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Effect of Cardiac Surgery on Long-Term Outcome

Balancing Between Survival Benefit, Surgical Risk and Health-Related Quality of Life

Doctoral dissertation

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ABSTRACT

Survival, mortality, morbidity, complication rate, symptom recurrence and need for re-interventions have long been used as benchmarks of cardiac surgery. These variables are easily and reliably construed, they are easy to iterate, and they are comparable regardless of the patients' cultural, social, or educational background. The current trend, however, is also to assess the patients' subjective health-related quality of life (HRQoL), especially among the elderly and more morbid patients. The evaluation of the benefits of cardiac surgery should be a comprehensive integration of both objective and subjective outcome measures.

This study is based on a comprehensive outcome analysis of 604 cardiac operated patients at the Kuopio University Hospital during 1990 and 2007. It examines several clinically relevant factors contributing to objective and subjective outcome measures. The study consists of four papers (**I-IV**). The specific objectives were to assess the long-term effects of postoperative conduction abnormalities on survival after primary coronary artery bypass grafting (**I**), to analyze the differences between mitral valve plasty and mitral valve replacement on survival and HRQoL (**II**), to investigate the long-term benefits of cardiac surgery on survival and HRQoL of octogenarians (**III**), and to study the implications of pacemaker-requiring conduction abnormalities after tricuspid valve surgery and to assess its impact on long-term survival, mortality, morbidity, and HRQoL (**IV**).

The findings suggest: firstly, survival of the coronary artery bypass grafted patients is comparable to an age- and sex-matched reference population. However, coronary artery bypass-related permanent conduction abnormalities are associated with prolonged hospitalization, but they do not contribute to increased cardiac mortality during long-term follow-up (**I**).

Secondly, survival is longer after mitral valve plasty than after mitral valve replacement. However, the HRQoL of patients who have undergone mitral valve plasty is similar to the HRQoL after mitral valve replacement. In terms of the variables related to HRQoL, mitral valve operated patients do not differ markedly from the age- and sex-matched reference population (**II**).

Thirdly, the long-term HRQoL and survival of the patients who have undergone cardiac surgery at the age of ≥70 years are comparable to the age- and sex-matched reference population. The HRQoL does deteriorate after cardiac surgery, and this takes mainly place in the physical domains of HRQoL (**III**).

Fourthly, the need for a permanent pacemaker after tricuspid valve surgery is high, and permanent pacemakers are needed throughout the long-term follow-up. Also, the life expectancy of patients with a permanent pacemaker after tricuspid valve surgery is longer than of patients with no pacemaker. On the other hand, patients with a pacemaker had more thromboembolic complications and impaired HRQoL in the physical domains (**IV**).

National Library of Medicine Classification: WG 168, WG 169, WG 262, WG 268
Medical Subject Headings: Aged; Aged, 80 and over; Coronary Artery Bypass; Cardiac Surgical Procedure/mortality; Cardiac Surgical Procedures/adverse effects; Follow-Up Studies; Heart Block; Heart Valve Diseases/surgery; Life Expectancy; Mitral Valve/surgery; Pacemaker, Artificial/adverse effects; Postoperative Complications; Prospective Studies; Quality of Life; Risk; Survival Rate, Thromboembolism; Treatment Outcome; Tricuspid Valve/surgery

To Joel, Senni, Kasper, and Eeli

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Lahti, September 2009

Janne Jokinen

ABBREVIATIONS

AV	Atrioventricular
AVR	Aortic valve replacement
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CD	Conduction defect
CPB	Cardiopulmonary bypass
ECG	Electrocardiogram
HRQoL	Health-related quality of life
IABP	Intra-aortic balloon pump
LAHB	Left anterior hemiblock
LBBB	Left bundle branch block
LPHB	Left posterior hemiblock
MI	Myocardial infarction
MVP	Mitral valve plasty
MVR	Mitral valve replacement
NHP	Nottingham Health Profile
NYHA	New York Heart Association
PM	Permanent pacemaker
RBBB	Right bundle branch block
TR	Tricuspid regurgitation
TV	Tricuspid valve
TVP	Tricuspid valve plasty
TVR	Tricuspid valve replacement

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following articles, which are referred to in the text by their Roman numerals I-IV:

I Jokinen JJ, Mustonen PK, Hippeläinen MJ, Rehnberg LS, Hartikainen JEK. Effects of coronary artery bypass related conduction defects: a 10-year follow-up study. Scand Cardiovasc J 2004;38:235-9.

II Jokinen JJ, Hippeläinen MJ, Pitkänen OA, Hartikainen JEK. Mitral valve replacement versus repair: propensity-adjusted survival and quality-of-life analysis. Ann Thorac Surg 2007;84:451-8.

III Jokinen JJ, Hippeläinen MJ, Hänninen T, Turpeinen AK, Hartikainen JEK. Prospective assessment of quality of life of octogenarians after cardiac surgery: factors predicting long-term outcome. Interact Cardiovasc Thorac Surg 2008;7:813-8.

IV Jokinen JJ, Turpeinen A, Pitkänen O, Hippeläinen MJ, Hartikainen JEK. Pacemaker therapy after tricuspid valve operations: implications on mortality, morbidity and quality of life. Ann Thorac Surg 2009;87:1806-14.

CONTENTS

1. INTRODUCTION

Attempts to temporarily substitute a patient's heart and lungs with a mechanical device were originally made in 1812, when Julien Jean César LeGallois first presented the idea of artificial circulation (Griffenhagen and Hughes 1955). Since then, the history of the development of cardiopulmonary bypass (CPB) includes the first design of a CPB device by von Frey and Gruber in 1885 (von Frey and Gruber 1885) and the proposal in 1935 by Alexis Carrel and Charles Lindbergh (Carrel and Lindbergh 1935).

The modern era in cardiac surgery began in 1953, when John Gibbon reported the first successful use of extracorporeal circulation by means of an oxygenator (Gibbon 1954). The first successful coronary artery bypass grafting (CABG) was performed in 1964 by Vasilii Kolesov who grafted the left internal mammary artery (LITA) to the left anterior descending artery (LAD) without CPB (Kolesov 1965). Three years later René Favaloro began to use routinely the reversed greater saphenous vein for aortocoronary grafting (Favaloro 1969). The era of valve surgery started in 1948, when Dwight Harken performed the first closed mitral commissurotomy to relieve severe rheumatic mitral stenosis (Harken et al. 1948). In 1952, Charles Hufnagel implanted for the first time a prosthetic valve in the descending aorta (Hufnagel 1954), and in 1960, Nina Starr Braunwald successfully replaced a mitral valve in patient who lived about three months (Braunwald 1960).

Now the surgical treatment of various cardiac conditions, e.g., coronary artery disease (CAD), valve disorders, combination of these, and complex congenital heart diseases, is possible. Surgical treatment of adult cardiac diseases has become routine only during the past three decades - despite the fact that the feasibility of open heart surgery was shown already in the mid-1900s. There are a number of factors that have contributed to the improved outcomes of adult cardiac surgery patients, including the development of surgical technique as such, refinement of myocardial preservation and CPB, introduction of better pharmacological agents, and a more comprehensive understanding of the natural history of cardiac diseases. These allow more appropriate timing of interventions, and provide more accurate predictive models of operative risk and more optimal patient selection. As a result, the mortality of most cardiac operations of adults has dwindled – despite the fact that many high-risk patients undergo surgery. In the earlier decades, the benefit of open heart surgery was measured in terms of extended lifetime. Now, when cardiac operations are increasingly performed on elderly patients, the impact of cardiac intervention on subjectively experienced health-related quality of life (HRQoL) will perhaps be more important than its effect on longevity alone. Under these

circumstances, the survival variable no longer reflects the primary intention of treatment of cardiac surgery, although the outcome must also be evaluated in a more comprehensive context, including the impact of cardiac surgery on patient's self-perceived HRQoL.

2. REVIEW OF THE LITERATURE

2.1. Scope and importance of cardiac and cardiovascular conditions

Despite the fact that mortality from cardiovascular diseases has significantly decreased over the last decades, they are still the main reason for death and account for more than 40% of all deaths in Finland. In 2007, altogether 20,312 (383/100,000) deaths in Finland were due to cardiovascular diseases (Tilastokeskus 2009a), and CAD caused about one out of every four deaths (219/100,000) in Finland.

Treatment for CAD was needed in 2004 by 59,159 patients. This was equivalent to 75,964 hospital admission due to angina pectoris and 13,771 due to myocardial infarction. This caused a huge load to the Finnish healthcare system: there were 77,495 hospitalization periods and 660,085 patient hospital days. In 2008 the number of CABGs amounted to 4,017, the number of percutaneous coronary interventions to 8,597, and the number of coronary angiographies to 22,913 due to CAD (Suomen Kardiologinen Seura 2009).

According to the American Heart Association (AHA) in 2005 the overall mortality rate from cardiovascular diseases in United States was 279/100,000. CAD caused about one out of every five deaths in the United States, and CAD-related mortality in 2005 was 445,687 (148/100,000) patients (Lloyd-Jones et al. 2009). In 2009, 785,000 Americans will have a new myocardial infarction, and about 470,000 will have a recurrent infarction.

The overall total-mention mortality rate from valvular heart disease was 43,900. This is the number of death certificates in a year that mention the given disease classification either as the underlying cause or as a contributing cause. According to subgroup classification, the total-mention mortality from aortic valve disorder was 27,390 patients, from mitral valve disorder 6,210 patients, and from tricuspid valve disorder 114 patients. Arrhythmias were the reason of total-mention mortality of 466,750 patients (Lloyd-Jones et al. 2009).

2.2. Survival and mortality after cardiac surgery

The survival benefit acquired from cardiac surgery has steadily increased over the years despite the fact that there has been a marked increase in the average age of the cardiac surgical population over the last ten years. The average age of patients referred for cardiac surgery has increased from 58 to 64 years over the last decade – an average increase in age of one year for every two years (National Adult Cardiac Surgical Database Report 2000-2001). It is worth noting, however, that the survival benefits of cardiac surgery become evident only after long-term follow-up.

2.2.1. Postoperative conduction defects and survival

The impact of permanent postoperative conduction defects (CD) after cardiac surgery on mortality and morbidity has become less marked over the years since surgery-related CD is encountered more rarely. The recent study by Cook and colleagues reported a marked decrease in the incidence of new onset CD in CABG patients between 1991 and 2001. The early postoperative incidence of new CDs in 2001 was approximately one third of that of 1991 (19% vs. 6%, respectively). Also, 9% of the patients had a CD at the time of discharge in 1991, whereas the corresponding figure in 2001 was 7% (Cook et al. 2005). However, there is some evidence that a new, permanent CD after cardiac surgery may contribute negatively to long-term survival. Zeldis and co-workers reported that 20% of patients with a new left-sided CD died during the one to three years follow-up compared with only 7% of patients without a new permanent postoperative CD (Zeldis et al. 1978). Bateman and colleagues found in their series of 227 consecutive CABG-patients that among patients with preoperative or CABG-related left bundle branch block (LBBB) or intraventricular CD the mortality risk was no less than 38% during 5-years of follow-up compared to patients with right-sided or no CD whose risk was only 6%. Most of the deaths occurred during the first year after operation. The authors concluded that CD probably relates to cardiac mechanical dysfunction or ventricular arrhythmias and this poses initially a high risk for patients (Bateman et al. 1985). However, some reports from the same era have found no relation between CDs and survival. Wexelman and colleagues investigated 200 consecutive CABG-patients without a preoperative CD; 45 patients developed a new CD after CABG and 155 patients did not. The groups were relatively well-matched in terms of preoperative characteristics. As a result, the authors did not find any survival difference between the CD+ and CD- groups at 14 months follow-up regardless the type of CD, and concluded that the a new CD does not affect prognosis (Wexelman et al. 1986). Similar results were reported by Chu and co-workers in a series of 913 CABG-patients 17% of whom developed transient CD (resolved before discharge) and 14% permanent CD (until discharge). They reported that a new perioperative CD, including isolated new LBBB, did not impair the survival rate of patients who were followed for up to three years after surgery (Chu et al. 1987).

2.2.2. Survival of octogenarians after cardiac surgery

In a prospective study by Avery and co-workers of 104 cardiac operated octogenarians, the 30-day mortality was 13.5% as compared with 3.4% among 351 reference patients aged 65-75 years (Avery et al. 2001). Similarly, Chee and co-workers compared 2,272 patients over 75

years with 9,745 patients below 75 years and found, not surprisingly, that older age was associated with higher mortality rates during the in-hospital period and short-term follow-up. They reported a 3.4-fold (4.1% vs. 1.2%) increase in in-hospital mortality in patients >75 years compared to the younger age group (Chee et al. 2004). The long-term survival rates after isolated CABG of patients older than 75 years has increased in the United States from 92% in 1998 to 94% in 2001 (National Adult Cardiac Surgical Database Report 2000-2001). An analysis of Petersen and colleagues of 24,461 octogenarians who underwent CABG between 1987 and 1990 showed that the life span of the survivors was similar to that of the general population (Petersen 1995). Similarly, Ishikawa and associates found in 237 cardiac operated octogenarians that the early mortality rate was 9%, but that the 5-year actuarial survival rate of the hospital survivors was 75%. There were no significant differences in survival among CABG, valve or combination procedures. Although a marked increase in morbidity and mortality was noted among patients with urgent and emergent needs, the risk-benefit profile was considered acceptable (Ishikawa 2004). Improved surgical techniques have decreased operative mortality. Ivanov and colleagues reported a 34% reduction in the adjusted operative mortality risk among 3,330 consecutive patients aged 70 years and older who underwent isolated CABG between 1982 and 1996 (Ivanov et al. 1998).

2.2.3. Survival after mitral valve surgery

Studies on survival after mitral operations have shown that mitral valve plasty (MVP) is superior to mitral valve replacement (MVR). However, it is crucial to note that the etiology of mitral valve disease is decisive for selection of technique and patient outcome. In general, patients with degenerative mitral valve disease are most suitable for reconstructive surgery, and long-term results of repair are excellent in this group compared to the outcome of patients with rheumatic mitral valve disease, where repair is more difficult and less durable. In these selected cases, MVR may be the only feasible option for reconstruction of the diseased mitral valve apparatus. It is practically impossible, at least in valve surgery, to design prospective randomized clinical trials, since operative techniques cannot be selected randomly. Thus, the results regarding outcomes after mitral valve surgery are primarily based on non-randomized, register-based materials. The study reports are very heterogeneous regarding co-morbidities and etiologies of mitral disease.

MVP is currently applied to close to 60% of all patients who require surgery for mitral valve disease in the United States (Ad et al. 2008). In terms of operative and early (within 30 days) mortality, MVP seems to be superior to MVR. Akins and co-workers reported lower hospital mortality in patients who underwent MVP (3%) compared to patients who underwent MVR (12%; Akins et al. 1997). These results are corroborated by Enriquez-Sarano and Gogbashian, who found that operative mortality in 195 MVP patients was 2.6%, compared with 10.3% in 214 MVR patients who were operated due to organic mitral regurgitation (Enriquez-Sarano et al. 1995). Similarly, the in-hospital mortality among 218 MVP and 74 MVR patients who were operated on for degenerative mitral valve disease was 0.7% and 13.9%, respectively (Gogbashian et al. 2006). However, the long-term survival of the patients who had undergone concomitant CABG did not differ between these two groups (Gogbashian et al. 2006). The report by Mihaljevic and associates regarding 390 patients who had undergone CABG with (n=290) or without (n=100) MVP concluded by stating that although CABG in combination with MVP reduces postoperative mitral regurgitation and improves early symptoms compared with CABG alone, it does not improve the long-term functional status or survival of patients with severe functional ischemic mitral regurgitation (Mihaljevic et al. 2007).

Enriquez-Sarano and associates reported higher 10-year survival rates after MVP compared to MVR performed due to organic mitral regurgitation – 68% versus 52% (Enriquez-Sarano et al. 1995). Gillinov and colleagues studied a cohort of 482 patients who required surgery for ischemic mitral regurgitation and underwent either MVP or MVR and found that in combination with CAD, late survival was relatively poor. Overall, however, most patients with ischemic mitral regurgitation benefit from MVP compared to MVR in terms of survival. The 1- and 5-year survival rates were 82% and 58% compared with 56% and 36%, respectively. In the most complex, high-risk settings, survival after MVP and MVR were similar (Gillinov et al. 2001). In contrast, a more recent study of Gillinov and colleagues revealed that the 5-, 10-, and 15-year survival of 3,286 patients who had undergone either MVP or MVR due to isolated degenerative mitral valve disease (without CAD) was 95%, 87%, and 68% in MVP group, versus 80%, 60%, and 44% in MVR group. When the patients were propensity matched, the survival between the MVP and MVR groups was, unexpectedly, similar: 86%, 63%, and 43%, versus 83%, 62%, and 48%, respectively (Gillinov et al. 2008).

2.2.4. Survival after tricuspid valve surgery

Tricuspid regurgitation (TR) is a common echocardiographic finding that is present in 80% to 90% even of healthy individuals (Singh et al. 1999). The survival outcome is unambiguously related to the severity of TR. Nath and associates reviewed retrospectively the data of 5,223 patients who had undergone echocardiography over a period of four years in Veterans Affairs Medical Centers. They found that the prognosis was strictly dependent on the grade of TR. The 1-year survival of patients with severe, moderate, mild, and no TR was 64%, 79%, 90%, and 92%, respectively. The authors concluded that the severity of TR was associated with worse survival regardless of left ventricular ejection fraction or pulmonary artery pressure. In addition, severe TR was associated with a poor prognosis independent of age, biventricular systolic function, right ventricular size, and dilatation of the inferior vena cava (Nath et al. 2004). There is, regrettably, a paucity of survival data on patients who have undergone tricuspid valve (TV) surgery. The survival outcome after TV surgery is undoubtedly related to underlying cardiac disease and it might be related to the surgical technique. Ishan and colleagues reported 10- and 15-years survival rates of 37% and 30%, respectively, among 42 patients who underwent tricuspid valve replacement (TVR) for rheumatic disease (64%), Ebstein's anomaly (31%) or endocarditis (5%). They found that an elevated pulmonary artery pressure and a rheumatic etiology affected the long-term results unfavorably (Ishan et al. 2007). Ratnatunga and co-workers reported no survival difference between patients who had received a biological or a mechanical tricuspid valve: the 1-, 5-, and 10-year survival rates were 71%, 62%, and 48% for biological- and 74%, 58%, and 34% for mechanical prostheses, respectively (Ratnatunga et al. 1998).

There is some evidence that tricuspid valve plasty (TVP) may have some advantages over TVR – when feasible – in terms of survival. Guenther and associates reported that the survival among 416 patients ten years after TVP was 48% and after TVR 37 % (Guenther et al. 2008). McCarthy and colleagues reported an 8-year survival of 50% among 790 patients who underwent TVP (McCarthy et al. 2004).

2.3. Risk calculations and risk factors for mortality

Comprehensive mortality risk factor analysis after cardiac surgery based on individual studies is challenging. Study populations are heterogeneous, clinical practices and surgical techniques vary, follow-up periods are variable, and, ultimately, there are mixed results and conclusions drawn from the individual studies. This explains why predicting the outcome and

risk of single patients is practically impossible. The most feasible approach to assess the risk of operative mortality of cardiac surgery is to use validated risk scores calculators based on the large patient cohorts. The most common scoring systems are the European EuroSCORE, i.e., the European System for Cardiac Operative Risk Evaluation (Nashef et al. 1999 and 2002, Roques et al. 1999 and 2003, Pitkänen et al. 2000, EuroSCORE 2009) and the American STS risk calculator (Shroyer et al. 2003, STS 2009). EuroSCORE is based on risk factor analysis of 19,030 consecutive patients from 128 hospitals in eight European countries (Roques 1999), and the STS risk calculator refers to the Society of Thoracic Surgeons' National Cardiac Database (STS NCD; Shroyer et al. 2003, STS 2009). Both scoring systems predict the risk of operative mortality and morbidity related to cardiac surgery of adult patients based on patient demographics and a number of clinical variables. Although both systems have been shown to be a powerful and highly discriminatory risk predictor, there is evidence that as cardiac surgical outcomes have improved, both scoring systems tend to overestimate the actual risk (Ferguson et al. 2002, Karabulut et al. 2003, Osswald et al. 2009). This is especially true for valve surgery and high risk patients (Karabulut et al. 2003, Osswald et al. 2009), although EuroSCORE has also shown to be useful predictor of immediate and late outcome after mitral valve surgery (Heikkinen et al. 2007). However, more recent data suggest that STS risk calculator is more reliable in these situations than the EuroSCORE (Dewey et al. 2008). Van Gameren and associates have suggested that it might be reasonable to separate the risk stratification models for heart valve surgery and coronary artery surgery or a combination of these (van Gameren 2008).

In 2009, the STS working group (STS Quality Measurement Task Force) published three separate papers on the risk factors for mortality of patients who had undergone either CABG, isolated valve surgery or combined valve surgery and CABG (O'Brien et al. 2009, Shahian et al. 2009a, Shahian et al 2009b). These reports are based on cumulative information in the STS database that includes 774,881 isolated CABG patients, 67,292 isolated aortic valve replacement (AVR) patients, 21,229 isolated MVR patients, 21,238 isolated MVP patients, and 101,661 CABG and/or AVR and/or MVR or MVP patients. A summary of the relevant odds ratios and their 95% confidence intervals is shown in Table 1.

2.4. Incidence and morbidity risk factors

Cardiac surgery-related morbidity is closely associated to the patient's underlying medical condition. Stamou and associates reviewed 2,221 patients who had undergone either isolated

CABG, valve surgery or a combination of these. The postoperative morbidity figures for stroke was 2%, sepsis 3%, renal failure 7%, atrial fibrillation 29%, hemodialysis 2%, hemorrhage-related re-exploration 6%, blood transfusion 40%, cardiac tamponade 1%, mediastinitis 1%, re-admission to intensive care unit 8%, prolonged stay in hospital over nine days 22%, and prolonged intubation over 24 hours 11% (Stamou et al. 2008). Ruel and colleagues found in a study of 3,189 patients that approximately 20% of all patients with valve prostheses experience an embolic stroke within 15 years after valve replacement. Significant risk factors for late embolic stroke were female sex, age older than 75 years, left ventricular dysfunction, history of smoking or current smoking, and mechanical mitral prosthesis (Ruel et al. 2004).

In 2009, the STS working group (STS Quality Measurement Task Force) published three papers from the same patient cohorts and reported the risk factors for morbidity among patients who had undergone either CABG, isolated valve surgery or combined valve surgery and CABG (O'Brien et al. 2009, Shahian et al. 2009a, Shahian et al. 2009b). There were eight endpoints: cerebrovascular accident or stroke, renal failure, prolonged ventilation, deep sternal wound infection, reoperation, composite adverse outcome, prolonged duration of stay, and short duration of stay. Tables 2 and 3 show the odds ratios for morbidity outcomes related to cerebrovascular, renal, pulmonary, and infection endpoints, reoperations, and prolonged duration of stay after isolated CABG, isolated valve or combination procedures.

Table 1. Estimated odds ratios and 95% confidence intervals related to mortality after CABG, isolated valve surgery and combination procedures[a].

