The development of a CABG database, a never ending story

A risk analysis of morbidity and mortality in CABG surgery

Douglas P.B.Janssen

Printed by: Pasmans Offsetdrukkerij bv, Den Haag, The Netherlands

ISBN-10: 90 - 9020975 - 1

ISBN-13: 978 - 90 - 9020975 - 3

The development of a CABG database, a never ending story

A risk analysis of morbidity and mortality in CABG surgery

een wetenschappelijke proeve op het gebied van de
Medische Wetenschappen

Proefschrift

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen
op gezag van de Rector Magnificus prof. dr. C.W.P.M. Blom,
volgens besluit van het College van Decanen
in het openbaar te verdedigen op maandag 6 november 2006
des ochtends om 10.30 uur precies

door

Douglas Peter Bartel Janssen

geboren op 7 augustus 1960
te Amsterdam

Promotor:

Prof. dr. M.H.J. Brouwer

Co-promotor:

Dr. L. Noyez

Manuscript commissie

Prof. dr. F.W.A. Verheugt, voorzitter

Prof. dr. J.G. van der Hoeven

Prof. dr. G.J. van der Wilt

Prof. dr. G.J. Scheffer

Prof. dr. B. Mochtar, Academisch Ziekenhuis Maastricht

Financial support by the Netherlands Heart Foundation and the Jacques H. de Jong Stichting for the publication of this thesis is gratefully acknowledged.

Additional financial support provided by Edwards Lifesciences Cardiac Surgery, St. Jude Medical Nederland B.V., Sorin Group Nederland B.V., Bayer B.V. HealthCare, Biotronik Nederland B.V., Datascope B.V., Medtronic Trading NL B.V., Maquet, and Krijnen Medical Innovations B.V. is very much appreciated.

Aan: Mijn moeder

Katja, Lisa en ……… ?!

Contents

Chapter 1

Introduction

1.1 Clinical practice and database information

1.2 The CORRAD-database

1.3 From the bedside to the database and back again: objectives and outline of the study

1.1 Clinical practice and database information

Clinical database information is widely demanded. Everyone wants to review and comment on care, even without knowing the precise data. The idea that simple registration of data is sufficient, however, is wrong. We have not only to register simply the data, but we have also to known our own data and be effective in using these data.

Database information has a life cycle.[1] It begins with patient care, which is the basis for data-registration. Collecting data is, however, just the beginning. These data are used not only in descriptive reports as annual reviews, but are also the basis for smaller, mostly descriptive clinical studies. These smaller reports are sometimes underestimated, but they are a first step in quality control. The question is whether our data are comparable with other larger series? Furthermore, such reports will teach us how to manage data, and how to present them in a clinical manuscript. However, these reports are only intermediate steps towards reaching the real goal, which is the productive use of the gathered information to modify and improve patient care.

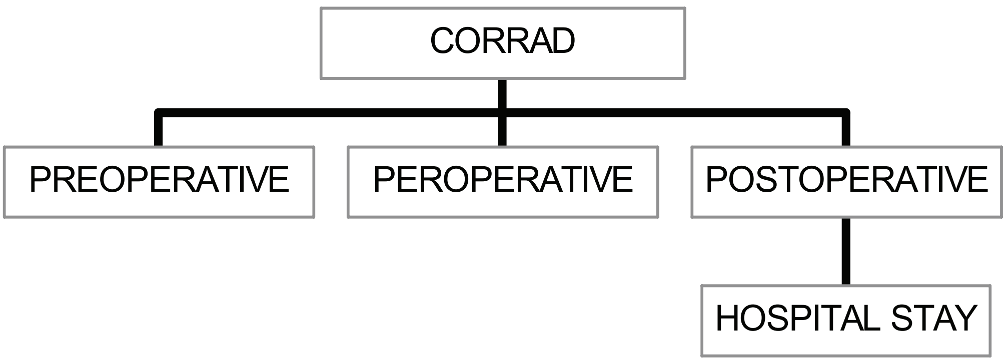
However, not only database information has a life cycle, also the database on itself has a life cycle.[1] With the set-up of a database much information is stored. But there is always a selection of data, because registration can never include all topics. By presenting our database information in reports, it will become clear that the importance of some topics will change. New topics will become more important and must necessarily be added to the database. Also this regular update of the database itself is a prerequisite, if we want to use our information to modify and improve patient care.

Only by recognizing these two life cycles of a database, we will be able to use our stored information.[1] This information allows a scientific approach of patient care and compare our results with external standards such as the Society of Thoracic Surgeons-database.[2] This scientific approach of our data gives us the opportunity to interact in processes were significant variation occurs, to use these data for science, and to consolidate our position when we are asked to provide data for different users. Database information can provide us with new perspectives and useful insights into our care. It can highlight both problems and opportunities that may not have been previously visible from a narrower perspective.[3]

1.2 The CORRAD-database

In January 1987 the CORRAD database was set up at the department of Thoracic, Cardiac and Vascular Surgery (presently: Thoracic and Cardiac Surgery) at the Radboud University Nijmegen (presently: Radboud University Medical Center Nijmegen) in The Netherlands. The intention of this database was to store pre-, per-, and postoperative (in hospital) information of all patients undergoing isolated coronary artery bypass surgery at the Radboud University Hospital (Figure 1). The name CORRAD refers to CORonary surgery RADboud University. The database of The Society of Thoracic Surgeons and the coronary artery surgery database of the University of Leuven (Belgium) were used as models for the set-up of the CORRAD database.

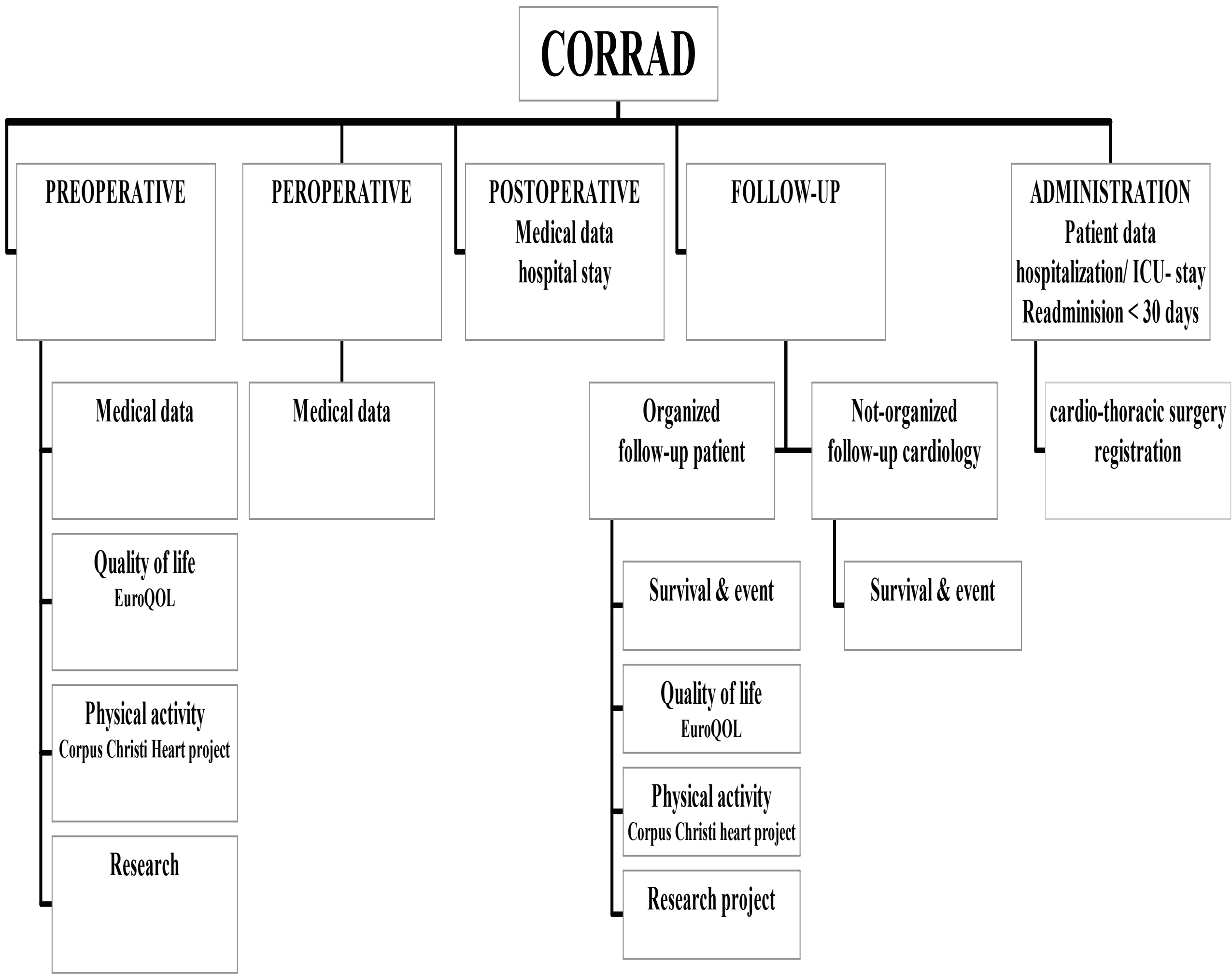
Figure 1. Coronary Artery Surgery Database in 1987.
 - **CORRAD** - **COR**onair St. **RAD**boud



Initially, only data of isolated myocardial revascularizations were stored in the CORRAD database. But during the past years, also data of valve surgery and other adult open-heart surgery procedures were added to the database. There was a growing interest, certainly from health care providers and the government in waiting lists, intensive care- and hospital stay. Therefore, the database was extended with a section 'administrative data', including more than only the initial information about birth date and date of operation of the patient. This administrative section is also connected to the cardiac surgery registration of the department of Thoracic and Cardiac surgery which is part of the hospital surgery-registration system -OKAPI -.

Because of the changed profile of our patient population,[4] the worldwide shortening of the postoperative hospital stay after cardiac surgery,[2] Blackstone's work[5] concerning the prolonged early phase in high risk patients, and our own experiences with mortality and morbidity registration after hospital discharge,[6] the database was extended with a follow-up section. Furthermore, preoperative- and follow-up registration of quality of life, using the EuroQOL registration and physical activity analogous to the Corpus Christi Heart Project, was included in the CORRAD database (Figure 2).[7,8]

Figure 2. Coronary Artery Surgery Database in 2005 (CORRAD database).



1.3 From the bedside to the database and back again: objectives and outline of the study

During the past years there is a trend towards surgically treating older and sicker patients, who have more complex and more preexisting diseases.[9-11] Ageing of the population is one of the reasons which contributes to the growing costs of healthcare.[12] The costs of coronary artery bypass grafting (CABG) can vary enormously between patients with uncomplicated postoperative stay and those who suffer from postoperative complications such as neurological, nephrological, or pulmonary problems. Duration of hospital stay and postoperative stay on the Intensive Care Unit (ICU) is lowest among patients who have a low morbidity risk.[13,14] Prediction of postoperative morbidity would facilitate decisions to operate, allocate resources and estimate costs.[15] Hospitals need to plan their operations to use available resources in an optimal fashion. This is especially true for CABG surgery, which is one of the most expensive elective procedures in a hospital.[13]

Furthermore, the preoperative identification of patients at high risk can be a basis for informed consent of the patient and their families and in selecting those patients whose operative risk may be unacceptably high.[14] Clinical predictions play an essential role in the practice of medicine because they are the basis for decisions involving diagnosis, prognosis, and therapy. Decision making in CABG requires an accurate assessment of the prognosis. Prognosis is generally affected by a large number of factors, including the patient's age, gender, severity of disease and symptoms, and coexisting medical disorders. Surgeons should inform the patient about the extent to which they are at risk for surgical mortality. Consequently, techniques are needed to identify prognostic factors, quantify their strength or importance, and construct a risk stratification model. Finally, risk stratification of patients who undergo open-heart surgery makes it feasible to analyze operative results by risk groups and to compare results in similar groups between institutions.[14,16,17]

The focus of this thesis is to show how a simple database was growing over the past years and how the stored information, initially used in a more descriptive way, became gradually useful to support patient care in a more scientific way. For that purpose, several questions were formulated:

- Is the profile of our group of patients undergoing isolated myocardial revascularization comparable with other institutions and what is changing through the years? The pre-, per- and postoperative data of 3834 patients undergoing primary isolated coronary bypass operations between January 1987 and December 1995 were analyzed (Chapter 2).
- Because of the increasing number of patients with neurological and nephrological morbidity after CABG, a further analysis of this postoperative morbidity was performed (Chapters 3 and 4). The following main questions were addressed:
    - Which of the variables measured pre-, and perioperatively could be considered as risk factors for postoperative neurological and nephrological morbidity?
    - Which of these factors contributed independently to an increased risk of postoperative neurological and nephrological complications?
    - Which of these independent predictors changed over time?
- Are elderly patients undergoing CABG at higher risk now than ten years ago? We analyzed the pre, per-, and postoperative data of patients aged between 70 and 77 years who underwent coronary artery bypass grafting between 1987 and 1996 (Chapter 5).
- Can patients, using our database information, be stratified according to their risk for prolonged stay in the Intensive Care Unit (Chapter 6)?
- Is it meaningful to develop institution-specific scoring systems besides the international used predictive systems, for predicting prolonged hospital and intensive care stay after CABG (Chapter 7)?

References

1. Dziuban SW Jr. Using database information in your clinical practice. Ann Thorac Surg 1999;68:350-352.
2. Society of Thoracic Surgeons - database www.sts.org
3. O'Connor GT, Eagle KA. How do we know how well we are doing ? J Am Coll Cardiol 1998;32:1000-1001.
4. Noyez L, Janssen DPB, van Druten JAM, Skotnicki SH, Lacquet LK. Coronary bypass surgery: what is changing ? Analysis of 3834 patients undergoing primary isolated myocardial revascularization. Eur J Cardio-thorac Surg 1998;13:365-369.
5. Blackstone EH. Outcome analysis using hazard function methodology. Ann Thorac Surg 1996;61:S2-7.
6. Wouters CW, Noyez L. Is no news good news ? Organized follow-up, an absolute necessity for the evaluation of myocardial revascularization. Eur J Cardio-thorac Surg 2004;26:667-670.
7. Brooks R, EuroQol group. EuroQol: The current state of play. Health Policy 1996;37:53-72.
8. Steffen-Batey L, Nichaman MZ, Goff DC, Frankowski RF, Hanis CL, Ramsey DJ, Labarthe DR. Change in level of physical activity and risk of all-cause mortality or reinfarction. The Corpus Christi Heart Project. Circulation 2000;102:2204-2209.
9. Jones ES, Weintraub WS, Craver JM, Guyton RA, Cohen CL. Coronary bypass surgery: is the operation different today ? J Thorac Surg 1991;101:108-115.
10. Katz NM, Chase GA. Risk of cardiac operations for elderly patients; reduction of age factor. Ann Thorac Surg 1997;63:1309-1314.
11. Magovern JA, Sakert T, Mogovern GJ, Benckart DH, Burkholder JA, Liebler GA, et al. A model that predicts morbidity and mortality after coronary artery bypass graft surgery. J Am Coll Cardiol 1996;28:1147-1153.
12. Weintraub WS, Craver JM, Jones EL Gott JP. Improving cost and outcome of coronary surgery. Circulation 1998;II:23-28.

13. Kurki TS, Häkkinen U, Lauharanta J, Rämö J, Leijala M. Evaluation of the relationship between preoperative risk scores, postoperative and total length of stays and hospital costs in coronary bypass surgery. Eur J Cardio-thorac Surg 2001;20:1183-1187.
14. Parsonnet V, Dean D, Bernstein AD. A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease. Circulation 1989;79(suppl I):I.3-I.12.
15. Ferraris VA, Ferraris SP, Singh A. Operative outcome and hospital cost. J Thorac Cardiovasc Surg 1998;115:593-603.
16. Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardio-thorac Surg 1999;16:9-13.
17. Gogbashian A, Sedrakyan A, Treasure T. EuroSCORE: a systematic review of international performance. Eur J Cardio-thorac Surg 2004;25:695-700.

Chapter 2

Coronary bypass surgery: what is changing? Analysis of 3834 patients undergoing primary isolated myocardial revascularization

Luc Noyez[1], Douglas P.B. Janssen[1], Johannes A. M. van Druten[2], Stefan Skotnicki[1], Leon K. Lacquet[1]

The Departments of [1]Thoracic and Cardiac Surgery, and [2]Medical Informatics, Epidemiology and Statistics, University Hospital Nijmegen, Nijmegen, The Netherlands

European Journal of Cardio-thoracic Surgery 1998;13: 365-369

Abstract

Objective: The patient population undergoing myocardial revascularization has changed during the last few years. Knowledge of these changes, and of the subsequent influence on morbidity and/or mortality is important, not only for up-dating quality control, but also to support decision-making in financial and economical aspects, and in further research concerning coronary artery surgery.

Methods: Pre-, per- and postoperative data of 3834 primary isolated coronary bypass operations, January 1987 - December 1995 were analyzed. The total group was divided into three time cohorts. Group A: 1987–1989 (n=1292); group B: 1990–1992 (n =1130); and group C: 1993–1995 (n =1412).

Results: Mean age increased from 60.4±9.0 (S.D.) years in group A to 62.9±9.9 (S.D.) years in group C (P < 0.0005). Patients with insulin-dependent diabetic (P = 0.005), uro-nephrological (P = 0.002), pulmonary (P < 0.0005) and neurological (P = 0.003) pathology increased significantly, and there was a significant increase in the use of arterial grafts (P < 0.05). Postoperative, hospital mortality remained stable (±2.5%). However, there was a significant increasing percentage of patients with pulmonary (P = 0.04), neurological (P = 0.02) and uro-nephrological (P < 0.0005) problems.

