio	1.08 ± 0.68	0.94 ± 0.41	1.0 ± 0.60	0.89 ± 0.35
Syst. RV pressure	36.0 ± 14.6	28.3 ± 9.0***	36.2 ± 10.3	30.5 ± 7.7***
Left atrium size	52.3 ± 8.9	50.8 ± 8.1**	53.4 ± 7.3	52.7 ± 7.8
Heart/Chest ratio	53.8 ± 5.5	50.7 ± 5.8***	54.7 ± 7.5	52.4 ± 5.6*

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Table 5.12. Nottingham Health Profile data. All data are mean ± standard deviation.

	Young			Old		
	Pre-op	2 months	6 months	Pre-op	2 months	6 months
Energy	48.4±40.9	24.6±32.8***	24.1±36.2***	40.2±36.0	27.2±35.1	25.2±34.4*
Emot. reactions	26.8±24.8	16.5±23.1***	16.8±23.7***	27.2±25.9	15.9±19.8*	17.5±21.2*
Pain*	17.8±22.4	14.1±22.8	10.9±18.5*	17.2±20.5	9.8±17.4*	13.8±19.8
Sleep	46.2±35.3	35.5±35.6**	31.2±34.5***	45.3±34.0	38.4±36.5	34.7±38.5*
Social isolation	11.5±21.8	7.7±17.1	8.8±19.5	11.3±18.6	11.0±19.6	7.3±15.1
Phys. mobility	31.8±27.0	18.0±25.0***	18.8±25.4***	33.0±26.2	25.5±23.2*	26.3±22.3
Social functions	2.6±1.9	1.8±1.9***	1.6±1.9***	1.9±1.9	1.5±1.5	1.3±1.7

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

QUALITY OF LIFE

The two questionnaires (Nottingham Health Profile and Hospital Anxiety and Depression scale) that were sent two months following surgery were returned by 113/126 (89.7%) Young and 55/64 (85.9%) Old surviving patients. After six months following surgery these questionnaires were returned by 116/122 (95.1%) Young and 54/62 (87.1%) Old surviving patients.

The Hospital Anxiety and Depression scale (HAD) showed a significant decrease of anxiety symptoms after surgery in both age groups ($P < 0.001$). The Young group also showed a significant reduction of depression symptoms following surgery ($P < 0.01$), which could not be demonstrated in the Old group (figure 5.4).

The Nottingham Health Profile (NHP) showed a significant improvement two months following surgery in the Old group in Emotional reactions, Pain and Physical mobility. After six months also a significant improvement of Energy and sleep disturbances was found. However at that time a significant increase of pain symptoms was observed, which was not present in the Young group (table 5.12). The amount of improvement in Physical mobility, Energy and sleep distur-

Figure 5.4. Score for anxiety and depression, before, 2 and 6 months after surgery.

bances was less in the Old age group. Since patients in the Old age group were usually not working, and less socially active, no improvement was seen in social functioning.

At the end of the follow-up period (median = 29 months) the surviving patients were asked by telephone about their subjective well being. 80.6% Young and 75% Old patients experienced an improvement of well being compared to before the operation. No changes were reported by 9.7% Young and 12.5% Old patients, and worsening was present in 9.7% Young and 12.5% Old patients ($P=n.s.$).

DISCUSSION

During the last decades degenerative calcified valvular disease has become a major indication for valvular surgery in the western society. The reason being the declining incidence of rheumatic valvular disease and increasing age limits for cardiac surgery.

The surgical mortality reported in several studies varies between 5.3% and 28%^{9; 10}, depending on the type of operation, riskfactors, lowest age limit and the surgical center¹¹⁻¹³. In our study we had a surgical mortality of 5.8% which was statistically not different from the Young group.

Late mortality varies between 8.1% and 39.8%^{14; 15} in several studies¹⁶⁻²¹, depending on the follow-up duration (1-5 years) and the lowest age limit for inclusion which varied from 65-80 years. We found a late mortality of 12.3% with a lower age limit of 75 years at a median follow-up duration of 29 months. The minimal follow-up duration of the surviving patients was 12 months, with a maximum of 51 months. With this follow-up duration there was again no statistical difference in mortality compared to Younger patients.

The best pre-operative predictors for mortality in the elderly were a pre-operative serum Creatinin value of more than 140 μ Mol/l and the presence of high right sided pressures (>45mmHg systolic) measured with an echocardiogram one day before surgery. We could not confirm the findings of several other studies^{10; 11; 16; 18-20; 22} that: combined coronary and valve surgery, multiple valve surgery, emergency surgery, low LV-ejection fraction, aortic insufficiency, posterior mitral annulus calcification, hypertension and male gender were independent risk factors for mortality. However the incidence of some of these variables was low in our study population, which could explain these differences.

The postoperative admission duration was similar in both groups. A striking difference in morbidity was a 2½ times higher incidence of postoperative mental confusion in the Old age group. One third of these patients had symptoms of

mental confusion. Nearly 1/2 of those patients needed temporary treatment with neuroleptic drugs (haloperidol). The incidence of mental confusion was clearly related to the length of the surgical procedure. Only a few studies looked at the incidence of postoperative confusion. Christenson²³ found a higher incidence of mental confusion in elderly patients after a reoperation for coronary bypass grafting. Craver⁹ found a significantly higher incidence of postoperative psychosis in elderly patients (>70 years) with aortic valve surgery, as compared to younger patients. Hofsté²⁴ found a high incidence of delirium and cognitive disorders in elderly patients over 70 years, especially after a prolonged cross-clamping time and an intra operative hemoglobin level of less than 5 mMol/l. This last riskfactor however was not of importance in our study.

The late results were nearly similar in both age groups, with a comparable improvement of symptoms, and a similar mortality rate. Only readmissions were 2.9 times higher in the Old group, especially in case of mitral surgery. In a retrospective study by Arcidi²⁵ in which mitral valve surgery was compared to conservative treatment in patients with moderate mitral incompetence undergoing CABG, conservative treatment of mitral valve disease had good hospital survival and long-term functional stability compared to those who underwent additional mitral valve surgery. This could justify a more conservative approach for moderate mitral valve disease in the elderly undergoing CABG.

Old patients showed a clear improvement of Quality of life after valvular surgery. The amount of improvement however is somewhat less than in Young patients.

In conclusion valvular surgery in patients older than 75 years can be performed with a low operative mortality and has a good prognosis also as to quality of life. However a higher morbidity rate (mental confusion) and a higher number of readmissions within one year following surgery was found in elderly patients who underwent mitral valve surgery.

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CHAPTER 6

Prophylactic β -blocking therapy for atrial fibrillation post cardiac surgery

Incidence and impact of contraindications for β -blockade, and the efficacy of low dose Sotalol in different age groups

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ABSTRACT

Background: The incidence of atrial fibrillation (AF) after cardiac surgery can be markedly reduced by β -blocking drugs.

Objectives: We compared the incidence of contraindications for β -blocking agents in elderly and younger subjects and evaluated the impact on routine use of low dose sotalol post cardiac surgery. We furthermore studied the prophylactic efficacy of sotalol for postoperative atrial fibrillation (POAF), and the effects on postoperative hospital stay.

Methods: 200 patients of 75 years and older (Old) admitted for cardiac surgery (CABG, valvular surgery or both) were compared with 400 gender- and procedure-matched subjects younger than 75 years of age (Young). The incidence of each of the following relative contraindications for β -blockers was determined: chronic obstructive pulmonary disease, pre- or postoperative heartfailure, impaired left ventricular function, prolonged postoperative ventilation and pre- or postoperative sinus node dysfunction or AV conduction disturbances. POAF was detected by telemetric ECG monitoring and by daily ECG's. The effects of low dose sotalol (40 mgr. b.i.d.) on incidence of POAF and length of postoperative hospital stay were determined.

Results: The incidence of contraindications for β -blockade was 57.5% in the Young versus 67% in the Old population ($p<0.05$). Preoperative heartfailure and postoperative sinus node dysfunction or AV conduction disturbances occurred more often in Young or Old patients subjected to valvular surgery. Prophylactic sotalol reduced the overall incidence of POAF in Young patients from 69% to 27.6% ($p<0.001$), and in Old subjects from 91.9% to 32.6% ($p<0.001$). Irrespective of age, POAF occurred significantly more often after valvular surgery than after CABG, but was prevented to a similar extent by sotalol. In Young patients prevention of POAF was associated with a 5-days shorter postoperative hospital admission, whereas this was only 2 days among Old patients.

Conclusions: Cardiac surgery patients show a high (>50%) incidence of contraindications for β -blocking agents which further increases with age. The incidence of postoperative atrial fibrillation is significantly higher in elderly patients, but can be markedly reduced by low dose sotalol at all ages. Postoperative atrial fibrillation is associated with a prolonged postoperative hospital stay.

CONDENSED ABSTRACT

We compared the incidence of contraindications to β -blockers in 200 elderly (≥ 75 yrs) and 400 younger cardiac surgery patients, and studied the efficacy of prophylactic low dose sotalol (40 mgr b.i.d.) in preventing postoperative atrial fibrillation (POAF). The incidence of contraindications in the elderly was 17% higher than in younger patients. In daily practice these contraindications did not preclude sotalol use in 20% of the cases. POAF occurred significantly more often with a preoperative history of AF, after valvular surgery, and in the elderly. Low dose sotalol caused a marked reduction in POAF. We conclude that effective prophylaxis of POAF by low dose sotalol is still markedly hampered by contraindications to β -blockade in all age groups.

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac tachyarrhythmia with an estimated incidence of 1.7% in the general population¹. Patients recovering from cardiothoracic surgery represent an independent risk group for developing atrial fibrillation on the second or third day postoperatively. Incidences between 11% and 100% have been reported depending on patients' age, previous history of atrial fibrillation, type of cardiac disease and means of postoperative AF detection²⁻⁷. A meta-analysis by Andrews et al. revealed a 27% incidence of atrial fibrillation after CABG⁸. Increased postoperative morbidity due to atrial fibrillation may have therapeutic consequences, may lengthen hospital stay and postoperative rehabilitation, and therefore must have an important impact on hospital resources^{2; 5; 9}.

The pathophysiologic mechanism underlying post cardiac surgery atrial fibrillation remains unclear. Sterile pericarditis, proarrhythmic autonomic or hemodynamic disturbances, atrial ischemia or fibrotic tissue changes all may play a role¹⁰. With respect to clinical management, several studies have shown that postoperative atrial fibrillation may be prevented by β -adrenergic blocking drugs^{8; 11-14}. Therefore routine administration of prophylactic β -blocking drugs post cardiac surgery has been advocated by several authors^{9; 15}.

The use of β -blocking agents to prevent postoperative atrial fibrillation is basically limited to patients free of contraindications for these drugs. Therefore, most clinical trials on this subject have excluded patients with contraindications to β -blockers. However, to the best of our knowledge no data exist on the incidence of (relative) contraindications for β -blocking drugs in cardiac surgery patients. Neither do we know whether these contraindications are related to the patients' age or cardiac disease, and to what extent these contraindications preclude the use

of β -blockers in daily practice. Finally, sotalol in moderate dosages appeared to be at least as effective as regular β -blocking drugs in preventing postoperative atrial fibrillation^{11, 16}. No data are available on the prophylactic efficacy of a minimal dose of sotalol in the elderly, whereas patients in their eighth or ninth decade represent a growing subpopulation of cardiac surgery patients.

In the present cohort study we determined the incidence of relative contra-indications for β -adrenergic blocking drugs in cardiac surgery patients. We furthermore studied the impact of these contraindications on the routine use of low dose sotalol (40 mgr. b.i.d.) in daily practice, and investigated the effectiveness of this prophylactic regimen against postoperative atrial fibrillation in different age groups and in relation to different types of surgery.

METHODS

PATIENT POPULATION

Between September 1993 and December 1996 six hundred patients were included in the study. During this period all patients (n=215) of 75 years or older and who were admitted for elective or emergency (< 48 hours after admission) coronary artery bypass grafting (CABG), aortic or mitral valve repair or replacement, or a combined valvular/coronary bypass procedure were considered for study inclusion. Two hundred of these patients were enrolled in the primary study (Old). Fifteen patients were not included for logistic reasons. For comparison, 400 sex- and procedure-matched patients younger than 75 years of age (on admission) were randomly included in the Young age group. The histogram in figure 1 illustrates age and gender distribution of both study groups. The median age in the Young group was 66.6 years, in the Old group 77.3 years. In both groups 46.5% of the patients were male, 65.5% had coronary artery bypass surgery, 18% valvular surgery (mitral, aortic or both) and 16.5% a combined valvular/coronary bypass procedure.

PRE-OPERATIVE SCREENING

After informed consent was obtained all patients were preoperatively evaluated by the same cardiologist (J.H.). Past and current medical history, functional class (NYHA), current medication, and risk factors for cardiovascular diseases were documented. Routine physical examination, blood and urine tests, a standard chest X-ray, a standard 12-lead electrocardiogram, a pulmonary plethysmogram, a transthoracic echocardiogram and a selective coronary angiogram were obtained. All data were stored in a patient database. This database was not accessible for clinical decision making by the attending physicians responsible for the management of the patient.

Figure 6.1. Age and gender distribution of both patients groups. The OLD patient group (75 years and older) contained all subjects admitted for cardiac surgery. The YNG group was selected to match the OLD population with respect to gender distribution and type of surgical procedure.

SURGICAL TECHNIQUES AND POSTOPERATIVE MANAGEMENT

All patients in both age groups were operated upon using the same standard anesthetic, surgical and hemodynamic monitoring techniques. Cardiopulmonary bypass was instituted with a flow rate of 2.4 L/min/m². After cross-clamping the aorta, antegrade infusion of St. Thomas crystalloid cardioplegic solution was combined with topical cooling of the heart using cold saline. The average bypass time was 104 ± 46 minutes (Young: 104 ± 48 ; Old: 104 ± 42 ; n.s.). The average aortic crossclamp-time was 68 ± 34 minutes (Young: 69 ± 36 ; Old: 67 ± 31). Moderate systemic hypothermia (28–32° Celsius in both groups) was used. Patients who were in atrial fibrillation before surgery and who were not converted into sinus rhythm during cardioplegia were cardioverted intrathoracically by DC shock (8 J/s).

PREVENTION OF POST-OPERATIVE ATRIAL FIBRILLATION

Prophylactic treatment for postoperative atrial fibrillation was standardized to sotalol 40 mgr b.i.d orally and was started during the first 24 hours post-operatively or as soon as possible. Basically, if no general contraindications for β -adrenergic blocking agents or sotalol in particular (QT-prolongation or Torsade de Pointes ventricular arrhythmias) were considered to be present, oral sotalol 40 mgr b.i.d. was given as soon as the patient was extubated (median in-

tubation time in both patient groups: < 24 hours). Sotalol was continued during post-operative hospital stay unless adverse effects required withdrawal of the drug. In daily practice prophylactic low dose sotalol was prescribed by the attending physician based upon clinical state and severity of contraindications for β -blocking drugs. Consequently, patients without contraindications could still be withheld from low dose sotalol for other reasons (gastrointestinal problems, infections, neurologic complications), whereas patients with mild contraindications could still receive low dose sotalol if the attending physician anticipated a prophylactic effect. If sotalol was contraindicated, no other prophylactic β -blocking or anti-arrhythmic agents were given.