	Isolated CABG	Isolated AVR	Isolated MVR	Isolated MVP	CABG + AVR	CABG + MVR	CABG + MVP
Age 60 vs. 50 years	1.36 (1.24-1.49)	1.43 (1.34-1.52)	1.65 (1.53-1.78)	1.80 (1.62-2.00)	1.29 (1.20-1.39)	1.51 (1.39-1.64)	1.46 (1.36-1.57)
Age 70 vs. 50 years	2.53 (2.31-2.76)	2.04 (1.79-2.32)	2.71 (2.33-3.17)	3.24 (2.63-4.00)	1.67 (1.45-1.92)	2.28 (1.94-2.68)	2.14 (1.86-2.46)
Age 80 vs. 50 years	4.70 (4.29-5.15)	3.34 (2.84-3.93)	5.14 (4.15-6.37)	6.72 (5.00-9.04)	2.47 (2.08-2.94)	3.95 (3.17-4.93)	3.60 (2.97-4.33)
Creatinine 1.5 vs. 1.0 mg/dl	1.66 (1.57-1.76)	NA	NA	NA	NA	NA	NA
Creatinine 2.0 vs. 1.0 mg/dl	1.94 (1.84-2.04)	NA	NA	NA	NA	NA	NA
Creatinine 2.5 vs. 1.0 mg/dl	2.26 (2.14-2.39)	NA	NA	NA	NA	NA	NA
Dialysis vs. no dialysis	3.84 (3.54-4.16)	2.85 (2.53-3.45)	4.59 (3.65-5.77)	6.24 (4.19-9.30)	3.20 (2.84-3.61)	3.20 (2.84-3.61)	3.20 (2.84-3.61)
EF per 10-unit decrease	1.19 (1.17-1.22)	NA	NA	NA	1.10 (1.06-1.15)	1.23 (1.16-1.30)	1.09 (1.04-1.15)
Preoperative atrial fibrillation	1.36 (1.28-1.44)	NA	NA	NA	NA	NA	NA
CHF not NYHA IV	1.21 (1.15-1.28)	1.29 (1.18-1.42)	1.29 (1.18-1.42)	1.29 (1.18-1.42)	1.24 (1.14-1.34)	0.91 (0.80-1.03)	0.96 (0.85-1.09)
CHF NYHA IV	1.39 (1.31-1.47)	1.83 (1.62-2.07)	1.83 (1.62-2.07)	1.83 (1.62-2.07)	1.48 (1.34-1.64)	1.09 (0.95-1.24)	1.16 (1.02-1.32)
Chronic lung disease (mild)	1.22 (1.16-1.29)	NA	NA	NA	NA	NA	NA
Chronic lung disease (moderate)	1.40 (1.32-1.49)	1.27 (1.21-1.33)	1.08 (1.01-1.16)	1.23 (1.09-1.43)	1.19 (1.16-1.23)	1.19 (1.16-1.23)	1.19 (1.16-1.23)
Chronic lung disease (severe)	2.35 (2.19-2.52)	1.27 (1.21-1.33)	1.08 (1.01-1.16)	1.23 (1.09-1.43)	1.19 (1.16-1.23)	1.19 (1.16-1.23)	1.19 (1.16-1.23)
CVD with CVA	1.31 (1.24-1.38)	NA	NA	NA	NA	NA	NA
CVD without CVA	1.14 (1.08-1.20)	NA	NA	NA	NA	NA	NA
Diabetes, insulin	1.30 (1.24-1.37)	1.62 (1.43-1.83)	1.62 (1.43-1.83)	1.62 (1.43-1.83)	NA	NA	NA
Diabetes, not insulin	1.01 (0.97-1.06)	1.27 (1.15-1.39)	1.27 (1.15-1.39)	1.27 (1.15-1.39)	NA	NA	NA
Diseased vessels (2 vs. 1, or 3 vs. 2)	1.17 (1.12-1.23)	NA	NA	NA	NA	NA	NA
Preoperative IABP / inotropes	1.41 (1.33-1.49)	1.47 (1.26-1.71)	1.47 (1.26-1.71)	1.47 (1.26-1.71)	1.43 (1.30-1.58)	1.43 (1.30-1.58)	1.43 (1.30-1.58)
Shock	2.29 (2.12-2.47)	1.62 (1.29-2.03)	1.62 (1.29-2.03)	1.62 (1.29-2.03)	1.68 (1.45-1.94)	1.68 (1.45-1.94)	1.68 (1.45-1.94)
Female vs. male	1.31 (1.25-1.36)	1.23 (1.10-1.36)	1.11 (0.97-1.27)	0.97 (0.77-1.21)	1.36 (1.26-1.47)	1.36 (1.26-1.47)	1.36 (1.26-1.47)
Active infectious endocarditis	NA	NA	NA	NA	2.04 (1.66-2.50)	2.04 (1.66-2.50)	2.04 (1.66-2.50)
Mitral insufficiency, moderate/severe	1.31 (1.21-1.41)	NA	NA	NA	NA	NA	NA
PCI ≤6 hours	1.37 (1.24-1.50)	NA	NA	NA	NA	NA	NA
Peripheral vascular disease	1.42 (1.36-1.48)	NA	NA	NA	NA	NA	NA
MI 1-21 days	1.37 (1.32-1.44)	NA	NA	NA	NA	NA	NA
MI >6 hours and <24 hours	1.59 (1.46-1.74)	NA	NA	NA	NA	NA	NA
MI ≤6 hours	1.70 (1.53-1.89)	NA	NA	NA	NA	NA	NA
Reoperation, 1 previous operation	3.13 (2.74-3.57)	2.11 (1.99-3.08)	2.11 (1.78-2.49)	2.11 (1.78-2.49)	2.20 (1.81-2.67)	2.20 (1.87-2.67)	2.20 (1.87-2.67)
Reoperation, ≥2 previous operation	4.19 (3.45-5.09)	2.48 (1.99-3.08)	2.48 (1.99-3.08)	2.48 (1.99-3.08)	2.46 (1.87-3.24)	2.46 (1.87-3.24)	2.46 (1.87-3.24)
Status urgent	1.16 (1.10-1.22)	NA	NA	NA	NA	NA	NA
Status emergent, no resuscitation	2.83 (2.52-3.18)	3.77 (2.75-5.16)	2.74 (1.99-3.78)	8.73 (4.84-15.74)	2.14 (1.62-2.81)	2.14 (1.62-2.81)	2.14 (1.62-2.81)
Status emergent, resuscitation	8.00 (6.91-9.29)	7.94 (5.40-11.66)	5.78 (3.77-8.85)	18.39 (9.68-34.96)	4.56 (3.31-6.29)	4.56 (3.31-6.29)	4.56 (3.31-6.29)
Unstable angina	1.12 (1.07-1.17)	NA	NA	NA	NA	NA	NA

[a]Modified from the three articles published in the Annals of Thoracic Surgery 2009;88:S2-S62. CHF = congestive heart failure, CVA = cerebrovascular accident, CVD = cerebrovascular disease, EF = ejection fraction, IABP = intra-aortic balloon pump, MI = myocardial infarction, NA = not applicable, NYHA = New York Heart Association, PCI = percutaneous coronary intervention.

Table 2. Estimated odds ratios related to morbidity after CABG, isolated valve surgery and combination procedures[a].

	Isolated CABG *CVA/RF/Vent*	**Isolated AVR** *CVA/RF/Vent*	**Isolated MVR** *CVA/RF/Vent*	**Isolated MVP** *CVA/RF/Vent*	**CABG + AVR** *CVA/RF/Vent*	**CABG + MVR** *CVA/RF/Vent*	**CABG + MVP** *CVA/RF/Vent*
Age 60 vs. 50 years	1.78 / 1.24 /1.06	1.48 / 1.38 / 1.31	1.48 / 1.35 / 1.31	1.48 / 1.55 / 1.31	1.28 / 1.39 / 1.23	1.28 / 1.39 / 1.23	1.28 / 1.39 / 1.23
Age 70 vs. 50 years	2.43 / 1.93 / 1.42	2.19 / 1.90 / 1.71	2.19 / 1.81 / 1.71	2.19 / 2.42 / 1.71	1.64 / 1.92 / 1.52	1.64 / 1.92 / 1.52	1.64 / 1.92 / 1.52
Age 80 vs. 50 years	3.34 / 3.01 / 1.90	3.21 / 2.88 / 2.31	3.21 / 2.67 / 2.31	3.21 / 4.11 / 2.31	2.03 / 2.76 / 1.96	2.03 / 2.76 / 1.96	2.03 / 2.76 / 1.96
Dialysis vs. no dialysis	1.67 / NA / 2.85	1.65 / NA / 3.07	1.65 / NA / 3.07	1.65 / NA / 3.07	1.42 / NA / 2.27	1.42 / NA / 2.27	1.42 / NA / 2.27
EF per 10-unit decrease	1.14 / 1.08 / 1.18	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / 1.06 / 1.12	NA / 1.06 / 1.12	NA / 1.06 / 1.12
Preoperative atrial fibrillation	1.21 / 1.24 / 1.20	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
CHF not NYHA IV	NA / 1.36 / 1.31	NA / 1.24 / 1.33	NA / 1.24 / 1.19	NA / 1.24 / 1.16	0.98 / 1.19 / 1.22	0.80 / 0.92 / 1.02	1.05 / 0.99 / 1.10
CHF NYHA IV	NA / 1.35 / 1.52	NA / 1.61 / 1.92	NA / 1.61 / 1.72	NA / 1.61 / 1.67	1.15 / 1.35 / 1.47	0.93 / 1.04 / 1.22	1.23 / 1.12 / 1.32
Chronic lung disease (mild)	NA / 1.14 / 1.36	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Chronic lung disease (moderate)	NA / 1.25 / 1.65	NA / 1.18 / 1.26	NA / 1.18 / 1.26	NA / 1.18 / 1.26	NA / 1.12 / 1.26	NA / 1.12 / 1.18	NA / 1.12 / 1.21
Chronic lung disease (severe)	NA / 1.66 / 2.37	NA / 1.18 / 1.26	NA / 1.18 / 1.26	NA / 1.18 / 1.26	NA / 1.12 / 1.26	NA / 1.12 / 1.18	NA / 1.12 / 1.21
CVD with CVA	2.09 / 1.18 / 1.35	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
CVD without CVA	1.65 / 1.11 / 1.15	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Diabetes, insulin	1.19 / 1.80 / 1.22	NA / NA / NA	NA / 1.91 / 1.66	NA / 1.91 / 1.68	NA / NA / NA	NA / NA / NA	NA / NA / NA
Diabetes, not insulin	1.16 / 1.32 / 1.04	NA / NA / NA	NA / 1.45 / 1.30	NA / 1.45 / 1.31	NA / NA / NA	NA / NA / NA	NA / NA / NA
Diseased vessels (2 vs. 1, or 3 vs. 2)	1.35 / 1.23 / 1.19	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Preoperative IABP / inotropes	NA / 1.43 / 2.56	NA / 1.34 / 1.78	NA / 1.34 / 2.21	NA / 1.34 / 2.90	NA / 1.27 / 2.18	NA / 1.27 / 2.18	NA / 1.27 / 2.18
Shock	1.38 / 1.65 / 2.08	1.65 / NA / 2.09	1.65 / NA / 2.09	1.65 / NA / 2.09	1.19 / 1.17 / 1.93	1.19 / 1.21 / 1.93	1.19 / 1.69 / 1.93
Female vs. male	1.32 / 1.25 / 1.33	1.25 / 0.97 / 1.29	1.25 / 0.97 / 1.06	1.25 / 0.97 / 1.23	1.19 / 1.18 / 1.52	1.19 / 1.18 / 1.17	1.19 / 1.18 / 1.25
Active infectious endocarditis	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	1.83 / 1.52 / 1.96	1.83 / 1.52 / 1.96	1.83 / 1.52 / 1.96
Mitral insufficiency, moderate/severe	NA / NA / 1.12	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
PCI ≤6 hours	NA / 1.29 / 1.21	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Peripheral vascular disease	1.32 / 1.21 / 1.22	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
MI 1-21 days	1.31 / 1.27 / 1.34	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
MI >6 hours and <24 hours	1.59 / 1.48 / 1.59	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
MI ≤6 hours	1.49 / 1.43 /1.56	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Reoperation, 1 previous operation	NA / 1.52 / 1.72	2.09 / 1.55 / 1.83	2.09 / 1.55 / 1.50	2.09 / 1.55 / 2.06	NA / 1.29 / 1.83	NA / 1.29 / 1.38	NA / 1.29 / 1.55
Reoperation, ≥2 previous operation	NA / 1.58 / 1.86	2.36 / 1.66 / 2.49	2.36 / 1.66 / 2.03	2.36 / 1.66 / 2.80	NA / 1.47 / 2.19	NA / 1.47 / 1.66	NA / 1.47 / 1.86
Status urgent	1.11 / 1.12 / 1.24	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Status emergent, no resuscitation	2.12 / 1.68 / 2.14	2.78 / 3.10 / 4.54	2.78 / 2.20 / 3.19	2.78 / 3.03 / 6.12	2.21 / 1.77 / 2.71	2.21 / 1.77 / 2.71	2.21 / 1.77 / 2.71
Status emergent, resuscitation	2.51 / 2.16 / 3.01	2.11 / 3.47 / 3.50	2.11 / 2.46 / 2.46	2.11 / 3.39 / 4.72	2.60 / 1.86 / 2.12	2.60 / 1.86 / 2.12	2.60 / 1.86 / 2.12
Unstable angina	NA / 1.11 / 1.05	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA

[a]Modified from the three articles published in the Annals of Thoracic Surgery 2009;88:S2-S62. CHF = congestive heart failure, CVA = cerebrovascular accident, CVD = cerebrovascular disease, EF = ejection fraction, IABP = intra-aortic balloon pump, MI = myocardial infarction, NA = not applicable, NYHA = New York Heart Association, PCI = percutaneous coronary intervention, RF = renal failure, Vent = prolonged ventilation.

Table 3. Estimated odds ratios related to morbidity after CABG, isolated valve surgery and combination procedures[a].

	Isolated CABG *DSWI/Re/PLOS*	**Isolated AVR** *DSWI/Re/PLOS*	**Isolated MVR** *DSWI/Re/PLOS*	**Isolated MVP** *DSWI/Re/PLOS*	**CABG + AVR** *DSWI/Re/PLOS*	**CABG + MVR** *DSWI/Re/PLOS*	**CABG + MVP** *DSWI/Re/PLOS*
Age 60 vs. 50 years	1.43 / 1.14 / 1.35	1.52 / 1.16 / 1.31	1.52 / 1.25 / 1.26	1.52 / 1.20 / 1.50	1.06 / 1.19 / 1.37	1.06 / 1.19 / 1.37	1.06 / 1.19 / 1.37
Age 70 vs. 50 years	1.70 / 1.45 / 2.17	2.31 / 1.35 / 1.71	2.31 / 1.56 / 1.60	2.31 / 1.44 / 2.25	1.11 / 1.41 / 1.86	1.11 / 1.41 / 1.86	1.11 / 1.41 / 1.86
Age 80 vs. 50 years	2.02 / 1.85 / 3.48	2.73 / 1.59 / 2.50	2.73 / 1.97 / 2.27	2.73 / 1.75 / 3.78	1.12 / 1.67 / 2.67	1.12 / 1.67 / 2.67	1.12 / 1.67 / 2.67
Dialysis vs. no dialysis	2.13 / 1.86 / 2.80	NA / 1.79 / 2.94	NA / 1.79 / 2.94	NA / 1.79 / 2.94	NA / 1.65 / 2.42	NA / 1.21 / 2.42	NA / 1.88 / 2.42
EF per 10-unit decrease	1.11 / 1.11 / 1.17	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / 1.08 / 1.10	NA / 1.08 / 1.10	NA / 1.08 / 1.10
Preoperative atrial fibrillation	NA / 1.26 / 1.42	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
CHF not NYHA IV	1.33 / 1.16 / 1.43	NA / NA / 1.25	NA / NA / 1.25	NA / NA / 1.25	NA / NA / 1.30	NA / NA / 1.03	NA / NA / 1.17
CHF NYHA IV	1.45 / 1.26 / 1.50	NA / 1.25 / 1.54	NA / 1.25 / 1.54	NA / 1.25 / 1.54	NA / 1.16 / 1.49	NA / 1.16 / 1.17	NA / 1.16 / 1.33
Chronic lung disease (mild)	1.56 / 1.11 / 1.34	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Chronic lung disease (moderate)	1.80 / 1.20 / 1.65	1.27 / 1.09 / 1.29	1.27 / 1.09 / 1.16	1.27 / 1.09 / 1.26	1.32 / 1.10 / 1.26	1.32 / 1.10 / 1.20	1.32 / 1.10 / 1.16
Chronic lung disease (severe)	2.40 / 1.54 / 2.46	1.27 / 1.09 / 1.29	1.27 / 1.09 / 1.16	1.27 / 1.09 / 1.26	1.32 / 1.10 / 1.26	1.32 / 1.10 / 1.20	1.32 / 1.10 / 1.16
CVD with CVA	NA / 1.21 / 1.45	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
CVD without CVA	NA / 1.12 / 1.14	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Diabetes, insulin	2.24 / 1.14 / 1.59	1.56 / 1.20 / 1.68	1.56 / 1.20 / 1.68	1.56 / 1.20 / 1.68	NA / NA / NA	NA / NA / NA	NA / NA / NA
Diabetes, not insulin	1.38 / 0.98 / 1.15	NA / NA / 1.22	NA / NA / 1.22	NA / NA / 1.22	NA / NA / NA	NA / NA / NA	NA / NA / NA
Diseased vessels (2 vs. 1, or 3 vs. 2)	1.15 / 1.07 / 1.15	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Preoperative IABP / inotropes	NA / 1.37 / 1.60	1.69 / 1.14 / 1.46	1.69 / 1.14 / 1.46	1.69 / 1.14 / 1.46	NA / 1.16 / 1.41	NA / 1.16 / 1.29	NA / 1.16 / 1.56
Shock	NA / 1.43 / 1.73	NA / 1.32 / 1.74	NA / 1.32 / 1.05	NA / 1.32 / 2.50	NA / 1.24 / 1.45	NA / 1.24 / 1.45	NA / 1.24 / 1.45
Female vs. male	1.19 / 0.90 / 1.24	0.98 / 0.86 / 1.25	0.98 / 0.79 / 1.09	0.98 / 0.90 / 1.28	1.11 / 0.92 / 1.31	1.11 / 0.92 / 1.31	1.11 / 0.92 / 1.31
Active infectious endocarditis	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / 1.56 / 1.81	NA / 1.56 / 2.08	NA / 1.56 / 2.98
Mitral insufficiency, moderate/severe	NA / 1.24 / 1.15	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
PCI ≤6 hours	NA / 1.30 / 1.17	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Peripheral vascular disease	1.36 / 1.24 / 1.31	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
MI 1-21 days	NA / NA / 1.22	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
MI >6 hours and <24 hours	NA / NA / 1.31	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
MI ≤6 hours	NA / NA / 1.30	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Reoperation, 1 previous operation	NA / 1.57 / 1.62	NA / 1.31 / 1.42	NA / 1.31 / 1.42	NA / 1.31 / 1.42	NA / 1.39 / 1.55	NA / 1.15 / 1.30	NA / 1.49 / 1.32
Reoperation, ≥2 previous operation	NA / 1.71 / 1.79	NA / 1.41 / 1.76	NA / 1.41 / 1.76	NA / 1.41 / 1.76	NA / 1.48 / 1.65	NA / 1.22 / 1.38	NA / 1.59 / 1.41
Status urgent	1.20 / 1.18 / 1.20	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA
Status emergent, no resuscitation	1.87 / 1.83 / 2.12	NA / 1.63 / 2.45	NA / 1.63 / 2.45	NA / 1.63 / 2.45	NA / 1.41 / 2.72	NA / 1.41 / 2.72	NA / 1.41 / 2.72
Status emergent, resuscitation	2.09 / 2.34 / 2.39	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / 1.76	NA / NA / 1.76	NA / NA / 1.76
Unstable angina	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA	NA / NA / NA

[a]Modified from the three articles published in the Annals of Thoracic Surgery 2009;88:S2-S62. CHF = congestive heart failure, CVA = cerebrovascular accident, CVD = cerebrovascular disease, DSWI = deep sternal wound infection, EF = ejection fraction, IABP = intra-aortic balloon pump, MI = myocardial infarction, NA = not applicable, NYHA = New York Heart Association, PCI = percutaneous coronary intervention, PLOS = prolonged length of stay, Re = reoperation.

2.5. HRQoL after cardiac surgery

In 1948, The World Health Organization (WHO) defined health as being not only the absence of disease and infirmity but also the presence of physical, mental, and social well-being (Constitution of the World Health Organization 1952). The term quality of life (QoL) and, more specifically, health-related quality of life (HRQoL) refers to physical, psychological, and social domains of health, seen as distinct domains that are influenced by a person's experience, beliefs, expectations, and perceptions (Brook et al. 1983, Testa and Simonson 1996). For clarity, the term HRQoL has been used through this study. An assessment of HRQoL has become increasingly important, both as a measure of risk assessment and as an outcome. Also, beyond subjective perception of the HRQoL, the impact of surgical intervention on HRQoL has become more relevant in today's health care practice where monetary measures do not readily apply. The growing fields of outcome research and health-technology assessment evaluate the efficacy, cost effectiveness, and net benefit of new therapeutic strategies to determine whether the associated increases in expenditures for health care are justified (Thier 1992, Taskinen et al. 2008).

Tools available for assessment of HRQoL require a shift in thinking from only exact mortality, morbidity, and survival figures to probabilities. In general, reports after cardiac surgical interventions show that HRQoL has improved or is at least equal to the matched reference population for most cardiac surgical patients (Sjöland et al. 1999, Rumsfeld et al. 2001, Järvinen et al. 2003, Maliwa et al. 2003, Welke et al. 2003, Koch et al. 2007). The greatest improvement in HRQoL occurs probably in patients with the worst preoperative, cardiac-symptoms related HRQoL, whereas patients with a relatively good HRQoL benefit little (Rumsfeld et al. 2001). Several investigators have reported that markedly impaired HRQoL preoperatively is associated with higher mortality (Rumsfeld et al. 1999, Curtis et al. 2002, Koch et al. 2007). Rumsfeld and co-workers reported that among 2,480 patients who underwent CABG the physical component of the SF-36 score was an independent risk factor for six months mortality. The risk for mortality was 1.39 times higher in patients who had a 10-point lower preoperative score in the physical well-being domain compared to patients with a normal value. In contrast, the baseline mental component summary score did not predict mortality (Rumsfeld et al. 1999). Similar findings were published by Ho and colleagues, who found that the preoperative physical and mental health status were independent predictors of mortality after cardiac surgery in patients 65 years or older but not in younger patients. A score 10 points below the healthy average in the domains of physical and mental well-being at baseline

increased the relative risk of postoperative mortality by 51% and 28%, respectively (Ho et al. 2005). Koch and associates examined the survival of 6,305 patients who underwent either CABG or a valve procedure or a combination of these. They found that a poor HRQoL after recovery from cardiac surgery identifies patients who are at risk for reduced long-term survival (Koch et al. 2007). Similarly, Curtis and colleagues reported that poor preoperative HRQoL is related to increased in-hospital mortality and prolonged hospital stay after CABG (Curtis et al. 2002). On the other hand, prolonged stay in intensive care unit over eight days after primary heart valve surgery has been associated with reduced HRQoL in terms of physical and mental health still five years after surgery (Hellgren and Ståhle 2005).

The impact of cardiac surgical techniques on HRQoL can be studied if there are two or more technical options to treat a certain heart condition. Two recent articles reported that MVP might be better than MVR in terms of HRQoL (Goldsmith et al. 2001, Sedrakyan et al. 2006). Immer and co-workers were not able to corroborate this finding in their study of 115 consecutive mitral valve patients; they found that the mid-term outcome in terms of survival and HRQoL was similar in the two groups (Immer et al. 2003). However, the HRQoL among long-term survivors after MVP have shown to be comparable to that of an age- and sex-matched general population. Heikkinen and colleagues investigated the HRQoL of 109 patients who had undergone MVP due to degenerative or ischemic mitral valve regurgitation, and found no significant differences in terms of HRQoL between MVP-operated patients and an age- and sex-adjusted Finnish general population (Heikkinen et al. 2005a).