Conclusion: During the last few years there has been a trend in myocardial revascularization of older patients, with more coexisting disease. Despite the fact that hospital mortality seems stable, there is an increase in major postoperative morbidity.

Introduction

During the last few years, cardiac surgeons, cardiologists and all concerned with patients undergoing coronary bypass artery grafting (CABG) have noted a trend towards surgically treating older, sicker patients who have more complex diseases.[1-3] There has also been an enormous impact on cardiac surgery with regard to the financial and economical aspects. Health care costs must decrease, and this can be done by decreasing the length of hospital stay. This is most effective in patients who have a low morbidity risk. This policy, however, can be dangerous for the high risk patients: they may become isolated, ‘expensive’ patients, for whom there is no place in our ‘low cost health care’.[2,3] Therefore it is important to study the evolutionary trends in the recent patient population, so that the problems can be identified and the support put in place for decision-making in financial and economical aspects and even in further research concerning coronary artery surgery. The purpose of this study was to outline the changes in the patient population during the last few years.

Material and methods

Patients

With the aid of our database, Coronary Surgery Database Radboud Hospital (CORRAD), a registry that stores pre-, per- and postoperative data of all patients undergoing isolated myocardial revascularization, we identified a series of 3834 patients undergoing primary isolated CABG from January 1987 to December 1995. These 9 years were subdivided into three time cohorts of 3 years. Group A (1292 patients) operated between January 1987 and December 1989, group B (1130 patients) operated between January 1990 and December 1992, and group C (1412 patients) operated between January 1993 and December 1995. Table 1 presents the studied variables, however only these with a statistical significance change over time or other importance were further noted in this study. Preoperatively, diabetes was defined when there was insulin dependency. Hypertension was defined as systolic blood pressure of greater than 160 mmHg or diastolic pressure of greater than 100 mmHg. Hyperlipidemia was defined as having a total cholesterol level of greater than 250 mg/dl or a triglyceride level of greater than 200 mg/dl. Neurological pathology was registered in patients with cerebrovascular accidents and/or transient ischaemic attack in their histories. Uro-nephrological pathology was defined as having a documented urological problem or operation or renal failure (creatinine $\geq$ 150 μmol/l), preoperative dialysis, or renal transplantation. Pulmonary pathology was registered in patients with chronic obstructive pulmonary disease, and/or a history of previous lung disease.

Table 1. Preoperative, operative and postoperative variables.

Preoperative	Operative	Postoperative
Sex	Bypass time	Mortality
Age	Aortic cross-clamp time	Myocardial infarction
Diabetes	Number of grafts	Reoperation for bleeding
Hypertension	Number of distal anastomoses	Low cardiac output
Hyperlipidemia	Number of arterial grafts	Ventilatory support >2 days
Peripheral vascular atherosclerosis		Wound problems
Neurologic pathology		Neurological problems
Uro-nephrological pathology		Uro-nephrological problems
Pulmonary pathology		Pulmonary problems
Gastrointestinal pathology		Gastrointestinal problems
PTCA		Vascular problems
Myocardial infarction		
Heart rhythm		
Combined valve disease (mild)		
Vessel disease		
NYHA – class/emergency		
Left main		

PTCA, percutaneous transluminal coronary angioplasty; NYHA: New York Heart Association classification.

Emergency operation was defined as an operation involving myocardial infarction, ischemia not responding to medical therapy, or cardiogenic shock. Left main was noted when there was a stenosis of 70% or more. Postoperatively, mortality was defined as operative, hospital and 30-day mortality. Myocardial infarction as a new postoperative Q wave or T wave accompanied by increased cardiac enzymes (CPK-MB>10%). Pulmonary problems were all infectious and other pulmonary problems. Neurological problems were defined as having a new cerebrovascular accident and/or transient ischaemic attack, but also when there was confusion for more than 12 h. Under uro-nephrological problems, postoperative dialysis, renal dysfunction (creatinine ≥ 150 μmol/l) and eventually other urological problems were noted.

Surgical technique

All patients were operated on using the standard cardiopulmonary bypass technique, aortic and right atrial (two stage) cannulation and hypothermia (28–32°C). Myocardial protection during aortic cross-clamping was performed with an infusion of cold (4°C) St. Thomas' Hospital cardioplegia until asystole occurred and was maintained by reinfusion of 100 ml/m^2 of the solution every 25–30 min or earlier, as needed. Over the time there was no significant difference in bypass and aortic-crossclamp time, neither in number of grafts and distal anastomoses. The only surgical change was the statistically significant increase in the use of arterial grafts (group A: 69%; group B: 78%; group C: 89%).

Statistical analysis

The characteristics of patients in groups A, B and C are presented as percentages for dichotome variables and as mean ±S.D. for age. Differences in age distribution in the three groups were tested with the *F*-test (one way analysis of variance) and differences in percentage were tested with the χ^2-test. Statistical significance was assumed at $P \leq 0.05$ ($P = 0.000$ means $P < 0.0005$).

Results

Table 2 presents the preoperative data of the patients. There is a statistical significant increase of the mean age of the patients ($P = 0.0001$) and of the percentage of patients 80 years and older. Also the percentage of patients with insulin-dependent diabetic, uro-nephrological and pulmonary pathology increased

Table 2. Preoperative variables.

Variable	**Group A** n=1292 (%)	**Group B** n=1130 (%)	**Group C** n=1412 (%)	***P*-value**
Sex				0.12
Men	954 (74)	851 (75)	1091 (77)	
Women	338 (26)	279 (25)	321 (23)	
Age (mean±S.D.) (years)	60.4 ± 9.0	62.2 ± 9.4	62.9 ± 9.9	0.000
range	29-84	34-84	13-89	
Patients ≥ 80 years	9 (0.7)	15 (1.3)	37 (2.6)	0.000
Diabetes:insulin-dependent	39 (3.0)	37 (3.3)	74 (5.2)	0.005
Hypertension	695 (54)	677 (60)	776 (55)	0.006
Hyperlipidemia	648 (50)	564 (50)	719 (51)	0.87
Peripheral vascular atherosclerosis	272 (21)	215 (19)	261 (18)	0.22
Neurological pathology	63 (4.9)	48 (4.3)	101 (7.2)	0.003
Uro-nephrological pathology	87 (6.7)	114 (10)	146 (10)	0.002
Pulmonary pathology	110 (8.5)	209 (13)	197 (14)	0.000
Single-vessel disease	97 (7.5)	73 (6.5)	58 (4.1)	0.001
Two-vessel disease	240 (19)	207 (18)	315 (22)	0.02
Three-vessel disease	955 (74)	850 (75)	1039 (74)	0.62
Previous successful PTCA	18 (1.4)	48 (4.3)	57 (4.0)	0.01
Preoperative myocardial infarction	648 (50)	552(49)	667 (47)	0.32
Emergency operation	118 (9.1)	81 (7.2)	80 (5.7)	0.002
Left main	108 (8.4)	113 (10)	125 (8.9)	0.36

PTCA, percutaneous transluminal coronary angioplasty

P = 0.000 means P < 0.0005

significantly. The statistically significant increase in patients with neurological pathology was a phenomenon of the last 3 years of the study (4.3–7.2%). The percentage of patients with hypertension is different in the three groups, but no clear trend is seen.

Concerning the cardiac preoperative data, the group of patients operated on for single-vessel disease decreased significantly. On the other hand, the number of patients with two-vessel disease increased from 19 to 22% (P = 0.02). The percentage of patients with three-vessel disease is not statistically significantly different in the three time cohorts. The emergency operations decreased also significantly and the percentage of patients with a successful PTCA in their history increased from 1.4 to 4.0% (P = 0.000).

Postoperatively (Table 3), there is statistically no difference between the three groups concerning mortality, perioperative myocardial infarction and percentage of patients that needed ventilatory support for more than 2 days. The percentage of patients with pulmonary problems seems to be different for the three groups (P = 0.04). The percentage of patients with neurological and uro-nephrological problems, increased over the years; this is especially clear for the uro-nephrological problems (P = 0.000).

Table 3. Postoperative variables.

Variable	**Group A** n=1292 (%)	**Group B** n=1130 (%)	**Group C** n=1412 (%)	***P*-value**
Mortality	35 (2.7)	30 (2.7)	34 (2.4)	0.87
Myocardial infarction	31 (2.4)	35 (3.1)	35 (2.5)	0.51
Ventilatory support > 2 days	207 (16)	191 (17)	231 (16)	0.84
Pulmonary problems	113 (8.8)	79 (7.0)	139 (9.8)	0.04
Neurological problems	18 (1.4)	25 (2.2)	42 (3.0)	0.02
Uro-nephrogical problems	24 (1.9)	45 (4.0)	67 (4.8)	0.000

P = 0.000 means P < 0.0005

Discussion

The increasing age of the patients, and/or the increasing number of patients of 80 years and older of the patients undergoing myocardial revascularization is confirmed by several studies. It is important that a higher age and certainly an age of 80 years or older, is accompanied with higher surgical risks and significant hospital expenses. Certainly for the older patients (≥ 80 years), with a limited long-time survival, it will be important to have studies, analyzing not only the survival, but also the quality of life to justify the costs of the myocardial revascularization of this group of elderly patients.[3,4] Also insulin-dependent diabetes, cerebrovascular, pulmonary and uro-nephrological (creatinine level) disease are preoperative variables with a relative strength in predicting postoperative morbidity and mortality. However, these variables are probably also influenced by the increasing age of the patient population.[5,6]

The statistically significant decrease in patients operated on for single-vessel disease is a result of the increasing number of percutaneous transluminal coronary angioplasties. At the same time the number of patients with a successful angioplasty in their preoperative history increased also significantly. The statistically significant decrease in emergency operations can be partially explained by angioplasty of the culprit lesion to stabilize patients. But also the use of fibrinolytic agents, the use of stents, and probably the use of the intraaortic balloon-pump preoperatively (not noted separately in our database) are important here.

Left ventricular function, ejection fraction, is not included as a parameter. In the patient population, the ejection fraction was not routinely calculated, mostly, only for patients with 'bad' ventricular function. Because of the missing information in more than 70% of the patients, we did not include this parameter in our study. This is of course a deficit, because an impaired left ventricular function is a strong predictor for postoperative mortality and morbidity.

Of the operative variables, only the use of arterial grafts changed significantly. The increasing use of one or more arterial grafts is of course a surgical decision and a consequence of the superiority of the arterial grafts.[7] Several studies proved already that the use of one, or more, arterial graft(s) did not increase postoperative morbidity and mortality.[8,9]

Postoperatively, there is a slight, just significant ($P = 0.04$) increase of patients with pulmonary problems. The percentage of patients with uro-nephrological and with neurological problems, increased significantly. These two postoperative problems are associated with special care and longer hospital stay.[10-13] It is important is to note that the neurological problems were defined not only by the occurrence of a new cerebrovascular accident or a transient ischemic attack but also when patients were confused for more than 12 h. Several studies are describing a depressed level of consciousness and/or confusion after CABG as a result of cerebral ischemia, and possible in relation to preoperative neurological events. It must be clear that this patient group has also a prolonged overall hospital stay.[12,13]

This study outlines the trends in patients undergoing primary isolated myocardial revascularization during the last few years using standard cardiopulmonary techniques. The results are good, and prove that mortality can be kept low, in spite of a statistically significant increasing number of older patients as well as associated coexisting diseases. The same trend has been documented by The society of Thoracic Surgeons National Database.[14] The reproducibility, durability and the strive for a complete revascularization are the fundamentals of the standard CABG, and it will be difficult for minimally invasive surgery to improve these overall results.[15,16]

In conclusion, during the last few years, in primary CABG, there has been an increasing number of older patients. Also, there has been an increase in variables, maybe in relation to increasing age, which are or may be strong predictors of postoperative morbidity. Postoperative morbidity increased, as there was an increasing number of neurological and nephrological problems. Further analysis of this postoperative morbidity in relation to preoperative variables will be essential for a better understanding and for prevention of these ‘expensive’ complications.

References

1. Jones ES, Weintraub WS, Craver JM, Guyton RA, Cohen CL. Coronary bypass surgery: is the operation different today?. J Thorac Surg 1991;101:108-115.

2. Magovern JA, Sakert T, Magovern GJ, Benckart DH, Burkholder JA, Liebler GA, Magovern GJ. A model that predicts morbidity and mortality after coronary artery bypass graft surgery. J Am Coll Cardiol 1996;28:1147-1153.
3. Katz NM, Chase GA. Risks of cardiac operations for elderly patients: reduction of age factor. Ann Thorac Surg 1997;63:1309-1314.
4. Peterson ED, Cowper PA, Jollis JG. Outcomes of coronary artery bypass graft surgery in 24461 patients aged 80 years or older. Circulation 1995;92(Suppl. II):85-91.
5. Jones RH, Hannan EL, Hammermeister KE, DeLong ER, O'Connor GT, Luepker RV, Parsonnet V, Pryor DB. Identification of preoperative variables needed for risk adjustment of short-term mortality after coronary artery bypass graft surgery. J Am Coll Cardiol 1996;28:1478-1487.
6. Williams DB, Carrillo RG, Traad EA, Wyatt CH, Grahowksi R, Wittels H, Ebra G. Determinants of operative mortality in octogenarians undergoing coronary bypass. Ann Thorac Surg 1995;60:1038-1043.
7. Loop FD, Lytle BW, Cosgrove DM, Stewart RW, Goormastic M, Williams GW, Leonard P, Golding AR, Gill CG, Taylor PC, Sheldon WC, Proudfit WL. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. New Engl J Med 1986;41:1-6.
8. Cosgrove DM, Loop FD, Lytle BW. Does mammary artery grafting increase surgical risk?. Circulation 1985;72(Suppl II):170-174.
9. Galbut DL, Traad EA, Dorman MJ, DeWitt PL, Larsen PB, Kurlansky PA, Button JH, Ally JM, Gentsch TO. Bilateral internal mammary artery grafts in reoperative and primary coronary bypass surgery. Ann Thorac Surg 1991;52:20-28.
10. Owen CH, Cummings RG, Timothy LS, Schwab SJ, Jones RH, Glower DD. Coronary artery bypass grafting in patients with dialysis-dependent renal failure. Ann Thorac Surg 1994;58:1729-1733.
11. Laws KH, Merril WH, Hammon JW, Prager RL, Bender HW. Cardiac surgery in patients with chronic renal disease. Ann Thorac Surg 1986;42:152-157.
12. Harrison MJ. Neurologic complications of coronary artery bypass grafting: diffuse or focal ischemia? Ann Thorac Surg 1995;59:1356-1358.

13. Redmond JM, Greene PS, Goldsborough MA, Cameron DE, Stuart RC, Sussman MS, Watkins L, Lashinger JC, McKhann GM, Johnston MV, Baumgartner WA. Neurologic injury in cardiac surgical patients with a history of stroke. Ann Thorac Surg 1996;61:42-47.
14. The Society of Thoracic Surgeons. Data analyses of The Society of Thoracic Surgeons National Cardiac Surgery Database, The 4th Year, Chicago, January 1995.
15. Reardon MJ, Espadea R, Letsou GV, Safi HJ, McCollum CH, Baldwin JC. Minimally invasive coronary artery surgery—a word of caution. J Thorac Surg 1997;114:419-420.
16. Ancalmo N, Busby J. Minimally invasive coronary artery bypass surgery: really minimal? Ann Thorac Surg 1997;64:928-929.

Chapter 3

Predictors of neurological morbidity after coronary artery bypass surgery

Douglas P.B. Janssen[1], Luc Noyez[1], Johannes A.M. van Druten[2], Stefan H. Skotnicki[1], Leon K. Lacquet[1]

The Departments of [1]Thoracic and Cardiac Surgery, and [2]Medical Informatics, Epidemiology and Statistics, University Hospital Nijmegen, Nijmegen, The Netherlands

European Journal of Cardio-thoracic Surgery 1999;15:166-172

Abstract

Objective: The aim of this study was to analyze the postoperative neurological complications after myocardial revascularization.

Methods: We analyzed the pre-, peri- and postoperative data of 3834 patients who underwent a primary isolated bypass grafting between January 1987 and December 1995. Postoperative neurological complications (A) were divided into mild complications (B) and major complications (C).

Results: The incidence of A increased, from 1.4% to 3.0%. Unifactor risk analysis identified: age>75 years, peripheral vascular atherosclerosis, neurological pathology, aorta-pathology and perioperative myocardial infarction as risk factors for A. Perioperative myocardial infarction and neurological pathology for B; age>75 years, peripheral vascular atherosclerosis, neurological pathology, perioperative myocardial infarction and aorta-pathology for C. Multifactor risk regression analysis identified peripheral vascular atherosclerosis, neurological pathology, aorta-pathology, perioperative myocardial infarction and the time cohort 1993–1995 as independent predictors for A; perioperative myocardial infarction and the time cohort 1993–1995 for B; neurological pathology, aorta-pathology and perioperative myocardial infarction for C.

Conclusions: Peripheral vascular atherosclerosis, neurological pathology, aorta-pathology, the occurrence of a perioperative myocardial infarction and the time cohort 1993–1995 were identified as independent risk factors for neurological complications.