CONTRAINDICATION FOR β -BLOCKERS

Relative contraindications for β -adrenergic blocking agents were defined as:

1. Chronic obstructive pulmonary disease requiring bronchodilating drugs on a dialy basis. (*COPD*)
2. A documented history of congestive heartfailure (NYHA 3-4). (*Preop. HeartFailure*)
3. An echocardiographically determined pre-operative left ventricular ejection fraction of less than 40%. (*LVEF < 40%*)
4. Post-operative heart failure requiring positive inotropic agents. (*Postop. HeartFailure*)
5. Post-operative respiratory insufficiency requiring prolonged (>24 hours) ventilation. (*Postop. Vent. > 24 h*)
6. Preoperative history of documented sinus bradycardia (< 50 bpm), sinus node dysfunction, significant atrioventricular conduction delay (PR > 0.26 sec) or high degree AV-block. (*Preop. SND/AV#*)
7. Peri- or postoperative (temporary) sinus node dysfunction or atrioventricular conduction disturbances (see 6). (*Postop. SND/AV#*)

POST-OPERATIVE DETECTION OF ATRIAL FIBRILLATION

Detection of atrial fibrillation was started immediately post surgery and continued until 1) in-hospital discontinuation of sotalol because of adverse drug effects; 2) hospital discharge or 3) in-hospital death. During the first 4 to 5 post-operative days atrial fibrillation was detected by continuous telemetric ECG monitoring (lead I, II or III; Hewlett Packard 78510B) visually interpreted by a trained intensive care nurse. An algorithm detecting ventricular arrhythmias and ventricular rates above 120 bpm was used for general arrhythmia scanning. Atrial tachyarrhythmias were discriminated from other rhythm disturbances and documented on paper for review and authorization by a cardiologist (J.H.). Electrocardiographically, atrial fibrillation was defined as an absence of regular P- or F-waves, and the presence of rapid irregular atrial activity with a continuous va-

riation in complex morphology. The moment of onset of the first detected episode of postoperative atrial fibrillation was documented. There was no minimal time duration for a tachyarrhythmia to be considered as atrial fibrillation. As a result, also short asymptomatic and clinically irrelevant episodes of atrial fibrillation were taken into account. In case of poor quality recordings or diagnostic difficulties, a standard 12-lead electrocardiogram was obtained. After 3–4 days of continuous telemetric ECG monitoring, detection of atrial fibrillation was based upon daily ECG's and on ECG's recorded for clinical indications.

STATISTICAL ANALYSIS

All data are expressed as mean $\pm$ standard deviation unless stated otherwise. Differences between two groups were evaluated using the unpaired Student's *t*-test if the groups were normally distributed. Otherwise the Mann-Whitney rank sum test for unpaired samples was applied. Frequencies were compared by using the Pearson χ^2 -test for equality of proportions with Yates correction for small numbers, or by using the Fisher exact test whenever appropriate (2×2 , expected value less than 5 in one cell). All data were analyzed using the SPSS 8.0 statistical package.

RESULTS

PATIENTS BASELINE CHARACTERISTICS

In table 1 the characteristics of all study patients are summarized. The queuelet index and body surface area (BSA) were significantly lower in the Old group. Preoperative left ventricular function and left atrial dimension were similar. Only the left ventricular enddiastolic diameter showed a slight but significant difference. Preoperative laboratory tests revealed a significantly higher BUN level and a slightly lower hemoglobin concentration in the elderly patients. Preoperative creatinine levels were similar. Regarding pulmonary function the Old patients showed a significantly lower mean vital capacity and FEV₁ value. However, this difference appeared to be age- and BSA-related. In both age groups more than 50% of the patients suffered a recent (≤ 2 mnths) or previous (> 2 mnths) myocardial infarction. A similar number of patients suffered from diabetes mellitus, peripheral arterial sclerosis or a previous cerebrovascular event. A positive smoking history and hypercholesterolemia (upper limit: 6.4 mmol/l) occurred more frequently in Young patients. The majority (94.5%) of patients in both groups were subjected to elective surgery. The in-hospital-mortality was 5% in the Young population, 4% in the Old group (n.s.), and was never related the use of low dose sotalol.

Table 6.1. Baseline characteristics of the patients studied.

	Young (n=400)	Old (n=200)
Male/Female	186/214	93/107
Age [range] (yrs)	65 ± 7 [35.2-74.9]	78 ± 3 [75.0-91.3]
Body mass index (g/m ²)	27.0 ± 4.3	25.7 ± 3.3**
Body surface area (m ²)	1.84 ± .18	1.77 ± .15**
<i>Cardiac measurements</i>		
LVEF pre-op (%)	55 ± 12	54 ± 11
LVEDD pre-op (mm)	50 ± 6	49 ± 6*
LV-mass index pre-op (g/m ²)	123.7 ± 32.4	128.2 ± 32.0
Left atrium pre-op (mm)	48 ± 7	49 ± 6
E/A-ratio pre-op	0.97 ± 0.44 (n=346)	0.89 ± 0.58
Syst RV-press. pre-op (mmHg)	29 ± 11	30 ± 10
LVEDP pré-cine (mmHg)	14 ± 8	15 ± 8
<i>Laboratory data</i>		
Creatinin pre-op (μMol/L)	97 ± 41	105 ± 73
BUN pre-op (mMol/L)	6.9 ± 3.0	7.7 ± 3.3**
Hb pre-op (mMol/L)	8.5 ± .9	8.1 ± .9**
<i>Pulmonary function</i>		
VC % / norm	99 ± 18	101 ± 20
FEV1 (l)	2.41 ± 0.85	1.97 ± 0.57***
FEV1 % / VC	72 ± 12	71 ± 12
<i>Cardiovascular riskfactors</i>		
Previous Myocardial Infarction [§]	28%	31%
Recent Myocardial Infarction [§]	12%	14%
History of Heart Failure (NYHA 3-4)	25%	26.5%
Diabetes Mellitus (type 1 or 2)	17%	19%
Peripheral Vascular Disease	17%	16%
History of Systemic Hypertension	45%	45%
Cerebrovascular Disease	9%	9%
Hypercholesterolemia (≥6.5 mMol/l)	33%	20%**
Smoking	27%	15%***

* P<0.05, ** P<0.01, *** P<0.001, §: previous MI: > 2 months, recent MI: ≤ 2 months.

Figure 6.2. Bar diagram illustrating the frequency distribution of relative contraindications for β -blockers in both age groups. The absolute number of patients in each subgroup is given in the box in top of each bar. As can be seen, less than 50% of the patients were free of contraindications. This means that more than half of all patients was no candidate for prophylactic treatment with β -blockers for postoperative atrial fibrillation. The elderly patient group showed a trend towards more than one contraindication. * $p < 0.05$.

CONTRA-INDICATIONS FOR B-ADRENERGIC BLOCKING DRUGS

None of the patients in either age group had a previous history of idiosyncratic reactions to β -blocking agents or sotalol, neither did anyone suffer from Torsade des Pointes arrhythmias ventricular arrhythmias. Figure 2 illustrates the incidence of contraindications for β -blockade in both age groups. 57.5% of the Young patients and 67% of the Old ones ($p < 0.05$) had one or more contraindications for β -blocker use. Of these patients 52.2% in the Young and 56% in the Old category (n.s.) had two or more contraindications. If these contraindications were strictly applied more than half of the cardiac surgery patients would not be a candidate for postoperative β -blocker use.

The incidence of each individual contraindication screened for is given in figure 3 for both age groups and for the different types of cardiac surgery. Overall, chronic obstructive pulmonary disease was present in 16.3% of the Young and 20% of the Old subjects. In CABG patients COPD occurred almost twice as often in the Old group ($p < 0.01$). However, in case of valvular surgery this age-related difference was reversed. Postoperative respiratory insufficiency requiring prolonged venti-

Incidence of contraindications

Figure 6.3. Incidence of the seven individual (relative) contraindications related to different types of cardiac surgery. Each bar diagram gives the incidence of the indicated contraindication for bypass grafting (CABG), mitral or aortic valve repair or replacement, or a combination of both. The numbers in top of each bar give the absolute number of patients in the respective subgroups. As can be seen, only preoperative heartfailure and postoperative sinus node dysfunction or AV conduction disturbances showed a clear positive relationship with the type of procedure.

lation occurred in 19% of the Young and 24% of the Old patients with a trend towards a higher incidence in valvular and combined procedures. The most frequent contraindication for β -blockade was a previous history of moderate or severe congestive heartfailure, occurring in about a quarter of patients in both age groups and showing an evident positive relationship with valvular surgery. A preoperative LVEF $< 40\%$ and postoperative heart failure both showed the lowest incidence, about 10%, in both age groups with a slight trend towards a higher incidence in case of combined surgery. Preoperative sinus node dysfunction or atrioventricular conduction disturbances were present in about 11% of the Young and almost in 16% of the Old patients with a somewhat lower incidence in case of valvular surgery. Finally, postoperative atrioventricular conduction disturbances or sinus node dysfunction occurred about 30% more often than preoperatively, with an overall incidence of 16% in the Young and 21% in the Old patients. In this case there was a clear positive relationship with valvular and valvular/coronary surgery.

A preoperative history of paroxysmal or chronic atrial fibrillation was associated with higher incidences of contraindications for β -blockade. Young patients with preoperative AF (19.8%) had significantly more often preoperative heartfailure (63% versus 16%; $p < 0.001$), postoperative heart failure (20% versus 8%; $p < 0.01$), prolonged postoperative ventilation (27% versus 17%; $p < 0.05$) or peri- or postoperative sinus node dysfunction or atrioventricular conduction disturbances (38% versus 11%). In the Old group a history of preoperative atrial fibrillation (28.5%) was only associated with a higher incidence of preoperative heart failure (49% versus 17%; $p < 0.001$).

In summary, preoperative heart failure, prolonged postoperative ventilation and postoperative sinus dysfunction or AV conduction disturbances were the most frequent contraindications for β -blockers, irrespective of age but with a clear positive relation to valvular or combined valvular/coronary surgery.

THE IMPACT OF CONTRAINDICATIONS ON POSTOPERATIVE LOW DOSE SOTALOL USE

After cardiac surgery the attending physicians decided upon the prophylactic use of low dose sotalol (40 mgr. b.i.d. orally) taking the patient's clinical situation and presence of contraindications into account. As a result, patients with relative contraindications for β -blockade could still receive low dose sotalol, whereas patients without contraindications could not receive the drug for other clinical reasons. Only in this way the impact of contraindications on the use of low dose sotalol in *daily practice* could be studied. In 57.0% of the Young patients and in 44.5% of the Old population sotalol was given (table 2). Of all Young patients with one or more contraindications 34.5% still received low dose sotalol because of a low risk profile for adverse drug effects according to the

Table 6.2. Presence of contraindications to beta-blocking drugs and incidence of prophylactic post-operative sotalol administration.

Contraindication:	Young		Old	
	Sotalol given	n (%)	Sotalol given	n (%)
None	149/170	(87.6%)	44/66	(67%)
One or more	79/229 [§]	(34.5%)	45/134	(33.6%)
COPD	16/64	(25%)	12/40	(30%)
PreOp HeartFailure	20/100	(20%)	16/53	(30.2%)
PreOp LVEF < 40%	6/44	(13.6%)	7/18	(38.9%)
PostOp HeartFailure	4/41	(9.8%)	1/15	(6.7%)
PostOp Vent. > 24h	18/75	(24%)	10/48	(20.8%)
PreOp SND/AV#	25/44	(56.8%)	13/31	(41.9%)
PostOp SND/AV#	11/64	(17.2%)	10/42	(23.8%)

[§]: one missing value, Data represent number of patients (n), * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

attending physician. On the other hand, 12.4% of the group of Young patients without any contraindication did not receive sotalol for other reasons like gastro-intestinal problems, infectious or neurologic complications. Similarly, also Old patients with relative contraindications still received low dose sotalol in 33.6% of the cases. However, it was also withheld in 33% of the elderly for other reasons than contraindications to β -blockade. In none of the Young or Old patients with contraindications who still received low dose sotalol the drug had to be withdrawn because of hemodynamic or pulmonic side effects. These findings indicate that general contraindications to β -blockade do not preclude the use of low dose sotalol in patients post cardiac surgery.

Postoperative use of low dose sotalol, despite of documented contraindications to β -blockers, was not specifically related to one of the defined contraindications screened for (table 2). Young patients receiving low dose sotalol could have each of the seven contraindications, although preoperative sinus dysfunction or AV conduction disturbances had by far the lowest impact on postoperative low dose sotalol use in daily practice. In the Old population only prolonged postoperative ventilation, postoperative AV block or sinus node dysfunction, and postoperative heartfailure were associated with a less than 25% prescription rate of prophylactic sotalol. Other contraindications had even less impact on prescription habits with a more than 30% use of sotalol. These findings indicate that general contraindications for β -blockers have only a moderate impact on low dose sotalol use in daily cardiosurgical practice. None of the defined contraindications turned out to be an absolute one.

THE EFFECTS OF LOW DOSE SOTALOL ON POSTOPERATIVE ATRIAL FIBRILLATION

In the Young group 19.8% of the patients had a documented history of chronic (8%) or paroxysmal (11.9%) atrial fibrillation. In the Old group this was the case in 28.5% ($P < 0.05$), due to a higher incidence (19.5%) of paroxysmal atrial fibrillation. Since a preoperative history of atrial fibrillation has been identified as an independent risk factor for the development of postoperative atrial fibrillation, this subpopulation was considered separately³. Overall, postoperative atrial fibrillation occurred in 83.8% of cases. Interestingly, there was no difference between the Young and Old patients, but the incidence increased with valvular surgery. In Young patients undergoing a combined valvular/coronary procedure the incidence was even 100%. Without sotalol the incidence of postoperative atrial fibrillation was almost 90% in the Young and even 100% in the elderly. This was reduced by almost 30% in the Young and by almost 50% in the elderly patients using prophylactic low dose sotalol. This antifibrillatory effect was greatest in CABG patients.

Among all 463 patients who were free of a previous history of atrial fibrillation the incidence of post-operative atrial fibrillation was 44.1% (table 4), being almost 50% lower than in patients with a preoperative history of atrial fibrillation. The incidence of postoperative AF was lowest after CABG (33.9%) but increased to more than 50% if valvular surgery was involved. In the elderly postoperative atrial fibrillation occurred significantly more often (61.5 versus 36.3% in the Young group). This was in contrast to the subpopulation of patients with a preoperative history of atrial fibrillation in which no such age-related difference was found (table 3). The highest incidence (70%) of new onset postoperative AF was found in elderly patients subjected to valvular surgery.