Identification and assessment of the predictors that contribute to the patient's postoperative HRQoL would be most useful for preoperative patient counseling and even patient selection. The anticipated HRQoL after surgery can provide valuable information for discharge planning (Elliot et al. 2006) and rehabilitation (Engblom et al. 1992, 1994 and 1997). A number of investigators have reported several circumstances that predict the postoperative HRQoL. Rumsfeld and colleagues analyzed risk factors related to impaired HRQoL after CABG among 1,973 male patients six months after operation. Factors that predicted a low postoperative score for the physical dimensions were: peripheral vascular disease, chronic obstructive pulmonary disease, hypertension, smoking, low left ventricular ejection fraction, and a history of neurological disease (Rumsfeld et al. 2004). Welke and associates identified diabetes, chronic obstructive pulmonary disease, peripheral vascular disease, obesity, and physical function at baseline as risk factors for impaired HRQoL after CABG (Welke 2003). In the case of mitral

surgery, high age, high preoperative and postoperative NYHA-class, a need for nitroglycerin and diuretics correlate with impaired HRQoL (Chocron et al. 1996).

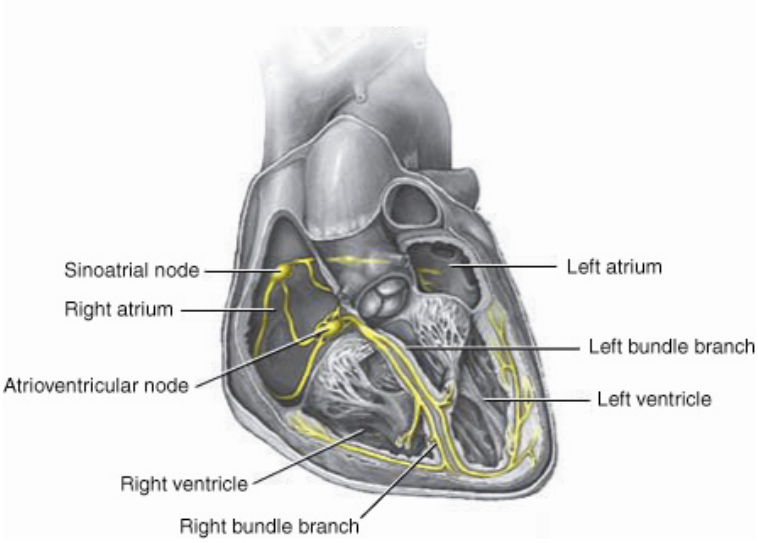
The relation between age and HRQoL has been investigated by Järvinen et al. (2003) and Loponen et al. (2007). During short-term follow-up, elderly patients derived less benefit in terms of HRQoL from cardiac surgery than younger patients. Järvinen and co-workers studied 508 patients who had undergone CABG and reported that patients aged >75 years had higher mortality and morbidity and a poorer HRQoL compared with younger patients. Age is a risk factor for reduced postoperative HRQoL after mitral valve surgery (Chocron et al. 1996).

The results regarding the association between TV surgery and HRQoL in adult cardiac surgery are very limited. Do and colleagues reviewed data regarding 454 patients who had undergone either TVR of TVP during the years 1978 and 1998. Although HRQoL was not specifically addressed, the authors concluded that most of the survivors after TV surgery could expect an improvement in their HRQoL as their NYHA-class declined (Do et al. 2000).

2.6. Conduction abnormalities

The conduction system of the heart is susceptible to reversible and irreversible damage at the time of cardiac surgery. The consequences are conduction abnormalities which are categorized as AV-blocks, bundle branch blocks, and hemiblocks. The course of the conduction system is shown in Figure 1.

Figure 1. Conduction system of the heart. Copyright 2009 ADAM Inc., Atlanta, Georgia, U.S. Figure is freely available from Medline Plus, a service of the U.S. National Library of Medicine and the National Institutes of Health: http://www.nlm.nih.gov/medlineplus/ency/imagepages/18052.htm



2.6.1. AV-blocks

AV-blocks are classified as first degree (1st degree), second degree (2nd degree), and third degree (3rd degree) AV-blocks.

The 1st degree AV-block is characterized by a prolonged delay in conduction at the AV-node or bundle of His. Corresponding ECG finding is a PR interval longer than 200 ms. In 1st degree AV-block every atrial impulse passes through the AV-node to the ventricles, and therefore, 1st degree AV-block is rather a delay than an actual block in the conduction system.

In 2nd degree AV-block, all atrial impulses do not pass through the AV-node resulting in more P waves than QRS complexes on the ECG. 2nd degree AV-blocks are subdivided into Mobitz I (Wenckebach block) and Mobitz II blocks. In Mobitz I the AV delay increases successively until one atrial impulse fails to reach the ventricle. A progressive lengthening of the PR-interval is seen on the ECG until a QRS complex is dropped. In Mobitz I, the AV-block usually resides in the AV-node. In the Mobitz II block, occasional atrial impulses are not conducted to the ventricles and there is no preceding progressive lengthening of the PR-interval. In Mobitz II, the block is usually located below the AV-node at the level of His-Purkinje system. A Mobitz I block can be a normal finding in healthy subjects caused by a high vagal tone, while the Mobitz II block is not dependent on autonomic tone and is usually considered to be pathological.

In 3rd degree AV-block (complete heart block) the atrial impulses are not conducted to the ventricles at all. The site of the block can be either at the level of AV-node or further down at the level of the His bundle. The lack of impulses from the atria leads to a ventricular escape rhythm that usually is 30-45 beats / minute.

2.6.2. Bundle branch blocks

Bundle branch blocks refer to abnormal conduction in either the left or right bundle branches (LBBB or RBBB) distal to the bundle of His. Both LBBB and RBBB cause typical findings in the ECG. In LBBB, left ventricular depolarization is delayed which results in wide QRS complexes (duration over 120 ms). Similarly, in RBBB, delay in right ventricle depolarization widens the QRS complex beyond 120 ms and, it too, has an easily identifiable form.

2.6.3. Hemiblocks

Hemiblock refers to a conduction block of one of the three separate fascicles of the left bundle branch. A block in the septal fascicle has little clinical relevance, whereas blocks in left

anterior (LAHB) and left posterior (LPHB) fascicles are clinically more important. The diagnosis of the hemiblocks is based on left or right deviation of the frontal QRS axis in combination with minor criteria.

2.7. Pacemaker therapy

The symptoms caused by conduction abnormalities (or bradycardia) after cardiac surgery are generally due low cardiac output or a transient loss of cerebral perfusion. The manifestations include fatigue, dyspnea, low exercise tolerance, dizziness, pulmonary congestion, presyncope, or syncope. The indications for implantation of a PM in adults have been published by the Task Force of the American College of Cardiology and American Heart Association (Gregoratos et al. 2002ab) and the Task Force of the European Society of Cardiology and the European Heart Rhythm Association in 2007 (Vardas et al. 2007). After cardiac surgery, the indications for PM are usually 3rd degree AV-block, symptomatic or significant sinus node dysfunction, slow ventricular rate during atrial fibrillation, tachycardia-bradycardia syndrome (fast atrial fibrillation alternating with slow sinus rhythm), and advanced 2nd degree AV-block with a slow ventricular response. The optimal time of implantation of a PM is difficult to determine because occasionally the need is transient. Since implantation of a PM carries a low complication rate, the greatest benefit of a PM is achieved if it is implanted about 4-5 days after surgery (Glikson et al. 1997).

2.8. Need for PM after cardiac surgery

A temporary need for pacing is very common immediately after cardiac surgery. Most patients with normal sinus rhythm before the operation will regain it within a few days after the operation (Glikson et al. 1997, Gordon et al. 1998).

The proportion of patients needing a PM after cardiac surgery ranges reportedly from 0.4% to as high as 28%. The incidence is related to the type of surgery; it is below 1% after CABG and 3%-6% after valve surgery (Gordon et al. 1998, Koplan et al. 2003, Limongelli et al. 2003, Dawkins et al. 2008, Onalan et al. 2008). Several studies have sought predictive factors for PM after cardiac surgery, and found that TV surgery unequivocally carries the highest risk for PM implantation compared with coronary, aortic, mitral, or multiple valve surgery (Koplan et al. 2003). Other predictors for PM include preoperative conduction abnormalities, re-operative surgery, type of cardioplegia, renal failure, endocarditis, prolonged aortic cross-clamp time, electrolyte imbalance, high age, female sex, previous MIs, left main coronary artery stenosis,

long-standing hypertension, preoperative digitalis treatment, and low myocardial temperature during surgery (Baerman et al. 1987, Caspi et al. 1987, Caretta et al. 1991, Salerno et al. 1991, Mustonen et al. 1995, Dawkins et al. 2008, Onalan et al. 2008).

Koplan and co-workers developed and validated a risk score calculator to predict the need for PM after valve surgery (Koplan et al. 2003). In their comprehensive series of 4,694 patients, they found that preoperative RBBB or LBBB, multivalve surgery (especially when including TV surgery), preoperative PR-interval >200 ms, prior valve surgery, and age over 70 years were the strongest independent predictors for the need of PM.

3. OBJECTIVES OF THE PRESENT STUDY

The purpose of this study was to do a comprehensive analysis of patient outcomes after cardiac surgery with regard to survival, mortality, morbidity, and HRQoL. The specific aims were:

1. To assess the effects of postoperative conduction abnormalities on long-term survival after primary CABG.

2. To analyze the differences between MVP and MVR on survival and HRQoL and to assess the risk factors for mortality and impaired HRQoL.

3. To investigate the long-term benefits of cardiac surgery on survival and HRQoL of octogenarians.

4. To study the impact of PM-requiring conduction abnormalities after TV surgery on long-term outcome in terms of survival, morbidity, and HRQoL.

4. PATIENTS AND METHODS

4.1. Study setting and patient population (I-IV)

This study is a composition of four single center registry studies carried out at the Department of Surgery at the Kuopio University Hospital. The study was approved by the Ethics Committee of the Kuopio University Hospital and written informed consent was obtained from all patients.

The departments of Surgery and Anesthesiology at the Kuopio University Hospital have since 1992 maintained prospectively a register of patients referred for cardiac surgery. This database includes comprehensive clinical data of all cardiac surgical patients operated at the Kuopio University Hospital in terms of demographics, underlying or contributing cardiac conditions, co-morbidities, and medication. In addition, factors related to cardiac surgery and perioperative or postoperative complications until discharge from the hospital have been recorded. To verify long-term survival and authentic causes of deaths, all patients were traced with respect to mortality data from the continuously updated National Cause of Death Register during the closing intervals of each study. The HRQoL was investigated cross-sectionally in Studies **II** and **IV**, and longitudinally in Study **III** by using the Nottingham Health Profile (NHP) HRQoL questionnaire. Comparisons regarding HRQoL were made between the appropriate study groups and age- and sex-matched Finnish reference population. Altogether 604 patients were included in this study.

I. The first patient cohort consisted of 180 consecutive, electively operated patients who underwent isolated CABG between June 1990 and March 1991, 63 of whom (35%) developed a new permanent CD during the CABG. Patients who underwent emergency operation or re-operation, and patients with any CD confirmed by preoperative ECG analysis were excluded.

II. The second patient cohort consisted of 184 consecutive patients who underwent primary MVP (n=85) or MVR (n=99) for mitral regurgitation between January 1992 and December 1996. Of these, 113 (61%) underwent concomitantly CABG (72% in the MVP group, and 53% in the MVR group, respectively). Exclusion criteria were mitral stenosis, aortic or tricuspid valve surgery, previous valve repair or replacement, or congenital heart disease.

III. The third patient cohort consisted of 104 consecutive patients who were older than 70 years at the time of primary cardiac surgery in 1993. Of these, 60 patients (58%) underwent CABG, 12 patients (11%) valve surgery, and 32 patients (31%) combined CABG and a valve procedure.

IV. The fourth patient cohort consisted of 136 consecutive patients who underwent either TVP or TVR between January 1992 and September 2007. Twenty-five patients (18%) had only TV surgery, 91 patients (67%) had double valve surgery, and 20 patients (15%) had triple valve surgery. CABG was performed concomitantly in 37 (27%) cases.

Patient data of Studies **I**, **II**, **III**, and **IV** are summarized in Table 4.

Table 4. Demographic and clinical data of patients (Studies **I**, **II**, **III**, and **IV)**.

Characteristic	**Study I (n=180)**	**Study II (n=184)**	**Study III (n=104)**	**Study IV (n=136)**
Sex				
male	148 (82)	126 (68)	50 (48)	54 (40)
female	32 (18)	58 (32)	54 (52)	82 (60)
Age at operation (years)	55.7 ± 8.6	61.8 ± 9.3	72.9 ± 2.9	65.0 ± 11
BMI (kg/m^2)	-	26.4 ± 3.2	-	25.5 ± 3.7
NYHA-class				
I	-	1 (1)	1 (1)	1 (1)
II	-	42 (23)	9 (9)	22 (16)
III	-	91 (49)	30 (29)	89 (65)
IV	-	50 (27)	64 (62)	24 (18)
Previous MI	119 (66)	60 (33)	54 (52)	15 (11)
1 or 2-vessel disease	-	-	-	18 (13)
3-vessel disease	-	74 (40)	80 (77)	31 (23)
LMCAS	35 (19)	25 (14)	24 (23)	-
Unstable angina pectoris	58 (32)	-	51 (49)	7 (5)
Cardiac rhythm				
sinus rhythm	180 (100)	134 (73)	-	32 (24)
atrial fibrillation	-	49 (26)	-	104 (76)
pacemaker rhythm	-	1 (1)	-	-
Preoperative CD				
RBBB	-	-	-	9 (7)
RBBB+LAHB/LPHB	-	-	-	2 (1)
LAHB	-	-	-	5 (4)
LBBB	-	-	-	6 (4)
Peripheral arterial disease	-	11 (6)	6 (6)	7 (5)
Cerebrovascular disorder	-	-	11 (11)	-
TIA	-	6 (3)	-	7 (5)
stroke	-	6 (3)	-	5 (4)
ICB	-	-	-	2 (1)
Severe renal failure	-	4 (2)[a]	26 (25)[a]	5 (4)[b]
Diabetes	23 (13)	24 (13)	21 (20)	14 (10)
Hyperlipidemia	-	-	39 (38)	62 (46)
Hypertension	127 (71)	-	44 (42)	72 (53)
Ejection fraction (%)	59 ± 11	58 ± 13	58 ± 16	54 ± 13
Pulmonary hypertension	-	-	-	26 (19)
Urgency of operation				
elective	180 (100)	135 (73)	40 (39)	105 (77)
urgent	-	35 (19)	55 (53)	22 (16)
emergency	-	14 (8)	9 (9)	9 (7)

Values denote number of patients (percentage) or mean ± standard deviation. BMI = body mass index; CD = conduction defect; ICB = intracerebral bleeding; LAHB = left anterior hemiblock; LBBB = left bundle branch block; LPHB = left posterior hemiblock; LMCAS = left main coronary artery stenosis; MI = myocardial infarction; NYHA = New York Heart Association; RBBB = right bundle branch block; TIA = transient ischemic attack; [a]Creatinine >105 μmol/l; [b]Glomerular filtration rate <29 $ml/kg/1.73m^2$.

4.2. Assessment of results of cardiac surgery

The outcomes after cardiac surgery may be divided into objectively measurable outcomes (by a clinician, researcher or statistician) and subjective outcomes (patient's subjective experience of the impact of the cardiac intervention on HRQoL).

Objective measures, i.e., survival and mortality, morbidity, complications, symptom recurrence, and need for re-interventions have long been used as the criteria of success of cardiac surgery. These variables are easily and reliably measured, they are easy to iterate and they are comparable regardless of the patients' cultural, social, or educational background. Albeit important, reporting only survival figures and the rate of complications are no longer the only acceptable benchmark in today's practice, because modern assessment of cardiac surgery needs to consider both objective and subjective outcome measures comprehensively.

Subjective measures, i.e., patient-related outcomes, have not been the primary focus for clinicians, maybe because HRQoL is a subjective and abstract outcome measure and because an objective comparison of HRQoL as an outcome is more tricky. Nevertheless, measuring HRQoL is gaining importance in surgical research because there is a growing societal interest in HRQoL after surgical intervention. Clinicians and researchers are also interested in additional measures to quantify the impact of specific interventions (Spertus et al. 2002, Rumsfeld 2003).

4.3. Reporting survival and mortality

Survival in medical research is defined as the fraction of patients living for a certain amount of time after a given treatment. Survival is closely associated with the underlying medical condition and its treatment. Actuarial and Kaplan-Meier survival analysis are two accepted methods to analyze survival information. An actuarial survival analysis is performed when the actual date of a survival event is not known. The known information is that the event has occurred between time *tn* and time *tn+1*. Actuarial analysis is carried out at specific time intervals, and the resulting graph will step only at those intervals.

The Kaplan-Meier method is used when the actual date of the end-point is known. End-points not reached are treated as censored at the date of last follow-up for the analysis. The curves change at every event, death, or censoring (Wormuth 1999).

The rationale for reporting mortality figures in cardiac surgery is published in the Guidelines for reporting mortality and morbidity after cardiac valve intervention by Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity (Edmunds et al. 1996, Akins et al. 2008). The committee states that early mortality is to be reported as all-cause

mortality at 30, 60, or 90 days after surgery and depicted by actuarial estimates, i.e., number of subjects remaining at risk and confidence intervals or as percentages. All-cause mortality includes all deaths from any cause after cardiac surgical intervention and survival should be compared with an age- and sex-matched sample from the general population whenever possible. Cardiac mortality includes all deaths resulting from cardiac causes and is subgrouped into valve-related deaths, sudden unexplained deaths, and deaths from other cardiac cause, e.g., from heart failure, acute myocardial infarction, or documented arrhythmias. A sudden unexplained death is one in which the cause of death has not been determined by clinical investigation or autopsy findings (Edmunds et al. 1996, Akins et al. 2008).

4.4. Morbidity

According to the committee, morbidity refers to a diseased state, disability, or poor health due to an underlying cardiac condition, intervention, or re-intervention related to it (Edmunds et al. 1996, Akins et al. 2008). Morbidity in cardiac surgery is closely related to embolism or bleeding events due to devices, most commonly mechanical valves, used in surgery or unavoidable medication related to these devices or underlying cardiac condition. Device-related morbidity is categorized as structural valve deterioration, nonstructural dysfunction, thromboembolism, and valve thrombosis. Embolism is any embolic event that occurs in the absence of infection after the immediate perioperative period, and it can be manifested by a neurological event or peripheral embolic event. A neurological event includes any central, new neurological deficit, whether temporary or permanent and whether focal or global, that occurs after awakening from anesthesia. Specific neurological events include stroke, transient ischemic attack, clusters (multiple or repeated transient events occurring during a short period), and psychomotor deficit. A non-cerebral embolic event is an embolus documented operatively, at autopsy, or clinically that produces signs or symptoms attributable to complete or partial obstruction of a peripheral artery. A major bleeding event includes any episode of major internal or external bleeding that causes death, hospitalization, or permanent injury or that necessitates transfusion regardless whether the patient has or has not been taking anticoagulants or antiplatelet drugs. Re-intervention is any surgical or percutaneous interventional catheter procedure that repairs, otherwise alters or adjusts, or replaces a previous intervention (Edmunds et al. 1996, Akins et al. 2008).

4.5. Measuring HRQoL

Unlike standard of living, HRQoL is not a tangible thing, and so cannot be measured directly. Measuring HRQoL requires a valid, reproducible, and sensitive method. In the context of medical research, both disease-specific and generic measurement can be utilized (Kind 2001).

A disease-specific measure reflects the experience of a particular illness or condition or its treatment and is specially designed for a particular disease, patient group, or areas of function. The typical disease-specific measurements of patients with cardiac disease are the New York Heart Association classification (NYHA; The Criteria Committee of the New York Heart Association) and the Canadian Cardiovascular Society's functional classification (CCS; Campeau 1976). The NYHA-classification categorizes heart failure patients into four groups based on their functional capacity (Table 5), and the CCS-classification categorizes patients into four groups according their severity of angina (Table 6). Other commonly used disease-specific measures are the Seattle Angina Questionnaire (Spertus et al. 1995), the Coronary Revascularization Outcome Questionnaire (Schroter et al. 2004), and the Minnesota Living with Heart Failure Questionnaire (Rector et al. 1987).

Table 5. New York Heart Association's functional classification (NYHA-classification).

Class I: Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.
Class II: Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
Class III: Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.
Class IV: Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

Table 6. Canadian Cardiovascular Society's grading of angina pectoris (CCS-classification).

Grade I: Ordinary physical activity does not cause angina, such as walking and climbing stairs. Angina with strenuous or rapid or prolonged exertion at work or recreation.
Grade II: Slight limitation of ordinary activity. Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during the few hours after awakening. Walking more than two blocks on the level and climbing more the one flight of ordinary stairs at a normal pace and in normal conditions.
Grade III: Marked limitation of ordinary physical activity. Walking one or two blocks on the level and climbing one flight of ordinary stairs in normal conditions and at normal pace.
Grade IV: Inability to carry any physical activity without discomfort, angina syndrome may be present at rest.

Generic instruments, on the other hand, should cover a broad range of dimensions of HRQoL and allow comparisons between different groups of patients. An ideal generic health assessment would include a comprehensive measure of a person's HRQoL. The World Health Organization QoL group (WHOQOL Group 1993) has recommended five dimensions that should be included in a generic HRQoL instrument. These are physical and psychological health, social relationship perceptions, function, and well-being.

The most common instruments to assess HRQoL in medical literature related to cardiac surgery are the Short-Form 36 (SF-36), The Nottingham Health Profile (NHP), EQ-5D, and the 15D (Hunt et al. 1981, Sintonen and Pekurinen 1989, Ware and Sherbourne 1992, Brooks et al. 2003). The Finnish version of the NHP questionnaire is shown in the Appendix.

4.6. Cardiopulmonary bypass

Cardiopulmonary bypass was performed by using a Stöckert heart-lung machine (Sorin Group GmbH, Munchen, Germany). A roller pump with a non-pulsatile flow, about 2.5 litres / body surface area (m^2) was used. Gas inflow to the oxygenator was adjusted using the alpha-stat method (Halstead et al. 2005). The temperature of venous blood was kept at 34°C. The arterial inflow was delivered through single cannulation of the ascending aorta or aortic arch. Venous drainage was through single venous cannulation inserted via the right atrial appendix in CABGs and aortic valve operations. Separate superior and inferior caval vein cannulations were utilized in mitral and tricuspid valve operations.

4.7. Myocardial protection (I, II, III, IV)

In Study **I** between the years 1991 and 1992, cardioplegia was performed with a modification of St. Thomas solution containing sodium 167 mmol/l, chloride 143 mmol/l, potassium 21 mmol/l, calcium gluconate 200 mg/l, magnesium 8 mmol/l, and nitroglycerin 2 mg/l; at 4°C the pH was 8.1. Initially, the cardioplegic solution was infused into the aortic root until the heart stopped fibrillating and the target temperature (10°-15°C) was reached. Additional dose of cardioplegic solution was given into the aortic root after every 1-2 anastomoses or at least every 20-30 minutes. The initial dose was usually less than 1000 ml, and subsequent doses were about 200-300 ml. No cardioplegic solution was given through the venous grafts.

Blood cardioplegia has been used in all valve and combined GABG-valve operations. Blood cardioplegia concentrate includes 400 ml of Ringer acetate, 100 ml of citrate-phosphate-dextrose (CPD) solution (Baxter Ltd., IL, USA), 5 ml of Addex Tham buffer (Fresenius-Kabi AG, Uppsala, Sweden), 10 mekv of magnesium sulfate ($MgSO_4$), and 50 mmol of potassium chloride (KCl). The temperature of blood cardioplegia was maintained before administration at 12°C. The initial dose of cardioplegia was given with blood/concentrate ratio of 4:1, and subsequent doses with ratio of 8:1, respectively. In the valve operations, cardioplegia was delivered either antegradely through aortic root into the coronary ostia or retrogradely via the coronary sinus.