Introduction

Neurological morbidity complicates myocardial revascularization in 2% to 6% of the patients. In addition, cognitive impairment occurs in up to 30% of the patients.[1-3] In a previous report, we described an increase of the postoperative neurological complications from 1.4% to 3.0% between 1987 and 1995.[4] Although most patients show a good functional recovery within the first half year, these neurological complications result in a prolonged hospital stay, with financial consequences.[5]

The purpose of this study was to analyze postoperative neurological complications in relation to pre- and perioperative risk factors, so that we can predict patients at increased risk. The following main questions were addressed: (a) which of the variables measured pre-, and perioperative could be considered as risk factors for postoperative neurological complications? (b) which of these factors contributed independently to an increased risk of postoperative neurological complications? (c) which of these independent predictors changed over time?

Materials and methods

Patients

With the aid of our database, Coronary Surgery Database Radboud Hospital (CORRAD), a registry that stores pre-, per-, and postoperative data of all patients undergoing isolated coronary bypass grafting (CABG), we identified a series of 3834 patients undergoing a primary isolated CABG from January 1987 to December 1995. These 9 years were subdivided into three time cohorts of 3 years. January 1987 to December 1989 (1292 patients), January 1990 to December 1992 (1130 patients), and January 1993 to December 1995 (1412 patients). Of these 3834 patients, 85 (2.2%) had postoperative neurological complications. Postoperative neurological complications were defined as when there was a new cerebrovascular accident and/or transient ischaemic attack, so called major complications, but also when there was confusion for more than 12 hours or memory disturbances, so called mild complications.[6] Table 1 presents the frequency of neurological complications (A) in the three time cohorts and also a division between mild complications (B) and major complications (C).

Preoperatively, diabetes was defined as having a positive glucose tolerance test, oral antidiabetic medication, or insulin dependency. Hypertension was defined as systolic blood pressure > 160 mmHg or diastolic pressure > 100 mmHg.

Peripheral vascular atherosclerosis was registered in patients with either central (carotic) or peripheral vascular disease or operations. Neurological pathology was registered in patients with a cerebrovascular accident, transient ischaemic attack, or a documented history of cognitive disturbances preoperatively. Emergency operation was defined as operation for involving myocardial infarction, ischaemia not responding to medical therapy, or cardiogenic shock. Perioperative, aorta-pathology was noted in patients, with severe calcification in the aorta ascendens. Perioperative myocardial infarction as a new postoperative Q wave or T wave accompanied by increased cardiac enzymes (CPK-MB >10%).

Surgical Technique

All patients were operated on using standard cardiopulmonary bypass techniques, aortic and right atrial (two stage) cannulation, and hypothermia (28°C - 32°C). Myocardial protection during aortic cross-clamping was performed with infusion of cold (4°C) St. Thomas' Hospital cardioplegia until asystole occurred and was maintained by reinfusion of 100 ml/m^2 of the solution every 25-30 minutes or earlier, as needed. Over the time there was no significant difference in bypass and aortic-crossclamp time, neither in number of grafts and distal anastomoses. The only surgical change was the increase in the use of arterial grafts.[4]

Statistical analysis

To test which variables can be considered risk factors for neurological complications, Fisher's exact test for 2 x 2 tables was used (unifactor risk analysis). Changes in the incidence of postoperative neurological complications and changes in the prevalence of risk factors in three time cohorts were examined with the χ^2 test. Multiple logistic regression analysis was used to identify risk factors which independently contribute to an increased risk of postoperative neurological complications (multifactor risk analysis). In the analysis the three time cohorts were represented by two indicator variables, the cohort 1987-1989 was used as reference for the other two cohorts. Statistical significance was assumed at $P < 0.05$.

Table 1. Incidence of postoperative neurological complications in the three time-cohorts.

	1987-1989 *n*=1292 (%)	1990-1992 *n*=1130 (%)	1993-1995 *n*=1412 (%)	1987-1995 *n*=3834 (%)	χ^2 test *P*-value
Neurological problems	18 (1.4)	25 (2.2)	42 (3.0)	85 (2.2)	0.02
Mild neurological problems	10 (0.8)	16 (1.4)	27 (1.9)	53 (1.4)	0.04
Severe neurological problems	8 (0.6)	9 (0.8)	15 (1.1)	32 (0.8)	0.44

Results

Table 1 shows that the incidence of postoperative neurological complications (A) increased with time, from 1.4% to 3.0% (*P* = 0.02). This increased risk was mainly due to an increased risk for mild complications (B).

Unifactor risk analysis

Table 2 lists the variables tested for postoperative neurological complications. For each variable the risk was calculated for complications A, B and C. Table 3 shows the results of the unifactor risk analysis; per variable the relative risk (RR), ratio of incidence rates, is shown for complications A, B and C. The risk for mild and/or severe neurological problems (A) was not related to sex, diabetes, perfusion time and aortic cross-clamp time. Hypertension and emergency operation just reached the significance level for complication A (*P* = 0.05). Clear risk factors for post-operative neurological complications (A) were: age >75 years, peripheral vascular atherosclerosis, neurological pathology, aorta-pathology and perioperative myocardial infarction. Neurological pathology (*P* = 0.03) and certainly perioperative myocardial infarction (*P* = 0.0005) were associated with an increased risk of mild neurological complications (B). Age (>75 years) (*P* = 0.008), peripheral vascular atherosclerosis (*P* = 0.02), perioperative myocardial infarction (*P* = 0.01), but certainly neurological pathology (*P* = 0.003), and most evident aorta-pathology (*P* < 0.0001) were strongly associated with a high relative risk for severe postoperative complications (C).

Table 2. Variables tested for postoperative neurological complications (A, B, C).

Variables	Number of patients	A: 2.2 %	B: 1.4%	C: 0.8%
Age				
≤ 75 years	3616	2.1	1.3	0.7
> 75 years	218	5.1	2.3	2.8
Sex				
Male	2896	2.2	1.5	0.7
Female	938	2.1	1.0	1.2
Diabetes				
Yes	501	3.4	2.0	1.4
No	3333	2.0	1.3	0.8
Hypertension				
Yes	2148	2.7	1.6	1.0
No	1686	1.7	1.1	0.6
Peripheral vascular atheroslerosis				
Yes	748	3.7	2.1	1.6
No	3086	1.9	1.2	0.7
Neurological pathology				
Yes	302	5.6	3.0	2.7
No	3532	1.9	1.3	0.7
Perfusion time (minutes)				
≤ 100	2134	2.1	1.4	0.7
> 100	1700	2.4	1.4	1.1
Aortic cross-clamp time (minutes)				
≤ 60	2287	2.2	1.4	0.8
> 60	1547	2.3	1.4	0.8
Elective / emergency operation				
Elective	3555	2.1	1.3	0.8
Emergency	279	3.9	2.2	1.8
Aorta-pathology				
Yes	32	15.6	0.0	15.6
No	3802	2.1	1.4	0.7
Perioperative myocardial infarction				
Yes	104	10.6	6.7	3.9
No	3730	2.0	1.2	0.8

A = B + C; B = mild neurological complications; C = severe neurological complications

Table 3. Unifactor risk analysis for neurological complications (A, B, C).

Variables	A RR (*P*-value*)	B RR (*P*-value*)	C RR (*P*-value*)
Age (> 75 years / ≤ 75 years)	2.4 (0.008)	1.8 (0.23)	4.0 (0.008)
Sex (male / female)	1.0 (0.90)	1.5 (0.26)	0.6 (0.21)
Diabetes (yes / no)	1.7 (0.07)	1.5 (0.22)	1.8 (0.18)
Hypertension (yes / no)	1.6 (0.05)	1.5 (0.16)	1.7 (0.16)
Peripheral vascular atherosclerosis (yes / no)	1.9 (0.003)	1.8 (0.06)	2.3 (0.02)
Neurological pathology (yes / no)	2.9 (0.0003)	2.3 (0.03)	3.9 (0.003)
Perfusion time (min) (>100 / ≤100)	1.1 (0.51)	1.0 (1.00)	1.6 (0.21)
Aortic cross-clamp time (min) (> 60 / ≤ 60)	1.0 (0.91)	1.0 (0.89)	1.0 (1.00)
Emergency / elective operation	1.9 (0.05)	1.7 (0.28)	2.3 (0.08)
Aorta-pathology (yes / no)	7.4 (0.0006)	- **	22 (< 0.0001)
Perioperative myocardial infarction (yes/no)	5.3 (<0.0001)	5.6 (0.0005)	4.9 (0.01)

Neurological complications, A = B + C; B = mild neurological complications;
C = severe neurological complications. RR = relative risk (ratio of incidence rates)
* = Fisher exact test.
** = No mild complications registered in the group with aorta-pathology, see Discussion.

Multifactor risk analysis

Table 4 shows the results of the multiple logistic regression analysis for neurological complications A, B and C. Independent predictors for postoperative complications (A) were peripheral vascular atherosclerosis (*P* = 0.03), neurological pathology (*P* = 0.006), aorta-pathology (*P* = 0.001), perioperative myocardial infarction (*P* = 0.0001), and the time cohort 1993 – 1995 (*P* = 0.03). Age, diabetes, hypertension and emergency operation were not independent predictors in the multifactor analysis. Only perioperative myocardial infarction (*P* = 0.0002) and the time cohort 1993 – 1995 (*P* = 0.03) were identified as predictors for mild neurological complications (B).

Table 4. Multifactor risk analysis (logistic regression) for neurological complications (A,B,C).

	***P*-value**			**Odds-ratio**		
Variables	A	B	C	A	B	C
Age (> 75 years / ≤ 75 years)	0.07	0.41	0.12	1.9	1.5	2.3
Sex (male / female)	0.46	0.11	0.38	1.2	1.8	0.7
Diabetes (yes / no)	0.38	0.39	0.83	1.3	1.4	1.1
Hypertension (yes / no)	0.13	0.23	0.41	1.4	1.4	1.4
Peripheral vascular atherosclerosis (yes / no)	0.03 *	0.15	0.14	1.7	1.6	1.8
Neurological pathology (yes / no)	0.006 *	0.13	0.02 *	2.3	1.8	3.0
Perfusion time (min) (>100 / ≤100)	0.97	0.44	0.29	1.0	0.7	1.6
Aortic cross-clamp time (min) (>60 / ≤60)	0.69	0.90	0.46	0.9	1.0	0.7
Emergency / elective operation	0.86	0.97	0.82	1.1	1.0	1.1
Aorta-pathology (yes / no) [a]	0.001 *		0.0001*	5.8		18.1
Perioperative myocardial infarction (yes / no)	0.0001*	0.0002*	0.04*	5.1	5.8	3.7
Time cohort 1990-1992 [b]	0.13	0.15	0.56	1.6	1.8	1.3
Time cohort 1993-1995 [b]	0.03 *	0.03 *	0.51	1.9	2.3	1.4

Neurological complications, A = B + C

B = mild neurological complications, C = severe neurological complications

* = Statistically significant

[a] Aorta-pathology is not included in the logistic regression risk analysis for complication B, see Discussion section.

[b] Reference time cohort: 1987-1989.

Predictors for severe postoperative complications (C) were neurological pathology (P = 0.02) and perioperative myocardial infarction (P = 0.04), but in the first place aorta-pathology (P = 0.0001) was an independent predictor.

Table 5. Change of prevalence of independent risk factors in the three time cohorts.

Independent risk factor	**1987-1989** n =1292 (%)	**1990-1992** n =1130 (%)	**1993-1995** n =1412 (%)	χ^2 test *P*-value
Peripheral vascular atherosclerosis	272 (21)	215 (19)	261 (18)	0.22
Neurological pathology	76 (5.9)	62 (5.5)	164 (11.6)	0.001
Aorta-pathology	11 (0.9)	3 (0.3)	18 (1.3)	0.02
Perioperative myocardial infarction	34 (2.6)	35 (3.1)	35 (2.5)	0.62

Table 5 shows the change of prevalence of the independent risk factors in the three time cohorts. Only the prevalence of preoperative neurological pathology was clearly increased in the time cohort 1993 - 1995 (*P* = 0.001). Table 6 shows the relation between the independent risk factors, peripheral vascular atherosclerosis, neurological pathology, aorta-pathology and perioperative myocardial infarction, and the risk factors, emergency operation and hypertension, identified in the unifactor analysis. Emergency operation was strongly related to an increased risk of perioperative myocardial infarction (elective 1.7%; emergency 15.4%). Hypertension was associated with an increased risk of peripheral vascular atherosclerosis, aorta-pathology and perioperative myocardial infarction.

Discussion

Neurological complications or problems represent one of the most costly complications of cardiac surgery. This morbidity is attended with prolonged ICU and/or hospital stay, and eventually rehabilitation programs.[1-3,5,7] Harrison showed that, severe postoperative neurological problems, such as stroke, is mostly due to macroembolism and that microembolism can cause mild neurological problems, such as confusion and memory disturbances.[6] We differentiated in our analysis between three groups of neurological complications, first the total number (severe

Table 6. Relationship between the risk factors emergency operation, hypertension and independent risk factors for postoperative neurological complications.

Independent risk factor	Elective		Emergency		Fisher-test
	n = 3555	(%)	n = 279	(%)	*P* – value
Peripheral vascular atherosclerosis	697	(19.6)	51	(18.3)	0.64
Neurological pathology	281	(7.9)	21	(7.5)	0.91
Aorta-pathology	26	(0.7)	6	(2.2)	0.03 *
Perioperative myocardial infarction	61	(1.7)	43	(15.4)	3.10^{-23} *
	No-hypertension		**Hypertension**		
	n =1686	(%)	n = 2148	(%)	
Peripheral vascular atherosclerosis	291	(17.2)	457	(21.3)	0.001 *
Neurological pathology	133	(7.9)	169	(7.9)	1.00
Aorta-pathology	8	(0.5)	24	(1.1)	0.03 *
Perioperative myocardial infarction	34	(2.0)	70	(3.3)	0.02 *

* statistically significant

and/or mild), second, the severe complications, which may hide mild complications, and third, only the mild complications.

This study demonstrated that the significant increase of overall neurological complications over the years was mainly due to an increase of mild neurological complications (Table 1). The unifactor risk analysis showed no predictive value of the variables sex, perfusion time > 100 minutes and aortic cross-clamp time > 60 min (Table 3). The question of a possible influence of bypass time on neurological complications is interesting, because of the evolution of coronary artery bypass surgery without pump. In a study of patients with a history of stroke, patients with postoperative neurological deficit had a significant longer bypass time than patients without deficit. However, those with a deficit were older, received more distal anastomoses, and more patients had a valve replacement. It is known that valve operations have a higher incidence of cerebral injuries compared with isolated myocardial revascularizations.[5] A recent study, comparing the serum S-100β levels, which are increasing with neurological injury, showed a significant greater elevation in intracardiac procedures as in CABG and a correlation with increasing patients-age, but not with bypass time.[8] However, Westaby[9] and colleagues demonstrated that the elevation in serum levels S-100β did not occur in patients who underwent CABG without bypass. A recent study of Browne *et al*., (Browne S, Westaby S, Taggart DP. Neuropsychological and respiratory injury following CABG surgery with and without cardiopulmonary bypass. Presented at the 11th Annual meeting of the European Association for Cardio-Thoracic Surgery, Copenhagen, Denmark, September 1997), comparing neuropsychological and respiratory injury following CABG with and without cardiopulmonary bypass showed that bypass does contribute to respiratory injury, but does not appear to be responsible for neuropsychological problems. The association between age and neurological complications is described in other studies, several mechanisms are therefore responsible, but the increasing prevalence of atherosclerosis as well as an increased risk of plaque embolization is more likely.[10,11] The fact that age is a significant predictor for severe neurological complications and not for confusion is supporting this theory. Hypertension and elective/emergency operation showed a weak, significant association with neurological complications, however, this association disposed when severe and mild complications were studied separately.

Neurological pathology and perioperative myocardial infarction were significant predictors for neurological problems, as well for severe as mild complications. The vulnerability of patients with a previous history of cerebrovascular accident and/or ischemic attack, is supported by several studies.[5] The recent study of Taggart[8], however, suggested that the period between the cerebral injury and the operation may be important. Perioperative myocardial infarction showed only a weak significant correlation with severe neurological problems, but a strong correlation with confusion. Peripheral vascular atherosclerosis, a significant predictor for neurological problems, tended to be significant for confusion, but was clearly significant for cerebrovascular accident and/or transischemic attack. Also here we see a support of the theory of Harrison.[6] Aorta-pathology, eventually resulting in disrupter of calcified plaques during aortic cross-clamping, macroembolisms, in the aortic wall, is a significant predictor for neurological problems, but extremely for postoperative stroke. In patients with aorta-pathology, we noted no isolated mild neurological complications. In the case of a severe stroke, mild complications may be masked by the severity of the major complication. Therefore we must take care with the interpretation of 'zero' patients in the group of mild neurological complications and we can only conclude that if patients have neurological complications due to aorta-pathology, this resulted in severe neurological complications. Therefore, but also because the power to detect a significant relationship between an independent risk factor and a neurological complication (A, B, or C) decreases if the number of persons with this risk factor is low. Only 32 patients (0.8%) had aorta-pathology risk, no mild complications were noted; because of this we excluded aorta-pathology as a possible risk factor for mild neurological problems in the logistic regression analysis.

Four independent risk factors were found for mild and/or severe complications (Table 4): peripheral vascular atherosclerosis, neurological pathology, aorta-pathology and perioperative myocardial infarction. Further analysis identified aorta-pathology, perioperative myocardial infarction and neurological pathology as independent predictors for severe neurological complications, what is again supporting the 'macroembolism'-theory of Harrison.[6] Peripheral vascular atherosclerosis matures as predictor for either severe or mild neurological complications. Only perioperative myocardial infarction was an indepent predictor for severe as well for mild neurological complications. Perioperative myocardial infarction can result in a low cardiac output syndrome, eventually a period of hypotension, inducing cerebral ischemia and mild neurological problems. On the other site, the occurrence of a perioperative myocardial infarction may also be the result of the severity of the atherosclerosis, in combination with the difficulties of the myocardial revascularization. And thus being an exponent of severe atherosclerosis, identified by the unifactor analysis as a predictor of severe neurological complications.