Overall, low dose sotalol reduced the incidence of new onset postoperative AF by more than 50% in both age groups. In case of valvular surgery a reduction of 60 to 85% was found. This was opposite to the patients with a positive history of atrial fibrillation where low dose sotalol was most effective in patients recovering from coronary bypass surgery. These results demonstrate sotalol's efficacy in reducing the incidence of postoperative atrial fibrillation, both in young and elderly patients with and without a preoperative history of atrial fibrillation.

DURATION OF HOSPITAL ADMISSION POST CARDIAC SURGERY

We determined the length of postoperative hospital admission in both age groups in relation to the occurrence of postoperative atrial fibrillation (table 5). The median length of postoperative admission was 13 days in Young patients with postoperative atrial fibrillation. This was 5 days longer than in Young patients in whom no atrial fibrillation was detected ($p < 0.001$). In the elderly, postoperative atrial fibrillation was associated with a median hospital admission

Table 6.3. Incidence of postoperative atrial fibrillation in patients with a preoperative history of atrial fibrillation.

	Young		Old	
	19.8% (79/400)		28.5% (57/200)	
CABG	69.2% (18/26)		76.9% (20/26)	
Valve	80% (24/30)		93.8% (15/16)	
CABG&Valve	100% (23/23)		93.3% (14/15)	
All procedures	82.3% (65/79)		86% (49/57)	
	Sotalol: -	Sotalol: +	Sotalol: -	Sotalol: +
CABG	86.7% (13/15)	45.5% (5/11)*	100% (16/16)	40.0% (4/10)**
Valve	84.6% (22/26)	50.0% (2/4)	100% (10/10)	83.3% (5/6)
CABG&Valve	100% (17/17)	100% (6/6)	100% (14/14)	0% (0/1)
All procedures	89.7% (52/58)	61.9% (13/21)*	100% (40/40)	52.9% (9/17)***

Absolute number of patients in each subgroup are given between brackets.

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

Table 6.4. Incidence of postoperative atrial fibrillation in patients without a preoperative history of atrial fibrillation.

	Young		Old	
	80% (320/400)		71.5% (143/200)	
CABG	31.4% (74/236)		60% (63/105)***	
Valve	45.2% (19/42)		70% (14/20)	
CABG&Valve	54.8% (23/42)		61.1% (11/18)	
All procedures	36.3% (116/320)		61.5% (88/143)***	
	Sotalol: -	Sotalol: +	Sotalol: -	Sotalol: +
CABG	50.8% (31/61)	24.6% (43/175)***	84.0% (42/50)	38.2% (21/55)***
Valve	63.0% (17/27)	13.3% (2/15)**	100% (10/10)	40% (4/10)*
CABG&Valve	72.0% (18/25)	29.4% (5/17)*	90.9% (10/11)	14.3% (1/7)**
All procedures	58.8% (66/113)	24.2%(50/207)***	87.3% (62/71)	36.1% (20/72)***

Absolute numbers of patients in each subgroup are given between brackets.

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

Table 6.5. Length of postoperative hospital stay (days).

Post-op. AF	Young	
	Yes	No
CABG	10 (92)	8 (170)***
Valve	14 (43)	10 (29)***
CABG&Valve	14 (46)	9 (20)
All procedures	13 (181)	8 (219)***

Post-op. AF	Old	
	Yes	No
CABG	13 (83)	12 (48)\$\$\$
Valve	16 (29)	9 (7)
CABG&Valve	15 (25)	12 (8)
All procedures	14 (137)	12 (63)* \$\$

Median length of postoperative hospital stay; number of patients between brackets.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ for post-operative AF; \$ $P < 0.05$, \$\$ $P < 0.01$, \$\$\$ $P < 0.001$ between both age groups

of 14 days which was only 2 days longer than when no postoperative atrial fibrillation was detected ($P < 0.05$). The median postoperative admission time of CABG patients was shorter than of patients who underwent valvular or combined surgery. If no postoperative atrial fibrillation occurred, this procedure related difference became less pronounced in either age group. The present data suggest that postoperative atrial fibrillation is associated with an increased length of postoperative in-hospital-stay in patients younger than 75 years of age, but less so in elderly patients. However, other factors may influence the postoperative length of hospital stay even to a greater extent.

ARE CONTRAINDICATIONS FOR β -BLOCKERS RISK FACTORS FOR POSTOPERATIVE ATRIAL FIBRILLATION?

We correlated the presence of general contraindications for β -blocking agents with the occurrence of postoperative atrial fibrillation in patients who were prophylactically treated with low dose sotalol and in patients who did not receive this drug. It appeared that only postoperative ventilation lasting longer than 24 hours was associated with a significantly ($P < 0.05$) increased risk for developing postoperative atrial fibrillation (relative risk 1.23, odds ratio 2.1). Treatment with low dose oral sotalol abolished this increased risk. There were no significant differences between both age groups.

DISCUSSION

The main findings of the present study are that more than 50% of the cardiac surgery patients below 75 years of age and more than 65% of those above this age have one or more (relative) contraindications for β -blocking drugs. This may have important implications for the routine use of β -blockers to prevent postoperative atrial fibrillation. It appeared that postoperative atrial fibrillation occurs in the majority of patients, and that oral sotalol in a very low dose can reduce the incidence atrial fibrillation by more than 50%. Finally, postoperative atrial fibrillation was statistically associated with a prolonged hospital admission period.

STUDY DESIGN

The main purpose of this study was to quantify the incidence of contraindications for β -blocking agents in cardiac surgery patients with special emphasis on the growing, elderly population. Since the average age of cardiac surgery patients is increasing, management and/or prevention of postoperative complications becomes more important. Risk-stratification of postoperative morbidity is mandatory for a realistic cost-benefit analysis in the era of decreased hospital resources and increasing age of cardiac surgery patients. Therefore the elderly patient population above 75 years of age was arbitrarily chosen as the primary study group. It should be realized that also this elderly study group represents a selected group of older patients with a relatively low risk profile regarding postoperative comorbidity and mortality. For age-related comparison a group of patients younger than 75 years of age was selected perfectly matching the elderly group as far as gender and surgical procedure were concerned. Only in this way differences in incidence of contraindications for β -blockers, postoperative atrial fibrillation or hospital admission time could be studied in relation to age and type of surgery. It should be emphasized that because of this matching procedure the Young patient group did not represent the normal population of cardiac surgery patients below 75 years of age which usually contains more coronary artery bypass grafting procedures and relatively more male patients than in our matched group.

The preoperative screening data including contraindications for β -blockade were not explicitly presented to the attending physicians when deciding upon the postoperative administration of low dose oral sotalol. The use of low dose sotalol was not directed by a study protocol. In this way the impact of contraindications on the use of low dose sotalol in *daily practice* could be investigated. This represents the 'real life' scenario as seen in most hospitals and gives us the real incidence of

atrial fibrillation as well as the clinical handling of contraindications for β -blockers.

Our detection criteria for postoperative atrial fibrillation were very strict. Each episode of atrial fibrillation was considered, regardless of its duration or clinical significance. To our opinion both the occurrence of nonsustained and persistent atrial fibrillation is an indicator for the presence of a pathoelectrophysiologic substrate for this arrhythmia. In other studies various AF detection criteria were applied including minimal AF durations between 16 seconds and 60 minutes,^{8: 11-14}. This may explain why reported incidences of postoperative atrial fibrillation differ so widely.

ATRIAL FIBRILLATION POST CARDIAC SURGERY

The pathophysiological mechanisms responsible for postoperative atrial fibrillation remain unclear. Surgical trauma of the right auricle due to venous cannulation or the occurrence of postoperative sterile pericarditis may play an important role in the development of postoperative atrial fibrillation. Also age-related tissue fibrosis, eventually in relation with hypertensive heart disease or perioperative atrial ischemia, has been postulated as a substrate for increased atrial vulnerability^{17; 18}. Furthermore, an increased adrenergic tone due to peri- and postoperative stress or an elevated circulatory volume causing increased atrial wall stretch and ANF release might be important factors in the development of postoperative atrial fibrillation. Frost et al. found an increased incidence of atrial ectopy and an elevated mean heart rate in the hours preceding the onset of atrial fibrillation post CABG¹⁹. This may explain the beneficial effect of β -blocking agents.

Atrial fibrillation post cardiac surgery has also been associated with several clinical or peri-operative risk factors. Age, male gender, systemic hypertension, intra-aortic balloon pumping, postoperative pneumonia, prolonged postoperative ventilation and repeated or valvular surgery all have been identified as independent risk factors^{5; 9}. Page et al. found a 25% AF incidence after coronary surgery and an 80% incidence after valvular procedures²⁰. Lowe et al. reported a 36% incidence of postoperative atrial fibrillation²¹. In general, the conclusions from these studies were confirmed by the present findings. The fact that we found higher incidences of postoperative atrial fibrillation than in most other studies can be explained by the criteria used. We included each episode of AF, no matter its duration, and no matter its clinical significance.

CONTRAINDICATIONS FOR β -BLOCKERS

Several studies have shown that β -adrenergic blocking agents may reduce or prevent the occurrence of postoperative atrial fibrillation. Therefore routine treatment with β -blockers post cardiac surgery is recommended if contraindica-

tions are absent. To the best of our knowledge the present literature does not provide systematic data on the incidence of contraindications for β -blocking agents in cardiac surgery patients and how these affect the routine use of β -blockers in daily practice.

Interestingly, we found that more than half of the Young and two third of the Old patients had at least one contraindication for treatment with β -blocking agents. In addition, patients of 75 years or older had more often multiple contraindications than the younger patients. This indicates that a considerable number of patients are no good candidates for prophylactic treatment with β -blockers. Therefore the efficacy of the lowest recommended dosage of sotalol is very interesting. Although the number of patients actually treated with low dose sotalol in our institution was somewhat higher than the number of patients free of contraindications, a considerable amount of patients remained unprotected against postoperative atrial fibrillation. In daily practice a number of patients with contraindications still received low dose sotalol without problems. Therefore, routine use of low dose sotalol in *all* patients irrespective of contraindications might turn out to be a safe and effective approach. Future studies are required to evaluate the risks and adverse effects of low dose sotalol in patients with relative contraindications for β -blocking agents and the feasibility of standard low dose sotalol use irrespective of contraindications.

THE EFFECTS OF β -BLOCKERS ON POST SURGERY ATRIAL FIBRILLATION

The prophylactic use of drugs to reduce the incidence of postoperative atrial fibrillation has been advocated by several authors. A meta-analysis by Kowey et al.¹² revealed that β -blockade significantly reduces the incidence of clinically important atrial fibrillation from 20.2% to 9.8%. This prophylactic action also appeared from a meta-analysis by Andrews et al.⁸ In other studies the efficacy of sotalol was only evaluated for CABG^{11; 15; 22; 23}. Janssen et al. showed that moderately high dosages of sotalol (80 mgr t.i.d.) were significantly more effective than metoprolol (50 mgr t.i.d) in preventing postoperative atrial fibrillation¹¹. This difference was attributed to the additional class III effects of sotalol. Suttrop et al. showed that even lower dosages of Sotalol (40 mgr t.i.d.) were equally effective but with significantly less side effects^{15; 16}. We showed that further lowering of the dosage of sotalol did not affect its efficacy both in younger and elderly patients.

THE VALUE OF PREVENTING ATRIAL FIBRILLATION POST CARDIAC SURGERY

The occurrence of atrial fibrillation after cardiac surgery has several consequences for postoperative management and recovery. One of the most important associations is the lengthening of postoperative in-hospital stay⁹. However,

these studies did not discriminate between different types of surgery or age groups. In patients younger than 75 years of age we found a similar increase in hospital admission length in the presence of postoperative AF as reported by others. However, in the elderly this difference was much less (2 versus 5 days). This might be explained by a higher degree of comorbidity than in Young patients or by a prolonged admission due to elderly related social or rehabilitation problems. It furthermore appeared that postoperative hospital stay shortened the most if no postoperative atrial fibrillation occurred in patients who underwent valvular surgery. In the CABG group the difference was only 1-2 days depending on the age group. It should be emphasized though that the statistical association between postoperative hospital admission length and the occurrence of postoperative atrial fibrillation does *not* implicate any causal relationship between these variables.

STUDY LIMITATIONS

The total number of patients included in the present study was sufficient to answer the primary study questions for patients with CABG, valvular or combined coronary/valvular surgery. The number was too low for further differentiation between various type of valvular surgery (aortic valve, mitral valve or both; replacement or repair). Another limitation is that the duration and frequency of individual episodes of atrial fibrillation were not assessed. This could have answered the question in how many patients low dose sotalol only reduced the number and duration of postoperative episodes of atrial fibrillation without completely eliminating the arrhythmia.

CONCLUSIONS

The present findings demonstrate that contraindications for β -blockers are present in more than 50% of all patients having cardiac surgery, with a trend to a higher incidence in the elderly. Low dose sotalol (40 mgr. b.i.d.) prevents postoperative atrial fibrillation in more than 50% of the cases. This reduction was associated with a 5 day shortening of postoperative hospital stay in young patients, but only 2 days in the elderly. Given the high number of patients with relative contraindications for β -blockade, we conclude that new therapies might be required to prevent post cardiac surgery atrial fibrillation. On the other hand, low dose sotalol might be used without causing serious adverse effects in the majority of patients with general contraindications for β -blockade. Future placebo-controlled studies are necessary to study this hypothesis.

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CHAPTER 7

Comparison of quality of life after coronary and/or valvular cardiac surgery in patients ≥ 75 years of age to younger patients

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Contemporary studies have indicated that open heart surgery in elderly patients can be performed with a low mortality rate¹⁻⁵. However only limited information is available about the quality of life following different types of open heart surgery in elderly as compared to younger patients. The effect of cardiac surgery on quality of life was studied prospectively in 200 elderly patients aged ≥ 75 years and 400 younger patients.

During a period of 3¼ years, starting September 22, 1993, until December 18, 1996, we included 200 patients who underwent open heart surgery, and were 75 years or older (Older group, mean age=78, range 75-91). Each of these patients was matched with 2 patients < 75 years (Younger group, mean age=65, range 35-74), having the same operative procedure, and being of the same sex (table 1). Sixty-six % had coronary surgery, the remaining patients had valvular surgery (18%) or combined coronary and valvular surgery (16%). Fifty-four % of all patients were female. The median follow-up duration of the surviving patients was 31 months and ranged from 12 to 52 months.

To evaluate quality of life, two tests were selected with a limited number of questions, easy to respond in a short time by the patient, but covering various aspects like mood, social functioning and physical condition. The first one is the Hospital Anxiety and Depression scale (H.A.D., after Zigmund and Snaith, 1983)^{6, 7} of which an official Dutch translation is available. This questionnaire has 14 multiple choice questions dealing with anxiety and depressive complaints, with a range from 0-21. A higher number means a worse score for that item. The second is the Nottingham Health Profile (N.H.P., after Hunt, McKenna, 1981)^{8, 9}, of which a Dutch translation exists since 1993. The first part of this questionnaire has six main items, consisting of: energy, pain, emotional reactions, sleep, social isolation, and physical mobility, with a total number of 38 questions, that can all be answered by filling out A "yes" or "no". The range for this scale is from 0-100. Also here a higher number means a worse score for that item. Part 2 of the NHP has seven questions concerning limitations in daily activities (work, house-keeping, social contacts in/outside home, sexual activity, hobbies and recreational activities). These items were put together into a sum score (range 0-7), in which a higher score means a higher limitation of social activities.