4.8. Surgical procedures

A summary of the surgical procedures and surgical details are shown in Table 7.

Table 7. Summary of indications, etiology and perioperative details of the Studies **I**, **II**, **III**, and **IV**.

Characteristic	Study I (n=180)	Study II (n=184)	Study III (n=104)	Study IV (n=136)
Indication for surgery				
isolated CAD	180 (100)	-	60 (58)	-
CAD + AS and / or MR	-	-	33 (32)	-
ischemic MR	-	114 (62)	-	-
degenerative MR	-	64 (35)	-	-
rheumatic MR	-	3 (2)	-	-
endocarditis	-	3 (2)	-	5 (4)
isolated TR	-	-	-	4 (3)
CAD + TR	-	-	-	3 (2)
ischemic MR + TR	-	-	-	18 (13)
degenerative MR + TR	-	-	-	61 (45)
rheumatic MR +TR	-	-	-	3 (2)
AS and / or MS	-	-	11 (11)	27 (20)
ASD	-	-	-	9 (7)
VSD	-	-	-	1 (1)
congenital	-	-	-	1 (1)
myxoma	-	-	-	2 (1)
other	-	-	-	2 (1)
Performed operations				
CABG	180 (100)	-	60 (58)	-
MVP	-	85 (46)	1 (1)	-
MVR	-	99 (54)	-	-
AVR	-	-	9 (9)	-
CABG + AVR and / or MVR or MVP	-	-	1 (1)	-
MVP or MVR	-	-	33 (32)	-
TVP	-	-	-	21 (15)
TVR	-	-	-	4 (3)
TVP + AVR	-	-	-	12 (9)
TVP + MVR	-	-	-	43 (32)
TVP + MVP	-	-	-	36 (26)
TVP + AVR + MVR	-	-	-	14 (10)
TVP + AVR + MVP	-	-	-	6 (4)
Concomitant CABG	180 (100)	113 (61)	93 (89)	37 (27)
Re-operation	-	-	-	21 (15)
Perfusion time (min)	150 ± 39	256 ± 58	151 ± 52 [63-333]	166 ± 67 [34-465]
AO-time (min)	98 ± 31	134 ± 48	127 ± 45 [46-279]	134 ± 55 [29-295]
Number of distal anastomoses	4.7 ± 1.4	2.5 ± 2.2	4.6 ± 1.5 [0-9]	0.76 ± 1.5 [0-6]
Number of arterial grafts	-	0.6 ± 0.5	-	0.14 ± 0.35 [0-1]
Number of venous grafts	-	1.9 ± 1.9	-	0.40 ± 0.76 [0-3]
Amount of cardioplegia (ml)	1866 ± 743	-	-	2023 ± 897
IABP	-	-	-	16 (12)
VAD	-	-	-	1 (1)
Perioperative MI	9 (5)	-	4 (4)	22 (16)
Stay in ICU (days)	2.6 ± 3.9	-	2.3 ± 2.9 [1-15]	2.9 ± 4.8 [1-35]
Stay in hospital (days)	9.4 ± 5.5	-	8.4 ± 4.7 [2-30]	9.2 ± 6.2 [2-44]

Values denote number of patients (percentages) or mean ± standard deviation [range]. AO-time = aortic occlusion time; AS = aortic stenosis; ASD = atrial septal defect; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CAD = coronary artery disease; IABP = intra-aortic balloon pump; ICU = intensive care unit; MI = myocardial infarction; MR = mitral regurgitation; MS = mitral stenosis; MVP = mitral valve plasty; MVR = mitral valve replacement; TR = tricuspid regurgitation; TVP = tricuspid valve plasty; TVR = tricuspid valve replacement; VAD = ventricular assist device; VSD = ventricular septal defect.

4.8.1. Coronary artery bypass grafting (I)

Between the years 1990 and 1991 CABGs were performed at the Kuopio University hospital as follows: anastomoses were performed with one or two sequential venous grafts and the use of at least one arterial graft. All vessels that had a stenosis of more than 50% of the lumen diameter at angiography and more than 1.5 mm in diameter were grafted. A membrane oxygenator was used, with bicaval cannulation by snaring of the cavae and venting of the left ventricle through the right upper pulmonary vein. General hypothermia of 25°-28°C was maintained during cardiac arrest. Rewarming was started at the beginning of the last distal anastomosis. Proximal anastomoses were performed with a sidebiting clamp after unclamping of the aorta. During that time only arterial grafts were open, and the heart usually started fibrillating. About 2-5 minutes after unclamping of the aorta, the first direct current (DC) shock of 8 to 10 J was given. The shock was repeated if fibrillation reappeared during the manipulation of the heart. Pacing wires were sutured to the myocardium of the right ventricle. The patient was weaned from the heart-lung machine when the rectal temperature was 34°C and the heart had received vented reperfusion through all the grafts for at least five minutes. Cardiac output and pressures were measured with a Swan-Ganz thermodilution catheter. The serum potassium concentrations were kept within the normal range in the operating room and in the intensive care unit.

4.8.2. Mitral valve surgery (II)

During the study period, the technique of mitral valve surgery began to shift from MVR to MVP. Between the years 1992 and 1996 mitral valve procedures were performed at the Kuopio University hospital as follows: a perioperative transesophageal echocardiography was done after anesthesia induction, and the pathophysiology of the mitral valve was classified according to Carpentier's nomenclature. A structurally normal mitral valve with normal leaflet motion but with annular dilation was Type I, increased leaflet motion indicating leaflet prolapse or flail was Type II, restricted leaflet motion in systole and diastole, usually associated with rheumatic leaflet and subvalvular thickening was Type IIIa, and restricted leaflet motion in systole, often seen in ischemic cardiomyopathy with history of myocardial infarction was Type IIIb. The grade of regurgitation was evaluated by mapping the spatial area of the color Doppler regurgitant jet and by measuring the regurgitant area or expressing the regurgitant area as a percentage of the left atrial size. In addition, pulmonary vein flow was recorded as regards blunting or systolic reversal of pulmonary vein flow during left ventricular systole and was

taken as an indicator of severity of mitral regurgitation. Using these two methods the severity of mitral regurgitation was graded as mild (1+), moderate (2+ to 3+), or severe (4+). Transesophageal echocardiography was repeated at the end of surgery and the surgical result was evaluated in the beating heart before decannulation of the aorta.

All mitral valve procedures were performed through a median sternotomy, and general hypothermia of 25°-28°C was maintained during the cardiac arrest. Arterial inflow was introduced via the ascending aorta and venous drainage was done through bicaval cannulation. Caval snares were used for inflow occlusion during the mitral valve exposure, and venting of the left ventricle through the apex of the heart was utilized. Cardioplegic solution was delivered both by the antegrade and the retrograde route.

The mitral valve apparatus was exposed either through interatrial Waterstons's or Sondergaard's groove or through the superior transseptal approach via the right atrium. The most common techniques to repair the mitral valve were quadrangular resection of the posterior leaflet with concomitant sliding plasty, annular plication, and triangular resection of the anterior leaflet.

All patients who underwent MVP received an annuloplasty ring. The most common device at that time was the rigid Carpentier-Edwards Classic® annuloplasty ring (Edwards Lifesciences Inc., CA, USA).

For patients undergoing MVR, Carbomedics® and Sorin Bicarbon® (Sorin Group Inc., CO, USA) were the most common prosthetic valves.

4.8.3. Tricuspid valve surgery (IV)

In the case of severe TR due to a dilated tricuspid annulus, the technique of De Vega's annuloplasty has been utilized until the end of the 1990's. Since the beginning of the millennium, flexible annuloplasty rings have been used. The most common devices are the Tailor® (St. Jude Medical Inc., MN, USA) and Duran® (Medtronic Inc., MN, USA) annuloplasty rings. Recently, incomplete Carpentier-Edwards® annuloplasty bands (Edwards Lifesciences Inc., CA, USA) have been used instead of complete tricuspid annuloplasty rings to avoid conduction disturbances which may arise from the closed ring structure.

4.9. ECG analysis, definition of CD, and indications and timing for PM (I, IV)

An immediate postoperative ECG was recorded soon after the patient had arrived in the intensive care unit, and thereafter ECGs were recorded every morning until the fifth

postoperative day and again at the day of discharge. Cardiac rhythm, atrioventricular conduction, intraventricular conduction, signs of myocardial infarction, and ST-segment and T-wave change were recorded. CDs were classified into seven categories based on Satinsky et al. (1974) and the World Health Organization (Willems 1985) 1. first degree atrioventricular block (1st degree AV-block, PR interval >200 ms) 2. partial or complete left bundle-branch block (LBBB/CLBBB), 3. partial or complete right bundle-branch block (RBBB/CRBBB), 4. RBBB and left anterior hemiblock or left posterior hemiblock (RBBB/CRBBB + LAHB/LPHB), 5. LAHB or LPHB, 6. second degree atrioventricular block (2nd degree AV-block), and 7. third degree atrioventricular block (3rd degree AV-block). All ECGs were interpreted by an experienced cardiologist. The indications for PM were 1. persistent 2nd or 3rd degree AV-block, 2. atrial fibrillation with a slow ventricular response, and 3. sinus node dysfunction. The decision to implant a PM and the timing of the implantation were always based on individual clinical judgment. The established policy at the Kuopio University Hospital is to wait until the fifth postoperative day before PM implantation in an attempt to allow time for transient conduction abnormalities to resolve. All PMs were implanted subcutaneously through the transvenous approach.

4.10. The Nottingham Health Profile HRQoL analysis (II, III, IV)

The Nottingham Health Profile (NHP) is a generic measure of self-perceived health status (Hunt et al. 1981). It has been shown to be valid, reliable, easily completed, and acceptable to cardiac patients (Caine et al. 1999, Chocron et al. 2000, Herlitz et al. 2005). The NHP consists of 38 statements covering six dimensions of perceived health status. The dimensions are emotional reactions, pain, energy, social isolation, mobility, and sleep. In the NHP questionnaire, the statements are presented randomly and the respondent is asked to indicate whether or not the statement applies to him or her at present. Each statement has been weighted empirically to indicate their perceived severity, allowing scores to range from 0 to 100. The score obtained indicates the level of dysfunction or disability in the different domains. The higher the score, the greater is the perceived dysfunction. The NHP was selected for this study because it has been applied and validated previously to a random population sample to obtain standard values for the Finnish adult population. This standardization specifies the means and standard deviations of the different dimensions of the instrument relative to age and sex (Koivukangas et al. 1995).

4.11. Statistical analysis

Definitions, data analyses, and reporting were based on the guidelines and recommendations of the Joint Society of Thoracic Surgeons and the American Association for Thoracic Surgery Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity (**II-IV**; Edmunds et al. 1996, Akins et al. 2008). Data in the Tables are expressed as number of patients and percentage or mean and standard deviation (**I-IV**). Differences between groups were compared with the χ^2-test or Fisher's exact test (**I, II, IV**) or Wilcoxon's signed-rank test, marginal homogeneity test, and McNemar's test (**III**). Continuous variables and proportions were compared with the non-parametric Mann-Whitney U-test or Student's *t*-test after analysis of normality of distribution by the Kolmogorov-Smirnov test (**I-IV**). Late survival and time-dependent events were depicted with Kaplan-Meier's survival curves. The log-rank test was used for univariate analysis of mortality and morbidity followed by Cox's multivariate analysis for statistically significant univariate factors (**I-IV**). Risk factors for impaired HRQoL and PM implantation were analyzed by binary logistic regression (**II-IV**). Differences with a p-value <0.05 were considered statistically significant.

Propensity score analysis was carried out in Study **II** to estimate the probability that a patient might undergo MVP or MVR and to eliminate the effect of non-randomization and selection bias. The theoretical basis of propensity score analysis has been published by Rosenbaum and Rubin (1983). Propensity scores are used to create matched pairs or matched sets that are balanced with respect to many observed covariates. The resulting matched sets are heterogeneous within the covariates, but the covariates aim to have uniform distributions in treated and control groups, which makes the groups as a whole comparable (Joffe and Rosenbaum 1999). As a result, logistic regression analysis of several preoperative variables was performed to generate a propensity score for each patient. In a subset analysis, patients were grouped according to the magnitude of their propensity score into quintiles, after which their characteristics and outcomes were compared within these quintiles. Groups with similar propensity scores were well matched with respect to all characteristics (**II**). Version 15.0 of the SPSS software was used to run the statistics (SPSS Inc., Chicago, Ill, USA).

5. RESULTS

5.1. Postoperative CDs and long-term effects on survival after CABG (I)

Early mortality (within 30 days) was 1% (2/180). The causes of early deaths were cerebral infarct and septic shock. Survival after 9.6±0.2 years was 86% (155/180).

CDs at the time of discharge from the hospital were recorded in 63 patients (35%). Five patients (3%) received a PM due to permanent or intermittent 3rd degree AV-block. The prognostic factors for the development of a new CD after CABG were left main coronary artery diameter narrowing below 50% (p=0.02), perioperative myocardial infarction (determined as a new Q-wave in the ECG; p=0.04), postoperative CK-MB enzyme release (p=0.002), low cardiac output syndrome (determined as cardiac output below 2.0 l/min/m^2; p=0.03), and prolonged postoperative care in a cardiac care unit (p=0.001).

Overall survival of the patients with a new CD (CD+ group) was significantly lower than in the CD- group (78% vs. 90%, p=0.02). Seven of the 14 deaths in the CD+ group (50%) and nine (82%) of the 11 deaths in the CD- group were of cardiac origin. Thus, cardiac mortality in the CD+ and CD- groups did not differ from each other (11% vs. 8%, p=NS). The overall mortality in the CD+ and CD- groups during the follow-up was lower than the predicted mortality of the age- and sex-matched reference population (18%). By multivariate analysis, five factors were significantly related to increased late mortality during the follow-up: diabetes, perfusion time, less than four distal anastomoses performed, a new CD, and an ejection fraction below 50% measured by preoperative transthoracal echocardiography. Detailed information on mortality predictors and risk ratios, 95% confidence intervals, and p-values are shown in Table 8.

In the entire cohort, 7% underwent coronary angiography, 5% percutaneous coronary interventions, and 1% re-CABG during the long-term follow-up.

Table 8. Risk factors related to late mortality in Studies **I**, **II**, **III**, and **IV**.

	RR	95 % CI	p-value
Perioperative need for hemofiltration (**IV**)	10.224	4.067-25.704	<0.0001
Preoperative UAP (**II**)	4.359	2.159-8.799	<0.0001
Diabetes (**I**)	5.990	2.430-14.780	<0.0001
Perioperative MI (**IV**)	3.000	1.561-5.766	0.001
Age >60 years (**II**)	1.070	1.027-1.115	0.001
Preoperative severe renal failure[a] (**IV**)	4.797	1.696-13.571	0.003
Use of mitral prosthesis (**II**)	2.713	1.391-5.289	0.003
Perfusion time (**I**)	1.020	1.010-1.030	0.003
Number of distal anastomoses <4 (**I**)	3.200	1.300-7.880	0.010
A new conduction defect (**I**)	2.830	1.240-6.490	0.010
Urgency of the operation (**III**)	2.027	1.151-3.569	0.014
Perioperative need for IABP (**IV**)	2.167	1.116-4.207	0.020
Postoperative PM (**IV**)	0.289	0.104-0.806	0.020
Ejection fraction <50% (**III**)	2.088	1.110-3.929	0.022
Preoperative severe renal failure[b] (**III**)	2.054	1.047-4.026	0.036
Ejection fraction <50% (**I**)	2.600	1.080-6.270	0.040
Preoperative severe renal failure[b] (**II**)	1.004	1.000-1.007	0.050
Preoperative cerebrovascular disorder (**II**)	2.713	0.985-5.289	0.054

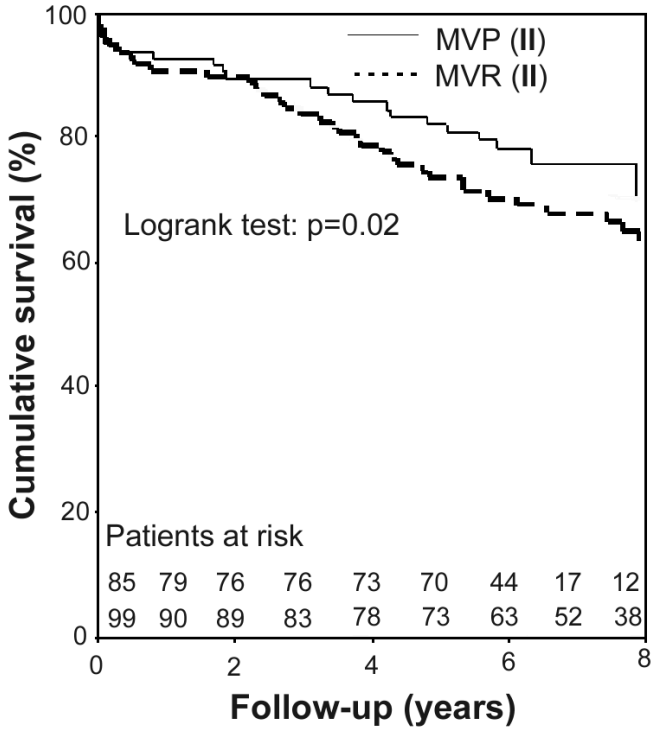
[a]renal failure (glomerular filtration rate <29 ml/min/1.73m^2); [b]renal failure (creatinine level more than 105μmol/l); 95% CI = 95% confidence interval; IABP = intra-aortic balloon pump; MI = myocardial infarction; PM = permanent pacemaker; RR = risk ratio; UAP = unstable angina pectoris.

5.2. Survival, morbidity and HRQoL differences between MVP and MVR (II)

CABG was simultaneously performed for 61 patients (72%) in the MVP group and 52 patients (53%) in the MVR group. Early mortality (within 30 days) was 4% (8/184). The 5-year and actual survival was 81% and 74% in the MVP group, and 74% and 60% in the MVR group, respectively. After adjustment for baseline characteristics by the propensity score method, there was a statistically significant survival benefit for the patients who had undergone MVP when all-cause mortality was included (p=0.02; Figure 2). However, when only cardiac-related mortality was included, the acquired survival benefit from MVP was not statistically significant. Thirty-three patients (18%) died later than 30 days after the mitral valve procedure because of acute myocardial infarction. Sixteen patients (19%) died of acute myocardial infarction in the MVP group and 17 patients (17%) in the MVR group (p=1.00). Five of the deaths were categorized as valve-related deaths (3%) in the whole cohort. The death of one patient was categorized as valve-related in the MVP group (1%) and four deaths were categorized as valve-related in the MVR group (4%; p=0.18). Among the 16 variables evaluated, five turned out to be statistically significantly associated with mortality. These were: preoperative unstable angina pectoris, age above 60 years, mitral valve prosthesis, preoperative renal failure, and

preoperative cerebrovascular disorder. Detailed information on the predictors of mortality and the risk ratios, 95% confidence intervals, and p-values are shown in Table 8.

Figure 2. Propensity-matched Kaplan-Meier survival curves of patients who underwent either mitral valve plasty (MVP, n=85) or mitral valve replacement (MVR, n=99, **II**).



A non-fatal myocardial infarction occurred in six patients (7%) in the MVP group and in three patients (3%) in the MVR group during follow-up (p=0.21). Thromboembolic or bleeding events, i.e., stroke, transient ischemic attack, or intracerebral bleeding occurred in seven patients (8%) in the MVP group and in three patients (3%) in the MVR group (p=0.18). Re-interventions (either coronary angiography alone or coronary angiography followed by percutaneous coronary interventions for ischemic symptoms) were done in two patients (2%) in the MVP group and in five patients (5%) in the MVR group, respectively, during the long-term follow-up. One patient (1%) underwent conversion from MVP to MVR later after primary

surgery. Three patients required a PM in the MVP group (4%) and two patients (2%) in the MVR group (p=0.83 for all interventions combined).

The HRQoL was studied on average 6.9 years after surgery in the MVP group and 8.2 years after surgery in the MVR group. There were no differences in the NHP-scores between the MVP and MVR groups in any of the six NHP-dimensions. However, the NHP-scores were statistically significantly higher in the study groups (MVP and MVR) than in the reference population concerning the dimensions describing energy (p=0.002 and p=0.004, respectively) and mobility (p=0.01 and p=0.03, respectively; Figure 3). Fourteen of the 37 tested variables had a statistically significant negative effect on HRQoL in the whole cohort. These contributors were mainly related to physical activity and physical performance (i.e., energy and mobility), but the dimensions describing pain and psychological dimensions, e.g., social isolation and emotion, were also affected by varying risk ratios. A summary of the statistically significant contributors to impaired HRQoL is shown in Table 9.

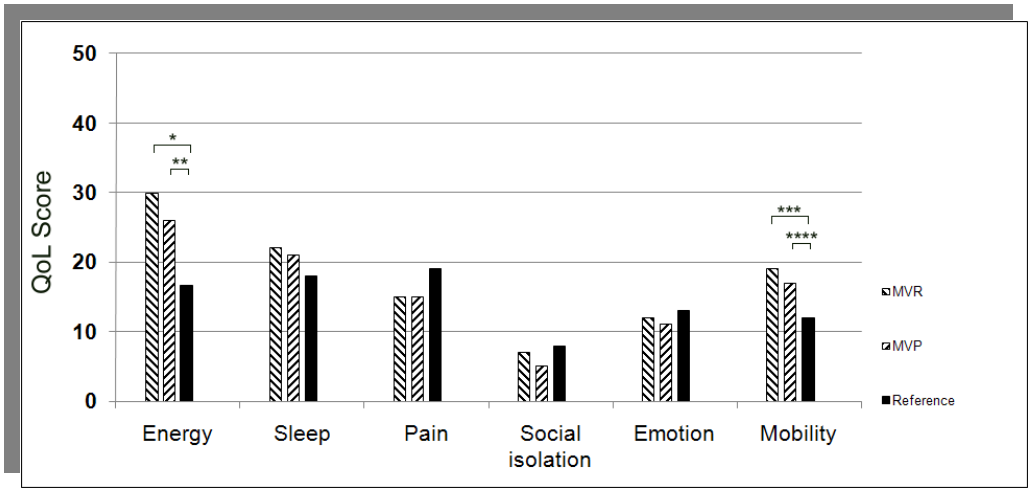


Figure 3. Nottingham Health Profile (NHP) health-related quality of life scores and statistical differences between the mitral valve plasty (MVP) and mitral valve replacement (MVR) groups versus an age- and sex-matched reference population (**II**). *p=0.002; **p=0.004; ***p=0.01; ****p=0.03.

Table 9. Factors associated with impaired health-related quality of life in Studies **II** and **III** according to the Nottingham Health Profile quality of life analysis.