The changes in prevalence of pre-operative neurological pathology (Table 5) is reason for concern. The prevalence in the 1993-1995 cohort was 11.6 %. This percentage is substantially larger than the prevalence observed in the time cohorts 1987-1989 and 1990-1992. Furthermore the cohort 1993-1995 appeared to be an independent predictor for increased risk for neurological complications (Table 4). Therefore, factors not included in this risk analysis, related to the time cohort, influence the risk for neurological complications. Possible the tendency, to accept lower perfusion pressure (50 - 60 mmHg) during cardiopulmonary bypass, could be a reason for the increased risk of neurological morbidity, as described by Gold et al.[12] An other explanation, is related to the definition and registration of "mild neurological" complications. Mild complications were defined as confusion or memory disturbances for more than 12 hours, without formal neurological or neuro-psychological examination. This is of course a serious deficit of our study, however, inevitable in a retrospective analysis. Therefore, it is possible that mild neurological problems were better registered during the period 1993-1995. Also, during this last period, patients were discharged faster from the intensive care to intermediate care or the ward. Mild neurological complications may be more registered, because on the intensive care these mild complications are more 'accepted' or 'hidden' in the whole of intensive care problems. In the unifactor analysis, neurological pathology was a predictor of mild neurological problems. So it is possible that the higher risk of especially mild neurological complications during the last time cohort is a consequence of the increasing number of patients with preoperative neurological pathology, who are more at risk for mild neurological complications in combination with our fast discharge policy. This is important, because on the ward, these patients need more care, what can be translated in more nursing costs. Furthermore, these patients are more likely to aspirate, to require reintubation because of hypoxia due to their confusion or depressed consciousness.[5] Concerning these two remarks, a logical question is: are all patients benefited with the maintenance of low perfusion pressure during bypass and with the fast-track policy? As it is known that patients who develop even minor postoperative complications have excess costs compared to patients who have no complications.[12,13]

The relation between elective/emergency operation and neurological problems is especially determined by the occurrence of a perioperative myocardial infarction and also, however to a lesser extent, by the presence of aorta-pathology. We know that patients operated in emergency, but in which we can prevent or limit a myocardial infarction, are mostly not causing any problem. It is the occurrence of a perioperative myocardial infarction that is responsible for the frequency of neurological problems after emergency operations. Hypertension, resulting in atherosclerotic degeneration of the vessels, lead to more neurological problems possible because the high frequency of peripheral vascular atherosclerosis and the higher incidence of perioperative myocardial infarction due to distal coronary pathology.

In this study, we analyzed neuro- and psychological disorders after coronary bypass surgery, and we accept the criticism of methodological limitations, as the definition of the 'mild neurological complications'. However, the importance of such studies is that they accentuate the problem, and serve as a source of ideas for design of prospective controlled studies.[14]

In conclusion, the present study emphasizes that peripheral vascular atherosclerosis, preoperative neurological pathology, aorta-pathology and the occurrence of a perioperative myocardial infarction, are predictors for neurological postoperative complications. In addition, we suggest that different strategies in patient care for patients with or without these risk factors, can be useful in reduction of postoperative (mild) neurological complications and eventually cost reduction.

References

1. Lynn GN, Stefanko K, Reed JF, Gee W, Nicholas G. Risk factors for stroke after coronary artery bypass. J Thorac Cardiovasc Surg 1992;104:1518-1523.
2. Newman S, Smith P, Treasure T, Joseph P, Ell P, Harrison M. Acute neuropsychological consequences of coronary artery bypass grafting. Curr Psychol Res Rev 1887;6:115-124.
3. Reed GL, Singer D, Picard E. Stroke following coronary artery bypass grafting. N Engl J Med 1988;319:1246-1250.
4. Noyez L, Janssen DPB, van Druten JAM, Skotnicki SH, Lacquet LK. Coronary bypass surgery: What is changing? Analysis of 3834 patients undergoing primary isolated myocardial revascularization. Eur J Cardio-thoracic Surg 1998;13:365-369.

5. Redmond JM, Greene PS, Goldsborough MA, Cameron DE, Stuart RS, Sussman MS, Watkins L, Lashinger JC, McKhann GM, Johnston MV, Baumgartner WA. Neurological injury in cardiac surgical patients with a history of stroke. Ann Thorac Surg 1996;61:42-47.
6. Harrison MJG. Neurological complications of coronary artery bypass grafting: diffuse or focal ischemia? Ann Thorac Surg 1995;59:1356-1358.
7. Christakis GT, Fremes SE, Naylor CD, Chen E, Roa V, Goldman BS. Impact of preoperative risk and perioperative morbidity on ICU stay following coronary bypass surgery. Cardiovasc Surgery 1996;4:29-35.
8. Taggart DT, Mazel JW, Bhattacharya K, Meston N, Standing SJ, Kay JDS, Pillai R, Johnsson P, Westaby S. Comparison of serum S-100β levels during CABG and intracardiac operations. Ann Thorac Surg 1997;63:492-496.
9. Westaby S, Johnsson P, Parry A. Serum S100 protein: a potential marker for cerebral events during cardiopulmonary bypass. Ann Thorac Surg 1996;61:88-92.
10. Tuman KJ, McCarthy RJ, Najafi H, Ivankovich AD. Differential effects of advanced age on neurological and cardiac risks of coronary artery operations. J Thorac Cardiovasc Surg 1992;104:1510-1517.
11. Heyer EJ, Delphin E, Adams DC, Cerebral dysfunction after cardiac operations in elderly patients. Ann Thorac Surg 1995;60:1716-1722.
12. Gold JP, Charlson ME, Williams-Russo P, Szatrowski TP, Peterson JC, Pirraglia PA, Hartmann GS, Yao FSF, Hollenberg JP, Barbut D, Hayes JG, Thomas SJ, Purcell MH, Mattis S, Gorkin L, Post M, Krieger KH, Isom OW. Improvement of outcomes after coronary bypass. A randomized trial comparing intraoperative high versus low mean arterial pressure. J Thorac Cardiovasc Surg 1995;110:1302-1314.
13. Magovern JA, Sakert T, Magovern GJ Jr., Benckart DH, Burkhoder JA, Liebler GA, Magovern GJ Sr. .A model that predicts morbidity and mortality after coronary artery bypass graft surgery. J Am Coll Cardiol 1996;28:1147-1153.
14. Engels EA, Spitz MR. PACE –setting reseach. The Lancet 1997;350:677-678.

Chapter 4

Predictors of nephrological morbidity after coronary artery bypass surgery

Douglas P.B. Janssen[1], Luc Noyez[1], Johannes A.M. van Druten[2], Stefan H. Skotnicki[1], Leon K. Lacquet[1]

The Departments of [1]Thoracic and Cardiac Surgery, and [2]Medical Informatics, Epidemiology and Statistics, University Hospital Nijmegen, Nijmegen, The Netherlands

Cardiovascular Surgery 2002;10:222-227

Abstract

Aim: The aim of this study was to analyze the nephrological morbidity after myocardial revascularization.

Methods and Results: We analyzed the pre-, peri-, and postoperative data of 3815 patients who underwent a primary isolated coronary bypass grafting between January 1987 and December 1995. Nephrological complications were divided into renal dysfunction and requiring dialysis. The increase in nephrological complications (1.2 - 4%) is the result of an increase of patients with renal dysfunction. Unifactor risk analysis identified age, diabetes, hypertension, nephrological pathology, perfusion time, aortic cross-clamp time, emergency operation and perioperative myocardial infarction as risk factors. Multifactor risk analysis identified diabetes, hypertension, nephrological pathology, perfusion time, perioperative myocardial infarction and the cohorts operated upon in 1990 -1992, 1993 -1995 as independent risk factors for renal dysfunction; and age, nephrological pathology and perioperative myocardial infarction for those needing dialysis.

Conclusion: Several variables have been identified as risk factors for nephrological complications; especially important are pre-existing nephrological pathology and perioperative myocardial infarction.

Introduction

In a previous report, based on an analysis of 3834 patients undergoing primary isolated myocardial revascularization, we described a significant increase of the nephrological morbidity from 1.9% to 4.8% between 1987 and 1995.[1] The data of the STS National cardiac surgery database also showed an increase of the percentage of renal complications after primary isolated CABG during the latter years.[2] Renal failure and postoperative dialysis results in a prolonged hospital stay and increased costs. Renal dysfunction also seems to be an independent predictor of morbidity and mortality after CABG.[3]

The purpose of this study was to analyze the postoperative nephrological morbidity in relation to pre- and perioperative risk factors, so that patients at increased risk can be predicted. The following main questions were addressed: (a) which of the variables measured pre- or perioperatively are risk factors for post-operative nephrological complications? (b) which of these factors contributed independently to an increased risk of postoperative nephrological complications? And (c) which of these independent predictors changed over time?

Material and methods

Patients

With the aid of our database, Coronary Surgery Database Radboud Hospital (CORRAD), a registry that stores pre-, per-, and postoperative data of all patients undergoing isolated coronary bypass grafting (CABG), we identified a series of 3834 patients undergoing a primary isolated CABG from January 1987 to December 1995. Of these 3834 patients, 12 dialysis-dependent and seven renal transplant patients were excluded from this study. So, 3815 patients were included in the study. The nine years were subdivided into three cohorts of three years. January 1987 to December 1989 (1283 patients), January 1990 to December 1992 (1126 patients), and January 1993 to December 1995 (1406 patients). One hundred and four (2.7%) of these 3815 patients had postoperative nephrological complications. Postoperative nephrological morbidity was accepted when there was renal dysfunction (creatinine $\geq$ 150 μmol/l) and/or patients required dialysis. Dialysis (hemodialysis or peritoneal dialysis) was only started after a nephrology consultation. Table 1 presents the frequency of nephrological complications in the three time cohorts and also shows the division between renal dysfunction (creatinine $\geq$ 150 μmol/l) and those requiring dialysis. Preoperatively, diabetes was defined as patients having a positive glucose tolerance test, requiring oral antidiabetic medication, or insulin treatment. Hypertension was defined as a systolic blood pressure > 160 mmHg or a diastolic pressure > 100 mmHg. Peripheral vascular atherosclerosis was registered in patients with signs of peripheral vascular disease or requiring operations. Nephrological pathology was registered in patients with a documented history of renal dysfunction (creatinine $\geq$ 150 μmol/l) preoperatively. Emergency operation was defined as an operation for evolving myocardial infarction, ischaemia not responding to medical therapy, or cardiogenic shock. Perioperative, aortic pathology was noted in patients, with severe calcification in the ascending aorta. Perioperative myocardial infarction was defined as a new postoperative Q wave or T wave accompanied by increased cardiac enzymes (CPK-MB >10%).

Surgical Technique

All patients were operated on using standard cardiopulmonary bypass technique, aortic and right atrial (two stage) cannulation, and hypothermia (28 - 32°C). Myocardial protection during aortic cross-clamping was obtained by infusion of cold (4°C) St Thomas' Hospital cardioplegia until asystole occurred and was maintained by reinfusion of 100 ml/m^2 of the solution every 25-30 minutes or earlier, as needed. Over the study period there was no significant difference in bypass and aortic cross-clamp time, nor in the number of grafts and distal anastomoses that were made. The only surgical change was the increased use of arterial grafts.[1]

Statistical analysis

To test which variables can be considered risk factors for nephrological complications, Fisher's exact test for 2x2 tables was used (unifactor risk analysis). Changes in the incidence of postoperative nephrological complications and changes in the prevalence of risk factors in the three time cohorts were examined with the χ^2 test. Multiple logistic regression analysis was used to identify risk factors which independently contributed to an increased risk of postoperative nephrological complications (multifactor risk analysis). In the analysis the three time cohorts were represented by two indicator variables, the cohort 1987-1989 was used as reference for the other two cohorts. In the unifactor risk analysis we used three time cohorts to present and analyze the incidence of postoperative nephrological complications over time. In the logistic regression analysis (multifactor risk analysis) these three time cohorts were represented by two indicator variables (using as reference the time cohort 1987-1989). Such a representation model allows a priori different time effects for different cohorts. In the model we used two indicator time variables instead of one time continuous variable because we wanted to avoid the a priori assumption of a linear relationship with time. A postiori, if we had used one time continuous variable in the model (using the assumption of linearity) instead of two indicator time variables, we would have come to the same conclusions. Statistical significance was assumed at $P \leq 0.05$.

Table 1. Incidence of postoperative nephrological complications in the three time-cohorts.

	1987-1989 *n*=1283 (%)	1990-1992 *n*=1126 (%)	1993-1995 *n*=1406 (%)	1987-1995 *n*=3815 (%)	χ^2 test *P*-value
Nephrological problems	15 (1.2)	33 (2.9)	56 (4.0)	104 (2.7)	0.001
Renal dysfunction[a]	8 (0.6)	25 (2.2)	48 (3.4)	81 (2.1)	0.001
Dialysis	7 (0.6)	8 (0.7)	8 (0.6)	23 (0.6)	0.85[a]

[a] creatinine ≥ 150 μmol/l

Results

Table 1 shows that the incidence of postoperative nephrological complications increased with time, from 1.2% to 4.0% ($P = 0.001$). The increase in the overall incidence was the result of an increase of the number of patients with postoperative renal dysfunction (0.6% to 3.4%). The incidence of patients requiring postoperative dialysis remained stable in time ($P = 0.85$).

Unifactor risk analysis

Table 2 lists the variables tested for postoperative nephrological complications. For each variable the risk was calculated for complications as renal dysfunction and the need for dialysis. Patients with a known history of nephrological pathology ($n = 33$) had an increased risk of postoperative complications. Also patients who had a perioperative myocardial infarct ($n = 103$) clearly had an increased risk of post-

Table 2. Variables tested for postoperative nephrological complications (A, B, C)[a].

Variables	No. of patients	A: 2.7%	B: 2.1%	C: 0.6%
Age				
≤ 75 years	3597	2.5	2.0	0.5
> 75 years	218	7.3	4.6	2.8
Sex				
Male	2881	2.5	2.1	0.5
Female	934	3.3	2.4	1.0
Diabetes				
Yes	497	6.0	4.6	1.4
No	3318	2.2	1.8	0.5
Hypertension				
Yes	2137	3.7	2.9	0.8
No	1678	1.5	1.2	0.3
Peripheral vascular atherosclerosis				
Yes	744	3.6	2.6	1.1
No	3071	2.5	2.0	0.5
Nephrological pathology				
Yes	33	57.6	36.4	21.2
No	3782	2.3	1.8	0.4
Perfusion time (min)				
≤ 100	2129	1.4	1.1	0.3
> 100	1686	4.4	3.4	1.0
Aortic cross-clamp time (min)				
≤ 60	2278	2.1	1.6	0.5
> 60	1537	3.6	2.9	0.7
Elective / emergency operation				
Elective	3536	2.6	2.0	0.6
Emergency	279	5.0	3.9	1.1
Aorta-pathology				
Yes	32	9.4	6.3	3.1
No	3783	2.7	2.1	0.6
Perioperative myocardial infarction				
Yes	103	20.4	14.6	5.8
No	3712	2.2	1.8	0.5

[a]Nephrological complications, A = B + C

B = renal dysfunction (creatinine ≥ 150 μmol/l)

C = dialysis

Table 3. Unifactor risk analysis for nephrological complications (A, B, C)[a].

Variables	A RR (*P*-value*)	B RR (*P*-value*)	C RR (*P*-value*)
Age (> 75 years / ≤ 75 years)	2.9 (2.10^{-4})	2.3 (0.02)	5.6 (0.003)
Sex (male / female)	0.8 (0.20)	0.9 (0.60)	0.5 (0.14)
Diabetes (yes / no)	2.7 (2.10^{-5})	2.6(2.10^{-4})	2.8 (0.02)
Hypertension (yes / no)	2.5 (2.10^{-5})	2.4 (4.10^{-4})	2.7 (0.04)
Peripheral vascular atherosclerosis (yes / no)	1.4 (0.1)	1.3 (0.39)	2.2 (0.11)
Nephrological pathology (yes / no)	25.0 (2.10^{-22})	20.2 (9.10^{-13})	53.0 (4.10^{-10})
Perfusion time (min) (>100 / ≤100)	3.1 (3.10^{-8})	3.1 (2.10^{-6})	3.3 (5.10^{-3})
Aortic cross-clamp time (min) (>60 / ≤60)	1.7 (6.10^{-3})	1.8 (5.10^{-3})	1.4 (0.52)
Emergency / elective operation	1.9 (0.02)	2.0 (0.05)	1.8 (0.23)
Aorta-pathology (yes / no)	3.5 (0.06)	3.0 (0.15)	5.2 (0.18)
Perioperative myocardial infarction (yes / no)	9.3 (1.10^{-13})	8.1 (2.10^{-9})	11.6 (2.10^{-5})

[a]Nephrological complications, A = B + C, B = renal dysfunction (creatinine ≥ 150 μmol/l), C = dialysis. *Fisher exact test

operative nephrological morbidity. The relative risks (RR) and the results of the Fisher's exact test (*P*-value) are shown in Table 3 for each variable (unifactor analysis). Most of the variables tested in the unifactor analysis were associated with postoperative complications; some very strong with a very large relative risk, especially patients with a known history of nephrological pathology, or perioperative myocardial infarction. Peripheral vascular atherosclerosis and aortic pathology were only weakly associated with postoperative nephrological complications (*P*-values not clearly significant); gender was not a predictor for nephrological complications.