Both questionnaires were filled out by the patient 1) one day before surgery, 2) two months after surgery, and 3) six months after surgery. The time that is needed to fill out these questionnaires varies between 5 and 15 minutes.

Several studies have shown that these questionnaires are suitable for serial comparison, and have been useful in showing changes of quality of life after surgery. Validation studies have also been performed of the Dutch version of these questionnaires.^{10; 11}

Table 7.1. Type of surgery in the patients studied.

	Age group			
	Young		Old	
	Nb	%	Nb	%
CABG	262	65.5%	131	65.5%
klep	72	18.0%	36	18.0%
CABG+valve	66	16.5%	33	16.5%
Total	400	100.0%	200	100.0%

Abbreviations: CABG=coronary artery bypass grafting; Nb=number

At the end of the follow-up period (median 31 months) 161 Younger and 83 Older randomly selected patients from the study population were asked by telephone about their subjective opinion concerning the final surgical outcome. These results were graded into three categories: 1) patients felt better compared to before the operation, 2) patients without change in well-being, 3) patients who experienced permanent worsening after the operation.

Elderly patients (≥ 75 years) referred for coronary surgery had more often 3-vessel disease (81.7% vs. 66.3%), a higher incidence of severe left main stenosis (13.7% vs. 7.7%) and more often reported angina in rest (69% vs. 56%). The incidence of hypercholesterolemia (24.7% versus 37.9%, $P=0.002$) and smoking (13.8% versus 24%, $P=0.001$) was clearly lower in the elderly. This might explain why the onset of coronary insufficiency is on a more advanced age. No differences were seen in renal function, LV-ejection fraction, pulmonary function. In elderly patients referred for valvular surgery a higher incidence of diabetes mellitus (15.9% versus 12.3%), and a lower incidence of treated hypertension (20.3% versus 33.3%) was found. Elderly patients had a higher incidence of urgent surgery (53.0% versus 43.5%, $P<0.05$). This was defined as surgery during the same hospital admission as the cardiac catheterisation.

The unpaired *t*-test was used to demonstrate differences in Interval variables between both age groups. For nominal variables chi-square analysis of contingency was used. In case of ordinal variables the Mann-Whitney rank-sum test was performed. To demonstrate changes in each treatment group after surgery the paired *t*-test was used for interval variables, McNemar's test for nominal variables and Wilcoxon signed rank test for ordinal variables. A *P*-value <0.05 was considered statistically significant. Analyses were conducted using SPSS for Windows, release 8.0 (©SPSS Inc, Chicago, Illinois.)

The hospital mortality (defined as mortality within 30 days following surgery) was 22 patients (5.5%) in the Younger and 9 patients (4.5%) in the Older group ($P=n.s.$). The one-year mortality (including hospital-mortality) was 32 patients (8.0%) in the Younger and 15 patients (7.5%) in the Older group ($P=n.s.$).

Table 7.2. Hospital Anxiety and Depression Scale[#] & Nottingham Health Profile*. All data are mean $\pm$ standard deviation. *P*-values represent differences to pre-operative values.

	Young			Old		
	Pre-op	2 months	6 months	Pre-op	2 months	6 months
Anxiety [#]	8.24 $\pm$ 4.45	5.44 $\pm$ 4.28***	5.91 $\pm$ 4.61***	7.65 $\pm$ 4.40	4.88 $\pm$ 3.73***	5.15 $\pm$ 4.13***
Depression [#]	6.44 $\pm$ 3.99	5.07 $\pm$ 4.39***	5.26 $\pm$ 4.54***	6.63 $\pm$ 4.41	5.37 $\pm$ 4.45**	5.19 $\pm$ 4.36**
Energy*	48.5 $\pm$ 40.4	24.4 $\pm$ 33.9***	24.8 $\pm$ 34.5***	44.3 $\pm$ 39.1	27.9 $\pm$ 34.0***	26.2 $\pm$ 35.0***
Emot. reactions*	29.1 $\pm$ 25.8	15.1 $\pm$ 21.9***	16.9 $\pm$ 23.1***	27.4 $\pm$ 25.9	15.7 $\pm$ 22.2***	16.6 $\pm$ 22.7***
Pain*	23.2 $\pm$ 24.8	14.9 $\pm$ 23.2***	12.8 $\pm$ 20.5***	22.8 $\pm$ 23.2	12.3 $\pm$ 20.4***	16.2 $\pm$ 23.0**
Sleep*	43.4 $\pm$ 33.7	35.2 $\pm$ 34.8***	32.3 $\pm$ 33.8***	44.8 $\pm$ 35.8	33.5 $\pm$ 35.6***	33.3 $\pm$ 37.3***
Social isolation*	10.5 $\pm$ 19.5	6.54 $\pm$ 15.3**	8.91 $\pm$ 19.3	11.0 $\pm$ 17.6	8.70 $\pm$ 17.6	6.67 $\pm$ 15.5**
Physical mobility*	30.8 $\pm$ 27.1	17.2 $\pm$ 22.7***	16.6 $\pm$ 23.3***	35.9 $\pm$ 26.6	23.9 $\pm$ 24.2***	25.0 $\pm$ 25.0***
Daily activities*	2.81 $\pm$ 1.9	1.71 $\pm$ 1.89***	1.53 $\pm$ 1.85***	2.40 $\pm$ 1.8	1.59 $\pm$ 1.7***	1.42 $\pm$ 1.76***

* *P*<0.05, ** *P*<0.01, *** *P*<0.001

The quality of life questionnaires were filled out 2 and 6 months following surgery by 352/373 (94.3%) surviving Younger patients and 170/188 (90.4%) surviving Older patients. Both groups showed a significant improvement of anxiety and depression scores two months following surgery. No significant changes were seen in the time between 2 and 6 months following surgery (figure 1). Patients who had pre-operative signs of depression (HAD score ≥ 12 , *n*=44) had the same 1-year mortality (6.9%) in both age groups as patients without depression (7.9%, *P*=n.s.). However, general well-being at a median follow-up time of 32 months was less if signs of pre-operative depression were present, especially in the Older group (figure 2). There were no significant differences in NYHA class 6 months following surgery between depressed (76% improvement) and non-depressed patients (81% improvement).

All items of the NHP except social isolation showed a clear improvement in the two months following surgery, with again no significant changes in the period between 2 and 6 months following surgery (table 2). Symptoms of social isolation before surgery were very mild in both age groups. This may explain why there are only minimal changes for that variable after surgery. Both groups showed a similar improvement of daily activities 2 months following surgery, as measured in part 2 of the NHP, which further improved 6 months following surgery. Younger patients had pre-operatively more limitations in social activities, due to the fact that elderly patients had usually retired from working.

Questioning by telephone at the end of the follow-up (12–52, median 31 months) revealed a clear improvement of general well-being in 73.3% Younger and 69.9% Older patients. This includes depressed and non-depressed patients. No differences in well-being compared to before the operation were present in 13.7% Young and 15.7% Old patients, and a worsening of general well-being following surgery was present in 13.0% Younger and 14.5% Older patients (*P*=n.s.).

Figure 7.1. Hospital Anxiety and Depression scale.

Figure 7.2. General wellbeing at the end of the follow-up period (range 12-52 months), in comparison to pre-operative situation.

Figure 7.3. Changes in complaints of angina and dyspnea following surgery in both age groups.

Pre-operatively more elderly people had angina at rest compared to young patients (50.5% versus 41%, $P < 0.05$). After six and twelve months following surgery all patients were again asked about anginal and dyspnea complaints. Compared to pre-operative values there was a clear improvement of complaints in both groups ($P < 0.001$) without any differences between the age groups. In the time between 6 and 12 months following surgery a moderate increase in anginal complaints was seen ($P < 0.01$) and to a lesser extent in complaints of dyspnea ($P < 0.05$) in both age groups (figure 3).

In our study we found that although elderly patients had more severe coronary artery disease and more often urgent surgery, their surgical and one-year mortality were identical to younger patients. Both quality of life questionnaires showed improvement in nearly all aspects of quality of life in both age groups. Also relief of anginal and dyspnea complaints were similar in both groups. Several studies have already shown that there is an improvement of quality of life in elderly patients^{1; 12-16}. Our study indicates that this improvement is independent of the age of the patient.

Some studies suggest that pre-operative signs of depression are predictive for a worse outcome following cardiac surgery¹⁷⁻¹⁹. We found that the mortality and NYHA class were identical in depressed and non-depressed patients. However the subjective signs of general well-being were worse in elderly depressed patients.

In conclusion there is a definite improvement in quality of life following cardiac surgery, which is independent of the age of the patient.

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CHAPTER 8

The incidence and consequences of mental disturbances in elderly patients post cardiac surgery

A comparison with younger patients

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ABSTRACT

Background: Limited data exists about the incidence and consequences of mental confusion following open heart surgery in different age groups. Also little is known about pre-operative predictors of mental confusion.

Methods: Two-hundred consecutive patients, aged 75 years or more (Old group), and four-hundred procedure and gender-matched younger patients (Young group) who underwent coronary or valvular surgery were included in a prospective study. The relation between postoperative mental confusion, mortality, morbidity and quality of life were studied.

Results: Mental confusion was present in 11.8% Young and 22.6% Old patients. The incidence was higher after valvular surgery. Pre-operative risk factors in Old patients were: Diabetes Mellitus, a history of heart failure, weak carotid pulsations and a re-operation. Late mortality, after a median follow-up duration of 31 months, was significantly worse in patients that were confused, which was related to the underlying disease. Recovery of quality of life was clearly diminished in elderly patients with confusion in contrast to younger patients.

Conclusion: Postoperative mental confusion has a high incidence in the elderly population, and is associated with a diminished quality of life.

CONDENSED ABSTRACT

The incidence of postoperative mental confusion was prospectively studied in 200 subsequent patients ≥ 75 years and 400 procedure and gender matched younger patients undergoing open heart surgery. Mental confusion was present in 22.6% of the older and 11.8% of the younger patients. Preoperative riskfactors were: valvular surgery, diabetes, heart failure, weak carotid pulsations and re-operation. Mental confusion was associated with a diminished recovery of quality of life, and a higher late mortality rate.

INTRODUCTION

It is well known that elderly people are more prone to develop mental confusion after a surgical procedure, which is also called the postoperative delirium syndrome. Only limited data exists about the incidence and the predisposing factors of mental confusion after open heart surgery in different age groups. Pre-operative screening with the "Mini Mental State Exam" appeared to be of no value in predicting which patient will develop mental confusion.¹ Also the consequences of mental confusion on the final outcome of the procedure including quality of life have not been studied so far.

In order to investigate the incidence and outcome of patients developing mental confusion after open heart surgery we performed a prospective study in 200 consecutive patients of 75 years or older, and 400 younger patients.

MATERIALS AND METHODS

In order to investigate the incidence of mental confusion following cardiac surgery in elderly patients as compared to younger patients we designed a prospective observational study. During a period of 3¼ years, starting September 22nd 1993 until December 18th 1996 we included 200 patients who underwent open heart surgery, and were 75 years or older (Old group, range 75–91 years, median=77.3 years). Each of these patients were matched with two patients less than 75 years (Young group, range 35–74 years, median=66.5 years), having the same operative procedure, and being of the same sex. The data analyzed include medical data, information about admission duration, and assessment of the quality of life. The follow up duration of all surviving patients was at least one year. All patients were operated upon in the Academic Hospital of Maastricht (Department of Cardio Thoracic surgery). Two-third of all patients had coronary surgery, the others having valvular or combined valvular and coronary surgery (table 1).

Mental confusion following surgery was defined as a mental state in which the patient had signs of disorientation in time, place or person, with or without hallucinations. The incidence of mental confusion was registered from the first day following surgery until discharge from hospital. Its appearance however, was nearly always in the first days following surgery, and the duration of symptoms varied between 1 and 7 days. All patients were mentally healthy and not confused prior to surgery.

Quality of life assessment was done using the Dutch version of the Nottingham Health Profile (NHP)²⁻⁴ and the Hospital Anxiety and Depression scale

Table 8.1. Type of surgery in the patients studied. Abbreviations: CABG=coronary artery bypass grafting; Nb=number.

	Age group			
	Young		Old	
	Nb	%	Nb	%
CABG	262	65.5%	131	65.5%
klep	72	18.0%	36	18.0%
CABG+valve	66	16.5%	33	16.5%
Total	400	100.0%	200	100.0%

(HAD)⁵⁻⁷. These questionnaires were filled out by the patient one day before surgery, and repeated two and six months following surgery.

Data recorded from the clinical history included: cardiac risk factors (smoking, hypercholesterolemia, diabetes mellitus, hypertension), presence of an old or recent myocardial infarction (<2 months old), history of congestive heart failure, previous cardiac operation, history of non-cardiac atherosclerotic vascular disease (cerebral, peripheral, kidney), history of arrhythmias, hypertension, chronic obstructive pulmonary disease and medication use.

An echocardiogram was performed one day prior to surgery to evaluate left ventricular function and the hemodynamic status of the patients.

OPERATIVE PROCEDURE

The operative technique included a standard median sternotomy, and routine aortic and right atrial cannulation.

Data was collected on type of surgery, first or re-operation, use of intra-aortic balloon pump (IABP), quantity and type of grafts (arterial, venous), quality of vein grafts and native vessels, types of valve surgery (mechanical, biological, or reconstruction).

ANESTHESIA AND MYOCARDIAL PERFUSION DURING SURGERY

Standard anesthetic (lorazepam, fentanyl citrate, sufentanil citrate, alfentanil hydrochloride, midazolam hydrochloride, pancuronium bromide) and monitoring techniques (electrocardiogram, central venous/pulmonary and arterial pressure monitoring, urinary output, rectal and skin temperature monitoring) were used in both groups.

The main components in the extra corporeal circuit consisted of a hollow fiber membrane oxygenator (Univox; Bentley/Baxter Inc.), a venous reservoir (BMR-1900), a cardiomy reservoir: William Harvey H4700 and an arterial line filter. The standard priming of the extra corporeal circuit was 1300 ml Haemaccel 3.5%, 200 ml Mannitol 20%, 100 ml Human-Albumin 20%, 50 ml NaHCO₃

8.4%, 20 ml KCl 7.45% and 6500 IU Heparin Leo. After institution of cardiopulmonary bypass at a flow rate of 2.4 L/min/m^2 , and after reaching a blood temperature below 28°C , the heart was topically cooled till fibrillation using cold saline 0.9% at 4°C . The aorta was then cross clamped and a single dose of approximately 800 ml of St. Thomas I cardioplegic solution at 4°C was infused into the aortic root in a period of 4 minutes (3–5 minutes) to provide myocardial preservation. Topic cooling was maintained during the infusion of the cardioplegic solution. Target flow rates of 2.4 L/min/m^2 were maintained at normothermia and correspondingly lower rates of 2.0 L/min/m^2 ($1.8\text{--}2.2 \text{ L/min/m}^2$) were maintained at moderate hypothermia of 28°C , depending on the venous oxygen saturation and the arterial pressure. Pulsatile perfusion was used throughout the period of aorta cross clamping.