	Energy	Sleep	Pain	Social isolation	Emotion	Mobility
Study II						
Male sex	-	-	-	2.6 (1.0-6.6)	-	-
Age >60 years	2.1 (1.0-4.5)	-	3.2 (1.5-7.0)	-	-	3.3 (1.5-7.1)
Preoperative NYHA III/IV vs. I/II	3.6 (1.5-8.7)	-	4.7 (1.8-12.3)	5.4 (1.2-24.4)	-	3.8 (1.6-8.9)
Preoperative myocardial infarction	-	-	-	-	-	2.7 (1.0-6.9)
Other severe disease	-	-	-	5.8 (1.2-28.1)	-	-
3-vessel disease	-	-	-	-	-	2.5 (1.0-6.0)
Number of anastomoses 1-3 vs. 4-7	-	-	-	-	-	2.5 (1.1-5.8)
Postoperative NYHA III/IV vs. I/II	27.4 (7.7-97.8)	-	24.0 (6.7-86.1)	4.7 (1.9-11.9)	4.1 (1.7-9.9)	18.1 (4.1-80.6)
Postoperative cardiac symptoms	2.5 (1.2-5.3)	-	-	-	-	-
Postoperative cerebrovascular disorder	-	-	-	5.9 (1.5-24.1)	-	-
Beta-blocker	-	-	-	-	-	2.5 (1.1-5.9)
ACE-inhibitor	-	-	-	2.6 (1.2-5.6)	-	-
Nitroglycerin	11.7 (2.5-54.2)	-	10.2 (2.2-47.5)	3.5 (1.2-10.7)	3.9 (1.2-13.2)	5.8 (1.2-26.8)
Diuretics	3.2 (1.5-7.1)	-	3.4 (1.5-7.6)	-	2.3 (1.0-5.1)	3.3 (1.4-7.8)
Study III						
Diabetes	1.03 (1.0-1.1)	-	1.05 (1.0-1.1)	-	-	1.06 (1.1-1.1)
High energy score at 15 months	1.03 (1.0-1.1)	-	-	-	-	1.05 (1.0-1.1)
High pain score at 15 months	-	1.04 (1.0-1.1)	-	-	-	-
Use of HMG-CoA-reductase inhibitors	0.97 (0.95-1.0)	-	-	-	-	-
Stay in ICU >3 days	1.04 (1.0-1.1)	-	-	-	-	-
Duration of cardiac symptoms preoperatively >120 days	-	-	-	-	1.07 (1.0-1.1)	-

Risk ratios and 95% confidence intervals (in parenthesis). All p-values are <0.05. ACE = angiotensin-converting enzyme; ICU = intensive care unit; NYHA = New York Heart Association.

5.3. Cardiac surgery, survival and HRQoL of octogenarians (III)

Early mortality (within 30 days) was 4% (4/104). The causes of deaths were acute myocardial infarction for two patients (50%) and underlying valvular disease for two patients, as well 50%. 1-year, 5-year, and actual survival rates were 94%, 76%, and 59%, respectively. These did not differ from the predicted survival of the age- and sex-matched reference population (58%) after nine years (Figure 4). The actual survival of patients who had undergone CABG, valve surgery, or a combination procedure was 65%, 58%, and 47%, respectively (p=0.188).

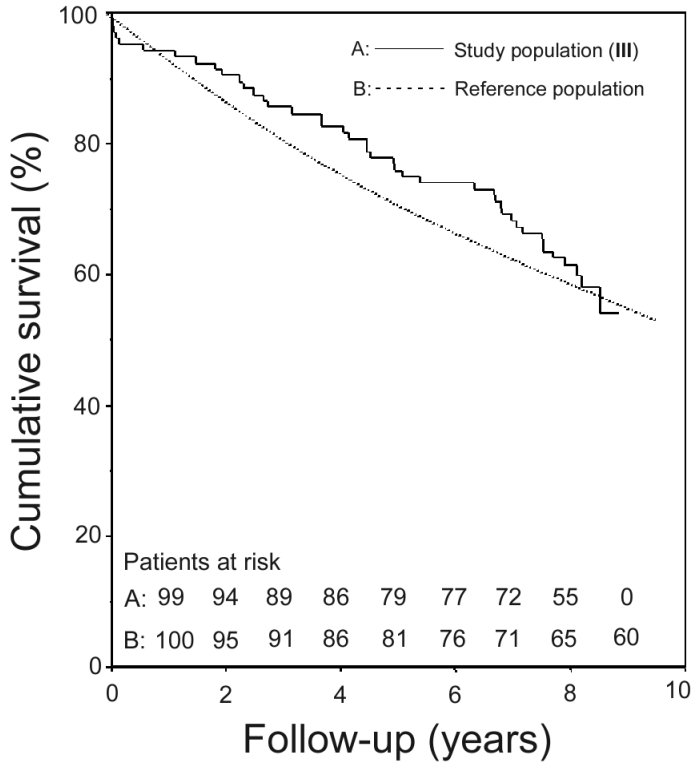


Figure 4. Kaplan-Meier survival curves of 104 cardiac operated octogenarians versus age- and sex-matched reference population during 8.2-years of follow-up (**III**).

There were 18 cardiac deaths (42%, 18/43) during the follow-up. Fifteen were categorized as ischemic (35%) and three as valve-related deaths (7%). Among the 17 variables that were evaluated, four turned out to be statistically significantly associated with mortality by univariate

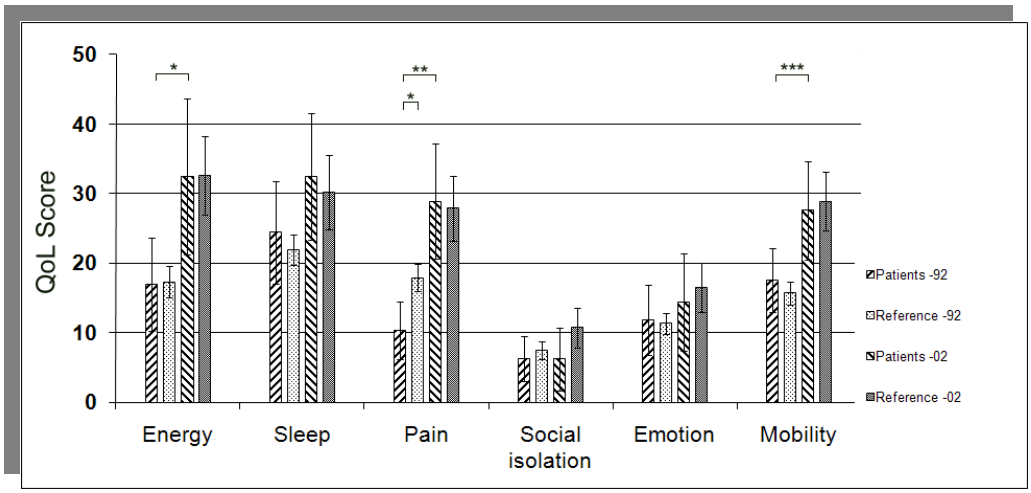
analysis. Three were associated with increased mortality by multivariate analysis: urgency of the operation, preoperative ejection fraction below 50%, and preoperative renal failure. Detailed information on the predictors contributing to mortality together with the risk ratios, 95% confidence intervals, and p-values are shown in Table 8.

In terms of morbidity, non-fatal myocardial infarction occurred in four (9%) of the survivors. The cumulative number of thromboembolic or bleeding events, i.e., stroke, transient ischemic attack, or intra-cerebral bleeding, was 13 (28%). Coronary angiography due to ischemic symptoms but without re-interventions was done in one patient (1%). One patient (1%) had valve replacement 119 days after a previous mitral repair. Four patients required a PM (9%).

The HRQoL was studied 15±3.2 months and 8.2±0.27 years after surgery with the NHP-questionnaire. The scores were compared with the scores standardized for the Finnish age- and sex-matched adult reference population at two time-points (65-74 years in 1993, and 75-80 years in 2002). The score reflecting the experience of pain was statistically lower ($p=0.001$) in the study group than in the reference population 15 months after cardiac surgery, but eight years after surgery the study group did not differ from the reference population in terms of any of the HRQoL dimensions. Within the study group itself, however, the scores for energy ($p=0.001$), pain ($p=0.003$), and mobility ($p=0.042$) increased from 15 months to eight years after surgery. The NHP-scores in patients with CABG, valve surgery, or combination procedure groups differed from each other neither at 15 months nor at eight years of follow-up (Figure 5).

Six of the 40 tested presumptive variables turned out to be statistically significantly related to HRQoL (Table 9). Diabetes, a high energy score, and a high pain score at 15 months, treatment in an intensive care unit for more than three days, and a duration of cardiac symptoms before surgery for more than 120 days emerged as statistically significant predictors of impaired HRQoL in the dimensions describing energy, sleep, pain, emotion, and mobility. Patients using HMG-CoA-reductase inhibitors scored lower than the reference population in the dimension describing energy.

Figure 5. Nottingham Health Profile (NHP) health-related quality of life scores and 95% confidence intervals of the study group (Patients), and an age- and sex-matched reference population (Reference) at two different time-points in 1992 (92) and in 2002 (02, **III**). *p=0.001; **p=0.003; ***p=0.042.



5.4. PM therapy and survival, morbidity, and HRQoL after TV surgery (IV)

PM implantation was required by 28 of all reported 136 patients (21%) during follow-up (PM+ group). The mean time of implantation was 562±954 days [range, 5 to 3108 days] after surgery. Fifteen (54%) of the PMs were implanted already before hospital discharge. Fifty-two patients (39%) had needed temporary pacing immediately after the operation. Of these, 18 (35%) received a PM either before hospital discharge or later during follow-up. Indications for PM were atrial fibrillation with slow ventricular rate in 16 (57%), sinus node dysfunction in 4 (14%), and 3rd degree AV-block in eight (29%) patients. Among the tested variables, five emerged as statistically significant predictors or showed a marked trend for PM implantation: need for temporary pacing during the immediate postoperative period, female gender, lack of adequate cardiac rhythm on the first postoperative day, use of TV annuloplasty ring, and LBBB before the operation (Table 10).

Table 10. Risk factors for the need of PM after tricuspid valve surgery (Study **IV**).

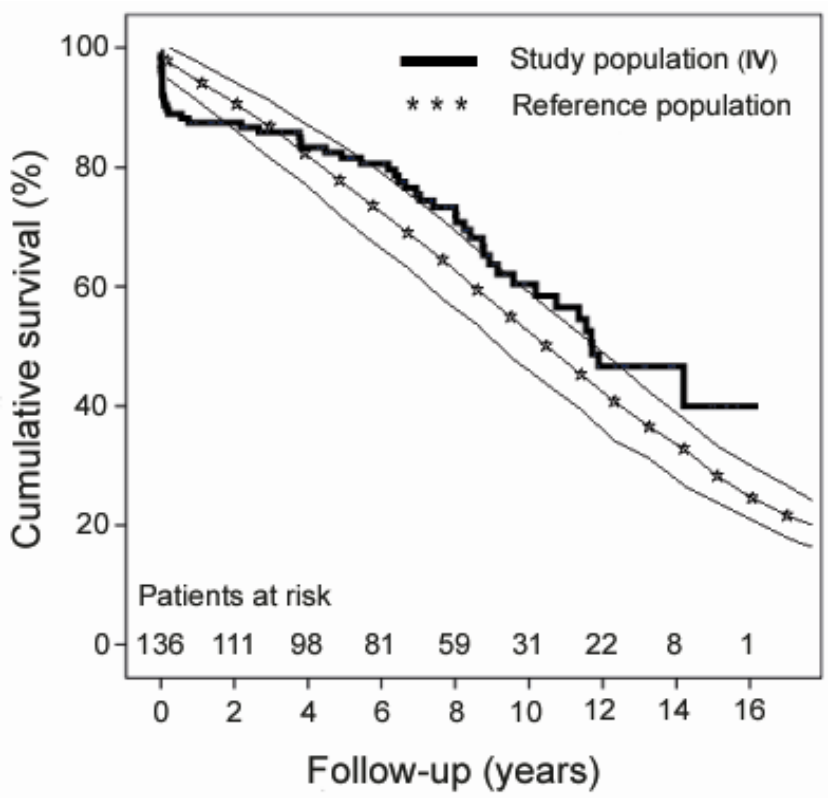
Variable	RR	95% CI	p-value
Need for temporary pacing postoperatively	3.865	1.613-9.258	0.002
Female sex	3.820	1.352-10.794	0.01
No adequate cardiac rhythm at the 1st POD	2.387	1.160-4.915	0.02
Use of annuloplasty ring vs. other methods to repair TR[a]	2.732	1.072-6.965	0.04
Preoperative LBBB	5.640	0.893-35.610	0.07

95% CI = 95% confidence interval; LBBB = left bundle branch block; POD = postoperative day; RR = risk ratio; TR = tricuspid regurgitation. [a]Other methods include tricuspid valve replacement with prosthesis or De Vega annuloplasty.

Eleven patients (8%) died within 30 days after the operation. The causes of early deaths were valve-related in eight cases (73%), ischemic-related in two cases (18%), and respiratory insufficiency due to pulmonary fibrosis in one case (9%). All early deaths occurred in the PM- group. The 5-year, 10-year, and actual survival of the entire study population were 82%, 60%, and 63%, respectively (Figure 6). Survival in group PM+ was 100%, 94%, and 86%, and in group PM- 77%, 53%, and 57% respectively (p=0.01). Thus, after exclusion of the early deaths, the late survival figures in group PM- were 85%, 59%, and 64% (PM+ vs. PM-, p=0.05; Figure 7).

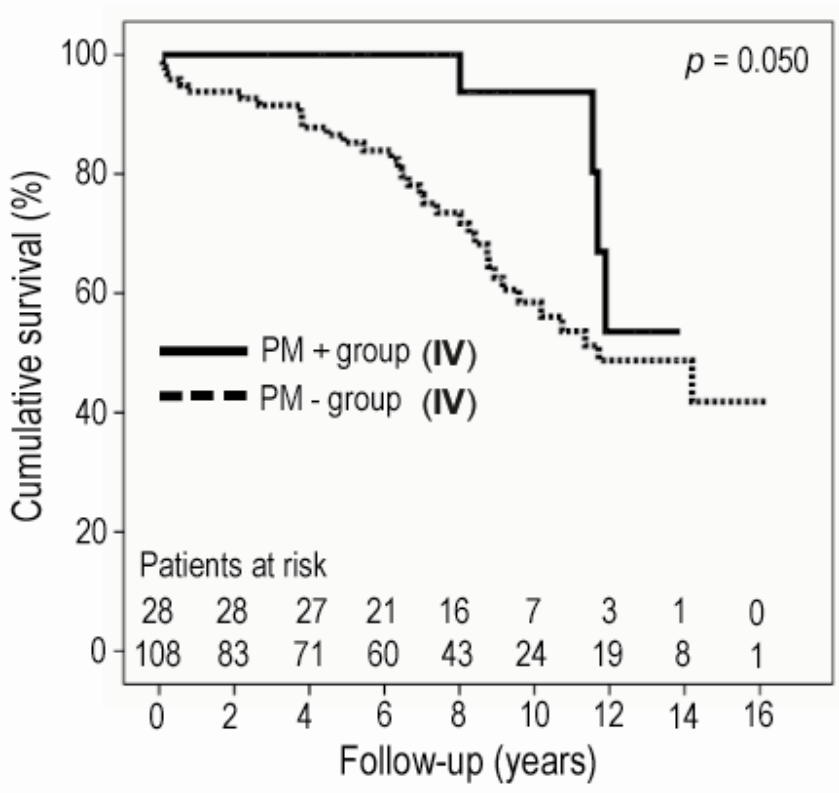
Ten of the tested variables were significantly associated with mortality by univariate analysis: perioperative need of hemofiltration, perioperative MI determined as a new Q-wave in ECG or postoperative CK-MB enzyme release over 100 μg/l, preoperative severe renal failure, need for a new PM, perioperative need for an IABP, preoperative MI, TR grade, unstable angina pectoris, stroke, and severe CAD. By multivariate analysis, five of the ten variables emerged as statistically significant predictors of late mortality. The multivariate model also showed that a new PM carried a protective effect against late death (Table 8).

Figure 6. Kaplan-Meier survival curve of 136 tricuspid valve operated patients versus an age- and sex-matched reference population. Parallel gray lines indicate 95% confidence intervals for the reference population (**IV**).



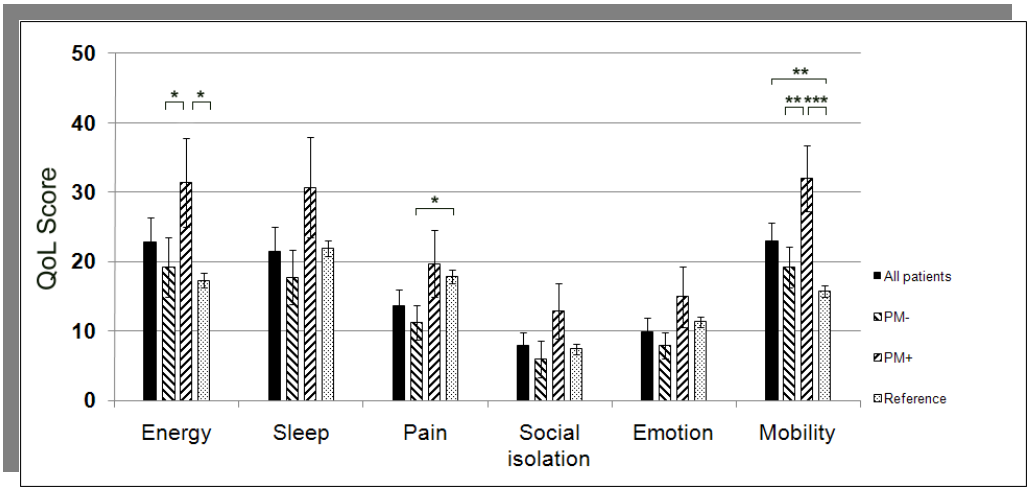
In terms of late morbidity (>30 days after operation), non-fatal myocardial infarction occurred in one patient (4%) in group PM+ and in one patient in group PM- (2%, p=0.52). In terms of re-interventions, the number of patients who underwent coronary angiography due to ischemic symptoms or percutaneous coronary intervention during long-term follow-up was one (4%) in group PM+, and two (4%) in group PM- (p=0.21). Emergent CDs increased patient morbidity. The need for a PM prolonged hospitalization significantly (p=0.009). During the long-term follow-up, PM was significantly related to a higher incidence of thromboembolic complications in terms of transient ischemic attacks (PM+ vs. PM-; 30% vs. 6%, p=0.004) and strokes (PM+ vs. PM-; 9% vs. 4%, p=0.008).

Figure 7. Kaplan-Meier survival curves of 136 patients who needed a pacemaker (PM+) and those who did not (PM-) after tricuspid valve surgery. Early mortality (deaths within 30 days after the operation) is excluded (**IV**).



The HRQoL was studied cross-sectionally. Figure 8 shows the NHP scores of the study population by need of PM together with the scores standardized to the Finnish age- and sex-matched reference population. Compared with the reference population, the entire patient population had significantly impaired mobility (p=0.007). The need for a PM was closely related to impaired HRQoL. Patients in group PM+ had significantly impaired HRQoL in the dimensions describing energy (p=0.01; p=0.04) and mobility (p=0.005; p=0.001) compared with group PM- and the reference population, respectively. Significantly more patients in group PM+ were in NYHA-class III and IV than in NYHA-class I and II compared to group PM- (p=0.03). On the other hand, group PM+ had a lower score for pain than the reference population (p=0.05).

Figure 8. Nottingham Health Profile (NHP) health-related quality of life scores and 95% confidence intervals for patients who required a pacemaker (PM+) compared with those who did not (PM-) need a permanent pacemaker after surgery (**IV**). *p<0.05; **p<0.01; ***p<0.001.



6. DISCUSSION

6.1. Postoperative CDs and long-term effects on survival after CABG (I)

The effect of permanent CDs on prognosis after heart surgery has been controversial. Earlier reports have found that RBBB is the most frequent conduction abnormality after CABG and, at the same time, the most benign of all CDs. The incidence of left-sided blocks is lower, but they have been associated with an adverse outcome (Zeldis et al. 1978, Bateman at al. 1985). Current data also suggests that the type of CD after CABG has changed from the RBBB to 1st degree AV-block (Cook et al. 2005). Other have found no difference in prognosis of patients with or without CDs after CABG (Wexelman et al. 1986, Tuzcu et al. 1990), although there is some evidence that patients with a CD have poorer left ventricular systolic function and more often chest pain or dyspnea as the exercise-limiting symptom than patients without CDs (Mustonen et al. 1998). The largest of these studies included 2,000 patients 111 (6%) of whom developed a CD (Tuzcu et al. 1990). The 5-year overall survival was 86% in patients with and 87% in patients without CDs, and the cardiac survival rate was 95% in patients with and 93% in patients without CDs. Our results agree with these findings. The 5- and 10-year cardiac survival in our study was 95% and 92%, versus 92% and 89%, in group CD- and CD+, respectively.

Herlitz and co-workers reported 11 independent predictors of reduced survival during a 5-year follow-up after isolated CABG (Herlitz et al. 1998): smoking, impairment of left ventricular function, a history of congestive heart failure, high age, arrhythmia 4-7 days after CABG, intermittent claudication, diabetes, prolonged ventilator time, history of cerebrovascular disease, treatment with digitalis at days 4-7 postoperatively, and cardiac enzyme release as a marker of myocardial injury. We found five independent predictors of all cause deaths: diabetes, perfusion time, number of distal anastomoses, permanent postoperative CDs, and preoperative left ventricular ejection fraction less than 50%. Four of these predictors have been documented previously by other authors (Herlitz et al. 1998, Myers et al. 1999). The effect of CDs on very long-term survival has not been reported previously. We found that not only rightsided, but also leftsided CDs are not related with inferior cardiac survival after CABG. However, 3rd degree AV-block emerged as a strong predictor of mortality. By multivariate analysis, 3rd degree AV-block was the only CD that was an independent risk factor for death.

The incidence of CDs in our study was relatively high (35%) and the spectrum wide but in line with clinical experience and results of some earlier studies (Caspi et al. 1987, Chu et al. 1987, Caretta et al. 1991, Mustonen et al. 1995). One of three patients was discharged from the hospital with a new CD, but PMs were needed in less than 10% of them. The causes of post-

CABG CDs seem to be multifactorial and some major contributors have been proposed. The main reason for the high incidence of CDs in our study was probably the myocardial preservation method used. A previously published analysis of the same patient cohort showed that in patients with a new permanent post-CABG CD, the perioperative myocardial temperature had been significantly lower than in patients with preserved conduction (Mustonen et al. 1995). It has been suggested that permanent damage of the conduction system after hypothermic myocardial protection is caused by temperature-induced changes in vital cellular functions of the conduction tissue during the post-ischemic period (Gozal et al. 1996). In our study, four of the studied variables remained significant predictors of permanent CDs by multivariate analysis: preoperative left main coronary artery stenosis, perioperative myocardial infarction determined as a new Q-wave in the ECG, postoperative CK-MB enzyme release, and prolonged stay in cardiac care unit. These contributors have been reported previously by other authors (Caspi et al. 1987, Chu et al. 1987, Caretta et al. 1991). The most recently published study corroborated these findings: Cook and colleagues found that the year of operation, age, use of intra-aortic balloon pump, number of vessels bypassed, and use of crystalloid cardioplegia were the most important predictors of emergent CDs after CABG (Cook et al. 2005).

6.2. Survival, morbidity and HRQoL differences between MVP and MVR (II)

The reconstructive techniques of mitral repair developed by Carpentier and colleagues have been suggested to be superior to mitral replacement in terms of survival (Braunberger et al. 2001, Mohty et al. 2001, Suri et al. 2006). Moss and colleagues published the results of a population of 322 patients whom they had followed-up for 3.4 years (Moss et al. 2003). They concluded that MVP improved survival, but also that the number of re-operations increased. In our study of 184 patients with a mean follow-up of 7.3±1.4 years we found no significant differences in the rate of re-evaluations for surgery or re-operations between the MVP and MVR groups. Two authors have recently reported the results of lower mortality and morbidity after MVP compared to MVR, especially in late valve-related complications, e.g., thromboembolism and bleeding events (Lee et al. 1997, Yau et al. 2000). In Study **II**, we found no difference in the frequency of late complications between the MVP and MVR groups.