Multifactor risk analysis

Table 4 shows the results of the multiple logistic regression analysis. Independent predictors for postoperative complications were; age (*P* = 0.02), diabetes (*P* = 0.04),

Table 4. Multifactor risk analysis (logistic regression) for nephrological complications[a].

Variables	*P*-value A	*P*-value B	*P*-value C	Odds ratio A	Odds ratio B	Odds ratio C
Age (> 75 years / ≤ 75 years)	0.02	0.38	0.02	2.2	1.4	3.8
Sex (male/female)	0.85	0.83	0.57	1.0	1.1	0.8
Diabetes (yes/no)	0.04	0.05	0.88	1.8	1.8	1.1
Hypertension (yes/no)	0.01	0.03	0.22	1.9	1.8	2.0
Peripheral vascular atherosclerosis (yes/no)	0.66	0.49	0.56	0.9	0.8	1.3
Nephrological pathology	0.0001	0.0001	0.0001	48.3	21.2	56.0
Perfusion time (>100/≤100 min)	0.002	0.01	0.07	2.4	2.2	2.9
Aortic cross-clamp time (>60/≤60min)	0.44	0.77	0.22	0.8	0.9	0.5
Emergency / elective operation	0.23	0.57	0.19	0.6	0.8	0.3
Aorta-pathology (yes/no)	0.39	0.75	0.78	2.1	1.3	1.6
Perioperative myocardial infarction (yes/no)	0.0001	0.0001	0.0001	11.5	8.7	15.7
Time cohort 1990-1992 [b]	0.006	0.002	0.69	2.5	3.7	1.3
Time cohort 1993-1995 [b]	0.0003	0.0001	0.51	3.2	5.3	0.7

[a]Nephrological complications, A = B + C; B = renal dysfunction (creatinine ≥ 150 μmol/l); C = dialysis. [b]Reference time cohort: 1987-1989

hypertension (*P* = 0.01), nephrological pathology (*P* = 0.0001), perfusion time > 100 minutes (*P* = 0.002), perioperative myocardial infarction (*P* = 0.0001), and the time cohorts 1990-1992 (*P* = 0.006), 1993-1995 (*P* = 0.0003). Diabetes (*P* = 0.05), hypertension (*P* = 0.03), nephrological pathology (*P* = 0.0001), perfusion time (*P* = 0.01), perioperative myocardial infarction (*P* = 0.0001) and the time cohorts 1990-1992 (*P* = 0.002), 1993-1995 (*P* = 0.0001) were identified as independent predictors for renal dysfunction. For postoperative dialysis, age (*P* = 0.02), nephrological pathology (*P* = 0.0001) and perioperative myocardial infarction (*P* = 0.001) were identified as independent predictors. In contrast with the unifactor analysis, the variables aortic cross-clamp time and emergency/elective operation were no independent predictors in the multifactor analysis.

Table 5. Change of prevalence of independent risk factors in the three time cohorts.

Independent risk factor	**1987-1989** *n*=1283 (%)	**1990-1992** *n*=1126 (%)	**1993-1995** *n*=1406 (%)	χ^2 **test** *P*-value
Age > 75 years	41 (3.2)	68 (6.0)	109 (7.8)	0.001
Diabetes	168 (5.9)	128 (11)	201 (14)	0.09
Hypertension	692 (54)	673 (60)	772 (55)	0.009
Nephrological pathology	7 (0.6)	7 (0.6)	19 (1.4)	0.05
Perfusion time (>100 min)	490 (38)	562 (50)	634 (45)	0.001
Perioperative myocardial infarction	34 (2.7)	34 (3.0)	35 (2.5)	0.71

The prevalence of nearly all-independent risk factors was associated with time (Table 5). The pattern with time was however not systematic. The percentage of patients above 75 yr was clearly increasing, 3.2% in 1987-1989 to 7.8% in the cohort 1993-1995. Table 6 shows the relationship between the independent risk factors age, diabetes, hypertension, nephrological pathology, perfusion time > 100 min, perioperative myocardial infarction, and the risk factors, aortic cross-clamp time, and emergency operation, identified in the unifactor analysis. A long aortic cross-clamp time was associated with longer perfusion times and a relatively higher risk of perioperative myocardial infarction. Emergency operation was associated with nearly all-independent risk factors, but strongly related to an increased risk of perioperative myocardial infarction (elective 1.7%; emergency 15.4%).

Discussion

This study demonstrated that the significant increase in nephrological complications after CABG, was mainly because of the significant increase in the percentage of patients with renal dysfunction (Table 1). The same trend has been documented by The Society of Thoracic Surgeons National Database. Over the period 1991-1993, 1.78% of the patients developed renal failure and 0.62% required dialysis after

Table 6. Relationship between the risk factors aortic cross-clamp time (AoX), emergency/elective operation and independent risk factors for postoperative nephrological complications.

Independent risk factor	**AoX ≤ 60 min.** *n* = 2278 (%)	**AoX > 60 min** *n* =1537 (%)	Fisher-test *P* – value
Age > 75 years	124 (5.4)	94 (6.1)	0.39
Diabetes	287 (13)	210 (14)	0.35
Hypertension	1267 (56)	870 (57)	0.55
Nephrological pathology	17 (0.8)	16 (1.0)	0.37
Perfusion time > 100 min	409 (18)	1277 (83)	0.001
Perioperative myocardial infarction	47 (2.1)	56 (3.6)	0.004
	Elective *n* = 3536 (%)	**Emergency** *n* = 279 (%)	Fisher-test *P* - value
Age > 75 years	188 (5.3)	30 (10.8)	0.0006
Diabetes	448 (13)	49 (18)	0.03
Hypertension	1935 (55)	202 (72)	6.10^{-9}
Nephrological pathology	28 (0.8)	5 (1.8)	0.09
Perfusion time > 100 min	1534 (43)	152 (54)	0.0004
Perioperative myocardial infarction	60 (1.7)	43 (15.4)	3.10^{-23}

primary isolated CABG, versus 2.7% renal failure and 0.83% dialysis over the years 1995-1996.[2]

The unifactor risk analysis showed no clear association for the variables of gender, peripheral vascular atherosclerosis, and perioperative detected aortic pathology (Tables 2 and 3). The strong association between nephrological pathology and postoperative nephrological morbidity (renal dysfunction and dialysis) has already been described by Dish et al.[4] The routine administration of a renal dose of dopamine to patients with nephrological pathology, is possibly a reason that the nephrological morbidity did not increase in a recent study describing the changes in risk and morbidity of CABG.[5]

Two independent risk factors were found for renal dysfunction as well as dialysis: nephrological pathology and perioperative myocardial infarction (Table 4). The vulnerability of patients with a prior diagnosis of nephrological pathology has already been reported.[4] Perioperative myocardial infarction can be associated with a postoperative low cardiac output syndrome resulting in severe renal dysfunction leading to dialysis. Some patients who develop a perioperative myocardial infarction require emergency surgery which may lead to a low cardiac output resulting in renal dysfunction.

Age (> 75 yr) was associated with an increased risk of dialysis (Table 4, P = 0.02). Diabetes, hypertension and perfusion time (> 100 minutes) were predictors of renal dysfunction (P = 0.05). However, the significance of these predictors was clearly inferior to the presence of nephrological pathology and a perioperative myocardial infarction. Age was an independent predictor of nephrological morbidity (Table 4, P = 0.02), and it is known that there is a relation between age and other comorbidity and postoperative morbidity.[6] Age did not appear to be a predictor for renal dysfunction (P = 0.38) but was a significant predictor for dialysis (P = 0.02). This is possibly because in elderly patients, the decision to start dialysis is made earlier. Age is an important predictor, because it is an independent factor, which clearly increased during the study[1] and will be even more important in the future.

Also the time cohorts 1990-1992 and 1993-1995 were independent predictors of an increased risk of nephrological morbidity, especially renal dysfunction. Apparently there are factors not included in the risk analysis, related to the time cohorts, which have had an effect on the incidence of renal dysfunction. Possibly, the acceptance of lower mean arterial pressure during cardiopulmonary bypass or in the perioperative period, during the last years, is a reason for renal dysfunction. However, the role of perfusion pressure in organ dysfunction is still controversial,[7,8] but a possibility that needs further investigation. The increase of nephrological morbidity with time requires more investigation of patients at risk and eventually the development of specific protocols to manage these patients.[3]

The relation between aortic cross-clamp time (> 60 min) and the independent risk factors was especially determined by longer perfusion times (Table 6, P =

0.001) and the occurrence of a perioperative myocardial infarction (*P* = 0.004). Longer aortic cross-clamp times result mostly in longer perfusion times. During prolonged aortic cross-clamp times there is the problem of myocardial protection, and sometimes longer aortic cross-clamp times are the consequence of perioperative difficulties, which both may result in perioperative myocardial damage and myocardial infarction.

Emergency operation was associated with nearly all independent risk factors. This was very strongly related to the risk of a peri-operative myocardial infarction ($P = 3.10^{-23}$). These associations with independent risk factors may explain the observation that aortic cross-clamp time and elective/emergency operation were risk factors in the unifactor analysis but were not relevant when taken with other independent factors. Their relationship with an increased risk of nephrological morbidity is by association with other independent factors. We excluded dialysis-dependent and renal transplant patients in this study because these patients are special groups with their own complications and associated impact on the perioperative morbidity.[9]

Acknowledgements

We thank Mrs Lisette Peters for her work in the secretarial function of the CORRAD database.

References

1. Noyez L, Janssen DPB, van Druten JAM, Skotnicki SH, Lacquet LK. Coronary bypass surgery: What is changing? Analysis of 3834 patients undergoing primary isolated myocardial revascularization. Eur J Cardio-thoracic Surg 1998;13:365-369.
2. The Society of Thoracic Surgeons. Data analyses of The Society of Thoracic Surgeons National Cardiac Surgery Database.

3. Magovern JA, Sakert T, Magovern GJ Jr, Benckart DH, Burkhoder JA, Liebler GA, et al. A model that predicts morbidity and mortality after coronary artery bypass graft surgery. J Am Coll Cardiol 1996;28:1147-1153.
4. Dish DL, Oçonnor GT, Birkmeyer JD, Olmstead EM, Levy DG, Plume SK. Changes in patients undergoing coronary artery bypass grafting; 1987-1990. Northern New England Cardiovascular Disease Study Group. Ann Thorac Surg 1994;57:416-423.
5. Estafanous FG, Loop FD, Higgings TL, Tekyi-Mensah S, Lytle BW, Cosgrove DM, et al. Increased risk and decreased morbidity of coronary artery bypass grafting between 1986 and 1996. Ann Thorac Surg 1998;65:383-389.
6. Williams DB, Carrillo RG, Traad EA, Wyatt CH, Grahowski R, Wittels H, et al. Determinants of operative mortality in octogenarians undergoing coronary bypass. Ann Thorac Surg 1995;60:1038-1043.
7. Slogoff S, Reul GJ, Keats AS, Curry GR, Crum ME, Elmquist BA, et al. Role of perfusion pressure and flow in major organ dysfunction after cardiopulmonary bypass. Ann Thorac Surg 1990;50:911-918.
8. Gold JP, Charlson ME, Williams-Russo P, Szatrowski TP, Peterson JC, Pirraglia PA, et al. Improvement of outcomes after coronary bypass. A randomized trial comparing intraoperative high versus low mean arterial pressure. J Thorac Cardiovasc Surg 1995;110:1302-1314.
9. Owen CH, Cummings RG, Sell TL, Schwab SJ, Jones RH, Glower DD. Coronary artery bypass grafting in patients with dialysis-dependent renal failure. Ann Thorac Surg 1994;58:1729-1733.

Chapter 5

Coronary artery bypass grafting in elderly patients: analysis of the outcome changes in patients aged between 70 and 77 years

Douglas P.B. Janssen[1], Luc Noyez[1], Stefan H. Skotnicki[1], Leon K. Lacquet[1]

The Departments of [1]Thoracic and Cardiac Surgery, University Hospital Nijmegen, Nijmegen, The Netherlands

Cardiologie 1999;6:297-302

Abstract

Objective: Are patients aged between 70 and 77 years who undergo CABG at higher risk now than ten years ago?

Methods: We compared the pre-, peri-, and postoperative data of patients of this age, operated between 1 January 1987 and 31 December 1988 (group A, n=112), 1 January 1990 and 31 December 1991 (group B, n= 185), and 1 January 1995 and 31 December 1996 (group C, n= 273).

Results: Neurological pathology increased, emergency operations decreased and elective operations increased significantly. The use of arterial grafts increased significantly. Mortality decreased significantly. Multifactor analysis selected emergency operations as independent risk factors for mortality. Analyzing the elective operations, there was a significant increase of patients with neurological pathology and diabetes, but no change in mortality and morbidity.

Conclusion: Our data suggest that patients aged ≥ 70 and < 77 years now undergoing CABG are at significantly greater preoperative risk. However, the mortality rate, strongly influenced by the emergency operations, remained stable.

Introduction

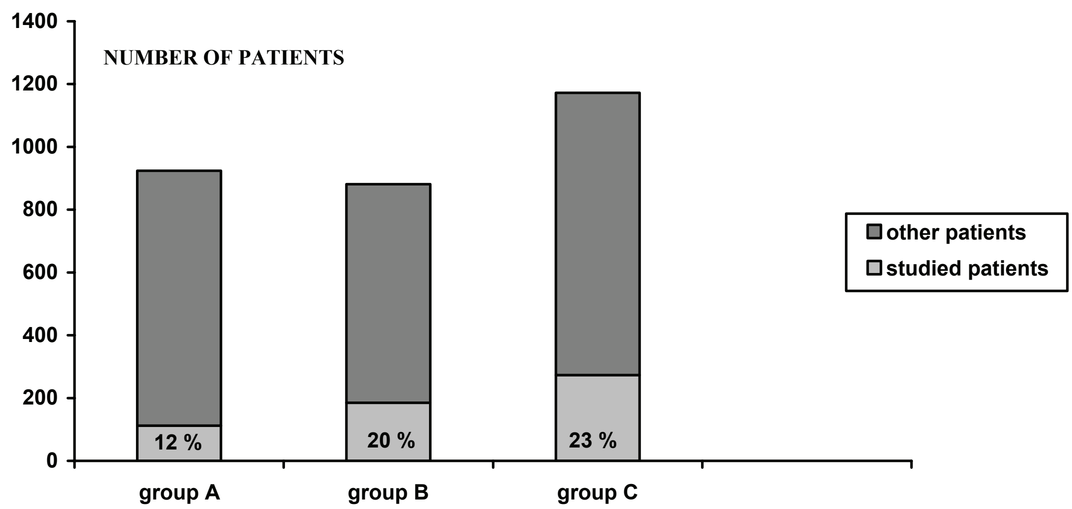
In the mid 1980s, several reports were published concerning myocardial revascularization (CABG) in patients older than 70 years.[1-3] Recently, several studies have been presented on coronary operations in octogenarians.[4-6] Despite the ten years between most publications, and the ten-year differences in age of the studied patient populations, there is a similar trend in the conclusions of these reports.[1-6] The patient population is limited, but growing; only the ‘best’ low-risk patients used to be operated and so the morbidity and mortality was acceptable. However, during the last 10 years, an increasing number of patients older than 70 years are undergoing a CABG, and we can suppose that the initial hesitation to accept this patient population has disappeared with time. In other words, are higher-risk patients being operated today?

Material and methods

Patients

With the aid of our database, Coronary Surgery Database Radboud Hospital (CORRAD), a registry that stores pre-, peri-, and postoperative data of all patients undergoing isolated CABG, we identified 4868 myocardial revascularizations performed from January 1987 to December 1997. Of these operations, 926 (18%) were performed on patients 70 years of age or older, but younger than 77 years. We limited age to 77 years because we wanted to have groups with comparable age distribution. The increasing number of patients older than 77 years operated on during recent years could disturb this age distribution. Three groups of patients were identified for this study; group A, 112 patients operated between 1 January 1987 and 31 December 1988, group B, 185 patients operated between 1 January 1990 and 31 December 1991, and group C, 273 patients operated between 1 January 1995 and 31 December 1996. Figure 1 shows the patient distribution over the time cohorts.

Figure 1. Number of patients aged ≥ 70 and < 77 years versus the total number of patients operated during the same time cohort.



Preoperatively, diabetes was defined as having a positive glucose tolerance test, oral antidiabetic medication, or insulin dependency. Hypertension was defined as systolic blood pressure > 160 mmHg or diastolic pressure > 100 mmHg. Peripheral vascular atherosclerosis was registered in patients with either central (carotic) or peripheral vascular disease or operations. Neurological pathology was registered in patients with a cerebrovascular accident, transient ischaemic attack, or a documented history of cognitive disturbances preoperatively. Nephrological pathology was recorded when there was a documented urological problem or operation or renal failure (creatinine ≥ 150 μmol/l), preoperative dialysis, or renal transplantation. Pulmonary pathology was registered in patients with chronic obstructive pulmonary disease, and/or a history of previous lung disease. Emergency operation was defined as an operation for evolving myocardial infarction, ischaemia not responding to medical therapy, or cardiogenic shock.

Perioperative myocardial infarction was defined as a new postoperative Q wave or T wave accompanied by increased cardiac enzymes (CPK-MB>10%). Wound problems were defined as all sternal wound problems. Pulmonary problems were all infectious and other pulmonary problems, neurological problems were defined as incidence of a new cerebrovascular accident and/or transient ischaemic attack but also when there was confusion for more than 12 hours. Under nephrological problems, postoperative dialysis, renal dysfunction (creatinine ≥ 150 μmol/l) and eventually other urological problems were noted. Mortality was classified as operative, hospital and thirty-day mortality.