Data was collected about bypass time, aortic cross clamping time, arterial blood pressure, central venous pressure, diastolic pulmonary artery pressure, circulatory arrest time, lowest temperature, lowest hematocrit during perfusion, cardioplegia, venous O_2 saturation, and the need for inotropic support, temporary pacing or intra-aortic balloon pumping (IABP) at the end of the procedure.

POSTOPERATIVE COURSE

Information was collected about mortality and morbidity. The last one included the need for inotropic support, use of IABP, duration of ventilatory support, occurrence of post operative arrhythmias especially atrial fibrillation or flutter. Data on complications were divided in cardiac complications (infarction, heart failure, conduction disturbances) and non-cardiac complications (e.g. bleeding, infections, renal failure, need for rethoracotomy).

STATISTICAL METHODS

The Unpaired *t*-test was used to demonstrate differences in Interval variables between both age groups. For Nominal variables Chi-square analysis of contingency was used. In case of Ordinal variables, or in case of no normal distribution of the interval variables (e.g. Age-group) the Mann-Whitney rank-sum test was performed. To demonstrate changes in each treatment group after surgery the Paired *t*-test was used for Interval variables, McNemar's test for Nominal variables and Wilcoxon signed rank test for Ordinal variables. To analyze predictors of mortality Stepwise Logistic regression was performed. Survival analysis was done using the Kaplan-Meier method, with differences calculated using the Log rank test. Analyses were conducted using SPSS for Windows, release 8.0 (©SPSS Inc, Chicago, Illinois.)

RESULTS

The overall incidence of mental confusion following surgery in all procedures was 11.8% in the Young group and 22.6% in the Old group ($P=0.001$). As shown in table 2 the incidence was higher in case of valve surgery. 399 Young and 199 Old patients could be analyzed in our study (2 patients excluded because of peri-operative mortality).

Table 8.2. Incidence of Mental Confusion following surgery. († a bioprosthesis in the mitral position was only implanted in 2 Young and 1 Old patient). *P*-values represent differences in incidence of mental confusion between both age groups. The percentages mentioned refer to the total number of patients in the sub-groups.

Mental Confusion	Young	Old
Total study group	47 (11.8%)	45 (22.6%)
Coronary surgery	29 (11.1%)	22 (16.9%)
Valve surgery	12 (16.7%)	11 (30.6%)
Combined valve + coronary surgery	6 (9.2%)	12 (36.4%)**
Aortic valve (mechanical)	11 (13.3%)	10 (34.5%)*
Aortic valve (biological)	2 (20.0%)	10 (37.0%)
Mitral valve (mechanical)†	7 (15.9%)	5 (50%)*
Mitral valve (reconstruction)	1 (8.3%)	1 (16.7%)

* $P<0.05$, ** $P<0.01$

Risk factors for mental confusion in elderly people were: prolonged bypass time, aortic cross clamp time, together with increased use of cardioplegic solution and prolonged duration of surgery (table 3). Also a lower temperature during perfusion appeared to be a risk factor. In the Young group a prolonged bypass time, a higher diastolic pulmonary artery pressure at the end of surgery and a lower LV-ejection fraction were predictors for mental confusion.

Insulin dependent diabetes mellitus was an independent risk factor for mental confusion in both age groups. Non-insulin dependent diabetes mellitus was only a riskfactor in the Old group (table 4).

Other pre-operative predictors in elderly patients were: a history of heart failure, presence of weak carotid pulsations and a re-operation (table 5).

A complicated post-operative course resulting in prolonged mechanical ventilation, inotropic support, heart-failure, rethoracotomy or acute tubular necrosis was also associated with a higher incidence of mental confusion, especially in the elderly patient (table 5).

Table 8.3. Riskfactors for mental confusion in both age groups.

Age group		Confusion present	N	Mean	Std. Deviation	Std. Error Mean
Young	Bypass time	No	348	101.39	47.13	2.526*
		Yes	47	116.06	44.30	6.46
	Cross clamp time	No	347	67.73	35.49	1.91
		Yes	47	77.43	37.75	5.51
	Duration of surgery	No	352	201.49	72.65	3.87
		Yes	47	220.40	60.71	8.86
	Cardioplegic solution (ml)	No	347	943.62	473.93	25.44
		Yes	47	1021.28	524.27	76.47
	Lowest hematocrit during surgery	No	349	22.12	3.29	.18
		Yes	47	21.83	3.21	.47
	Lowest temperature during perfusion (°C)	No	350	23.56	4.35	.23
		Yes	47	22.91	4.23	.62
	Lowest venous O2-sat during surgery	No	349	77.19	7.76	.42
		Yes	47	77.51	7.17	1.05
	Diastolic Pulmonary Art. Pres. at end of surgery	No	324	15.57	4.34	0.241*
		Yes	46	17.04	5.24	.77
	Lowest ABP during surgery (mmHg)	No	349	44.37	9.27	.50
		Yes	47	44.15	13.57	1.98
	Creatin pre-operative (µMol/l)	No	352	95.62	42.27	2.25
		Yes	47	103.68	31.01	4.52
	LVEF pre-operative	No	351	55.59	11.23	*0.599
		Yes	47	51.62	13.16	1.92
	Syst. RV-pressure pre-operative	No	351	28.49	10.55	.56
		Yes	47	30.60	14.77	2.15
	Forced Expiratory 1 second Volume (l)	No	178	2.4375	.8812	6.605E-02
		Yes	24	2.2371	.5257	.1073
Old	Bypass time	No	153	96.05	35.09	2.837***
		Yes	45	128.71	54.81	8.17
	Cross clamp time	No	152	61.99	25.16	2.041***
		Yes	44	85.66	42.52	6.41
	Duration of surgery	No	154	180.71	51.16	4.122***
		Yes	45	230.13	75.33	11.23
	Cardioplegic solution (ml)	No	151	914.57	355.74	28.94***
		Yes	44	1204.55	636.20	95.91
	Lowest hematocrit during surgery	No	154	21.20	2.86	.23
		Yes	45	21.09	3.00	.45
	Lowest temperature during perfusion (°C)	No	154	23.58	4.32	0.348**
		Yes	45	21.62	3.61	.54
	Lowest venous O2-sat during surgery	No	153	78.54	8.05	.65
		Yes	45	76.84	7.95	1.19
	Diastolic Pulmonary Art. Pres. at end of surgery	No	144	15.94	4.46	.37
		Yes	40	16.27	5.41	.86
	Lowest ABP during surgery (mmHg)	No	153	43.31	9.20	.74
		Yes	45	42.16	9.46	1.41
	Creatin pre-operative (µMol/l)	No	154	100.22	38.40	3.09
		Yes	45	101.98	24.90	3.71
	LVEF pre-operative	No	152	53.83	10.38	.84
		Yes	44	53.86	12.11	1.82
	Syst. RV-pressure pre-operative	No	150	29.38	9.24	.75
		Yes	44	32.41	12.12	1.83
	Forced Expiratory 1 second Volume (l)	No	67	1.9803	.5572	6.808E-02
		Yes	24	1.8933	.6226	.1271

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Table 8.4. Effect of the presence of Diabetes on the incidence of mental confusion ($P<0.01$).

Mental confusion	Young	Old
No Diabetes	33/330 (10%)	30/162 (18.5%)
Non Insulin Dependent DM	5/42 (11.9%)	12/33 (36.4%)
Insulin Dependent DM	9/27 (33.3%)	3/4 (75%)

Table 8.5. Pre- and postoperative predictors for mental confusion in both age groups.

Mental confusion		Young	Old
History of congestive heart failure	No	32/299 (10.7%)	27/146 (18.5%)
	Yes	15/100 (15.0%)	18/53 (34.0%)*
Re-operation	No	41/333 (12.3%)	35/177 (19.8%)
	Yes	6/66 (9.1%)	10/22 (45.5%)**
History of cerebro-vascular disease	No	40/361 (11.1%)	38/178 (21.3%)
	Yes	7/38 (18.4%)	7/21 (33.3%)
Weak carotid pulsations	No	49/352 (13.9%)	26/154 (16.9%)
	Yes	9/47 (19.1%)	14/45 (33.4%)*
Carotid bruit present	No	24/352 (6.9%)	8/154 (5.1%)
	Yes	7/47 (14.9%)	3/45 (6.6%)
Inotropic support > 24 hours	No	34/356 (9.6%)	31/175 (17.7%)
	Yes	13/43 (30.2%)*	14/24 (58.3%)*
Mech. ventilation > 24 hours	No	24/324 (7.4%)	21/152 (13.8%)
	Yes	23/75 (30.7%)*	24/47 (51.1%)*
Atrial fibrillation post operative	No	16/218 (7.3%)	8/62 (12.9%)
	Yes	31/181(17.1%)*	37/137 (27.0%)*
Killip 3-4 heart failure post operative	No	36/358 (10.1%)	37/185 (20.0%)
	Yes	11/41 (26.8%)*	8/14 (57.1%)*
Rethoracotomy required	No	36/353 (10.2%)	36/182 (19.8%)
	Yes	11/46 (23.9%)*	9/17 (52.9%) **
Acute Tubular Necrosis	No	39/367 (10.6%)	33/181 (18.2%)
	Yes	8/31 (25.8%)*	12/18 (66.7%)*
Cerebrovascular accident post-op.	No	2/351 (0.6%)	4/154 (2.5%)
	Yes	7/47 (14.9%)*	4/45 (4.0%)*

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

CONSEQUENCES OF MENTAL CONFUSION

The hospital mortality (defined as mortality within 30 days following surgery or during the initial admission) in the Young / Old group was 4.5% / 2.6% if no confusion was present and 10.6% / 8.9% in case of mental confusion ($P=n.s.$). The late mortality was measured after a median follow-up duration of 29 months. The minimal follow-up duration of the surviving patients was 12

Figure 8.1. Four year survival in both age groups, and the effect of mental confusion ($P < 0.01$). Y=Young group, O=Old group, conf.=confusion present.

months (maximum=52 months). The late mortality was significantly worse in both age groups if mental confusion has occurred (figure 1).

QUALITY OF LIFE

Both quality of life questionnaires were filled out by 352/373 (94.3%) surviving Young patients and 170/188 (90.4%) surviving Old patients. The Hospital Anxiety and Depression scale has two items (anxiety and depression) with a range from 0-21. A higher number means a worse score for that item. Patients with mental confusion in both age groups showed no improvement of symptoms from depression following surgery, in contrast to non-confused patients (table 6). The Nottingham Health Profile has six items (energy, emotional reactions, pain, sleep, social isolation and physical mobility) with a range from 0-100. Also here a higher number means a worse score for that item. Elderly patients with mental confusion showed no significant improvement in symptoms of emotional reactions, pain, sleep disorders, and physical mobility following surgery, in contrast to younger or non-confused patients (table 6).

Table 8.6. Hospital Anxiety and Depression Scale[#] & Nottingham Health Profile^{*}. All data are mean $\pm$ standard deviation. *P*-values represent differences to pre-operative values.

	Confusion	Young			Old		
		Pre-op	2 months		Pre-op	2 months	
			6 months	6 months		6 months	6 months
Anxiety [#]	No	8.3 $\pm$ 4.4	5.4 $\pm$ 4.3***	5.9 $\pm$ 4.7***	7.9 $\pm$ 4.4	4.9 $\pm$ 3.8***	5.3 $\pm$ 4.2***
	Yes	8.1 $\pm$ 3.5	5.9 $\pm$ 4.1**	6.4 $\pm$ 4.1*	6.7 $\pm$ 4.4	4.6 $\pm$ 3.7*	4.5 $\pm$ 3.8*
Depression [#]	No	6.5 $\pm$ 4.0	5.0 $\pm$ 4.5***	5.2 $\pm$ 4.6***	6.4 $\pm$ 4.4	5.2 $\pm$ 4.4**	4.9 $\pm$ 4.2***
	Yes	5.4 $\pm$ 2.9	6.0 $\pm$ 3.5	6.1 $\pm$ 4.4	6.9 $\pm$ 4.3	6.2 $\pm$ 4.5	6.5 $\pm$ 4.7
Energy [*]	No	46.2 $\pm$ 39.7	23.4 $\pm$ 33.8***	24.9 $\pm$ 34.9***	42.3 $\pm$ 39.0	25.4 $\pm$ 32.6***	25.8 $\pm$ 35.9***
	Yes	54.1 $\pm$ 39.5	33.3 $\pm$ 34.9*	24.2 $\pm$ 31.5**	43.0 $\pm$ 40.5	38.7 $\pm$ 37.6	28.3 $\pm$ 32.4*
Emotional reactions [*]	No	29.2 $\pm$ 25.9	14.6 $\pm$ 22.1***	16.8 $\pm$ 23.2***	27.6 $\pm$ 25.3	15.4 $\pm$ 23.1***	16.0 $\pm$ 22.6***
	Yes	31.2 $\pm$ 22.5	19.1 $\pm$ 19.8*	19.2 $\pm$ 22.9**	26.1 $\pm$ 24.2	16.8 $\pm$ 19.0	19.2 $\pm$ 23.1
Pain [*]	No	22.9 $\pm$ 24.6	14.4 $\pm$ 22.9***	12.8 $\pm$ 20.6***	23.6 $\pm$ 22.7	11.9 $\pm$ 19.5***	16.2 $\pm$ 22.2***
	Yes	25.5 $\pm$ 28.3	19.1 $\pm$ 25.6**	12.5 $\pm$ 19.5*	16.9 $\pm$ 22.0	13.8 $\pm$ 24.2	16.3 $\pm$ 26.4
Sleep [*]	No	43.4 $\pm$ 33.8	34.2 $\pm$ 34.4***	31.8 $\pm$ 33.4***	48.5 $\pm$ 37.1	34.4 $\pm$ 35.1***	34.9 $\pm$ 38.1***
	Yes	48.1 $\pm$ 34.8	44.4 $\pm$ 37.6	37.0 $\pm$ 37.5*	33.5 $\pm$ 29.8	31.0 $\pm$ 37.9	27.3 $\pm$ 34.6
Social isolation [*]	No	10.2 $\pm$ 19.9	6.3 $\pm$ 15.2**	8.5 $\pm$ 19.0	10.0 $\pm$ 17.7	8.2 $\pm$ 17.8	6.1 $\pm$ 15.1*
	Yes	8.8 $\pm$ 14.3	8.8 $\pm$ 16.9	12.7 $\pm$ 21.7	13.5 $\pm$ 18.2	11.0 $\pm$ 17.0	9.1 $\pm$ 17.4
Physical mobility [*]	No	29.5 $\pm$ 27.5	16.8 $\pm$ 22.8***	16.3 $\pm$ 23.3***	35.1 $\pm$ 25.5	21.7 $\pm$ 22.6***	25.1 $\pm$ 25.1***
	Yes	34.4 $\pm$ 23.5	21.1 $\pm$ 21.7**	19.3 $\pm$ 23.2**	33.5 $\pm$ 30.2	32.3 $\pm$ 28.8	25.4 $\pm$ 25.1

* *P* < 0.05, ** *P* < 0.01, *** *P* < 0.001

Table 8.7. Value of mental confusion as a separate risk factor for one year mortality in patients with different risk profiles.