It has been clearly demonstrated that, in addition to the operative technique, underlying pathophysiologic mechanism of mitral valve disease contribute essentially to outcome (Cohn et al. 1995). The most common etiologies of mitral valve dysfunction are degenerative mitral valve

disease due to fibroelastic deficiency, Barlow's disease, and mitral insufficiency due to ischemic cardiomyopathy (Filsoufi et al. 2005). Fibroelastic deficiency is common among elderly patients with a relatively short history of mitral regurgitation, whereas Barlow's disease appears early in life, and patients typically have a long history of a systolic murmur. Ischemic mitral valve disease develops in parallel with CAD and causes mitral regurgitation by several mechanisms: typical clinical manifestations of ischemic mitral valve disease are annular dilatation, papillary muscle rupture, or leaflet prolapse due to fibrotic and elongated papillary muscles after myocardial infarction. In addition, myocardial infarction leads to left ventricular remodeling that changes the ventricular shape from ellipsoidal to spherical; such remodeling leads ultimately to papillary muscle displacement, reduced leaflet coaptation, and mitral regurgitation (Filsoufi et al. 2005). It is generally accepted that moderately severe to severe (grade 3+ or 4+) ischemic mitral regurgitation should be corrected at the time of CABG, but the optimal management of moderate (grade 2+) ischemic mitral regurgitation is still controversial (Raja et al. 2007). Srivastava and co-workers concluded in their review article that there is relatively good evidence that moderate mitral regurgitation in patients undergoing isolated CABG affects survival adversely and that mitral regurgitation does not with certainty improve after CABG alone. However, the evidence to support MVP or MVR at the time of CABG in the case of moderate or even mild mitral regurgitation to improve long-term survival is still weak (Srivastava et al. 2007). In this context, however, it is noteworthy to recall again that the results of MVP and MVR are essentially related to the underlying mitral valve pathology. In some cases, MVR may be the only feasible method to reconstruct mitral valve, e.g., in severe mitral stenosis or in mitral regurgitation, where MVP might be at first undertaken but then due to unsatisfactory outcome converted to MVR. In those cases where MVP is feasible, repair result has shown to be important predictor of the long-term outcome and recurrence rate. The immediate postoperative rate of residual regurgitation >1 predicts late failures requiring re-operations (Heikkinen et al. 2005b).

The combination of mitral regurgitation and CAD is a growing challenge, where two separate but interdependent pathophysiologic mechanisms potentiate each other. An increasing number of patients with these coexisting diseases are offered the option to have cardiac surgery. Recently published data demonstrates that mitral insufficiency is an independent risk factor for reduced survival with CAD (Diodato et al. 2004, Grossi et al. 2006), but, unexpectedly, the selected technique to repair ischemic mitral regurgitation (MVP vs. MVR) does not contribute to the long-term outcome (Mantovani et al. 2004). Herlitz and co-workers studied 35 patients

who underwent both mitral valve surgery and CABG. They reported that the combination of valve surgery and CABG was independently associated with increased death rates and re-hospitalizations. Early mortality was 11% and the 5-year survival 45%. The only independent predictor of an adverse outcome was a low ejection fraction (Herlitz et al. 1997). Mortality and survival figures were better in our Study (**II**): the early and 5-year survivals were 96% and 81%, respectively. In Study **II**, the survival difference between MVP and MVR groups was statistically significant only for all-cause mortality. In case of cardiac-only mortality, a long-term survival difference did not emerge. Because life expectancy is affected by CAD and underlying poor ventricular function, patients with severe CAD have often reduced survival. One might argue that our results are preferentially CAD-related rather than valve-related, because patients with CABG were included. In our series, CABG was performed concomitantly with MVP for 72% of the patients and with MVR for 53%. The mean ejection fractions were 54% and 63%, respectively. Thus, the patients in the MVP group presented with more severe CAD and worse left ventricular function than the patients in the MVR group. One would thus expect that the cardiac mortality in MVP group should be worse than in MVR group, but this was not a case (**II**).

In our study CABG done for unstable angina pectoris turned out to be an independent predictor of late mortality, whereas CABG for stable CAD was not significantly associated with mortality. Flameng and colleagues (Flameng et al. 1996) studied 741 patients who underwent a combination procedure (32 MVP and 180 MVR) and concluded that demographic variables, i.e., age (>70 years vs. 60>70 years vs. <60 years), female sex, renal failure, high NYHA-class III or IV, left ventricular dysfunction, amount of mitral regurgitation, CAD, non-sinus rhythm, and long aortic cross-clamp time were important predictors of early and late mortality in patients undergoing a mitral valve operation and CABG simultaneously. Our results agree very well with these findings, since we found that the following variables were associated with reduced survival: preoperative unstable angina pectoris, age older than 60 years, use of mitral prosthesis instead of valvular repair, preoperative renal failure, and preoperative cerebrovascular disorder.

Study **II** showed that HRQoL assessed with NHP was similar for patients who had undergone MVP or MVR. However, there was a statistical difference in the dimensions describing energy and mobility between the MVP and the MVR groups, on the one hand, and the standardized reference population on the other hand. No other HRQoL variable differed from the age- and sex-matched reference population. Two articles have reported that MVP might be superior to MVR as regards HRQoL (Goldsmith et al. 2001, Sedrakyan et al. 2006),

which stands in contrast to our study and the study by Immer and co-workers (Immer et al. 2003).

In Study **II** we also assessed the determinants of impaired HRQoL of the patients who had undergone either MVP or MVR. Among the 37 tested variables, 14 were associated with an inferior HRQoL. The risk factors that affected more than three dimensions of the NHP did so mainly on physical dimensions (energy, mobility, and pain) and less on mental dimensions (sleep, social isolation, and emotion). The most significant variables associated with a poor HRQoL were high NYHA-class, age above 60 years, and need for nitroglycerin and diuretics. This is not unexpected, because these variables portray a symptomatic ischemic heart condition and heart failure, which are known to impair HRQoL. The relation between age and NYHA-class with regard to impaired HRQoL has been reported previously (Chocron et al. 1996).

6.3. Cardiac surgery, survival and HRQoL of octogenarians (III)

The patients' own perception of their HRQoL is particularly important in older age: patients often value HRQoL above longevity. In Study **III**, the 1-year, 5-year, and actual survival rates of the patients who were operated at the age of 70 or older, were 94%, 76% and 59%, respectively. These survival rates are somewhat better than reported by Engoren and co-workers (Engoren et al. 2002) who studied 103 randomly selected septuagenarians undergoing cardiac surgery in 1998-1999, and reported 1-year and 2-year survival rates of all-patients of 83% and 82%, respectively. In the CABG-only group, both the 1-year and the 2-year survival rates were 90%. Survival in Study **III** is more in line with the results reported by Kolh and colleagues (Kolh et al. 2007). In their study of 220 octogenarians who were discharged from the hospital after aortic valve surgery (74%) with or without CABG (26%), the 1-year, 3-year, and 5-year survival rates for the entire study population were 86%, 80%, and 73%, respectively. Similarly to Kolh and associates, the actual survival rates in our study after combined valve- and CABG operations (47%) were lower than after isolated CABG (65%).

We sought to define risk factors that might predict death in the population who is operated at age 70 years or above. Multivariate analysis showed that risk factors for death were: urgency of operation, ejection fraction below 50%, and preoperative renal failure. Our results agree with previous findings (Kolh et al. 2007), which have shown that age, preoperative myocardial infarction, urgency of operation, and prolonged treatment in an intensive care unit were independently associated with high late mortality. The detrimental effect of preoperative renal failure on survival after cardiac surgery has been unambiguously reported earlier (Flameng et al.

1996, Melby et al. 2007). It is noteworthy that, in our series, the proportion of patients who had renal failure declined over time from 25% at baseline to 17% at 15 months and to only 4% at 8.2 years. This underscores the importance of renal failure as a predictor of an extremely poor survival outcome.

The postoperative morbidity in Study **III** was not very high. Given that the patients were rather old, a rate of nonfatal myocardial infarctions of only 9% during follow-up was not very high. One patient underwent conversion to valve replacement after previous mitral repair, one patient underwent cardiac catheterization without further interventions, and four patients received a PM. The cumulative incidence of thromboembolic or bleeding events, i.e., stroke, transient ischemic attack, or intra-cerebral bleeding was 28% at 8.2 years, which is well in line with previous reports (Huber et al. 2007).

Three reports have addressed the question of the long-term effect of cardiac surgery on HRQoL in elderly patients (Järvinen et al. 2003, Huber et al. 2007, Loponen et al. 2007). During short-term follow-up, elderly patients have derived less HRQoL benefit from cardiac surgery than younger patients. Järvinen and co-workers (Järvinen et al. 2003) found, in a study of 508 patients who had undergone CABG one year earlier, that patients aged >75 years had higher mortality and morbidity and also a poorer HRQoL compared to younger patients. Similar findings have been reported by Loponen and colleagues (Loponen et al. 2007): after initial improvement in HRQoL, the HRQoL of 56 patients who were older than 75 years at the time of CABG, returned to the preoperative level by 18 months after surgery. The study by Kolh and associates (Kolh et al. 2007) reported relatively good results in terms of HRQoL on average five years after aortic valve surgery, although the improvement in HRQoL was significantly associated with the preoperative status of the patients. A poor long-term HRQoL outcome may, in the elderly, be due to the natural progression of the underlying cardiac disease after surgery and to the co-morbidities related to old age.

In our study, cardiac operated septuagenarians at 15 months after surgery had less self-reported pain than the age- and sex-matched reference population. Also, on average eight years after surgery, the study group did not differ from the reference population in terms of any HRQoL dimensions. The HRQoL of the patients decreased during eight years of follow-up in the dimensions describing energy, pain, and mobility, but that was the case in the reference population, as well. Thus, although cardiac operated septuagenarians coped as well as their age- and sex-matched controls, they did not present with better HRQoL in any specific dimensions at age of 80 years. At baseline, the cardiac operated patients are physically restricted by their

underlying cardiac disease. Our results imply that the efforts to relieve the symptoms related to the underlying cardiac disease by surgical means were successful.

Unexpectedly, the type of cardiac surgery did not contribute with any dimension of the HRQoL in our study: patients who had undergone CABG, valve surgery, or a combination of both all had similar HRQoL scores. However, it is known that the type of cardiac surgery is related to the postoperative perception of HRQoL. In a study by Falcoz, CABG-operated patients did not recover as well as patients who had undergone valve surgery (Falcoz et al. 2003). In contrast, Huber and colleagues showed that octogenarians who had undergone either AVR or the combination procedure experienced more anxiety and worried more about dying than patients who had undergone isolated CABG (Huber et al. 2007). These mixed results reflect only too well the complexity related to the assessment of HRQoL.

We also studied the determinants of a poor HRQoL that affected the patients' own perception of their HRQoL. Among 40 tested variables, five were associated with an inferior HRQoL: diabetes, high energy score at 15 months, high pain score at 15 months, treatment in an intensive care unit more than three days, and preoperative symptoms for more than 120 days were associated with poorer scores for energy, sleep, pain, emotion, and mobility after the long-term follow-up. Patients on HMG-CoA-reductase inhibitors had a lower energy score.

The risk factors that had an impact on more than two dimensions of NHP influenced preferentially physical (i.e., energy and mobility) rather than mental domains. The most significant variables associated with impaired HRQoL in terms of physical conditions were diabetes and a high energy score at 15 months. In contrast to earlier studies (Falcoz et al. 2003, Peric et al. 2006), NYHA-class III and IV did not emerge as significant predictors of impaired HRQoL, although transition from NYHA-class I/II to class III/IV was statistically significant during the follow-up. However, the fact that this transition significantly increased the need for nitroglycerin during the follow-up supports the notion that the variables related to physical conditions are invariably more often affected than the mental dimensions, also among octogenarians.

In agreement with earlier reports (Kolh et al. 2007), diabetes with renal failure emerged as the most hazardous predictors for poor HRQoL outcome. Having diabetes predicted poor HRQoL as regards dimensions of energy, mobility, and pain. Regarding patient selection, a high energy score, and a high pain score at 15 months, and prolonged duration of symptoms preoperatively reflect the fact that decision-making whether to operate or not should be done without delay in order to achieve the optimum surgical results in terms of long-term HRQoL.

6.4. PM therapy and survival, morbidity, and HRQoL after TV surgery (IV)

The main finding in Study **IV** was that the need for a PM after TV surgery was high – 21% of the operated patients – and PMs were continuously needed during follow-up. Life expectancy among the PM-treated patients was higher than among the patients who did not need a PM. However, patients with a PM had a higher rate of thromboembolic complications and poorer HRQoL in terms of physical capacity than patients without a PM.

The incidence of PM after cardiac surgery is related to the type of operation. This is obvious for anatomical reasons. The early perioperative need for PM has been reported to be less than 1% after CABG, and 3% to 6% after aortic valve and mitral valve or combination procedures (Morell et al. 1996, Gordon et al. 1998, Limongelli et al. 2003, Dawkins et al. 2008). However, the long-term need for a PM after cardiac surgery has not been thoroughly examined. The report of Onalan et al. (2008) seems to be the only one addressing the question of the need of PM after CABG or mitral and aortic valve surgery over time. They reported that 23% of the patients needed a PM during ten years follow-up.

The need and clinical implications of PM implantation after TV surgery is even less well documented. A limited number of studies imply that the need of PMs after TV surgery during the early perioperative phase is higher than after other valve surgery (13%-28%; Scully et al. 1995, Do et al. 2000). More data regarding the general results and the need for PM after TV surgery are needed, because the current recommendations emphasize proactive and aggressive repair of secondary TR concomitantly with mitral surgery and revascularization. It has been predicted that the rate of TV surgery will increase along with the increasing rate of mitral repair and CABG (Tang et al. 2006). In Study **IV** we found that the incidence of PM after TV surgery is higher than after other valve surgery (Gordon et al. 1998, Koplan et al. 2003, Limongelli et al. 2003). Although PMs were often implanted before the patient was discharged from the hospital, nearly half of them were implanted later. The mean time from surgery to PM implantation was 562 days and the last PM in Study **IV** was implanted later than eight years after TV surgery.

Koplan et al. (2003) developed and validated a useful risk score to predict the need for PM after valve surgery. In their comprehensive series of 4,694 patients they found that preoperative RBBB or LBBB, multivalve surgery, especially when including TV surgery, preoperative PR-interval >200 ms, prior valve surgery, and age >70 years were the strongest independent predictors for the need of PM. We found that the need for temporary postoperative pacing and the lack of adequate cardiac rhythm during the first postoperative day, as well as preoperative LBBB, and female sex were independent predictors of PM. An interesting finding in Study **IV**

was that the use of the annuloplasty ring rather than De Vega's annuloplasty or prosthetic TV was an independent predictor of PM. De Vega's annuloplasty was the standard procedure for TV repair at Kuopio University Hospital until the end of the 1990's. In the beginning of the millennium, we used complete Tailor® (St. Jude Medical Inc., MN, USA) or Duran® (Medtronic Inc., MN, USA) flexible annuloplasty rings to repair the dilated tricuspid annulus if the patient had severe TR. Still more recently, we have used incomplete Carpentier-Edwards® annuloplasty bands (Edwards Lifesciences Inc., CA, USA) instead of complete tricuspid annuloplasty rings to avoid the development of conduction disturbances which may arise from to the closed ring structure.

The 5-year, 10-year, and actual survival was 82%, 60%, and 63%, respectively. In the report of Guenther et al. (2008) 416 patients underwent TV surgery; the 10-year survival was 48% in the TVP group and 37% in the TVR group. McCarthy et al. (2004) reported an 8-year survival of 50% among 790 patients who underwent TVP. Thus, the long-term survival in our study appears to be higher than in these studies. However, it is noteworthy that in our study most (95%) of the TV operations were repairs, whereas in the series of Guenther the proportion of repair was 75%.

The survival of patients who needed a PM after TV surgery was significantly higher than of those who did not. The survival rates at 5 years were 100% vs. 77%, and at 10 years 94% vs. 53%. This marked survival difference remained significant after exclusion of early mortality in the group who never received a PM. The reasons for this difference are not clear, but one may speculate that PM patients are under more careful observation and – maybe more importantly – that the PM protected against fatal bradyarrhythmias. In our series there was only one death in the group of patients who received a PM that was categorized as cardiac-related (25%, 1/4 patients), compared to 66% (33/50 patients) in the group who did not receive a PM. This hypothesis is difficult to verify, since bradyarrhythmias as the cause of death cannot be identified nor excluded postmortem by clinical examination or autopsy. However, risk factor analysis supported the hypothesis that PM improves survival, since the need for PM was ultimately the only protective factor against mortality during late follow-up. At the same time, we corroborated the findings of some previous studies (Gordon et al. 1998) on the impact of other risk factors on late mortality: preoperative or perioperative renal failure, perioperative MI, and perioperative need for IABP. This being the case the need for a PM as a protective factor against death gets some additional support.

The need for a PM has been related to increased morbidity because the incidence of atrial fibrillation and cardiac failure increases. The development of PM-related cardiac morbidity is apparently related to the pacing site and to the duration of pacing (Sharma et al. 2005). Physiological pacing (AAI or DDDR) reduces the risk of cardiovascular end-points more than ventricular pacing (VVI; Tang et al. 2001, Nielsen et al. 2003). In Study **IV**, VVI was the most common pacing mode, which was related to the high prevalence of atrial fibrillation in this group of patients. Although PM patients had better survival, they also had an increased risk of thromboembolic complications and impaired HRQoL. The rates of transient ischemic attacks and strokes were significantly higher in the group of patients who received a PM than among those who did not. It is not clear why the rate of neurological events was higher among the patients who received a PM than among those who did not, since the higher rate of thromboembolic complications is not associated with the fact that a PM is placed in a patient's right ventricle.

Data on HRQoL in the context of TV surgery is limited, but cardiac surgery is known to ameliorate HRQoL regardless of the type of underlying cardiac disease (Koch et al. 2007, Koch et al. 2008). In Study **IV**, the entire patient population coped similarly as the Finnish age- and sex-matched reference population, but the group of patients with a PM reported higher NHP-scores in the dimensions describing energy and mobility. Another reflection of this increased morbidity in patients with PMs and impaired HRQoL was the fact that patients with a PM were, on average, more often of NYHA functional class III or IV compared to the patients who did not need a PM. It is noteworthy that disadvantageous outcomes, i.e., higher rates of neurological events, higher NYHA-classes, and impaired HRQoL, were not related to the rate of left-sided valve surgery, to the presence of atrial fibrillation, or to impaired left ventricular function. These circumstances support the assumption that PM implantation is related to increased morbidity and poor HRQoL.

6.5. Integration of objective and subjective outcomes after cardiac surgery

Life expectancy has increased during the recent decades. The population of elderly citizens is growing in the Western world, including Finland. During the pioneer era of cardiac surgery in Finland in the mid-1950's, life expectancy at birth for the overall population was approximately 62 years (Tilastokeskus 2009b). Today, life expectancy has risen to 75.9 years for males and 82.9 years for females (Tilastokeskus 2009b). By 2030, the proportion of persons aged over 65 in the population is estimated to rise from the present 16% to 26%, and then to remain more or

less constant for the next decade. The proportion of persons aged over 85 in the population is predicted to rise from the current 1.8% to 6.1% by 2040. Thus, the number of people aged 80 and above will rise from 94,000 today to 349,000 in 2040 (Tilastokeskus 2009c). Considering that heart diseases are the leading cause of death in the Western world and that the prevalence of heart diseases is steadily increasing, the amount of patients seeking treatment or referred for cardiac surgery will by necessity increase. This is also supported by the observation that despite maximal medical therapy many elderly patients remain severely symptomatic due to their cardiovascular disease, and they experience significant functional limitations.

Continuous advances in operative techniques, myocardial protection, and perioperative care have led to a steady decline in operative mortality. Cardiac surgery can be performed safely in patients aged 80 years and above, still with acceptable results (Fruitman et al. 1999, Kolh et al. 2001, Engoren et al. 2002, Sedrakyan et al. 2003, Huber et al. 2007). Until very recently hard, objective variables like survival, mortality, morbidity, complication rate, symptom recurrence, and need for re-interventions were considered to be the only valid method to assess the outcome of patients undergoing cardiac surgery. Since the octogenarians and even older patients referred for cardiac surgery are approaching their maximum life expectancy, emphasis on survival alone in these patients following cardiac surgery may not be appropriate. Instead, patient selection criteria, comprehensive risk-factor analysis including outcome, HRQoL, and future hospital use may be the most important factors to influence surgical recommendations (Khan et al. 1998). The benchmark of cardiac surgical results should be a comprehensive integration of the both objective and subjective outcomes, or hard and soft endpoints.

In this study we showed that the life expectancy of patients who have undergone cardiac surgery, including septuagenarians, is comparable to the age- and sex-matched Finnish reference population. However, age over 60 years was an independent risk factor for mortality in patients undergoing mitral valve surgery (**II**). This observation is corroborated by other authors, as well (Brown et al. 2009, Maganti et al. 2009, Zingone et al. 2009). Not unexpectedly, survival outcome was closely related to the type of surgery. The 5-year survival rates in Studies **II**, **III**, and **IV** were 77%, 59%, and 82%, respectively, underlining the fact that older patients (**III**) do not survive as long as younger patients despite successful cardiac surgery. On the other hand, the survival difference between cohorts **II** and **IV** was small implying that tricuspid valve surgery in combination with CABG and/or aortic- and/or mitral valve surgery does not markedly reduce survival. In fact, the 5-year survival was longer in the

patients who had undergone concomitant tricuspid valve surgery (82%; **IV**) compared to those patients who had undergone only mitral valve surgery (77%, **II**).

In terms of risk factor analysis, renal failure and diabetes, either in combination or as separate entities, are the most important predictors of increased mortality after cardiac surgery. The importance of preoperative, perioperative, and postoperative renal failure and/or diabetes emerged as significant predictors of mortality in Studies **I**, **III**, and **IV**. This finding is well in line with previous studies (Flameng et al. 1996, Kolh et al. 2007, Melby et al. 2007). Cardiac interventions, if feasible, should be carried out before the underlying cardiac disease affects irreversibly cardiac and renal function. In Studies **I** and **III**, an ejection fraction below 50% emerged as a significant risk factor for mortality; this means that ischemic cardiomyopathy or cardiomyopathy due to other causes has proceeded to an irreversible state. The need for a PM after TV surgery emerged, unexpectedly, as a protective factor against mortality. The reason for this is not clear, but one may speculate that the PM patients after TV surgery were under more careful follow-up and – maybe more importantly – that the PM protected against fatal bradyarrhythmias. This hypothesis is difficult to verify since bradyarrhythmias as the cause of death cannot be identified or excluded by clinical examination or postmortem. However, risk factor analysis supported the hypothesis that PM improves survival, since the need for PM was ultimately the only protective factor against mortality during late follow-up. This finding is new and first published by our group (**IV)**.

The HRQoL after cardiac surgery was comparable to the age- and sex-matched Finnish reference population in Studies **II**, **III**, and **IV**. However, several factors contributing to impaired postoperative HRQoL outcome could be adduced. There was more homogeneity within the factors related to physical capacity and exercise tolerance than to the factors related to mental conditions. It is also noteworthy that the risk profile of factors that were associated with impaired HRQoL varied significantly between Studies **II** and **III**. This is probably due to differences between patient demographics and operations performed: in Study **II**, patients were younger (62 years) and underwent primarily mitral valve-related procedures whereas in Study **III**, patients were markedly older (73 years) and underwent mainly CABG. However, age over 60 years, higher pre- or postoperative NYHA-class, need for nitroglycerin or diuretics, and diabetes were the most important predictors of poor HRQoL after cardiac surgery in terms of physical dimensions (energy, pain and mobility). Higher NYHA-class and need for preceding medication affected also the mental dimensions (social isolation and emotion). Impaired physical capacity is likely to cause dejection in otherwise active cardiac patients. In general,

cardiac operated patients experienced less pain than the age- and sex-matched reference population. This observation has been made previously (Sjöland et al. 1997, Herlitz et al. 1999). Unexpectedly, the type of cardiac surgery did not contribute to any dimension of HRQoL (**II, III, IV)**. Patients who had undergone either CABG, valve surgery, or a combination procedure performed similarly on both physical and mental HRQoL scores.