Surgical technique

All patients were operated on using standard cardiopulmonary bypass technique, aortic and right atrial (two stage) cannulation, and hypothermia (28°C - 32°C). Myocardial protection during aortic cross-clamping was performed with infusion of cold (4°C) St. Thomas' Hospital cardioplegia until asystole occurred and was maintained by reinfusion of 100 ml/m^2 of the solution every 25-30 minutes or earlier, as needed.

Statistical analysis

Characteristics of patients in group A, B, and C are presented as percentages for dichotome variables and as mean ± standard deviation. Differences in the three groups were tested with the F test or the Chi-squared test, when appropriate. To test which variables can be considered risk factors for mortality, Fisher's exact test for 2*2 tables was used (unifactor risk analysis). Multiple logistic regression analysis was used to identify risk factors which independently contribute to an increased risk of postoperative mortality. Statistical significance was assumed at $P \leq 0.05$ ($P = 0.000$ means $P < 0.0005$).

Table 1. Preoperative demographic and cardiac variables.

Variable	**Group A** n=112 (%)	**Group B** n=185 (%)	**Group C** n=273 (%)	***P-value***
Demographic				
Men	71 (63)	116 (62)	181 (66)	ns
Women	41 (37)	69 (38)	92 (34)	ns
Age (mean ± SD) (years)	72.8 ± 1.8	73.1 ± 2.01	73.4 ± 1.9	ns
Diabetes	16 (14.2)	22 (12)	52 (19)	ns
Hypertension	55 (49.1)	104 (56)	133 (48.7)	ns
Peripheral vascular atherosclerosis	32 (28.5)	35 (19)	68 (24.9)	ns
Neurological pathology	7 (6.2)	9 (4.8)	44 (16.1)	0.000
Nephrological pathology	14 (12,5)	25 (15)	44 (15)	ns
Pulmonary pathology	13 (11,6)	30 (16,2)	55 (20,1)	ns
Cardiac				
Single-vessel disease	7 (6.2)	7 (3.7)	10 (3.6)	ns
Two-vessel disease	18 (16.0)	25 (13.5)	53 (19.4)	ns
Three-vessel disease	87 (77.6)	153 (82.7)	210 (76.9)	ns
Previous successful PTCA	7 (6.5)	11 (5.9)	18 (6.5)	ns
Preoperative myocardial infarction	55 (49.1)	105 (56.7)	157 (57.5)	ns
Reoperation	8 (7.1)	14 (7.5)	24 (8.7)	ns
Operation-elective	65 (58.0)	121 (65.4)	213 (78,0)	0.000
Operation-emergency	47 (41.9)	64 (34.5)	60 (21.9)	0.000

ns = not significant; $P = 0.000$ means $P < 0.0005$

Results

Over the studied time cohorts, there was a significant increase in the percentage of patients aged between ≥ 70 and < 77 years (*P* = 0.000), as shown in Figure 1. Table 1 presents the preoperative data of the patients. During this period there was a significant increase in the percentage of patients with preoperative neurological pathology (*P* = 0.000). Concerning the cardiac preoperative data, the percentage of emergency operations decreased significantly (*P* = 0.000) and at the same time the percentage of elective operations increased significantly (*P* = 0.000).

Perioperative data are presented in Table 2. Over time, there was no significant difference in bypass and aortic cross-clamp times, nor in the number of grafts and distal anastomoses. Only the increasing use of at least one arterial graft, mostly the left internal mammary artery, was significant.

Table 2. Perioperative variables.

Variable	**group A** n=112	**group B** n=185	**group C** n=273	***P* - value**
Extracorporeal bypass time[a]				ns
mean ± SD	104 ± 44.3	110 ± 38	105 ± 39	
range	30 – 331	30 - 301	33 - 363	
Aortic cross-clamping time[a]				ns
mean ± SD	53 ± 19	61 ± 20	62 ± 25	
range	12 - 110	9 - 151	11 - 108	
Number of grafts				ns
mean ± SD	2.5 ± 0.7	2.3 ± 0.5	2.2 ± 0.6	
range	1 – 4	1 - 4	1 – 4	
Number of distal anastomoses				ns
mean ± SD	3.7 ± 1.3	4.0 ± 1.2	3.7 ± 1.0	
range	1 – 7	1 - 7	1 – 6	
Number of arterial grafts ≥1(%)	49 (43.7)	124 (67,0)	242 (88.6)	0.000

[a] time in minutes; ns = not significant; *P* = 0.000 means *P* < 0.0005

Table 3. Postoperative variables.

Variable	Group A n = 112 (%)	Group B n = 185 (%)	Group C n = 273 (%)	*P*-value
Perioperative myocardial infarction	5 (4.6)	12 (6.4)	9 (3.2)	ns
Wound problems	3 (2.6)	7 (3.7)	12 (4.3)	ns
Nephrological problems	9 (8.0)	10 (5.4)	24 (8.7)	ns
Neurological problems	5 (4.4)	8 (4.3)	15 (5.4)	ns
Pulmonary problems	14 (12.5)	12 (6.4)	28 (10.2)	ns
Mortality	8 (7.1)	11 (5.9)	4 (1.4)	0.01

ns = not significant

Postoperatively (Table 3), there was only one statistical significant difference between the three groups, namely the decrease of mortality ($P = 0.01$). Unifactor analysis (Table 4) identified emergency operation ($P = 0.000$), perioperative myocardial infarction ($P = 0.000$), reoperation ($P = 0.014$) and to a lesser extent preoperative myocardial infarction ($P = 0.03$) and postoperative nephrological problems ($P = 0.03$), as variables associated with a high relative risk for mortality. The only multivariate predictor of mortality was emergency operation ($P = 0.000$). Because of this relationship between emergency operations and mortality, we analyzed separately the elective operations (Table 5). In the latter group, there was preoperatively a significant increase of patients with neurological and diabetic pathology. Postoperatively, morbidity and mortality did not change over the years for the electively operated patients.

Discussion

In this study we analyzed the evolution in our patient population 70 years of age or older but younger than 77 years. The ageing of the surgical population is a well-known phenomenon, not only in age itself, but also in the number of elderly patients

Table 4. Variables tested for mortality by univariate analysis.

Variable		Mortality Number	(%)	*P*-value
Sex	Male	14 / 368	(3.8)	0.07
	Female	9 / 102	(8.8)	
Diabetes	yes	3 / 90	(3.3)	1.0
	no	20 / 480	(4.1)	
Hypertension	yes	13 / 292	(4.4)	0.67
	no	10 / 278	(3.5)	
Peripheral vascular atherosclerosis	yes	6 / 135	(4.4)	0.80
	no	17 / 445	(3.8)	
Neurological pathology	yes	4 / 60	(6.6)	0.29
	no	19 / 510	(3.2)	
Pulmonary pathology	yes	4 / 98	(4.0)	1.00
	no	19 / 472	(4.0)	
Nephrological pathology	yes	3 / 83	(3.6)	1.00
	no	20 / 487	(4.1)	
Preoperative myocardial infarction	yes	18 / 317	(5.6)	0.03
	no	5 / 253	(1.9)	
Three-vessel disease	yes	17 / 450	(3.7)	0.6
	no	6 / 120	(8.3)	
Reoperation	yes	5 / 35	(15)	0.014
	no	18 / 535	(3.3)	
Emergency operation	yes	17 / 173	(9.8)	0.000 *
	no	6 / 397	(1.5)	
Perioperative myocardial infarction	yes	8 / 36	(22.2)	0.000 *
	no	15 / 534	(2.8)	
Nephrological problems	yes	5 / 43	(11.6)	0.03
	no	18 / 527	(3.4)	
Neurological problems	yes	3 / 28	(10.7)	0.11
	no	20 / 542	(3.6)	

*P = 0.000 means $P < 0.0005$

Table 5. Variables of the elective operations.

Variable	Group A n=65 (%)	Group B n=121 (%)	Group C n=213 (%)	*P* -value
Preoperative				
Men	44 (67)	73 (60)	138 (66)	ns
Women	21 (33)	48 (40)	75 (34)	ns
Diabetes	6 (9.2)	10 (8.2)	31 (14.1)	0.001
Hypertension	29 (44.6)	68 (56.1)	102 (47.8)	ns
Peripheral vascular atherosclerosis	22 (33.8)	22 (18.1)	53 (24.1)	ns
Neurological pathology	3 (4.6)	6 (4.9)	33 (15.4)	0.0025
Nephrological pathology	10 (15.3)	18 (14.9)	36 (16.9)	ns
Pulmonary pathology	8 (12.3)	20 (16.5)	41 (19.2)	ns
Postoperative				
Myocardial infarction	1 (1.5)	4 (3.7)	4 (1.8)	ns
Wound problems	1 (1.5)	3 (2.4)	8 (3.7)	ns
Nephrological problems	6 (9.2)	4 (3.3)	19 (8.9)	ns
Neurological problems	2 (3.0)	1 (0.8)	10 (4.7)	ns
Pulmonary problems	5 (7.6)	4 (3.3)	20 (9.3)	ns
Mortality	2 (3.0)	4 (3.3)	1 (0.4)	ns

ns = not significant

undergoing myocardial revascularization.[7,8] Analyzing the preoperative data of the whole group, we see a significant increase of patients with neurological pathology. The increasing number of patients with a preoperative neurological problem is common, but certainly influenced by the increasing age of the patient population.[8,9] However, this analysis shows that over years, in the same age group, this coexisting disease is increasing significantly.

The statistical significant increase of elective CABG, and decrease of emergency CABG is certainly associated with the use of fibrinolytic agents, angioplasty of the culprit lesion, and use of stents in acute situations,[8] but also with a difference in referring these patients for surgery. In the beginning of our study period, patients aged between 70 and 77 were referred for surgery only as a last resort. Nowadays, surgery for patients aged 70 years or older is generally accepted, so that these patients are more easily referred for CABG.

The only surgical change over study period was the statistically significant increase in the use of (at least one) arterial graft. This is of course a surgical decision and a consequence of the superiority of the arterial grafts, also for elderly patients.[10,11]

Postoperatively there were no significant differences in morbidity, but there was a significant decrease in mortality. Univariate analysis identified five predictors of this mortality. The higher mortality rates in reoperations versus primary operations and in emergency operations, certainly when there is a perioperative myocardial infarction, are well known,[12] as is the importance of these variables in the risk adjustment of mortality after CABG.[13,14] We also identified a preoperative myocardial infarction as a predictor for perioperative mortality, although with a low significance (P = 0.03). We suppose that the identification of a preoperative myocardial infarction as predictor of mortality is due to the decrease of ventricular function after the infarction. As each myocardial infarction decreases (left) ventricular function, ejection fraction is a strong predictor of mortality and morbidity.[13,14] It is, of course, a shortcoming of our study that we did not include this parameter, however, ejection fraction is not routinely calculated and missing in approximately 70% of the patients.[8] Nephrological problems were also identified as a predictor for postoperative mortality (P = 0.03). Probably these nephrological problems are secondary to preoperative myocardial infarction, low cardiac output syndrome and therefore only of limited significance.

Multivariate analysis identified only emergency operations as an independent predictor of mortality. Therefore and because of the significant difference between the percentage of emergency operations over the studied period, we repeated our analysis for the elective patients only. This analysis showed that there was not only a significant increase in patients with neurological pathology but with diabetes, two factors with a relative strength in predicting postoperative morbidity and mortality.[13,14] Despite the significant increase of these two risk factors, there was no difference in morbidity and mortality. Based on these results, we can conclude that in our institution the patients aged 70-77 years undergoing CABG are now at greater preoperative risk, but the morbidity and mortality rates are unchanged. However, before we conclude that patients, aged 70-77 years, are undergoing a CABG without any special selection, we compared these results with our previously published analysis of the total group of patients undergoing isolated CABG.[8] For this total group of 3834 patients there was a significant increase not only of diabetic patients and patients with neurological pathology, but also with nephrological and pulmonary pathology. The mortality rate was unchanged, but there was a higher pulmonary, neurological and nephrological morbidity.[8] It seems that the trend to operate patients with more co-existing comorbidity is more avowed in the total patient population than in the elderly. So we can assume that despite the increasing number of at-risk patients of 70-77 years of age undergoing a CABG, many (higher) risk patients of this age are not operated, or not referred for operation.

Based on our single-center study concerning patients of 70-77 years of age undergoing CABG, we conclude that an increasing number of patients of this age are undergoing CABG. The percentage of emergency operations is decreasing, resulting in a decrease of mortality. There is a significant increasing percentage of risk patients, without an increase in mortality and morbidity rates. However, this last conclusion must be viewed with care.

References

1. Kamel E, Pelletier LC. Morbidity and mortality of coronary artery surgery after the age of 70 years. Ann Thorac Surg 1986;42:197-200.
2. Rose DM, Gelbfish J, Jacobwitz I et al. Analysis of morbidity and mortality in patients 70 years of age and older undergoing isolated coronary artery bypass surgery. Am Heart J 1985;110:341-346.
3. Montague NT, Kouchoukos NT, Wilson TA, et al. Morbidity and mortality of coronary bypass grafting in patients 70 years of age and older. Ann Thorac Surg 1985;39:552-557.

4. Peterson ED, Cowper PA, Jollis JG, et al. Outcomes of coronary artery bypass graft surgery in 24461 patients aged 80 years or older. Circulation 1995;92[suppl II]:85-91.
5. Cane ME, Chen C, Bailey BM, et al. CABG in octogenarians: early and late events and actuarial survival in comparison with a matched population. Ann Thorac Surg 1995;60:1033-1037.
6. Weintraub WS. Coronary operations in octogenarians: can we select the patients? Ann Thorac Surg 1995;60:875-876.
7. The Society of Thoracic Surgeons. Data analysis of The Society of Thoracic Surgeons National Cardiac Surgery Database, The 4th Year, Chicago, January 1995.
8. Noyez L, Janssen DPB, van Druten JAM, Skotnicki SH, Lacquet LK. Coronary bypass surgery: what is changing? Analysis of 3834 patients undergoing primary isolated myocardial revascularization. Eur J Cardio-thorac Surg 1998;13:365-369.
9. Tuman KJ, McCarthy RJ, Najfi H, Ivankovich AD. Differential effects of advanced age on neurological and cardiac risk of coronary artery operations. J Thorac Cardiovasc Surg 1992;104:1510-1517.
10. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10-year survival on other cardiac events. New Engl J Med 1986;41:1-6.
11. Cosgrove DM, Loop FD, Lytle BW. Does mammary artery grafting increase surgical risk? Circulation 1985;75 (suppl II):170-174.
12. Noyez L, Skotnicki SH, Lacquet LK. Morbidity and mortality in 200 consecutive coronary reoperations. Eur J Cardio-thorac Surg 1997;11:528-532.
13. Parsonnet V, Dean D, Bernstein AD. A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease. Circulation 19989;79 suppl I.I-3-12.
14. Magovern JA, Sakert T, Magovern GJ, et al. A model that predicts morbidity and mortality after coronary bypass graft surgery. J Am Coll Cardiol 1996;28:1147-1153.

Chapter 6

Preoperative prediction of prolonged stay in the intensive care unit for coronary bypass surgery

Douglas P.B. Janssen[1], Luc Noyez[2], Constantijn Wouters[2], René M.H.J. Brouwer[2]

Department of [1]Thoracic and Cardiac Surgery, Free University Medical Center, Amsterdam; and Department of [2]Thoracic and Cardiac Surgery, University Hospital Nijmegen, Nijmegen, The Netherlands

European Journal of Cardio-thoracic Surgery 2004;25:203-207

Abstract

Objective: To construct a predictive model for a prolonged stay in the intensive care unit (ICU) for coronary artery bypass surgery (CABG).
Methods: Eight hundred eighty-eight patients undergoing CABG were studied by univariate and multivariate analysis. Prolonged stay in the ICU was defined as ≥ 3 days stay. Stepwise selective procedure ($P \leq 0.05$) was used to identify a subset of variables with prognostic value for prolonged stay. This subset was used to calculate a prognostic score S and predicted probability P (P=1/1+e $^{-S}$). Sensitivity analysis was used for evaluation.
Results: Significant risk factors for prolonged stay in the ICU were: lung disease, no-sinus rhythm, no-mild valve pathology, reoperation, no-elective operation, and no-off-pump procedure. The receiver operating characteristic curve gave an area under the curve value of 0.68 for prolonged stay in ICU. Observed probabilities compared well with the predicted probabilities. Patients were classified into low (5%), intermediate (15%), high (30%), and very high-risk groups (40%). A predicted probability of ≥ 0.40 was used as cut-off point for the prognostic test. The specificity of this test for prolonged stay in the ICU was 99%; sensitivity 9%; positive predictive value 60%; and negative predictive value 89%.
Conclusions: The results show that individual patients presented for CABG, can be stratified according to their risk for prolonged stay ≥ 3 days in the ICU.