Subgroup	Mortality Young		Mortality Old	
	No confusion	Confusion	No confusion	Confusion
All patients	23/352 (6.5%)	8/47 (17%)*	8/154 (5.2%)	6/45 (13.3%)
Pre-operative heartfailure	14/85 (16.5%)	3/15 (20%)	4/35 (11.4%)	3/18 (16.7%)
Creatinin > 140µMol/l pre-op	5/32 (15.6%)	1/6 (16.7%)	4/14 (28.6%)	2/5 (40%)
Valvular surgery	15/119 (12.6%)	2/18 (11.1%)	4/46 (6.7%)	4/23 (17.4%)
Re-operation	7/60 (11.7%)	1/6 (16.7%)	0/12 (0%)	2/10 (20%)
Diabetes Mellitus	3/55 (5.5%)	3/14 (21.4%)	3/22 (13.6%)	1/15 (6.7%)
Acute tubular necrosis post-op	10/23 (43.5%)	3/8 (37.5%)	2/6 (33.3%)	2/12 (16.7%)
Mechanical ventilation > 1 day	13/52 (25%)	7/23 (30.4%)	5/23 (21.7%)	4/24 (16.7%)
Inotropic support > 1 day	13/30 (43.4%)	6/13 (46.2%)	2/10 (20%)	2/14 (14.3%)
Re-thoracotomy needed	10/35 (28.6%)	3/11 (27.3%)	0/8 (0%)	2/9 (22.2%)

* $P < 0.05$

MENTAL CONFUSION AS A SEPARATE RISKFACTOR IN DIFFERENT PATIENT GROUPS

To evaluate the additional effect of mental confusion on one-year mortality we performed a subgroup analysis in patients with several risk profiles (table 7). It appeared that the presence of mental confusion within these subgroups was not an independent predictor for mortality.

DISCUSSION

In a prospective study by Gokgoz⁸ in 50 patients following coronary bypass surgery a significantly reduced perfusion of certain cerebral lobes using single photon emission computed tomography was found in those patients developing a postoperative delirium syndrome. Possible risk factors in that study were: advanced age, long aortic cross-clamp time, high dose inotropic support and excessive blood transfusion. Newman⁹, who did a study on cerebral autoregulation during cardiopulmonary bypass, found that an increased age predisposes to impaired cognition after cardiac surgery. This decline in cognitive function in the elderly however was not associated with age-related changes in cerebral blood flow auto regulation. Hofsté¹⁰ found that a pathologic intra-operative quantitative electroencephalogram and an intra-operative hemoglobin value of less than 5 mMol/l were predictors for delirium following surgery. Christenson¹¹ found a higher incidence of mental confusion in elderly patients after a reoperative CABG.

In our study we found that insulin dependent diabetes mellitus was an independent pre-operative predictor for mental confusion in all patients. In addition to this we found that valvular surgery (especially mitral valve surgery or combined surgery), a history of congestive heart failure and a re-operation were pre-operative predictors in patients more than 75 years old. Peri- and postoperative predictors for confusion were variables that were related to the duration of the surgical procedure, hemodynamic status, and post-operative complications. Surprisingly a longer cross clamp time was only a risk factor in the Old group.

The presence of weak carotid pulsations was the only neurologic pre-operative factor in the elderly patient that was predictive. A carotid bruit was not helpful for predicting postoperative confusion (radiated bruits from aortic stenosis or sclerosis were excluded). Apparently the presence of a bruit does not sufficiently reflect the severity of a carotid stenosis. A doppler examination of the carotid arteries was not routinely performed in our study. However this might more accurately discriminate patients at risk for mental confusion.

A history of a transient ischemic attack or a cerebrovascular accident before surgery was not a significant predictor for postoperative confusion. A reason for this might be that the incidence of ischemic cerebrovascular disease in our study population was only 8.5%.

The duration of the operative procedure (and perfusion time) was more important for predicting confusion than a lower oxygen saturation, a lower hematocrit level or a lower blood pressure during the procedure. The reduced perfusion of the brain during aortic cross clamping during a longer time is probably the major cause of mental confusion. Postoperative cerebrovascular accidents of ischemic origin were also associated with mental confusion in both age groups. However its incidence is rather low, which makes this a less important etiologic factor. Mental confusion was associated with a 2.4 times higher hospital mortality in the Young group, and a 3.4 times higher mortality in the Old group. The four years survival dropped from 87% to 74% in the Young and from 81% to 58% in the Old group when mental confusion was present following surgery. However this excess in mortality is due to the underlying riskfactors and morbidity of these patients and is not the result of mental confusion itself. However the recovery of quality of life following surgery in elderly patients who are confused is clearly diminished in the first six months following surgery.

Considering the fact the number of elderly patients that is undergoing open heart surgery is increasing, more attention should be paid to the mentioned risk factors for postoperative confusion. Postoperative confusion has a higher incidence in the elderly population and is clearly related to quality of life following surgery. A risk stratification can be made in the elderly patient summarizing the number of risk factors for confusion. In cases of multiple risk factors a conservative approach in treating the patient might be considered. Since the length of the surgical proce-

ture is a major factor, more attention should be paid in shorter surgical techniques in the elderly patient.

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CHAPTER 9

Observations on the effect of cardiac surgery on long-term survival patterns

A comparison with the general population

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ABSTRACT

Background: The number of aged people referred for open heart surgery is gradually increasing. Only limited data exists about the long-term survival of elderly patients after open heart surgery, in comparison to the general population.

Methods: Two-hundred consecutive patients, aged 75 years or more (Old group), and four-hundred procedure and gender-matched younger patients (Young group) who underwent coronary or valvular surgery were included in a prospective study. The median follow-up duration was 31 months. Survival curves from each age group were compared with survival curves for the Dutch population in general.

Results: In the first three years no significant differences in mortality are seen in both age groups. After that an increased mortality is seen in patients over 80 years, which is equal to the general population. After 36 months the survival of the elderly (70-80y) male patient is better, and the elderly female patient is equal to that of the general population. Mitral valve surgery was associated with a higher mortality in patients > 65 years.

Conclusion: Apart from a higher initial mortality due to the surgical procedure, the survival of elderly patients undergoing open heart surgery in the first three years is comparable to that of the general population.

INTRODUCTION

The relative number of patients older than 75 years that have undergone open heart surgery has increased 4–6 times in the last decade^{1,2}. Several studies have indicated that the initial results are good regarding surgical mortality and morbidity^{3–8}. The late mortality is always higher in elderly patients. This can be due to a lower life expectancy of elderly patients, or may reflect a worse surgical outcome in the elderly. Cane⁹ already suggested in a retrospective study in octogenarians after coronary surgery that the long-term prognosis was worse than from an age, sex, and race-matched general population. To analyze differences in outcome between various age groups we performed a prospective study in 600 patients undergoing open heart surgery. Of these patients 200 were 75 years or older. The remaining 400 patients were younger patients. The survival curves of these patients were compared to the survival curves of the general Dutch population, which were available from the Dutch National Institute of Statistics (CBS)^{10,11}.

METHODS

During a period of 3½ years, starting September 22nd 1993 until December 18th 1996 we included 200 consecutive patients who underwent open heart surgery, and were 75 years or older (Old group). During the inclusion period 290 old patients were operated. The remaining 90 patients were not included for logistic reasons (mostly because of matching problems). In that period 2499 younger patients were operated. Each of the old patients were matched with two patients less than 75 years (Young group), having the same operative procedure, and being of the same sex. These variables were chosen to analyze procedure related mortality, and the fact that life expectancy is gender dependent. Because of a relative small number of patients no further variables were used for matching. For matching the first young patient was chosen with the same gender and type of operation as the included old patient. 66% had coronary surgery, the remaining patients had valvular surgery (18%) or combined coronary + valvular surgery (16%). 53.5% of all patients were female (table 1). These female patients were relatively older than male patients. The majority of patients being operated was between 60 and 80 years old (figure 1). The median follow-up duration of the surviving patients was 31 months and ranged from 12 to 52 months. Due to intensive follow-up techniques no patients were lost to follow-up. In case the patient could not be reached, data from follow-up were obtained from the general physician. Pre-operative data were collected one day prior to surgery by interviewing and examining the patient, together with data

Table 9.1. Patient population

	Young		Old	
	male	female	male	female
CABG	132 (71.0%)	130 (60.7%)	66 (71.0%)	65 (60.7%)
Valve	24 (12.9%)	48 (22.4%)	12 (12.9%)	24 (22.4%)
CABG+Valve	30 (16.1%)	36 (16.9%)	15 (16.1%)	18 (16.9%)
Total	186 (100%)	214 (100%)	93 (100%)	107 (100%)

Figure 9.1. Age and gender of the patients studied. Abbreviations: Nb pts = Number of patients.

from the clinical chart. Data on follow-up were retrieved by calling the patient by telephone, after checking the hospital computer system that the patient did not die in the meantime. Since this is a prospective study data from clinical history, physical examination, ECG, and laboratory values were available from all patients. A pre-operative echocardiogram was available in 593/600 (98.8%) patients, and a pre-operative LV ejection fraction in 596/600 (99.3%) patients. All patients were operated in the academic hospital of Maastricht. Due to its unique geographical location this hospital is the only hospital in the wide neighborhood that offers cardiac surgery. Therefore many centers refer patients to Maastricht, which could make the study population representative for a major part of the general Dutch population.

STATISTICAL METHODS

The Unpaired *t*-test was used to demonstrate differences in Interval variables between both age groups. For Nominal variables Chi-square analysis of contingency was used. In case of Ordinal variables the Mann-Whitney rank-sum test was performed. To demonstrate changes in each treatment group after surgery the Paired *t*-test was used for Interval variables and Wilcoxon signed rank test for Ordinal variables. Survival analysis was done using the Kaplan-Meier method, with differences calculated using the Log rank test. Analyses were conducted using SPSS for Windows, release 8.0 (©SPSS Inc, Chicago, Illinois.)

BASELINE DIFFERENCES

Elderly patients (≥ 75 years) referred for coronary surgery had more often 3-vessel disease (81.7% vs 66.3%), had a higher incidence of severe left main stenosis (13.7% vs 7.7%) and had more often angina in rest (69% vs 56%). The incidence of hypercholesterolemia (24.7% versus 37.9%) and smoking (13.8% versus 24%) was clearly lower in the elderly. No differences were seen in renal function, LV-ejection fraction, pulmonary function. In elderly patients referred for valvular surgery a higher incidence of diabetes mellitus (15.9% versus 12.3%), and a lower incidence of treated hypertension (20.3% versus 33.3%) was found (table 2). Elderly patients had a higher incidence of urgent surgery (53.0% versus 43.5%, $P < 0.05$). This is defined as surgery within 2 weeks following referral, and during the same hospital admission.

RESULTS

The operative mortality (within 30 days following surgery) in the Young group was 10/186 (4.3%) in the Male, and 14/214 (6.5%) in the Female population. In the Old group this was 5/93 (5.4%) in the Male, and 4/107 (3.7%) in the Female population ($P = \text{n.s.}$).

When comparing the two age groups (Young and Old) no significant differences were found in mortality in the first three years following coronary, valvular or combined surgery. Even if more age categories are created no significant changes in mortality are seen in the first 40 months following surgery (figure 2). Only after 42 months there is a tendency to a higher mortality in patients older than 80 years. The youngest age group had the best long-term prognosis.

The same pattern is seen for coronary surgery and aortic valve surgery (figure 3+4). Only for mitral valve surgery a higher mortality rate is found ($P < 0.001$) compared to other types of surgery (figure 5).

Table 9.2. Baseline characteristics.

CABG patients	Young (n=262)	Old (n=131)
Age (yrs)	65.0 $\pm$ 7.2	77.8 $\pm$ 2.3
Angina in rest, NYHA=4 (n)	146 (56%)	90 (69%)*
Hypercholesterolemia (≥ 6.5 mMol/l)	99 (37.9%)	32 (24.7%)**
Smoking	63 (24%)	18 (13.8%)**
Body mass index (g/m ²)	27.4 $\pm$ 4.2	25.7 $\pm$ 3.4***
Anti-anginal triple medication	134 (51.1%)	71 (54.2%)
LV Ejection Fraction pre-op (%)	54.9 $\pm$ 10.6	53.0 $\pm$ 9.9
Syst RV-press. pre-op (mmHg)	24.8 $\pm$ 5.8	26.2 $\pm$ 5.8*
3 Vessel disease (n)	173 (66.3%)	107 (81.7%)*
Left Main stenosis >70% (n)	20 (7.7%)	18 (13.7%)*
Creatinin >200 μ Mol/l (n)	6 (2.3%)	3 (2.3%)
Pulmonary Vital capacity % / norm	101.1 $\pm$ 15.6	99.5 $\pm$ 19.7
Hemoglobin pre-op (mMol/l)	8.6 $\pm$.9	8.1 $\pm$.8***
Number of anastomosis	3.6 $\pm$ 1.3	3.95 $\pm$ 1.2**
Left internal mammary used (n)	233 (89%)	100 (76%)*
Re-operation	40 (15.2%)	15 (11.5%)
Valvular surgery	Young (n=138)	Old (n=69)
Age (yrs)	64.8 $\pm$ 7.5	78.2 $\pm$ 3.1
Dyspnea in rest, NYHA=4 (n)	36 (26.1%)	15 (21.7%)
History of congestive Heart Failure	74 (53.6%)	40 (57.9%)
Diabetes Mellitus (type 1 or 2)	17 (12.3%)	11 (15.9%)*
Systemic Hypertension (treated with drugs)	46 (33.3%)	14 (20.3%)*
Smoking	43 (31.1%)	11 (15.9%)*
Body mass index (g/m ²)	26.3 $\pm$ 4.5	25.7 $\pm$ 3.3
LV Ejection Fraction pre-op (%)	55.6 $\pm$ 13.1	55.5 $\pm$ 12.0
Posterior wall enddiast wall thickness (mm)	10.4 $\pm$ 1.4	11.2 $\pm$ 1.5***
Syst RV-press. pre-op (mmHg)	36.6 $\pm$ 14.7	37.0 $\pm$ 13.8
Pulmonary Vital capacity % / norm	95.2 $\pm$ 19.9	101.6 $\pm$ 19.9
Use of bioprosthesis	10 (11%)	27 (48%)*
Re-operation	26 (18.8%)	7 (10.1%)

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Figure 9.2. Life table showing survival in all age categories in all procedures ($P=n.s.$), including number of patients at risk during follow up.