6.6. Study limitations

From a methodological perspective, an obvious limitation of this study is the lack of randomization. However, it is very difficult to design prospective randomized clinical trials that compare only, e.g., the effect of the type of cardiac surgery in terms of outcome (Blackstone 2001 and 2002). The obvious reasons are that such studies carry great heterogeneity of patients and for ethical reasons the operative techniques cannot be selected randomly. Thus, treatment is confounded by selection bias, and any observed outcome differences could relate to a number of concealed underlying causes. In this study, we attempted to adjust for selection factors by using multivariate analysis, by investigating objective outcomes by logistic regression, and by stabilizing unavoidable patient heterogeneity by propensity score matching (**II**). Another limitation of this study is the cross-sectional composition of the HRQoL analysis in Studies **II** and **IV**, and the lack of preoperative HRQoL assessment. Data on HRQoL were not routinely collected in the 1990's, and thus we were not able to assess the change in the HRQoL longitudinally over time, except in Study **II**. We were, however, able to compare the HRQoL of the cardiac operated patients with an age- and sex-matched Finnish reference population. So far, there are not any approved methods to standardize subjective outcomes, such as HRQoL.

The single-center nature and the obligatory loss of patients inherent to long-term follow-up studies are also potential methodological restriction of this study. The loss of only 25% of elderly patients during eight years follow-up (**III**) is, on the other hand, quite small and does not invalidate the major results. From the HRQoL perspective, it is impossible to standardize all demographic characteristics of all patients in terms of education, profession, social status, and cultural background.

In Study **I**, the last ECG recording was performed on the day of discharge, and no additional recordings were routinely done. Thus, some of the CDs might still have resolved after discharge from hospital. Although Study **I** shed light on the survival of CABG patients compared with the age- and sex-matched Finnish reference population, the study does not present any direct

information on the survival of CABG patients in comparison with similar patients who were not treated in the same way.

In Study **IV**, patients who underwent TV surgery were a very heterogeneous group. Tricuspid valve regurgitation is nearly always secondary to mitral or aortic valve pathology or CAD, and mitral and/or aortic valve surgery or CABG is often performed concomitantly with tricuspid repair. Many of the patients had also undergone cardiac surgery previously. Thus, one has to be careful when applying these results to isolated TV surgery.

7. CONCLUSIONS

In this study, we reviewed comprehensively both objective and subjective outcome variables of patients who were referred for cardiac surgery. We addressed several clinically relevant risk factors contributing to impaired outcome and made the following specific observations:

1. Survival of CABG patients is comparable to an age- and sex-matched reference population. CABG-related permanent CDs are associated with prolonged hospitalization, but CABG-related CDs do not contribute to increased cardiac mortality during long-term (9.6±0.2 years) follow-up.

2. Survival is longer after MVP than after MVR. The HRQoL of MVP and MVR patients is similar. In terms of the variables related to HRQoL, mitral valve operated patients do not differ markedly from the age- and sex-matched reference population.

3. The long-term HRQoL and survival of octogenarians who have undergone cardiac surgery at the age of ≥70 years is comparable to the HRQoL and survival of the age- and sex-matched reference population. The HRQoL of octogenarians deteriorates over the years after cardiac surgery especially of the physical domains.

4. The need for a new PM after TV surgery is high – and PMs are continuously needed during long-term follow-up. Still, life expectancy among PM-treated patients is longer than among the patients who did not need a PM after TV surgery. Although PM treatment improves survival, the patients who have a PM implanted have an increased risk of thromboembolic complications and impaired HRQoL in terms of physical domains.

8. YHTEENVETO (FINNISH SUMMARY)

Sydänkirurgian tuloksia on perinteisesti arvioitu objektiivisilla mittareilla kuten sydänleikkaukseen liittyvällä kuolleisuudella, vertaamalla sydänleikkauspotilaiden elinaikaennustetta ikä- ja sukupuolivakioituun normaaliväestöön, sydänleikkaukseen liittyvien komplikaatioiden laadulla ja määrällä sekä uusintaoperaatioiden tarpeella. Vaikka objektiivisesti mitattavat suureet ovat keskenään vertailukelpoisia, ne eivät kerro mitään sydänkirurgialla saavutettavasta subjektiivisesta hyödystä potilaalle. Sydänleikkauksella saavutettava subjektiivinen hyöty voidaan arvioida sydänleikkauksen jälkeisenä parantuneena elämänlaatuna. Sydänleikkauksen vaikutus elämänlaatuun tulee tulevina vuosina entisestään korostumaan, koska sydänleikkaus on mahdollista tehdä entistä pienemmällä riskillä yhä iäkkäämmille ja aikaisempaa huonokuntoisemmille potilaille. Erityisesti iäkkäiden potilaiden kohdalla sydänkirurgian merkitys subjektiivisesti koettuun elämänlaatuun korostuu, kun taas objektiivisesti saavutettavan hyödyn, kuten elinaikaennusteen, merkitys vähenee. Toisaalta myös rajallisten terveydenhuollon resurssien vuoksi on perusteltua, että tehdyillä hoitotoimenpiteillä on todellinen potilasta hyödyttävä vaikutus. Terveyteen liittyvän elämänlaadun mittaamisesta on tullut keskeinen väline sydänkirurgisten hoitotulosten arvioinnissa ja potilaan kokemusta sydänleikkauksen vaikutuksesta elämänlaatuun on pidettävä nykyään vähintään yhtä tärkeänä hoidon onnistumisen mittarina kuin pidentynyttä elinaikaennustetta.

Väitöskirjatyössä selvitettiin sydänkirurgisen hoidon vaikuttavuutta tutkimalla Kuopion yliopistollisessa sairaalassa vuosien 1990–2007 välisenä aikana sydänleikattujen potilaiden elinaikaennustetta, sydänleikkauksen jälkeistä sairastavuutta, uusintaoperaatioiden tarvetta, elämänlaatua ja edellä mainittuihin vaikuttavia riskitekijöitä. Väitöskirjatyö koostui neljästä osatyöstä. Ensimmäisessä ja neljännessä osatyössä tarkasteltiin erityisesti sydänkirurgiaan liittyvien johtumishäiriöiden vaikutusta elinaikaennusteeseen ja elämänlaatuun. Tutkimusaineistona oli 604 potilaasta, joiden tiedot saatiin kirurgian ja anestesiologian klinikoiden yhteisestä prospektiivisesti kertyvästä sydänleikkausrekisteristä. Potilaiden seurantatiedot kerättiin poliklinikkakäyntien yhteydessä, Tilastokeskuksen ylläpitämästä kuolemansyyrekisteristä ja potilaille lähetetyillä kyselylomakkeilla.

Ensimmäisessä osatyössä selvitettiin 180 peräkkäisen elektiivisesti leikatun ohitusleikkauspotilaan elinaikaennustetta ja leikkauksessa syntyneen pysyvän johtumishäiriön vaikutusta elinaikaennusteeseen. Elektiivisesti ohitusleikattujen potilaiden elinaikaennuste oli yhtä hyvä kuin ikä- ja sukupuolivakioidun verrokkiväestön elinaikaennuste. Kuolemanriskiä lisääviä

tekijöitä kaikki kuolemansyyt huomioivassa monimuuttujamallissa olivat ohitusleikkauksen yhteydessä syntynyt pysyvä johtumishäiriö, diabetes, perfuusioaika, ohitusten lukumäärä ja heikentynyt vasemman kammion funktio. Pysyvä johtumishäiriö ei kuitenkaan lisännyt sydänperäisten kuolemien määrää.

Toisessa osatyössä verrattiin mitraaliplastia- (n=85) ja mitraalitekoläppäleikkauksen (n=99) vaikutuksia potilaiden elinaikaennusteeseen ja elämänlaatuun. Vertailu tehtiin vakioimalla potilaat leikkausta edeltävien muuttujien suhteen propensity score -menetelmällä. Mitraaliplastiapotilaiden elinaikaennuste oli tilastollisesti merkitsevästi parempi kuin mitraalitekoläppäpotilaiden, ja mitraalitekoläpän käyttö osoittautui itsenäiseksi kuolemanriskiä lisääväksi tekijäksi monimuuttujamallissa. Muita kuolemanriskiä lisääviä tekijöitä olivat leikkausta edeltävä epästabiili angina pectoris -oire, yli 60 vuoden ikä, leikkausta edeltänyt munuaisten vajaatoiminta ja iskeeminen aivotapahtuma. Valitulla leikkaustekniikalla (mitraaliplastia vs. mitraaliproteesi) ei ollut vaikutusta potilaiden subjektiivisesti kokemaan leikkauksen jälkeiseen elämänlaatuun. Mitraaliläppäleikattujen potilaiden elämänlaatu vastasi ikä- ja sukupuolivakioidun verrokkiväestön elämänlaatua lukuun ottamatta fyysistä suorituskykyä kuvaavia Nottingham Health Profile -elämänlaatumittarin ”tarmokkuus” ja ”liikkuminen” ulottuvuuksia. Tutkimuksessa löydettiin 14 muuttujaa, jotka osoittautuivat mitraaliläppäleikkauksen jälkeistä elämänlaatu heikentäviksi itsenäisiksi riskitekijöiksi.

Kolmannessa osatyössä selvitettiin 104:n yli 70 vuoden ikäisenä sydänleikatun potilaan elinaikaennustetta, ennusteeseen vaikuttavia tekijöitä ja elämänlaatua keskimäärin 15 kuukauden ja 8 vuoden jälkeen leikkauksesta sekä elämänlaatuun vaikuttavia tekijöitä. Yli 70-vuotiaana sydänleikattujen potilaiden elinaikaennuste oli vastaava kuin ikä- ja sukupuolivakioidun verrokkiväestön. Itsenäisiä kuolemanriskiä lisääviä tekijöitä olivat leikkauksen kiireellisyys, heikentynyt vasemman kammion funktio, leikkausta edeltänyt munuaisten vajaatoiminta ja pitkittynyt leikkauksen jälkeinen tehohoitojakso. Potilaiden subjektiivisesti kokema elämänlaatu vastasi ikä- ja sukupuolivakioidun verrokkiväestön elämänlaatua 15 kuukauden ja 8 vuoden seurannassa lukuun ottamatta kipua kuvaavaa ulottuvuutta: 15 kuukauden kohdalla sydänleikatut potilaat kokivat vähemmän elämänlaatua haittaavaa kipuoiretta kuin verrokkiväestö. Kuitenkin 8 vuoden seurannan aikana sydänleikattujen potilaiden subjektiivisesti kokema elämänlaatu heikkeni samalla tavalla kuin verrokkiväestönkin ”tarmokkuutta”, ”kipua” ja ”liikkumista” kuvaavissa ulottuvuuksissa. Tutkimuksessa löydettiin 7 muuttujaa, jotka osoittautuivat sydänleikkauksen jälkeistä

elämänlaatua heikentäviksi itsenäisiksi riskitekijöiksi yhdessä tai useammassa elämänlaatua kuvaavassa ulottuvuudessa.

Neljännessä osatyössä tutkittiin 136:n trikuspidaaliläppäleikatun potilaan leikkauksen jälkeistä pysyvän tahdistimen tarvetta, elinaikaennustetta, elämänlaatua ja näihin vaikuttajia tekijöitä. Välittömästi trikuspidaaliläppäleikkauksen jälkeen tai keskimäärin 8 vuoden seuranta-aikana pysyvän tahdistimen tarvitsi johtumishäiriön vuoksi 21 % potilaista. Määrä on poikkeuksellisen suuri yleisesti sydänkirurgiaan liittyvän pysyvän tahdistimen tarpeeseen verrattuna. Pysyvällä tahdistimella oli yllättäen elinaikaennustetta parantava vaikutus, sillä se oletettavasti suojasi potilaita rytmi- tai johtumishäiriöperäiseltä äkkikuolemalta. Pysyvän tahdistimen tarve lisäsi kuitenkin tromboembolisten komplikaatioiden ilmaantuvuutta ja heikensi potilaiden elämänlaatua erityisesti fyysistä suorituskykyä kuvaavissa ulottuvuuksissa. Trikuspidaaliläppäleikattujen potilaiden elinaikaennuste oli yhtä hyvä kuin ikä- ja sukupuolivakioidun verrokkiväestön. Itsenäisiä kuoleman riskiä lisääviä tekijöitä olivat välitön leikkauksen jälkeinen dialyysiä vaatinut munuaisten vajaatoiminta, leikkauksen aikainen sydäninfarkti, leikkausta edeltänyt munuaisten vajaatoiminta ja leikkauksen jälkeinen kontrapulsaattorin tarve.

Väitöskirjatutkimuksesta saatu tieto auttaa suuntaamaan potilasvalintaa siten, että sydänkirurgisen hoidon piiriin valikoituvat potilaat, jotka sekä objektiivisilla että subjektiivisilla mittareilla arvioituna sydänleikkauksesta oletettavasti eniten hyötyvät. Toisaalta tutkimus auttaa tunnistamaan riskipotilaat, joiden leikkaukseen, leikkauksen jälkeiseen toipumiseen ja leikkauksen jälkeiseen elämänlaatuun liittyy todennäköisesti ongelmia. Vaikka pysyvä tahdistin saattaa suojata potilaita johtumishäiriöperäiseltä kuolemalta, se heikentää elämänlaatua erityisesti fyysistä suorituskykyä kuvaavissa ulottuvuuksissa.

9. REFERENCES

Ad N, Barnett SD, Speir AM, Massimiano PS. Institutional and national trends in isolated mitral valve surgery over the past decade. Curr Opin Cardiol 2008;23:99-104.

Akins CW, Daggett WM, Vlahakes GJ, et al. Cardiac operations in patients 80 years old and older. Ann Thorac Surg 1997;64:606-14.

Akins CW, Miller DC, Turina MI, et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. J Thorac Cardiovasc Surg 2008;135:732-8.

Avery GJ, Ley SJ, Hill JD, Hershon JJ, Dick SE. Cardiac surgery in the octogenarian: evaluation of risk, cost, and outcome. Ann Thorac Surg 2001;71:591-6.

Baerman JM, Kirsh MM, deBuitleir M. Natural history and determinants of conduction defects following coronary artery bypass surgery. Ann Thorac Surg 1987;44:150-3.

Bateman TM, Weiss MH, Czer LS, et al. Fascicular conduction disturbances and ischemic heart disease: adverse prognosis despite coronary revascularization. J Am Coll Cardiol 1985;5:632-9.

Blackstone EH. Breaking down barriers: helpful breakthrough statistical methods you need to understand better. J Thorac Cardiovasc Surg 2001;122:430-9.

Blackstone EH. Comparing apples and oranges. J Thorac Cardiovasc Surg 2002;123:8-15.

Braunberger E, Deloche A, Berrebi A, et al. Very long-term results (more than 20 years) of valve repair with Carpentier's techniques in nonrheumatic mitral valve insufficiency. Circulation 2001;104:8-11.

Braunwald NS, Cooper T, Morrow AG. Complete replacement of the mitral valve. Successful clinical application of a flexible polyurethane prosthesis. J Thorac Cardiovasc Surg 1960;40:1-11.

Brook RH, Ware JE Jr, Rogers WH, et al. Does free care improve adults' health? Results from a randomized controlled trial. N Engl J Med 1983;309:1426-34.

Brooks R, Rabin R, de Charro F, Eds. The Measurement and valuation of health status using EQ-5D: a European perspective. Kluwer Academic Publishers 2003.

Brown JM, O'Brien SM, Wu C, Sikora JA, Griffith BP, Gammie JS. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. J Thorac Cardiovasc Surg 2009;137:82-90.

Caine N, Sharples LD, Wallwork J. Prospective study of health related quality of life before and after coronary artery bypass grafting: outcome at five years. Heart 1999;81:347-51.

Campeau L. Letter: Grading of angina pectoris. Circulation 1976;54:522-3.

Caretta Q, Mercanti CA, De Nardo D, et al. Ventricular conduction defects and atrial fibrillation after coronary artery bypass grafting. Multivariate analysis of preoperative, intraoperative and postoperative variables. Eur Heart J 1991;12:1107-11.

Carrel A, Lindbergh CA. Culture of whole organs. Science 1935;31:621.

Carrel A. On the experimental surgery of the thoracic aorta and heart. Ann Surg 1910;52:83-95.

Caspi Y, Safadi T, Ammar R, Elamy A, Fishman NH, Merin G. The significance of bundle-branch block in the immediate postoperative electrocardiograms of patients undergoing coronary artery bypass. J Thorac Cardiovasc Surg 1987;93:442-6.

Chee JH, Filion KB, Haider S, Pilote L, Eisenberg MJ. Impact of age on hospital course and cost of coronary artery bypass grafting. Am J Cardiol 2004;93:768-71.

Chocron S, Etievent J-M, Viel JF, et al. Prospective study of quality of life before and after open heart operations. Ann Thorac Surg 1996;61:153-7.

Chocron S, Etievent JP, Viel JF, et al. Preoperative quality of life as a predictive factor of 3-year survival after open heart operations. Ann Thorac Surg 2000;69:722-7.

Chu A, Califf RM, Pryor DB, et al. Prognostic effect of bundle branch block related to coronary artery bypass grafting. Am J Cardiol 1987;59:798-803.

Cohn LH, Rizzo RJ, Adams DH, et al. The effect of pathophysiology on the surgical treatment of ischemic mitral regurgitation: operative and late risks of repair versus replacement. Eur J Cardiothorac Surg 1995;9:568-74.

Constitution of the World Health Organization. In: World Health Organization. Handbook of basic documents. 5th edition. Geneva: Palais des Nations, 1952:3-20.

Cook DJ, Bailon JM, Douglas TT, et al. Changing incidence, type, and natural history of conduction defects after coronary artery bypass grafting. Ann Thorac Surg 2005;80:1732-7.

Curtis LH, Phelps CE, McDermott MP, Rubin HR. The value of patient-reported health status in predicting short-term outcomes after coronary artery bypass graft surgery. Med Care 2002;40:1090-100.

Dawkins S, Hobson AR, Kalra PR, Tang AT, Monro JL, Dawkins KD. Permanent pacemaker implantation after isolated aortic valve replacement: incidence, indications, and predictors. Ann Thorac Surg 2008;85:108-12.

Dewey TM, Brown D, Ryan WH, Herbert MA, Prince SL, Mack MJ. Reliability of risk algorithms in predicting early and late operative outcomes in high-risk patients undergoing aortic valve replacement. J Thorac Cardiovasc Surg 2008;135:180-7.

Diodato MD, Moon MR, Pasque MK, et al. Repair of ischemic mitral regurgitation does not increase mortality or improve long-term survival in patients undergoing coronary artery revascularization: a propensity analysis. Ann Thorac Surg 2004;78:794-9.

Do QB, Pellerin M, Carrier M, et al. Clinical outcome after isolated tricuspid valve replacement: 20-year experience. Can J Cardiol 2000;16:489-93.

Edmunds LH Jr, Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. Ann Thorac Surg 1996;62:932-5.

Elliott D, Lazarus R, Leeder SR. Health outcomes of patients undergoing cardiac surgery: repeated measures using Short Form-36 and 15 Dimensions of Quality of Life questionnaire. Heart Lung 2006;35:245-51.

Engblom E, Hämäläinen H, Lind J, et al. Quality of life during rehabilitation after coronary artery bypass surgery. Qual Life Res 1992;1:167-75.

Engblom E, Hämäläinen H, Rönnemaa T, Vänttinen E, Kallio V, Knuts LR. Cardiac rehabilitation and return to work after coronary artery bypass surgery. Qual Life Res 1994;3:207-13.

Engblom E, Korpilahti K, Hämäläinen H, Rönnemaa T, Puukka P. Quality of life and return to work 5 years after coronary artery bypass surgery. Long-term results of cardiac rehabilitation. J Cardiopulm Rehabil 1997;17:29-36.

Engoren M, Arslanian-Engoren C, Steckel D, Neihardt J, Fenn-Buderer N. Cost, outcome, and functional status in octogenarians and septuagenarians after cardiac surgery. Chest 2002;122:1309-15.

Enriquez-Sarano M, Schaff HV, Orszulak TA, Bailey KR, Tajik AJ, Frye RL. Congestive heart failure after surgical correction of mitral regurgitation. A long-term study. Circulation 1995;92:2496-503.

Enriquez-Sarano M, Schaff HV, Orszulak TA, Tajik AJ, Bailey KR, Frye RL. Valve repair improves the outcome of surgery for mitral regurgitation. A multivariate analysis. Circulation 1995;91:1022-8.

EuroSCORE Web-based interactive risk calculator. EuroSCORE Web site. Available at: http://www.euroscore.org/index.htm

Falcoz PE, Chocron S, Stoica L, et al. Open heart surgery: one-year self-assessment of quality of life and functional outcome. Ann Thorac Surg 2003;76:1598-604.

Favaloro RG. Saphenous vein graft in the surgical treatment of coronary artery disease. Operative technique. J Thorac Cardiovasc Surg 1969;58:178-85.

Ferguson TB Jr, Hammill BG, Peterson ED, DeLong ER, Grover FL; STS National Database Committee. A decade of change - risk profiles and outcomes for isolated coronary artery bypass grafting procedures. Ann Thorac Surg 2002;73:480-9.

Filsoufi F, Salzberg SP, Aklog L, Adams DH. Aqcuired disease of the mitral valve. In: Sabiston and Spencer, Surgery of the chest, 7th Edition, pp1299-1333, Elsevier Saunders, Philadelphia 2005.

Flameng WJ, Herijgers P, Szécsi J, Sergeant PT, Daenen WJ, Scheys I. Determinants of early and late results of combined valve operations and coronary artery bypass grafting. Ann Thorac Surg 1996;61:621-8.

Fruitman DS, MacDougall CE, Ross DB. Cardiac surgery in octogenarians: can elderly patients benefit? Quality of life after cardiac surgery. Ann Thorac Surg 1999;68:2129-35.

Gibbon JH Jr. Application of a mechanical heart and lung apparatus to cardiac surgery. Minn Med 1954;37:171-80.

Gillinov AM, Wierup PN, Blackstone EH, et al. Is repair preferable to replacement for ischemic mitral regurgitation? J Thorac Cardiovasc Surg 2001;122:1125-41.

Gillinov AM, Blackstone EH, Nowicki ER, et al. Valve repair versus valve replacement for degenerative mitral valve disease. J Thorac Cardiovasc Surg 2008;135:885-93.

Glikson M, Dearani JA, Hyberger LK, Schaff HV, Hammill SC, Hayes DL. Indications, effectiveness, and long-term dependency in permanent pacing after cardiac surgery. Am J Cardiol 1997;80:1309-13.

Gogbashian A, Sepic J, Soltesz EG, Nascimben L, Cohn LH. Operative and long-term survival of elderly is significantly improved by mitral valve repair. Am Heart J 2006;151:1325-33.

Goldsmith IRA, Lip GYH, Patel RL. A prospective study of changes in the quality of life of patients following mitral valve repair and replacement. Eur J Cardio-thorac Surg 2001;20:949-55.

Gordon RS, Ivanov J, Cohen G, Ralph-Edwards AL. Permanent cardiac pacing after a cardiac operation: predicting the use of permanent pacemakers. Ann Thorac Surg 1998;66:1698-704.

Gozal Y, Glantz L, Luria MH, Milgalter E, Shimon D, Drenger B. Normothermic continuos blood cardioplegia improves electrophysiocally recovery after open heart surgery. Anesthesiology 1996;84:1298-1306.

Gregoratos G, Abrams J, Epstein AE, et al. ACC / AHA / NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices (a). J Am Coll Cardiol 2002;40:1703-19.