Introduction

One of the factors contributing to the increasing costs of health care is the use of expensive technology such as coronary artery bypass graft (CABG) surgery.[1] The costs of CABG surgery depend on the costs of the operation, the length of hospital stay, and duration of stay on the Intensive Care Unit (ICU). Several risk models such as the Cleveland model, EuroSCORE, CORRADscore, and Parsonnet model have been developed to predict postoperative morbidity and mortality of patients undergoing CABG.[1-5] Furthermore, it has been shown that a multivariate statistical model improves the accuracy of subjective predictions.[6] A risk model based on preoperative risk factors can be an essential tool for risk assessment and cost-benefit analysis. Kurki et al.[1] found a close relationship between preoperative risk scores as measured by the Cleveland model on one hand, and postoperative and total lengths of stay and total cost on the other hand. Increased preoperative risk scores were associated with longer postoperative hospital length of stay and increased total costs.[1]

During the last few years there has been a trend in myocardial revascularization of older patients with more preoperative coexisting morbidity.[7] We reported that despite the fact that hospital mortality seemed stable, there was an increase in major postoperative morbidity in a cohort of 3834 patients undergoing CABG surgery between 1987 and 1995.[7] An increased postoperative morbidity is a reason for obstruction of the throughput of patients and probably related to longer postoperative stay and higher total costs. As ICUs are the most expensive part of a hospital, it is important to assess which risk factors contribute to a prolonged stay in the ICU. The focus of this study was to develop a specific risk model or risk score for a prolonged stay (≥ 3 days) in the ICU. These results may help to estimate required resources in CABG surgery dependent on the risk profile of patients, and efforts to control costs of CABG surgery and general healthcare.

Patients and methods

Between January 2000 and December 2001 a cohort of 888 patients underwent isolated coronary bypass surgery at the University Medical Center Nijmegen, St. Radboud. Pre-, per-, and postoperative data of all patients were regularly stored in our Coronary Surgery Database Radboud Hospital (CORRAD Database). Table 1 presents the pre- and peroperative variables and their definitions, which were analyzed to identify risk factors for prolonged stay in the ICU. The variable mild valve pathology indicates the presence of mild valve pathology versus no-mild valve pathology. Patients with severe valve pathology requiring valve surgery were not included in this study group. Also the composition of the studied population related to

Table 1. Studied variables – definition and patient population.

Variable			Total group patients 888 (100 %)	IC ≥ 3 days patients 104 (11.7 %)
Age (years)	≤ 55		150 (16.9)	11 (10.6)
	55 > age <70		458 (51.6)	50 (48.1)
	70 ≤ age < 80		258 (29.1)	36 (34.6)
	age ≥80		22 (2.5)	7 (6.7)
Sex	Female		223 (25.1)	30 (28.8)
	Male		665 (74.9)	74 (71.2)
Body Surface Area (BSA)		BSA < 1.6	40 (4.5)	5 (4.8)
		2.1 ≥ BSA ≥ 1.6	763 (85.9)	90 (86.5)
		BSA > 2.1	85 (9.6)	9 (8.7)
Diabetes: diet-controlled, oral therapy or insulin dependent			171 (19.3)	25 (24.0)
Hypertension: systolic blood pressure > 160 mmHg, or diastolic pressure > 100 mmHg,or antihypertensive medication			516 (58.1)	69 (66.3)
Hyperlipidemia: total cholesterol > 250mg/dl or triglyceride> 200 mg/dl			534 (60.1)	57 (54.8)
Neurological disease: cerebrovascular accidents and /or transient ischemic attack			78 (8.8)	8 (7.7)
Nephrological disease: creatinine ≥ 150 μmol /l, preoperative dialysis, renal transplantation			32 (3.6)	4 (3.8)
Lung disease: chronic obstructive pulmonary disease / history of previous lung disease			78 (8.8)	16 (15.4)
PTCA: previous percutaneous transluminal coronary angioplasty			124 (14)	17 (16.3)
Pre-myocardial infarction (MI): history of MI before operation			405 (45.6)	59 (56.7)
Recent MI: history of MI<30 days before the operation			31 (3.5)	8 (7.7)
Rhythm: no-preoperative sinus rhythm			40 (4.5)	13 (12.5)
Left main: left main stenosis > 70%			143 (16.1)	18 (17.3)
Mild valve disease: combined valve disease, not requiring surgery			50 (5.6)	4 (3.8)
Left ventricular function (ejection fraction)				
EF ≥ 50% good			840 (94.6)	88 (84.6)
50%> EF >30% poor			38 (4.3)	12 (11.5)
EF ≤ 30%			10 (1.1)	4 (3.8)
Redo-surgery: history of previous cardiac surgery			55 (6.2)	16 (15.4)
Operative status				
Elective: stable cardiac function, usually scheduled at least one day prior to the surgical procedure.			847 (95.4)	91 (87.5)
Urgent: surgery is required within 24 hours after admission			33 (3.7)	13 (12.5)
Emergency: evolving infarction, ischemia not responding to medical therapy, or cardiogenic shock.			8 (0.9)	
Off-pump procedure			141 (15.9)	5 (4.8)

the variables is presented in Table 1. Our surgical technique is described in previous papers.[7]

A stay of 3 days or more in the ICU was defined as a prolonged stay being the 90th percentile of admission for this group of patients. Indication for a prolonged ICU stay were prolonged ventilation, low-cardiac output defined as need for inotropic support and a Cardiac-Index < 2.2 $l/min/m^2$, need for continous hemodynamic monitoring using Swan ganz-catheter.

Univariate analysis, Fischer's exact test, was used to test, which variables contributed to a prolonged stay in the ICU. Odds ratios were also presented for the binominal variables. Multiple logistic regression analysis was used to identify risk factors that independently contributed to a prolonged stay. The odds ratios derived from the parameter estimates in the logistic regression analysis can be considered estimates of risk for prolonged stay. To identify a subset of variables with prognostic value for prolonged stay a stepwise logistic regression analysis was used. A *P*-value of ≤ 0.05 was defined as a significant level for entry, and respectively stay into the prognostic model. A receiver operating characteristic (ROC) curve was calculated to measure the prognostic value of this subset of variables. This subset was then used to calculate a prognostic score *S* and a predicted probability *P* for prolonged stay. The prognostic score *S* is a linear function of the variables included in the selected subset. If the variables are selected the *S* score is represented by $S = b_0 + b_1x_1 + b_2x_2 + \ldots b_hx_h$. The predicted probability *P* for prolonged stay was calculated by $P = 1/1 + e^{-s}$. Sensitivity analysis was used for evaluating the effect of the initial estimate on the final decision.

The percentages of mortality and the result of the evaluation of the predictive model were presented with the 95% confidence interval (CI).

Results

Of the 888 patients, who underwent isolated CABG, 104 (12%) stayed for 3 days or more in the ICU. The mean ICU-stay was 2.2 ± 5.1 days with a median of 1 day (range 0-79 days). Hospital mortality was 2.8% (1 - 4.6 , 95% CI).

Important risk factors in the univariate analysis for prolonged stay in the ICU were: age (*P* = 0.005); lung disease (*P* = 0.016; OR = 2.1); history of myocardial infarction (*P* = 0.01; OR = 1.6); recent myocardial infarction (*P* = 0.02; OR = 2.7); no-sinus rhythm (*P* < 0.001; OR = 2.1); no-mild valve pathology (*P* = 0.05; OR = 0.6); poor or bad left ventricular function (*P* < 0.001; OR = 4.5); reoperation (*P* < 0.001; OR = 3.4); no-elective operation (*P* < 0.001; OR = 3.8); and no off-pump procedure (*P* = 0.001; OR = 4).

The following risk factors were independent risk factors in the multivariate analysis for prolonged stay in the ICU: 55 < age < 70 years (*P* = 0.03; OR = 0.24) versus age ≤ 55 years; lung disease (*P* = 0.02; OR = 2.28); no-sinus rhythm (*P* = 0.002; OR = 3.67); no-mild valve pathology (*P* = 0.01; OR = 0.19) versus mild valve pathology; reoperation (*P* < 0.001; OR = 4.04); and no-off pump procedure (*P* = 0.004; OR = 5). The *P*-value of the variable urgent and emergency operation (i.e. no-elective operation) versus elective operation was not significant. However, the odds ratios for urgent and emergency operation versus elective operation were 276.38 and 685.24, respectively.

Using stepwise logistic regression analysis, the following variables were selected for prediction of prolonged stay in the ICU: lung disease, no-sinus rhythm, mild valve pathology, reoperation, no-elective operation, and off-pump procedure (Table 2).

Table 2. Stepwise logistic regression analysis of variables selected for prediction of prolonged stay in ICU.

Variables	Regression b_i coefficients (± SE)	Odds ratio	*P* - value
Intercept	– 2.23 (0.13)		
Lung disease (yes/no)	0.90 (0.32)	2.46	0.006
No-sinus rhythm (yes/no)	1.52 (0.38)	4.60	< 0.001
Mild valve pathology (yes/no)	– 1.20 (0.60)	0.30	0.046
Reoperation (yes/no)	1.38 (0.35)	4.00	< 0.001
No-elective operation (yes/no)	1.39 (0.40)	4.01	0.001
Off pump procedure (yes/no)	– 1.56 (0.48)	0.20	0.001

Table 3. Distribution of the *S*-scores in the group of patients with (*n* = 104) and without (*n* = 784) prolonged stay (≥ 3 days) in ICU (*S*-score divided into discrete classes).

Group	*S*-score							Total
	– 5	– 4	– 3	–2	– 1	0	1	
ICU < 3 days	4	105	39	541	89	2	4	784
ICU ≥ 3 days		1	4	59	31	4	5	104

Score – 2 means between – 2.5 and – 1.5.

The associated regression coefficients, odds ratios, and *P*-values are presented in Table 2. The regression coefficients show that the presence of mild valve pathology instead of no-mild valve pathology decreased the risk of prolonged stay in the ICU (OR = 0.30). Also off-pump procedure decreased the risk of prolonged stay (OR of off-pump = 1/OR of no-off pump, 1/5= 0.20). The ROC curve gave an area under the curve value of 0.68 for prolonged stay in the ICU.

The *S*-score for an individual patient with respect to prolonged stay in the ICU was calculated as follows: S = – 2.23 + 0.90 (lung disease) + 1.52 (no-sinus rhythm) – 1.2 (mild valve pathology) + 1.38 (reoperation) + 1.39 (no-elective operation) – 1.56 (off-pump procedure).

The distribution of the *S*-scores and predicted probabilities *P* for prolonged stay in the ICU in the group with (n = 104) and without (n = 784) prolonged stay is presented in Tables 3 and 4. The *S*-scores were classified into the following classes: – 5 (between –5.5 and – 4.5): – 4 (between – 4.5 and – 3.5): – 3 (between – 3.5 and 2.5): – 2 (between – 2.5 and 1.5): – 1 (between – 1.5 and – 0.5): 0 (between – 0.5 and 0.5): 1 (between 0.5 and 1.5). For probability the following classification was used: 0 ($0 \leq P < 0.10$): 1 ($0.10 \leq P < 0.20$);….8 ($0.80 \leq P < 0.90$). The observed probabilities in these discrete classes compared well with the midpoints of the predicted probabilities (Table 4).

The a priori average risk of prolonged stay in ICU was 104/888 (12%). Using the *S*-score and predicted probability *P*, patients were classified into low (5%), intermediate (15%), high (30%), and very high-risk groups (≥ 40%) for prolonged

Table 4. Distribution of predicted probabilities (*P*) in group of patients with (*n* = 104) and without (*n* = 784) prolonged stay (≥ 3 days) in ICU .

	Predicted probability									Total
	0	1	2	3	4	5	6	7	8	
ICU < 3 days	681	8	61	28		2	4			784
ICU ≥ 3 days	63	1	16	15		4	4		1	104
Observed with prolonged stay (%)	8	11	21	35		67	50		100	

Classes defined as: 0 = 0 ≤ *P* < 0.10; 1 = 0.10 ≤ *P* < 0.20; …8 = 0.80 ≤ *P* < 0.90

stay in the ICU (Table 5). The observed prolonged stay in the ICU of these different risk groups compared well with the predicted probability of prolonged stay (8, 11, 26, 60%). We used a predicted probability *P* ≥ 40% (risk group very high) as cut-off point for constructing a prognostic test for prolonged stay. The specificity and sensitivity of this test was calculated at 99% (95% CI: 98.4 - 99.6) and 9%, (95% CI: 4 -14) respectively. The positive predictive value was 60% (95% CI: 36 - 84) and the negative predictive value was 89% (95% CI:87-91) (Table 6).

Table 5. Classification of patients in low, intermediate, high, and very high-risk groups for prolonged stay (≥ 3 days) in ICU.

	Risk group				**Total**
	Low	Intermediate	High	Very-high	
Predicted probability	5 %	15 %	30 %	≥ 40 %	
Class	0 ≤ *P* < 0.10	0.10 ≤ *P* < 0.20	0.20 ≤ *P* < 0.40	*P* ≥ 0.40	
ICU < 3 days	681	8	89	6	784
ICU ≥ 3 days	63 (8%)	1 (11%)	31 (26%)	9 (60%)	104
Total	744	9	120	15	888

Table 6. 2 x 2 Table for the evaluation of the predictive model for prolonged stay (≥ 3 days) in ICU.

ICU ≥ 3 days	**Prognostic test**		**Total**
	P < 0.40	*P* ≥ 0.40	
No	778	6	784
Yes	95	9	104
Total	873	15	888

Discussion

The focus of this study was to construct a specific risk model or risk score for a prolonged stay (≥ 3 days) in the ICU. The variables: lung disease, no-sinus rhythm, reoperation, and no-elective operation were independent risk factors increasing the risk of prolonged stay. The presence of mild valve pathology and off-pump procedure were independent risk factors decreasing the risk of prolonged stay.

It is remarkable that the presence of mild valve pathology, instead of the absence of mild valve pathology, decreased the risk of prolonged stay. However, the odds ratio of 0.19 in the multivariate analysis indicates that the impact of this risk factor was limited. The variable off-pump or no-off pump surgery is of course a point of discussion. Can (no)-off-pump surgery be considered as a preoperative variable or is it a peroperative variable? We considered it as a preoperative variable because the decision to perform off-pump surgery is a preoperative decision. We admit that, certainly in the studied patient population, mostly low-risk patients were included in the 'off-pump' group, and that surgeon's preference and experience influenced this decision.

The most important risk factors increasing the risk of prolonged stay were: lung disease (OR = 2.28), no-sinus rhythm (OR = 3.67), reoperation (OR = 4.04), urgent (OR = 276.38), and emergency (OR = 685.24) operation. It is surprising that nephrological disease was not identified because in a previous study we identified nephrological disease as an independent risk factor for postoperative nephrological morbidity.[8] The limited number of patients (36) is probably the reason; on the other hand 4/36 (11%) had an ICU-stay > 3 days.

Using the risk model, the observed prolonged stay in the ICU of the different risk groups compared well with the predicted probability of prolonged stay. A predicted probability $P \geq 40\%$ (risk group very-high) was used as cut-off point for constructing a prognostic test for prolonged stay. The specificity of 99% (95% CI: 98.4-99.6) and negative predictive value of 89% (95%CI: 87-91) of this test was good. However, the sensitivity of only 9% (95% CI: 4-14) and positive predictive value of 60% (95% CI: 36-84) was disappointing. This means that a patient without lung disease and reoperation, with preoperative sinus rhythm, mild valve pathology, elective operation, and off-pump procedure will have a low risk (11%) for prolonged stay in the ICU. On the other hand, the presence of these risk factors does not indicate that the patient will have a prolonged stay in the ICU, as the positive predictive value was only 60%. Forty percent of patients with a positive prognostic test will not suffer a prolonged stay in the ICU.

Although the risk model, i.e. prognostic test does not predict outcome of the individual patient, it gives more insight in preoperative risk factors related to prolonged stay in the ICU. This can improve prediction of required resources and hospital cost. In a previous study, we found that there has been a trend in myocardial revascularization of older patients, with more coexisting disease during the last years.[7] Preoperative risk factors such as age, insulin-dependent diabetes, nephrological, pulmonary, and neurological pathology increased significantly. Despite the fact that hospital mortality seemed stable in this study, there was an increase in major postoperative morbidity. The percentage of patients with postoperative pulmonary, neurological, and nephrological problems increased from 1987 until 1995. The increased pre- and postoperative pathology of patients undergoing CABG may result in a prolonged stay in the ICU. However, the current prognostic test for prolonged stay in the ICU showed that lung disease was the only significant preoperative risk factor for prolonged stay. The preoperative variables neurological and nephrological pathology did not increase the risk of prolonged stay.

Kurki et al.[1] showed that increased preoperative risk scores were associated with longer postoperative hospital length of stay and increased total costs. An age over 74 years appeared to be an independent risk factor for increased postoperative length of stay, hospital length of stay, and with increased total costs.[1] In our study, an age > 55 years was significantly related to a prolonged stay in the ICU in the univariate analysis. However, in the multivariate analysis, age between 55 and 70 years (P = 0.03; OR = 0.24) was the only significant age cohort associated with prolonged stay. No difference was found between age ≤ 55 years versus age between 70 and 80 years or 80 years and older. We found that the presence of co-morbidity such as lung disease and no-sinus rhythm, were more important risk factors in predicting prolonged stay in the ICU.

A point of criticism in our study can be the absence of the costs-aspects of a prolonged ICU stay. However, the aim of this study was to develop a specific risk model for prolonged stay in the ICU. This model can be helpful in decision-making and probably results in a more efficient throughput of patients in the ICU resulting in more cost effective use of the ICU.

Finally, it has become evident that the presence of full-time intensivists in the ICU leads to better outcomes for patients and more efficient resource use. The so-called closed ICUs operate as functional units with a competent on-site team and their own management under the supervision of a full-time intensivist directly responsible for the treatment. It has been reported that a reduction in mortality and cost is associated with intensivist-model ICUs.[9,10]

In conclusion, with our risk model we can stratify patients presented for CABG, according to their risk of prolonged stay in the ICU. Based on this stratification, we have more insight into the risk factors contributing to the costs of CABG and therefore costs of general healthcare.

References

1. Kurki TS, Häkkinen U, Lauharanta J, Rämö J, Leijala M. Evaluation of the relationship between preoperative risk scores, postoperative and total length of stays and hospital costs in coronary bypass surgery. Eur J Cardio-thorac Surg 2001;20:1183-1187.