Figure 9.3. Coronary surgery ($n=393$, $P=n.s.$)

Figure 9.4. Aortic valve surgery. (n=149, $P=n.s.$)

Figure 9.5. Mitral valve surgery. (n=76, $P=n.s.$ within age groups, $P<0.001$ compared to coronary and aortic valve surgery), no pts>80years.

Table 9.3. Pre-operative Predictors of 1-year mortality after cardiac surgery.

Coronary surgery	Young (n=262)	Old (n=131)
Pre-operative Creatinin >140μMol/l	4/22 (18.2%)*	2/13 (15.4%)
Previous Myocardial infarction	9/135 (6.7%)	7/77 (9.1%)**
Diabetes Mellitus	4/52 (7.7%)	2/26 (7.7%)
LVEF <53%	8/103 (7.8%)	6/71 (8.5%)
Re-operation	3/40 (7.5%)	1/15 (6.7%)
Pre-operative Heart-failure	6/27(22.2%***	1/13 (7.7%)
Congestion on chest X-ray	2/9 (22.2%)*	1/8 (12.5%)
One-sided carotid murmur	4/13 (30.8%***	1/7 (14.3%)
Ischemia on pre-operative ECG	11/95 (11.6%)**	5/73 (6.8%)
Emergency surgery	1/16 (6.3%)	0/9 (0%)

Valvular surgery	Young (n=138)	Old (n=69)
Pre-operative Creatinin >140μMol/l	2/15 (13.3%)	4/5 (80%***
FEV1 < 1 liter	11/36 (30.6%)*	2/19 (10.5%)
Previous Myocardial infarction	7/24 (29%)**	1/11 (9.1%)
Diabetes Mellitus	2/17 (11.8%)	2/11 (18.2%)
LVEF <53%	10/44 (22.7%)*	5/25 (20%)
Re-operation	5/26 (19.2%)	1/7 (14.3%)
RV Syst.>45mmHg Pre-operative	5/30 (16.7%)	6/11 (55%)**
Additional coronary surgery	12/66 (18.2%)	6/33 (18.2%)
Mitral valve surgery	11/59 (18.6%)	4/17 (23.5%)
Emergency surgery	0/1 (0%)	0/2 (0%)

Abbreviations: LVEF = Left Ventricular Ejection Fraction, FEV1 = First Expiratory 1-Second Volume, RV Syst = Right Ventricular Systolic Pressure. * $P<0.05$ ** $P<0.01$ *** $P<0.001$

Major pre-operative predictors for 1 year mortality including hospital mortality in the CABG patients were: A history of pre-operative heartfailure, an increased Creatinin value >140μMol/l, persisting ischemia on the last pre-operative ECG, previous myocardial infarction, and a one-sided carotid murmur (table 3). In the group with valvular heart surgery major pre-operative predictors for mortality were: An increased Creatinin value >140μMol/l, previous myocardial infarction, poor pulmonary function with a FEV1<1 liter, and increased right sided pressures >45mmHg systolic (table 3).

Patients aged 75 years or older had a higher incidence of postoperative atrial fibrillation. In case of coronary surgery the postoperative admission duration was longer and the incidence of postoperative heartfailure was higher. In case of valvular surgery a higher incidence of post-operative mental confusion was found (table 4). There was no difference in stroke incidence.

Table 9.4. Postoperative morbidity.

Coronary surgery	Young (n=262)	Old (n=131)
Atrial fibrillation	92 (35.1%)	83 (63.4%)*
Ventricular tachycardia/fibrillation	6 (2.3%)	5 (3.8%)
Myocardial infarction	33 (12.6%)	22 (16.8%)
Congestive heart failure (Killip 2-4)	81 (30.9%)	56 (42.7%)*
AV-conduction disturbances requiring pacing	20 (7.6%)	19 (14.5%)*
Rethoracotomy performed	24 (9.2%)	11 (8.4%)
Respiratory infection	16 (6.1%)	13 (9.9%)
Mediastinitis	6 (2.3%)	6 (4.6%)
Acute Tubular Necrosis	13 (5.0%)	7 (5.3%)
Cerebrovascular accidents	6 (2.3%)	5 (3.8%)
Mental confusion	29 (11.1%)	22 (16.9%)
Postoperative admission duration (median/std)	9 ± 9	12 ± 10***

Valvular surgery	Young (n=138)	Old (n=69)
Atrial fibrillation	89 (64.5%)	54 (78.3%)*
Ventricular tachycardia/fibrillation	6 (4.3%)	1 (1.4%)
Myocardial infarction	16 (11.6%)	8 (11.6%)
Congestive heart failure (Killip 2-4)	61 (44.5%)	34 (49.3%)
AV-conduction disturbances requiring pacing	44 (32.1%)	23 (33.3%)
Rethoracotomy performed	22 (16.1%)	7 (10.1%)
Respiratory infection	25 (18.2%)	13 (18.8%)
Mediastinitis	5 (3.7%)	1 (1.4%)
Acute Tubular Necrosis	18 (13.2%)	11 (15.9%)
Cerebrovascular Accidents	5 (3.7%)	4 (5.8%)
Mental confusion	18 (13.1%)	23(33.3%)*
Postoperative admission duration (median ±std)	13 ± 16	14 ± 12

* $P \leq 0.05$, *** $P < 0.001$

GENERAL POPULATION LIFE TABLES

To compare the long term results regarding survival with the general population, we analyzed period life tables from the Netherlands (1992-1996), obtained from C.B.S. (Dutch National Institute for Statistics)^{10,11}. From that data we constructed two survival curves for a period of 5 years using the life table method, one for men and one for women (figure 6,7). The lines plotted in each of these age categories represent the survival curve for the median age of our study population in that age group.

Figure 9.6. Survival curves from the Dutch general Male population (source: C.B.S. 1997).

Figure 9.8. Survival curves of Male study population, all procedures (n=279).

Figure 9.7. Survival curves from the Dutch general Female population (source: C.B.S. 1997).

Figure 9.9. Survival curves of Female study population, all procedures (n=321).

Below these two figures we plotted the same graphs, also divided by gender, but now for our study population, which includes both coronary surgery and valvular surgery (figure 8,9).

Comparing these figures reveals a higher early mortality in nearly each age group in the study population, due to the surgical mortality. After 36 months following surgery the survival of the elderly patient is better than the general population for both men and women. After 48 months the survival of female patients over 80 years is equal to the general population, for male patients over 80 years the prognosis looks slightly worse, but is statistically also not different from the general population. For patients between 70 and 80 years old the prognosis is still better after 48 months than in the general population.

DISCUSSION

No significant differences in operative mortality were found between both age groups and between both genders. This is in contrast to the observations of Edwards et al¹² who found a higher operative mortality in female patients. Also several studies report a higher surgical mortality in elderly patients^{9,13,14}. This might be explained by a more careful selection of the elderly patient presented for surgery. Since only 1/600 (0.2%) patients had acute surgery and 27/600 (4.5%) patients had emergency surgery (within 2 days) with only 3 deaths (11.1%), we could not confirm this as a risk-factor.

Our study demonstrates that the mortality after 36 months of male patients older than 75 years was lower than from the general population (figure 6,8). In female elderly patients the mortality after 36 months was equal to that of the general population (figure 7,9). This difference can be explained by the lower life expectancy of male subjects. In octogenarians the mortality rate dramatically increased after three years following surgery, but that appeared to be in concordance with the general life expectancy of octogenarians. Since the number of octogenarians in our study was relatively low, the presented increase of mortality between 36 and 48 months could be overestimated.

The mortality in patients younger than 60 years was always higher than that of the general population. The explanation for this is probably the low mortality rate of the general (young) population, and the effect of the surgical mortality.

This study however has several limitations. The relative small number of the study population makes subgroup analysis less reliable. Especially because there are also some biases in the baseline characteristics between the age groups. Also a median follow-up duration of 31 months has limitations for predicting long term prognosis.

CONCLUSIONS

Apart from a higher initial mortality due to the surgical procedure, the survival of elderly patients undergoing open heart surgery in the first three years is comparable to that of the general population.

Mitral valve surgery in patients over 65 years is associated with a >40% higher mortality in the first year. Therefore a cautious approach in this patient group should be considered.

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CHAPTER 10

General discussion

INTRODUCTION

From the data described in this thesis and from the literature it can be concluded that the results from cardiac surgery in the elderly patient are favorable in many aspects. This resulted in a larger number of elderly patients currently referred for open heart surgery.¹⁻⁴

However success of a surgical procedure can be measured in many ways. Most studies from the literature were retrospective, and their data limited to mortality rates and description of complications.⁵⁻¹⁴ Also the majority of those studies did not include a control group. Since results may also vary between surgical centers, a control group with younger patients from the same center is needed to examine differences in results between the younger and the elderly population.

The unique aspect of our study is that we prospectively analyzed 200 patients aged 75 years or older referred for CABG and/or valve surgery and that they were matched with 400 gender and procedure matched younger patients as a control group. Besides the collection of medical data also quality of life analysis was performed before and after surgery.

PATIENT CHARACTERISTICS

Elderly patients referred for cardiac surgery are more compromised than younger patients. They have more angina in rest (69% vs 56%), a higher incidence of 3-vessel disease (82% vs 66%) and left main stenosis (14% vs 8%), and a higher incidence of urgent surgery (53% vs 44%). On the other hand the number of risk factors is clearly lower in the elderly. Smoking is less (14% vs 24%), obesity (BMI>30) is less (13% vs 23%), hypercholesterolemia is less (25% vs 38%), and also hypertension (20% vs 33%, in the valve surgery group). The incidence of concomitant diseases (COPD, renal failure, diabetes) was low in our study group, with no clear differences with the young group. Also the incidence of heart failure was low (10%, CABG group).

MORTALITY AND MORBIDITY

The low incidence of risk factors and concomitant diseases makes the study population except for cardiac disease relatively healthy, compared to the general population. This might explain why the surgical mortality had a tendency to be lower in the elderly (4.5% vs 6%). As can be seen in chapter 9 the long term survival after surgery is similar or even better than that from the general elderly population. This can be explained by patient selection with a higher incidence of chronic diseases in the elderly population in general.¹⁵

Atrial fibrillation is the most common complication after open heart surgery in the elderly patient. Since the size of the left atrium, which was measured pre-operatively in all patients, did not differ between the age groups, other age-related factors have to explain this finding. Probably the most important factor is age-related myocardial fibrosis. Another important factor we found in our study is the low incidence of prophylactic use of betablockers to prevent atrial fibrillation due to a higher incidence of contra-indications for β -blockade. Since atrial fibrillation results in a longer admission duration, there is a need for the development of anti-arrhythmic agents with less side-effects for the elderly population, which can be given prophylactically.

Mental confusion following open heart surgery is more common in the elderly. Its incidence is especially high after long operative procedures (bypass-time >114 minutes, cross-clamp time >76 minutes) as in valvular surgery. We also found that diabetes, pre-operative heart failure, weak carotid pulsations and a re-operation were risk factors. Probably diabetes causes some cerebral vasculopathy which enhances the occurrence of confusion in case of hypoperfusion of the brain. Also the presence of heart failure causes lower arterial oxygen saturations, which causes worsening of hypoxemia of the brain during surgery. Weak carotid pulsations can be a sign of carotid stenosis. Since this is a known risk factor for surgery, several authors suggest pre-operative carotid screening by duplex scanning if a carotid stenosis is suspected. The presence of a carotid stenosis >75% is associated with a 15% chance of a postoperative cerebrovascular accident.^{16; 17} A re-operation is a time-consuming procedure which because of its longer duration might explain the higher incidence of mental confusion.

The results of mitral valve surgery were less good in the elderly. The 1-year mortality was higher (24% vs 19%), and also the number of re-admissions within one year (47% vs 15%). A possible explanation for this can be a higher incidence of mitral annulus calcification in the elderly (56% vs 34%).¹⁸ This makes the surgical procedure more difficult. Also the possibilities to do a mitral valve reconstruction are limited in the presence of annular calcification. Elderly patients also had a higher incidence of inadequate functioning of the mitral valve when measured 6 months later by echocardiography. That finding was present in 29% vs 16%. This

was especially the case when mitral valve reconstruction was performed (75% vs 45%). These results suggest that mitral valve reconstruction is less successful in the elderly, and its use should probably be limited.

QUALITY OF LIFE

Both age groups showed a significant and similar improvement of the quality of life variables measured after surgery. The only pre-operative difference was a higher incidence of physical immobility in the elderly, which is a normal age-related phenomenon. The presence of pre-operative signs for depression appeared to be a predictor for less improvement of general well being in the elderly patient (57% vs 72%). In another study it has been described that pre-operative depression has a bad influence on rehabilitation after cardiac surgery, which will contribute to a poor outcome.¹⁹

CONCLUSIONS

Using the current selection criteria for open heart surgery in the elderly excellent results can be achieved regarding surgical mortality, morbidity and quality of life.

Further improvement is needed in the development for new anti-arrhythmic drugs for the prevention of atrial fibrillation following surgery. Also the development of surgical techniques resulting in shortening of the perfusion time are needed to diminish mental confusion in the elderly. Alternative surgical techniques for the management of mitral valve incompetence in the elderly patient should be considered.

Advanced age should not be a contra-indication for open heart surgery, especially when there is little comorbidity.

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CHAPTER 11

Summary

The number of patients older than 75 years that have undergone open heart surgery has increased significantly during the last decade. To answer the question if there are differences in outcome of open heart surgery in elderly patients we prospectively studied 200 patients aged 75 years or older in comparison to 400 procedure and gender matched younger patients. Data were collected regarding clinical parameters and quality of life.

BASELINE DIFFERENCES

Gender: As shown in chapter 3 female patients were relatively older at the time of surgery compared to male patients.

Severity of the disease: Elderly patients (≥ 75 years) referred for coronary surgery had more often 3-vessel disease (81.7% vs 66.3%), had a higher incidence of severe left main stenosis (13.7% vs 7.7%) and had more often angina in rest (69% vs 56%). The incidence of diabetes, renal disease and COPD did not differ. Risk factors for coronary artery disease (hypercholesterolemia and smoking) were less present in elderly patients. Elderly patients also had a higher incidence of pre-operative mitral insufficiency, a higher RV-systolic pressure and a higher LV-end diastolic pressure.

In elderly patients referred for valvular surgery the incidence of hypertension and smoking was less compared to younger patients. The incidence of left ventricular hypertrophy was slightly higher in the elderly. Findings on hemodynamic measurements were similar in both groups.

SURVIVAL

When comparing two age groups (above and below 75 years) no significant differences were found in mortality in the first three years following coronary, valvular and combined surgery. Hospital mortality (up to 30 days following surgery) was 4.5% in the Old group and 6.0% in the Young group. The One-year mortality (including hospital mortality) was 7.5% of the Old and 8.0% of the Young group. Only after 42 months a higher mortality rate was found in elderly patients, especially in those older than 80 years. This can be explained by

the lower life expectancy of octogenarians. In agreement with this observation is the fact that the youngest age group always had the best long-term prognosis. When the type of surgery was taken in account, the same pattern is seen for coronary surgery and aortic valve surgery. Only for mitral valve surgery a higher one year mortality rate is found in patients older than 75 years (23.5 vs 18.6%). Major pre-operative predictors for 1 year mortality including hospital mortality in the CABG patients were: A history of cardiac asthma, the presence of pleural fluid on a chest X-ray, persisting ischemia on the last pre-operative ECG and symptomatic cerebrovascular disease. In the group with valvular heart disease major pre-operative predictors for mortality in the elderly were: An increased creatinin value $>140\mu\text{Mol/l}$ and increased right sided pressures $>45\text{mmHg}$ systolic.