Gregoratos G, Abrams J, Epstein AE, et al. American College of Cardiology / American Heart Association Task Force on Practice Guidelines / North American Society for Pacing and Electrophysiology Committee to Update the 1998 Pacemaker Guidelines (b). Circulation 2002;106:2145-61.

Griffenhagen GB, Hughes CH. The history of the mechanical heart. Annu Rep Smithsonian Inst 1955;4241:339-56. Original citation: LeGallois JJC. Experiences sur le principle de la vie. Paris: D'Hautel, 1812. Translation by Nancrede NC, Nancrede JG. Experiments on the principle of life. Philadelphia, 1813.

Grossi EA, Crooke GA, DiGiorgi PL, et al. Impact of moderate functional mitral insufficiency in patients undergoing surgical revascularization. Circulation 2006;114:573-6.

Guenther T, Noebauer C, Mazzitelli D, Busch R, Tassani-Prell P, Lange R. Tricuspid valve surgery: a thirty-year assessment of early and late outcome. Eur J Cardiothorac Surg 2008;34:402-9.

Halstead JC, Spielvogel D, Meier DM, et al. Optimal pH strategy for selective cerebral perfusion. Eur J Cardiothorac Surg 2005;28:266-73.

Harken DE, Ellis LB, Ware PF, Norman LR. The surgical treatment of mitral stenosis. N Engl J Med 1948;239:801-9.

Heikkinen J, Biancari F, Satta J, Salmela E, Juvonen T, Lepojärvi M. Quality of life after mitral valve repair. J Heart Valve Dis 2005a;14:722-6.

Heikkinen J, Biancari F, Uusimaa P, et al. Long-term outcome after mitral valve repair. Scand Cardiovasc J 2005b;39:229-36.

Heikkinen J, Biancari F, Satta J, Salmela E, Mosorin M, Juvonen T, Lepojärvi M. Predicting immediate and late outcome after surgery for mitral valve regurgitation with EuroSCORE. J Heart Valve Dis 2007;16:116-21.

Hellgren L, Ståhle E. Quality of life after heart valve surgery with prolonged intensive care. Ann Thorac Surg 2005;80:1693-8.

Herlitz J, Brandrup-Wognsen G, Caidahl K, et al. Mortality and morbidity among patients who undergo combined valve and coronary artery bypass surgery. Early and late results. Eur J Cardio-thorac Surg 1997;12:836-46.

Herlitz J, Brandrup-Wognsen G, Caidahl K, et al. Determinants for an impaired quality of life 10 years after coronary artery bypass surgery. Int J Cardiol 2005;98:447-52.

Herlitz J, Brandrup-Wognsen G, Haglid M, Karlson BW, Hartford M, Karlsson T. Predictors of death during 5 years after coronary artery bypass grafting. Int J Cardiol 1998;64:15-23.

Herlitz J, Wiklund I, Caidahl K, et al. Determinants of an impaired quality of life five years after coronary artery bypass surgery. Heart 1999;81:342-6.

Ho PM, Masoudi FA, Peterson PN, et al. Health-related quality of life predicts mortality in older but not younger patients following cardiac surgery. Am J Geriatr Cardiol 2005;14:176-82.

Huber CH, Goeber V, Berdat P, Carrel T, Eckstein F. Benefits of cardiac surgery in octogenarians - a postoperative quality of life assessment. Eur J Cardiothorac Surg 2007;31:1099-105.

Hufnagel CA, Harvey WP, Rabil PJ, McDermott TF. Surgical correction of aortic insufficiency. Surgery 1954;35:673-83.

Hunt SM, McKenna SP, McEwen J, Williams J, Papp E. The Nottingham Health Profile: Subjective health status and medical consultations. Soc Sci Med 1981;15:221-9.

Immer FE, Donati O, Wyss T, et al. Quality of life after mitral valve surgery: differences between reconstruction and replacement. J Heart Valve Dis 2003;12:162-8.

Iscan ZH, Vural KM, Bahar I, Mavioglu L, Saritas A. What to expect after tricuspid valve replacement? Long-term results. Eur J Cardiothorac Surg 2007;32:296-300.

Ishikawa S, Buxton BF, Manson N, et al. Cardiac surgery in octogenarians. ANZ J Surg 2004;74:983-5.

Ivanov J, Weisel RD, David TE, Naylor CD. Fifteen-year trends in risk severity and operative mortality in elderly patients undergoing coronary artery bypass graft surgery. Circulation 1998;97:673-80.

Järvinen O, Saarinen T, Julkunen J, Huhtala H, Tarkka MR. Changes in health-related quality of life and functional capacity following coronary artery bypass graft surgery. Eur J Cardiothorac Surg 2003;24:750-6.

Joffe MM, Rosenbaum PR. Invited commentary: Propensity Scores. Am J Epidemiol 1999;150:327-33.

Karabulut H, Toraman F, Alhan C, et al. EuroSCORE overestimates the cardiac operative risk. Cardiovasc Surg 2003;11:295-8.

Khan JH, McElhinney DB, Hall TS, Merrick SH. Cardiac valve surgery in octogenarians: improving quality of life and functional status. Arch Surg 1998;133:887-93.

Kind P. Measuring quality of life in evaluating clinical interventions: an overview. Ann Med 2001;33:323-7.

Koch CG, Khandwala F, Blackstone EH. Health-related quality of life after cardiac surgery. Semin Cardiothorac Vasc Anesth 2008;12:203-17.

Koch CG, Li L, Lauer M, Sabik J, Starr NJ, Blackstone EH. Effect of functional health-related quality of life on long-term survival after cardiac surgery. Circulation 2007;115:692-9.

Koivukangas P, Ohinmaa A, Koivukangas J, eds. The Finnish version of the Nottingham Health Profile. Helsinki, Finland: The National Research and Development Centre for Welfare and Health 1995;187:1-94.

Kolesov VI, Potashov LV. [Surgery of coronary arteries]. Eksp Khir Anesteziol 1965;10:3-8.

Kolh P, Kerzmann A, Honore C, Comte L, Limet R. Aortic valve surgery in octogenarians: predictive factors for operative and long-term results. Eur J Cardiothorac Surg 2007;31:600-6.

Kolh P, Kerzmann A, Lahaye L, Gerard P, Limet R. Cardiac surgery in octogenarians. Perioperative outcome and long-term results. Eur Heart J 2001;22:1235-43.

Koplan BA, Stevenson WG, Epstein LM, Aranki SF, Maisel WH. Development and validation of a simple risk score to predict the need for permanent pacing after cardiac valve surgery. J Am Coll Cardiol 2003;41:795-801.

Lee EM, Shapiro LM, Wells FC. Superiority of mitral valve repair in surgery for degenerative mitral regurgitation. Eur Heart J 1997;18:655-63.

Limongelli G, Ducceschi V, D'Andrea A, et al. Risk factors for pacemaker implantation following aortic valve replacement: a single centre experience. Heart 2003;89:901-4.

Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics - 2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2009;119:480-6.

Loponen P, Luther M, Wistbacka JO, et al. Quality of life during 18 months after coronary artery bypass grafting. Eur J Cardiothorac Surg 2007;32:77-82.

Maganti M, Rao V, Brister S, Ivanov J. Decreasing mortality for coronary artery bypass surgery in octogenarians. Can J Cardiol 2009;25:32-5.

Maliwa MA, van der Heijden GJ, Bots ML, et al. Quality of life and NYHA class 30 years after mechanical aortic valve replacement. Cardiovasc Surg 2003;11:381-7.

Mantovani V, Mariscalco G, Leva C, Blanzola C, Cattaneo P, Sala A. Long-term results of the surgical treatment of chronic ischemic mitral regurgitation: comparison of repair and prosthetic replacement. J Heart Valve Dis 2004;13:421-8.

McCarthy PM, Bhudia SK, Rajeswaran J, et al. Tricuspid valve repair: durability and risk factors for failure. J Thorac Cardiovasc Surg 2004;127:674-85.

Melby SJ, Zierer A, Kaiser SP, et al. Aortic valve replacement in octogenarians: risk factors for early and late mortality. Ann Thorac Surg 2007;83:1651-6.

Mihaljevic T, Lam BK, Rajeswaran J, et al. Impact of mitral valve annuloplasty combined with revascularization in patients with functional ischemic mitral regurgitation. J Am Coll Cardiol 2007;49:2191-201.

Mohty D, Orszulak TA, Schaff HV, Avierinos JF, Tajik JA, Enriquez-Sarano M. Very long-term survival and durability of mitral valve repair for mitral valve prolapse. Circulation 2001;104:1-7.

Morell VO, Daggett WM, Pezzella AT, Moran JM, Bitran D. Aortic stenosis in the elderly: result of aortic valve replacement. J Cardiovasc Surg (Torino) 1996;37:33-5.

Moss RR, Humphries KH, Gao M, et al. Outcome of mitral valve repair or replacement: a comparison by propensity score analysis. Circulation 2003;108:90-7.

Mustonen P, Hippeläinen M, Rehnberg S. Low myocardial temperatures are associated with postoperative conduction defects after coronary artery bypass surgery. Ann Chir Gyn 1995;84:44-50.

Mustonen P, Hippeläinen M, Vanninen E, Rehnberg S, Tenhunen-Eskelinen M, Hartikainen J. Significance of coronary artery bypass grafting-associated conduction defects. Am J Cardiol 1998;81:558-63.

Myers WO, Blackstone EH, Davis K, Foster ED, Kaiser GC. CASS Registry. Long Term Surgical Survival. J Am Coll Cardiol 1999;33:488-98.

Nashef SA, Roques F, Hammill BG, et al. Validation of European System for Cardiac Operative Risk Evaluation (EuroSCORE) in North American cardiac surgery. Eur J Cardiothorac Surg 2002;22:101-5.

Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9-13.

Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. J Am Coll Cardiol 2004;43:405-9.

National Adult Cardiac Surgical Database Report 2000-2001. http://www.ctsnet.org/file/SCTS2000pages72-81Age.pdf

Nielsen JC, Kristensen L, Andersen HR, Mortensen PT, Pedersen OL, Pedersen AK. A randomized comparison of atrial and dual-chamber pacing in 177 consecutive patients with sick sinus syndrome: echocardiographic and clinical outcome. J Am Coll Cardiol 2003;42:614-23.

O'Brien SM, Shahian DM, Filardo G, et al. Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2 - isolated valve surgery. Ann Thorac Surg 2009;88:S23-42.

Onalan O, Crystal A, Lashevsky I, et al. Determinants of pacemaker dependency after coronary and/or mitral or aortic valve surgery with long-term follow-up. Am J Cardiol 2008;101:203-8.

Osswald BR, Gegouskov V, Badowski-Zyla D, et al. Overestimation of aortic valve replacement risk by EuroSCORE: implications for percutaneous valve replacement. Eur Heart J 2009;30:74-80.

Peric VM, Borzanovic MD, Stolic RV, Jovanovic AN, Sovtic SR. Severity of angina as a predictor of quality of life changes six months after coronary artery bypass surgery. Ann Thorac Surg 2006;81:2115-20.

Peterson ED, Cowper PA, Jollis JG, et al. Outcomes of coronary artery bypass graft surgery in 24,461 patients aged 80 years or older. Circulation 1995;92:85-91.

Pitkänen O, Niskanen M, Rehnberg S, Hippeläinen M, Hynynen M. Intra-institutional prediction of outcome after cardiac surgery: comparison between a locally derived model and the EuroSCORE. Eur J Cardiothorac Surg 2000;18:703-10.

Raja SG, Berg GA. Moderate ischemic mitral regurgitation: to treat or not to treat? J Card Surg 2007;22:362-9.

Ratnatunga CP, Edwards MB, Dore CJ, Taylor KM. Tricuspid valve replacement: UK Heart Valve Registry mid-term results comparing mechanical and biological prostheses. Ann Thorac Surg 1998;66:1940-7.

Rector TS, Kubo SH, Cohn JN. Patients' self-assessment of their congestive heart failure. Part 2: Content, reliability and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. Heart Failure 1987;10:198-209.

Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. Eur Heart J 2003;24:882-3

Roques F, Nashef SA, Michel P, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg 1999;15:816-22.

Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika 1983;70:41-55.

Ruel M, Masters RG, Rubens FD, et al. Late incidence and determinants of stroke after aortic and mitral valve replacement. Ann Thorac Surg 2004;78:77-83.

Rumsfeld JS, Ho PM, Magid DJ, et al. Predictors of health-related quality of life after coronary artery bypass surgery. Ann Thorac Surg 2004;77:1508-13.

Rumsfeld JS, Magid DJ, O'Brien M, et al. Processes, Structures, and Outcomes of Care in Cardiac Surgery. Changes in health-related quality of life following coronary artery bypass graft surgery. Ann Thorac Surg 2001;72:2026-32.

Rumsfeld JS, MaWhinney S, McCarthy M Jr, et al. Health-related quality of life as a predictor of mortality following coronary artery bypass graft surgery. JAMA 1999;281:1298-303.

Rumsfeld JS. Valve surgery in the elderly: question of quality (of life)? J Am Coll Cardiol 2003;42:1215-7.

Salerno T, Houck JP, Barrozo CA. Retrograde continuos warm blood cardioplegia: a new concept in myocardial protection. Ann Thorac Surg 1991;51:245-7.

Satinsky JD, Collins JJ, Dalen JE. Conduction defects after cardiac surgery. Circulation 1974;49:170-4.

Schroter S, Lamping DL. Coronary revascularisation outcome questionnaire (CROQ): development and validation of a new, patient based measure of outcome in coronary bypass surgery and angioplasty. Heart 2004;90:1460-6.

Scully HE, Armstrong CS. Tricuspid valve replacement. Fifteen years of experience with mechanical prostheses and bioprostheses. J Thorac Cardiovasc Surg 1995;109:1035-41.

Sedrakyan A, Vaccarino V, Eleteriades JA, et al. Health related quality of life after mitral valve repairs and replacements. Qual Life Res 2006;15:1153-60.

Sedrakyan A, Vaccarino V, Paltiel AD, et al. Age does not limit quality of life improvement in cardiac valve surgery. J Am Coll Cardiol 2003;42:1208-14.

Shahian DM, O'Brien SM, Filardo G, et al (a). Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1 - coronary artery bypass grafting surgery. Ann Thorac Surg 2009;88:S2-22.

Shahian DM, O'Brien SM, Filardo G, et al (b). Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 3 - valve plus coronary artery bypass grafting surgery. Ann Thorac Surg 2009;88:S43-62.

Sharma AD, Rizo-Patron C, Hallstrom AP, et al; DAVID Investigators. Percent right ventricular pacing predicts outcomes in the DAVID trial. Heart Rhythm 2005;2:830-4.

Shroyer AL, Coombs LP, Peterson ED, et al. Society of Thoracic Surgeons. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. Ann Thorac Surg 2003;75:1856-64.

Singh JP, Evans JC, Levy D, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study). Am J Cardiol 1999;83:897-902.

Sintonen H, Pekurinen M. A generic 15 dimensional measure of health related quality of life (15D). J Soc Med 1989;26:85–96.

Sjöland H, Caidahl K, Wiklund I, et al. Impact of coronary artery bypass grafting on various aspects of quality of life. Eur J Cardiothorac Surg 1997;12:612-9.

Sjöland H, Wiklund I, Caidahl K, Hartford M, Karlsson T, Herlitz J. Improvement in quality of life differs between women and men after coronary artery bypass surgery. J Intern Med 1999;245:445-54.

Spertus JA, Winder JA, Dewhurst TA, et al. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. J Am Coll Cardiol 1995;25:333-41.

Spertus JA, Jones P, McDonell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. Circulation 2002;106:43-9.

Srivastava AR, Banerjee A, Jacob S, Dunning J. Should patients undergoing coronary artery bypass grafting with mild to moderate ischaemic mitral regurgitation also undergo mitral valve repair or replacement? Interact Cardiovasc Thorac Surg 2007;6:538-46.

Stamou SC, Camp SL, Reames MK, et al. Continuous quality improvement program and major morbidity after cardiac surgery. Am J Cardiol 2008;102:772-7.

STS web-based risk calculator. STS Web site. Available at: http://www.sts.org/sections/stsnationaldatabase/riskcalculator/

Suri RM, Schaff HV, Dearani JA, et al. Survival advantage and improved durability of mitral repair for leaflet prolapse subsets in the current era. Ann Thorac Surg 2006;82:819-27.

Suomen Kardiologinen Seura. Sydänliitto web site. Statistics available at: www.sydanliitto.fi/kaikki_sydamesta /tilastot_ ja_rekisterit/fi_FI/yleistietoja/

Tang AS, Roberts RS, Kerr C, et al. Relationship between pacemaker dependency and the effect of pacing mode on cardiovascular outcomes. Circulation 2001;103:3081-5.

Tang GH, David TE, Singh SK, Maganti MD, Armstrong S, Borger MA. Tricuspid valve repair with an annuloplasty ring results in improved long-term outcomes. Circulation 2006;114:577-81.

Taskinen P, Kupari M, Hippeläinen M, Vuori I, Salonen TS. Aortan tekoläpän asennus katetrin kautta. Suomen Lääkärilehti 2008;63:3519-31.

Testa MA, Simonson DC. Assesment of quality-of-life outcomes. N Engl J Med 1996;334:835-40.

The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th ed. Boston, Mass: Little, Brown & Co; 1994:253-6.

Thier SO. Forces motivating the use of health status assessment measures in clinical settings and related clinical research. Med Care 1992;30:15-22.

Tilastokeskus (a). Mortality figures 2007. Web site. Available at: http://www.ktl.fi/attachments/suomi/terveydenhuollon_ammattilaisille/tapaturmat/kuolemansyyt/2008/cdc_taulukot.pdf

Tilastokeskus (b). Life-expectancy statistics. Web site. Available at: http://www.stat.fi/org/historia/elinajanodote.html

Tilastokeskus (c). Population projection 2007-2040. Web site. Available at: http://www.stat.fi/til/vaenn/2007/vaenn_2007_2007-05-31_tie_001.html.

Tuzcu EM, Emre A, Goormastic M, Loop FD, Underwood DA. Incidence and prognostic significance of intraventricular conduction abnormalities after coronary bypass surgery. J Am Coll Cardiol 1990;16:607-10.

van Gameren M, Kappetein AP, Steyerberg EW, et al. Do we need separate risk stratification models for hospital mortality after heart valve surgery? Ann Thorac Surg 2008;85:921-30.

Vardas PE, Auricchio A, Blanc JJ, et al. European Society of Cardiology; European Heart Rhythm Association. Guidelines for cardiac pacing and cardiac resynchronization therapy. Eur Heart J 2007;28:2256-95.

von Frey M, Gruber M. Untersuchungen über den stoff-wechsel isolierter organe. Ein respirations apparat für isolierte organe. Virchow's Arch Physiol 1885;9:519-32.

Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-83.

Welke KF, Stevens JP, Schults WC, Nelson EC, Beggs VL, Nugent WC. Patient characteristics can predict improvement in functional health after elective coronary artery bypass grafting. Ann Thorac Surg 2003;75:1849-55.

Wexelman W, Lichstein E, Cunningham JN, Hollander G, Greengart A, Shani J. Etiology and clinical significance of new fascicular conduction defects following coronary bypass surgery. Am Heart J 1986;111:923-7.

WHOQOL Group: Study protocol for the World Health Organization project to develop a quality of life assessment instrument (WHOQOL). Qual Life Res 1993;2:153-9.

Willems JL, and World Health Organization / International Society and Federation for Cardiology Task Force Ad Hoc. Criteria for intraventricular conduction disturbances and pre-excitation (WHO). J Am Coll Cardiol 1985;5:1261-75.

Wormuth DW. Actuarial and Kaplan-Meier survival analysis: there is a difference. J Thorac Cardiovasc Surg 1999;118:973-5.

Yau TM, El-Ghoneimi YA, Armstrong S, Ivanov J, David TE. Mitral valve repair and replacement for rheumatic disease. J Thorac Cardiovasc Surg 2000;119:53-61.

Zeldis SM, Morganroth J, Horowitz LN, et al. Fascicular conduction distrubances after coronary bypass surgery. Am J Cardiol 1978;41:860-4.

Zingone B, Gatti G, Rauber E, et al. Early and late outcomes of cardiac surgery in octogenarians. Ann Thorac Surg 2009;87:71-8.

NHP - TERVEYSPROFIILI

Miten kuvaisitte tämänhetkistä terveydentilaanne ?

Erittäin hyvä □
Hyvä □
Melko hyvä □
Huono □
Erittäin huono □

Päivämäärä_____

OSA I

Alla on lueteltu joitakin vaivoja, joita ihmisillä voi olla päivittäisessä elämässään. Käykää luettelo läpi ja merkitkää rasti KYLLÄ -ruutuun kaikkien niiden vaivojen kohdalle, joita teillä tällä hetkellä on. Merkitkää rasti EI -ruutuun aina kun teillä ei ole kyseistä vaivaa.
Olkaa hyvä ja vastatkaa jokaiseen kysymykseen. Mikäli olette epävarma siitä, onko vastauksenne kyllä vai ei, merkitkää se vaihtoehto, joka mielestänne on tällä hetkellä totuudenmukaisempi.

	KYLLÄ	EI
Olen koko ajan väsynyt	□	□
Minulla on kipuja öisin	□	□

	KYLLÄ	EI
Käytän lääkkeitä päästäkseni uneen	□	□

	KYLLÄ	EI
Asiat masentavat minua	□	□
Asennon vaihtaminen on minulle tuskallista	□	□
Hermoni ovat kireällä	□	□

	KYLLÄ	EI
Tunnen itseni yksinäiseksi	□	□
Pystyn kävelemään vain sisätiloissa	□	□
Minulla on sietämättömiä kipuja	□	□

	KYLLÄ	EI
Minun on vaikea kumartua	□	□
Kaikki asiat vaativat ponnistelua	□	□

	KYLLÄ	EI
En pysty lainkaan kävelemään	□	□
Herään hyvin aikaisin aamulla	□	□
Olen unohtanut, millaista on nauttia elämästä	□	□

	KYLLÄ	EI
Minun on vaikea lähestyä ihmisiä	□	□
Minulla on kipuja kävellessä	□	□
Päivät tuntuvat matelevan	□	□

	KYLLÄ	EI
Minun on vaikea nousta ja laskeutua portaita	□	□

Jos olette epävarma siitä, onko vastauksenne kyllä vai ei, merkitkää se vaihtoehto, joka mielestänne on tällä hetkellä totuudenmukaisempi.

	KYLLÄ	EI
Minun on vaikea kurottaa esineitä	□	□
Menetän nykyään malttini herkästi	□	□

	KYLLÄ	EI
Makaan valveilla suurimman osan yötä	□	□
Tuntuu kuin olisin menettämässä hallintani	□	□
Minulla on kipuja seistessä	□	□

	KYLLÄ	EI
Minusta tuntuu, että en ole läheinen kenellekään	□	□
Minun on vaikea pukea itseäni	□	□

	KYLLÄ	EI
Voimani loppuvat nopeasti	□	□
Minun on vaikea seistä pitkään	□	□
Minulla on jatkuvia kipuja	□	□

	KYLLÄ	EI
Minun on vaikea päästä uneen	□	□
Minusta tuntuu, että olen vaivaksi ihmisille	□	□

	KYLLÄ	EI
Huolet pitävät minut valveilla öisin	□	□
Tuntuu, että elämä ei ole elämisen arvoista	□	□

	KYLLÄ	EI
Nukun huonosti öisin	□	□
Tarvitsen apua kävellessäni ulkona	□	□

	KYLLÄ	EI
Tunnen kipua kulkiessani ylös ja alas portaita	□	□
Herään masentuneena	□	□

	KYLLÄ	EI
Minun on vaikea tulla toimeen ihmisten kanssa	□	□
Tunnen kipua istuessani	□	□

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