DIFFERENCES IN HOSPITAL MORBIDITY

One of the major differences in morbidity was a higher incidence of post-operative atrial fibrillation in the elderly patient. The incidence was especially higher when valvular surgery was performed. The presence of atrial fibrillation was associated with a longer admission duration. The higher incidence of atrial fibrillation can be partly explained by a higher incidence of atrial fibrillation in elderly people, because of a higher incidence of age-related myocardial fibrosis. However as shown by the high incidence of atrial fibrillation in valve surgery, other factors like atrial enlargement play a role. We also found that elderly patients were considered to have more contra-indications for prophylactic use of beta-blocking drugs.

Another striking difference is a 2.5 times higher incidence of temporary mental confusion of elderly patients after valvular surgery (found in $1/3$ of patients). Mental confusion was associated with a significantly longer aortic cross clamp time (mean=103.8 minutes in confused patients versus 79.89 minutes without confusion). The mean aortic cross clamp time in elderly patients undergoing coronary surgery was only 56.2 minutes, which can explain the relatively low incidence of 17.2% mental confusion following that operation. Other riskfactors for mental confusion were: diabetes mellitus, pre-operative heartfailure and a re-operation.

Another difference in morbidity include a median of four days longer postoperative admission duration of the elderly patient with coronary surgery (13 versus 9 days), but no significant difference in case of valvular surgery (14 versus 13 days). In the elderly group with coronary surgery the incidence of postoperative congestive heart failure (Killip class 2-4) was higher (41.9% versus 31.1%) and also the incidence of postoperative AV-conduction disturbances requiring pacing was higher (14.7% versus 7.6%).

DIFFERENCES DURING FOLLOW-UP

Elderly patients with valvular surgery had a 2.9 times higher incidence of readmissions (29.7% vs 10.4%) because of procedure related or new cardiac problems in the first year following surgery. This was especially the case in elderly patients with mitral valve surgery of whom 47% had readmissions. No differences in readmissions were seen in patients with coronary surgery.

A routine echocardiogram which was performed 6–7 months following surgery demonstrated a larger decrease of LV-end diastolic diameter following valvular surgery in the young patient. No differences were seen regarding LV and valvular function.

Elderly patients showed a similar improvement in anginal and dyspnea complaints 6 and 12 months following surgery. When compared to pre-operatively, general well-being improved one year after surgery in 73.3% of the Young and 69.9% of the Old patients ($P=n.s.$).

Quality of life assessment using the Nottingham Health Profile and Hospital Anxiety and Depression scale pre-operatively and two and six months after surgery, showed improvement in both age groups. However in case of valvular surgery the amount of improvement was less in the elderly, especially regarding energy, sleep and social functioning which did not significantly improve in the first 2 months following surgery. In case of coronary surgery all items regarding quality of life improved significantly in both groups. Elderly patients who were pre-operatively depressed, had less improvement of general well-being compared to younger depressed patients following surgery (57% versus 67%). The improvement of the non-depressed patients were similar in both groups (72–73%).

COSTS OF HOSPITAL STAY

Based on fixed prices for one day admission on a general care or an intensive care unit we calculated the approximate admission costs for each patient, including pre-operative admission duration and re-admissions until one year following surgery, and excluding costs of surgery and diagnostic procedures. For this calculation we used an amount of f 850.- per day for a bed of general care, and f 2500.- per day for an intensive care or coronary care unit bed. The costs for coronary surgery were significantly higher in the Old age group (table 1), because of a longer postoperative admission duration. Surprisingly no differences were seen in the other patient groups.

Table 1. Calculated costs (Mean $\pm$ Std in DFL) for admission duration and re-admissions within one year.

	Young	Old
CABG	24818 $\pm$ 20444	29860 $\pm$ 21176*
Valve	27028 $\pm$ 21670	27749 $\pm$ 20984
CABG + Valve	35105 $\pm$ 37876	33812 $\pm$ 31773
AVR	27212 $\pm$ 23162	27656 $\pm$ 17783
MVR	37452 $\pm$ 37365	39153 $\pm$ 42935
All procedures	26913 $\pm$ 24589	30132 $\pm$ 23152

* $P < 0.05$

CONCLUSIONS

Elderly patients admitted for coronary revascularisation or aortic valve surgery have excellent results regarding mortality, morbidity and quality of life, comparable to younger patients. An important factor explaining these results is the pre-operative selection of patients. The results of mitral valve surgery in elderly patients are more disappointing because of higher mortality and morbidity. These findings should be taken into account when cardiac surgery in the elderly is considered.

The finding that the overall life expectancy after cardiac surgery is similar to that of the general population, indicates that advanced age should not be seen as a contra-indication for surgery, especially when not too many riskfactors predicting mortality are present.

CHAPTER 12

Samenvatting

Het aantal patiënten ouder dan 75 jaar dat open hart chirurgie heeft ondergaan in de laatste tien jaar is in belangrijke mate toegenomen. Om de vraag te beantwoorden of er verschillen zijn in de uitkomst van open hart chirurgie bij oudere patiënten, hebben wij een prospectieve studie verricht bij 200 patiënten van 75 jaar en ouder, en 400 jongere patiënten met overeenkomstige procedure en geslacht. Gegevens werden verzameld betreffende klinische parameters en kwaliteit van leven.

BASIS KENMERKEN

Geslacht: Zoals aangetoond in hoofdstuk 3 zijn vrouwelijke patiënten relatief ouder op het tijdstip van de operatie vergeleken met mannelijke patiënten.

Ernst van de ziekte: Oudere patiënten (≥ 75 jaar) verwezen voor coronaire bypass chirurgie hadden vaker 3-taks lijden (81.7% vs 66.3%), hadden een hogere incidentie van ernstige hoofdstam stenose (13.7% vs 7.7%) en hadden vaker angina pectoris in rust (69% vs 56%). De incidentie van diabetes mellitus, nierfunctie stoornissen en CARA verschilde niet. Risico factoren voor coronaria lijden (hypercholesterolemie and roken) waren in mindere mate aanwezig bij oudere patiënten. Oudere patiënten hadden ook een hogere incidentie van een pré-operatieve mitralisinsufficiëntie, een hogere RV-systolische druk, en een hogere LV-einddiastolische druk.

Oudere patiënten verwezen voor klepchirurgie hadden een lagere incidentie van hypertensie en roken, vergeleken met jonge patiënten. De incidentie van linker ventrikel hypertrofie was iets hoger bij ouderen. Hemodynamische metingen waren identiek in beide groepen.

OVERLEVING

Wanneer we beide leeftijdsgroepen (ouder en jonger dan 75 jaar) vergelijken, dan zijn er geen verschillen in sterfte in de eerste 3 jaar na coronair, klep, en gecombineerde operaties. De ziekenhuis sterfte (tot 30 dagen na operatie) was 4.5% in de oude en 6.0% in de jonge groep. De 1-jaars sterfte (inclusief ziekenhuis sterfte) was 7.5% in de oude en 8.0% in de jonge groep. Alleen na 42 maanden werd een hogere sterfte gevonden bij oudere patiënten, met name in de leeftijds-

groep ouder dan 80 jaar. Dit kan verklaard worden door de lagere levensverwachting van 80-plussers. In overeenstemming met deze bevinding is het feit dat de jongste leeftijdsgroep altijd de beste lange-termijn prognose had.

Wanneer er gekeken wordt naar het type operatie, dan is hetzelfde patroon zichtbaar voor coronair chirurgie en aortaklep chirurgie. Alleen bij mitraalklep chirurgie werd een hogere 1-jaars sterfte gevonden bij patiënten ouder dan 75 jaar (23.5 vs 18.6%).

Belangrijke pré-operatieve voorspellers voor 1-jaars sterfte alsmede ziekenhuis sterfte bij coronair chirurgie zijn: Een astma cardiale in de voorgeschiedenis, de aanwezigheid van pleuravocht op een thoraxfoto, persisterende ischemie op het laatste pré-operatieve ECG, en symptomatisch cerebrovasculair lijden. In de groep met kleplijden waren de belangrijkste pré-operatieve voorspellers voor sterfte: Een verhoogd serum kreatinine van $>140\mu\text{Mol/l}$ alsmede verhoogde rechter ventrikel drukken van $>45\text{mmHg}$ systolisch.

VERSCHILLEN IN ZIEKENHUIS MORBIDITEIT

Een van de grootste verschillen in morbiditeit was een hogere incidentie van post-operatief boezemfibrilleren bij de oudere patiënt. De incidentie was met name hoger na klep-operaties. Het optreden van boezemfibrilleren ging gepaard met een langere opnameduur. De hogere incidentie van boezemfibrilleren kan gedeeltelijk worden verklaard door een hogere incidentie van boezemfibrilleren bij ouderen, ten gevolge van een hogere incidentie van leeftijdsgebonden hartspier fibrose. Echter zoals blijkt uit de hogere incidentie van boezemfibrilleren na klepoperaties, spelen ook andere factoren zoals boezem vergroting een rol. Tevens vonden we dat oudere patiënten meer contraïndicaties hadden voor het profylactisch gebruik van bèta-blokkers.

Een ander opvallend verschil is een 2.5 keer hogere incidentie van tijdelijke mentale verwardheid bij oudere patiënten na klepchirurgie (bij $1/3$ van de patiënten). Verwardheid was geassocieerd met een significant langere aorta klemtijd (gemiddeld=103.8 minuten bij verwarde patiënten versus 79.89 minuten zonder verwardheid). De gemiddelde aorta klemtijd bij oudere patiënten tijdens coronairchirurgie was slechts 56.2 minuten, hetgeen de relatief lage incidentie van 17.2% verwardheid kan verklaren bij die ingreep. Andere risicofactoren voor verwardheid waren: diabetes mellitus, pré-operatief pompfalen en een re-operatie.

Een ander verschil in morbiditeit is een vier dagen langere postoperatieve opnameduur bij de oudere patiënt na coronairchirurgie (13 versus 9 dagen), doch er is geen significant verschil na klepchirurgie (14 versus 13 dagen).

In de oudere groep met coronairchirurgie werd een hogere incidentie gevonden van postoperatief pompfalen in Killip klasse 2-4 (41.9% versus 31.1%). Ook de

incidentie van postoperatieve AV-geleidingsstoornissen waarvoor pacing noodzakelijk is was hoger (14.7% versus 7.6%).

VERSCHILLEN TIJDENS FOLLOW-UP

Oudere patiënten na klepchirurgie hadden een 2.9 keer hogere incidentie van heropnames (29.7% vs 10.4%) ten gevolge van procedure gerelateerde of nieuwe cardiale problemen in het eerste jaar na de operatie. Dit was met name het geval bij mitraalklep-chirurgie waarbij er 57% heropnames waren. Er waren geen verschillen in heropnames bij coronairchirurgie.

Een routine echocardiogram dat 6-7 maanden postoperatief werd verricht toonde een grotere afname van de LV-eind diastolische diameter bij jongere patiënten na een klepoperatie. Er waren geen verschillen zichtbaar in linker ventrikel en klepfunctie.

Oudere patiënten lieten een identieke verbetering zien van angina pectoris en dyspneu klachten 6 en 12 maanden na de operatie. Ten opzichte van pré-operatief is het algemene welbevinden na 1 jaar verbeterd bij 73.3% van de jonge en 69.9% van de oude patiënten ($P=n.s.$).

Kwaliteit van leven, gemeten met de Nottingham Health Profile en de Hospital Anxiety and Depression scale, zowel pré-operatief als twee en zes maanden post-operatief, liet verbetering zien in beide leeftijdsgroepen. Echter bij klepoperaties is de mate van verbetering minder bij de oudere groep, met name factoren zoals energie, slaap, en sociaal functioneren verbeterden niet significant in de eerste 2 maanden na de operatie. Bij coronairchirurgie trad er in alle gemeten variabelen een verbetering op van kwaliteit van leven in beide groepen. Oudere patiënten die pré-operatief depressief waren, toonden een geringere verbetering van het algemene welbevinden dan jongere depressieve patiënten na de operatie (57% versus 67%). De verbetering van niet depressieve patiënten was identiek in beide groepen (72-73%).

KOSTEN VAN ZIEKENHUISOPNAME

Uitgaande van vaste bedragen voor een dag opname op een algemene afdeling en een intensive care unit hebben we een berekening gemaakt van de geschatte opname kosten per patiënt. Hierbij werd gekeken naar zowel de pré- en post-operatieve opnameduur, alsmede de heropnames tot een jaar na de operatie (exclusief kosten van ingrepen en diagnostiek). Voor deze berekening werd een bedrag van f 850,- per dag gebruikt voor een bed op de algemene afdeling, en f 2500,- per dag op een intensive care of hartbewakings afdeling. De kosten voor coronair chirurgie waren significant hoger bij de oudere leeftijdsgroep (tabel 1), ten gevolge van een langere postoperatieve opnameduur. Opvallend genoeg waren er geen verschillen bij de andere patiënten groepen.

Tabel 1. Berekende kosten (Gemiddelde $\pm$ Std in DFL) voor opnameduur en heropnames binnen één jaar.

	Jong	Oud
Bypass	24818 $\pm$ 20444	29860 $\pm$ 21176*
Klep	27028 $\pm$ 21670	27749 $\pm$ 20984
Bypass+Klep	35105 $\pm$ 37876	33812 $\pm$ 31773
Aortaklep	27212 $\pm$ 23162	27656 $\pm$ 17783
Mitraalklep	37452 $\pm$ 37365	39153 $\pm$ 42935
Alle ingrepen	26913 $\pm$ 24589	30132 $\pm$ 23152

* $P<0.05$

CONCLUSIES

Oudere patiënten opgenomen voor coronair chirurgie of aortaklep vervanging hebben uitstekende resultaten betreffende mortaliteit, morbiditeit, en kwaliteit van leven, hetgeen vergelijkbaar is met jongere patiënten. Een belangrijke factor die deze resultaten verklaard is de pré-operatieve selectie van patiënten. De resultaten van mitraalklep chirurgie bij oudere patiënten zijn meer teleurstellend in verband met een hogere mortaliteit en morbiditeit. Met deze bevindingen dient rekening te worden gehouden indien open hart chirurgie wordt overwogen bij oudere patiënten.

De bevinding dat de levensverwachting na open hart chirurgie identiek is aan die van de algemene bevolking, geeft aan dat gevorderde leeftijd niet gezien mag worden als een contra-indicatie voor operatie, met name indien er niet te veel risicofactoren voor een slechte operatie uitkomst aanwezig zijn.

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