2. Wouters SCW, Noyez L, Verheugt FWA, Brouwer RMHJ. Preoperative prediction of early mortality and morbidity in coronary bypass surgery. Cardiovasc Surg 2002;10:500-505.
3. Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardio-thorac Surg 1999;16:9-13.
4. Parsonnet V, Dean D, Bernstein AD. A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease. Circulation 1989;79(suppl I):I.3-I.12.
5. Higgins TL, Estafanous FG, Loop FD, Beck GJ, Blum JM, Paranandi L. Stratification of morbidity and mortality outcome by preoperative risk factors in coronary artery bypass patients. A clinical severity score. JAMA 1992;267:2344-2348.
6. Pons JMV, Borras JM, Espinas JA, Moreno V, Cardona M, Granados A. Subjective versus statistical model assessment of mortality risk in open heart surgical procedures. Ann Thorac Surg 1999;67:635-640.
7. Noyez L, Janssen DPB, Van Druten JAM, Skotnicki SH, Lacquet LK. Coronary bypass surgery: what is changing ? Analysis of 3834 patients undergoing primary isolated myocardial revascularization. Eur J Cardio-thorac Surg 1998;13:365-369.
8. Janssen DPB, Noyez L, Van Druten JAM, Skotnicki SH, Lacquet LK. Predictors of nephrological morbidity after coronary artery bypass surgery. Cardiovascular Surgery 2002;10:222-227.
9. Young MP, Birkmeyer JD. Potential reduction in mortality rates using an intensivist model to manage intensive care units. Eff Clin Pract 2000;6:284-289.
10. Burchardi H, Moerer O. Twenty-four hour presence of physicians in the ICU. Critical Care 2001;5:131-137.

Chapter 7

The EuroSCORE as predictor for prolonged hospital and intensive care stay after cardiac surgery ?

Luc Noyez,[1] Douglas P.B. Janssen[2], Constantijn W.Wouters[1], René M.H.J Brouwer[1]

Department of [1]Thoracic and Cardiac Surgery, University Hospital Nijmegen, Nijmegen; and Department of [2]Thoracic and Cardiac Surgery, Free University Medical Center, Amsterdam, The Netherlands

Netherlands Heart Journal 2005; 13: 170-174

Abstract

Objective: Validation of the EuroScore as predictor for a prolonged hospital and intensive care stay after CABG vs. institution-specific scoring systems.

Methods: For the evaluation of a prolonged hospital stay, 3359 patients were included in the analysis of EuroSCORE vs. the CORRAD morbidity score. For a prolonged intensive care stay, 1638 patients were included in the analysis of the EuroSCORE vs. the PICUS score.

Results: There was no significant difference in hospital stay between the three different EuroSCORE risk groups. The difference in hospital stay between the high-risk and low-risk groups, identified by the CORRAD morbidity score, was significant (6.9 vs. 11.2 days). For a prolonged intensive care stay, the patients identified as high-risk by the EuroSCORE and by the PICUS score also had a significantly longer intensive care stay; however, the discriminatory power was low.

Conclusion: The EuroSCORE is not of value as a predictive system for a prolonged hospital stay. There is a relation between the high-risk patients identified by the EuroSCORE and a prolonged intensive care stay.

Introduction

With the increasing number of high-risk patients undergoing cardiac surgery, preoperative risk scores have become essential for risk analysis. Several systems have been developed to predict perioperative mortality.[1] The Parsonnet score, and EuroSCORE are the most popular predictive systems used in the Netherlands.[2,3]

Despite an increase in the average perioperative mortality risk, hospital mortality has remained unchanged.[4] However, as a consequence of the increased perioperative risk, there is an increase in postoperative complications. This results in a prolonged intensive care unit (ICU) stay and hospital stay for high-risk patients resulting in an increase in healthcare costs. In an attempt to decrease healthcare costs there is an increased interest in preoperative identification of patients at risk for prolonged ICU and hospital stay.[5,6]

At present there is no internationally validated system to predict hospital length or costs in cardiac surgery based on preoperative variables, and the Parsonnet score and EuroSCORE are usually used. Recently we published a CORRAD morbidity score which can be used for identifying a low-risk and a high-risk group for postoperative morbidity, related to the postoperative hospital stay, in patients undergoing coronary artery bypass grafting (CABG).[7] Furthermore, we reported a scoring system for predicting a prolonged ICU stay (PICUS).[8] The objective of the current study was to evaluate the EuroSCORE as predictor for prolonged hospital and ICU stay and compare this with the CORRAD morbidity score and the PICUS score.

Material and methods

Risk systems

Three predictive systems were compared in this study. The EuroSCORE, a simple, objective and up-to-date system based on one of the largest, most complete and accurate databases in European cardiac surgery history. It is a scoring system for the preoperative prediction of early mortality in cardiac surgery on the basis of objective risk factors. Three risk groups are identified: a low, medium and high-risk group.[3]

The CORRAD morbidity score and the PICUS score are two systems developed in our own cardiac center based on our CORRAD database.[7,8] The aim of the CORRAD morbidity score is the preoperative identification of CABG patients with a high risk for morbidity which is related to a prolonged hospital stay. A low-risk and a high-risk group are defined.[7] With the PICUS score, CABG patients are stratified according to their risk for a prolonged stay $\geq$ 3 days in the ICU.[8] Table 1 presents the variables and risk groups of EuroSCORE, CORRAD morbidity score and PICUS score.

Table 1. Variables and risk groups: EuroSCORE, CORRAD morbidity score, PICUS score.

	EuroSCORE[3]	**CORRAD**[7]	**PICUS**[8]
Variables	Age	Age	Lung disease
	Female gender	Diabetes	No sinus rhythm
	Chronic pulmonary disease	Hypertension	Mild valve disease
	Extracardiac arteriopathy	Kidney disease	Reoperation
	Neurological dysfunction	Chronic pulmonary disease	No elective operation
	Previous cardiac surgery	Reoperation	Off-pump procedure
	Serum creatine > 200 μmol/l	Operative state	
	Active endocarditis	Left ventricular function	
	Critical preoperative state		
	Unstable angina		
	Left ventricular dysfunction		
	Recent myocardial infarct		
	Pulmonary hypertension		
	Emergency		
	Other than isolated CABG		
	Surgery of thoracic aorta		
	Postinfarct septal rupture		
Risk groups	Low	Low	< 3 days
	Medium	High	≥ 3 days
	High		

Prolonged hospital stay

All 3359 patients undergoing an isolated myocardial revascularization at the University Medical Center Nijmegen, St. Radboud between January 1997 and December 2003 were included. For all of them, the EuroSCORE and CORRAD morbidity score were calculated. Endpoint of this evaluation was the length of postoperative hospital stay.

Prolonged Intensive Care Unit Stay

All 1638 patients undergoing an isolated myocardial revascularization at the St Radboud University Medical Center, Nijmegen between January 2000 and December 2003 were included. For all of them, the EuroSCORE and PICUS score were calculated. Endpoint of this evaluation was the length of postoperative stay in the intensive care and an ICU stay of longer than three days.

Statistical analysis

Mortality is presented as percentages with 95% confidence interval, time intervals as mean ± S.D.(range). Differences between the groups were tested with F-test (one-way analysis of variance) or with the χ^2 -test when appropriate. Statistical significance was assumed at $P \leq 0.05$.

The discriminatory power of the EuroSCORE and PICUS score for ICU-stay ≥ 3 days was evaluated by calculating the area under the receiver operating characteristics (ROC) curve. The area under curves is presented with 95% confidence interval. An area of 1.0 indicates a perfect discrimination, whereas an area of 0.50 indicates complete absence of discrimination.

Results

Hospital stay

For the total patient population, there was a hospital mortality of 107 of 3359 patients (3.1%); the mean hospital stay at the St Radboud University Medical Center was 7.8 ± 10.1 (0-307) days. This mortality and hospital stay remained stable during the course of the study and are comparable with the mortality and hospital stay described in the database of the Society of Thoracic Surgeons.[9] Hospital mortality of this patient population was also evaluated by the EuroSCORE (Table 2).

Table 2. EuroSCORE and mortality.

	Patients n=3359	Mortality n=107	95% confidence limits for mortality Observed	Expected
EuroSCORE				
Low risk	1667	5 (0.2%)	(0-1.0)	(1.27-1.29)
Medium risk	1204	38 (3.1%)	(0-6.4)	(2.90-2.94)
High risk	488	64 (13.1)	(5.5-19.7)	(10.9-11.54)

Table 3. Postoperative hospitalisation: EuroSCORE vs CORRAD score.

	Patients	Postoperative hospital stay (days)	*P*-value
EuroSCORE			0.23
Low risk	1667	7.5 ± 8.5 (0-119)	
Medium risk	1204	7.7 ± 11.0 (0-307)	
High risk	488	8.3 ± 11.4 (0-123)	
CORRAD score			0.00
Low risk	2816	6.9 ± 7.2 (0-119)	
High risk	543	11.2 ± 15.8 (0-307)	

Table 3 presents the postoperative hospital stay of the different risk groups identified by the EuroSCORE and CORRAD morbidity score. There was no significant difference in hospital stay between the different risk groups identified by the EuroSCORE. In contrast, the difference in hospital stay found between the low-risk and high-risk groups using the CORRAD morbidity score was statistically significant.

Intensive care stay

The mean postoperative ICU stay of the 1638 included patients was 2.8 ± 10.3 (0-300) days. Altogether, 215 patients (12%) had a prolonged ICU stay of longer than three days (9.0 ±17.5). The postoperative ICU stay remained stable during the course of the study.

Table 4 presents the postoperative ICU stay of the different risk groups identified by the EuroSCORE and PICUS score. There was a significant difference between the ICU stay of the high-risk EuroSCORE group compared with the medium-risk and low-risk groups (*P*=0.00). However, there was no difference in ICU stay between the low and medium group. The ICU stay for patients with a positive PICUS score (2.5± 9.6) was statistically significantly higher than for patients with a negative PICUS score. The evaluation of the discriminatory power of the PICUS score and the high-risk group of the EuroSCORE for an ICU stay of three days or longer by using the ROC curves was 0.62 (95% CI 0.58 - 0.66) for the EuroSCORE and 0.62 (95% CI 0.58 - 0.67) for the PICUS score.

Table 4. Postoperative intensive care stay: EuroSCORE and PICUS score.

	Patients	**Postoperative ICU stay (days)**	***P*-value**
EuroSCORE			0.00
Low risk	883	2.4 ± 11.7 (0-300)	
Medium risk	555	2.3 ± 9.4 (0-64)	
High risk	180	6.3 ± 14.2 (0-94)	
PICUS score			0.00
Low risk	1544	2.5 ± 9.6 (0-300)	
High risk	94	9.0 ± 17.5 (0-96)	

Discussion

Analysis of patient outcome has gained increasing importance, as institutions, healthcare providers, and even patients ask for data on risk and prognosis for procedures and therapies. The first question always concerns the risk of mortality, certainly because in cardiac surgery it has long been accepted that mortality is an indicator of quality of care. However, crude mortality fails as a measure of quality because of the variations in the patient populations and without risk stratification, surgeons and hospitals treating high-risk patients will appear to have worse results than others. With the introduction of several risk stratification models it became possible to relate perioperative mortality to the risk profile of the patients.[10] Presented in 1999, the EuroSCORE constructed three distinct risk groups for prediction of early mortality: patients at low, medium, and high risk.[3] As presented in the results, our hospital mortality correlates well with the expected mortality in the different EuroSCORE groups.

However, in recent years a major case-mix evolution has been observed in cardiac surgery. Despite the increase in average perioperative mortality risk, older patients, and more co-morbidity, hospital mortality remained unchanged.[11] Meanwhile, there was an increase in postoperative morbidity which led to an increase in surviving high-risk patients. This resulted in a prolonged ICU and hospital stay, correlating with an increase in financial costs.[1] For budgetary reasons but also for a fluent patient throughput in the organization of a cardiac surgery department, identification of patients at risk for a prolonged intensive care and hospital stay becomes interesting. The need for specific models is confirmed by the publication of several more institution-related predictive models for morbidity or length of hospital or ICU stay.[5-8,12] But because of the lack of international statistical models specifically validated to preoperatively predict ICU and hospital stay, and/or costs, the classic risk stratification models as the EuroSCORE are usually used.[13]

In this study we evaluated the postoperative hospital stay of 3359 patients at the St Radboud University Medical Center according to the risk groups of the EuroSCORE and to our own CORRAD morbidity score. From our data it is clear that there is no significant relation between the three different risk groups of the EuroSCORE and postoperative hospital stay. With our CORRAD morbidity score we found that the postoperative hospital stay of the high-risk group was significantly longer than for the low-risk group.

In the second part of our study we performed the same analysis for our PICUS score, but because we have only been registering ICU stay since 2001, we included only 1638 patients in this part of the study. Both with the EuroSCORE and our PICUS score we found a good relation between the high-risk group and a prolonged ICU stay (statistically significant). However, the discriminatory power, as presented by the ROC, was very low for both (0.62).

Based on our data, the use of the EuroSCORE fails to predict a prolonged postoperative hospital stay in the different risk groups. In contrast, we found a significant relation between the high-risk group as identified by the EuroSCORE and a prolonged ICU stay. With the identification of these high-risk EuroSCORE patients we identify patients at risk for perioperative hospital mortality. So several of these high-risk patients survived the initial operation, but died during their postoperative period. In our data we have the highest mortality in our high-risk group and most of these patients died during their (prolonged) intensive care stay. So this patient group increases the postoperative ICU stay, but because of their mortality they do not have an influence on the total postoperative hospital stay.

The low discriminatory power of our PICUS score for a prolonged ICU stay of three days or more is not surprising. Several predictive models were developed for postoperative morbidity, and related hospital stay, with comparable results. [7,8,10,12] The wide range of complications registered under morbidity and the possible different impact of these complications on IC and hospital stay, for example gastrointestinal bleeding treated either conservatively by medication or necessitating an operation, is a problem for development of a good discriminatory system.

Another point in the prediction of postoperative ICU and hospital stay is the preoperative intention. Sergeant *et al.* showed how important procedural variables as bypass conduits, quality of distal vessels, concomitant procedures and institutional experience variables are on the outcome, certainly in high-risk patients.[14] These variables can never be included in a preoperative model. Furthermore, we must realize that also the definition of endpoint as intensive care and hospital stay is specific for each institution. In this study prediction of postoperative hospital stay means hospital stay in the cardiac surgery center, not the total hospital stay of the patient because many patients were discharged to their referring hospital a few days after their operation. Finally, our PICUS score was developed on data before we had a medium care unit for early discharge of intensive care patients.

A point of criticism on our analysis can be that patient population operated on in 1998 (563 patients) and used for the development of the CORRAD score and the population (888 patients) operated on in 2000 and used for the development of the PICUS score were included in this analysis, resulting in an advantage compared to the EuroSCORE.

In conclusion, prediction of length in postoperative intensive care unit and hospital stay is desirable, not only because of the financial aspect of a prolonged stay, but also for a fluent patient throughput and efficient management of a cardiac surgery department. The well-known internationally accepted mortality risk systems are not adequate because of the heterogeneity of the 'events' as hospital and intensive care stay. As a consequence of this institution-related heterogeneity development of international predictive systems will be difficult, and institution-specific score systems with a regular update will be more valid.

References

1. Ferguson TB Jr, Dziuban SW Jr, Edwards FH, Eiken MC, Shroyer Al , Pairolero PC, Anderson RP, Grover FL, The STS National database: current changes and challenges for the new millennium. Ann Thorac Surg 2000;69:680-691.
2. Parsonnet V, Dean D, Bernstein AD. A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease. Circulation 1989;79(suppl I):I.3-I.12.
3. Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardio-thorac Surg 1999;16:9-13.

4. Warner CD, Weintraub WS, Craver JM, Jones EL, Gott JP, Guyton RA. Effect of cardiac surgery patient characteristics on patient outcomes from 1981 through 1995. Circulation 1997;96:1575-1579.
5. TU JV, Mazer CD, Levinton C, Armstrong PW, Naylor CD. A Predictive index for length of stay in the intensive care unit following cardiac surgery. Can Med Assoc J 1994;151:177-185.
6. Lazar HL, Fitzgerald C, Gross S, Heeren T, Aldea GS, Shemin RJ.Determinants of length of stay after coronary artery bypass graft surgery. Circulation 1995;92(Suppl):II20-24.
7. Wouters CW, Noyez L, Verheugt FWA, Brouwer RMHJ. Preoperative prediction of early mortality and morbidity in coronary bypass surgery. Cardiovasc Surg 2002;10:500-505.
8. Janssen DPB, Noyez L, Wouters CW, Brouwer RMHJ. Preoperative prediction of prolonged stay on intensive care unit in coronary bypass surgery. Eur J Cardio-thorac Surg 2004; 25:203-207.
9. STS on the web. http://www.sts.org/
10. Geissler HJ, Hölzl P, Marohl S, Kuhn-Régnier F, Mehlhorn U, Südkamp M, deVivie E.R. Risk stratification in heart surgery: comparison of six score systems Eur J Cardio-thorac Surg 2000; 17:400-406.
11. Pinna Pintor P, Colangelo S, Bobbio S. Evolution of case-mix in heart surgery: from mortalità risk to complication risk. Eur J Cardio-thorac Surg 2003; 23: 595-598.
12. Kurki TS, Häkkinen U, Lauharanta J, Rämö J, Leijala M. Evaluation of the relationship between preoperative risk scores, postoperative and total length of stays and hospital costs in coronary bypass surgery. Eur J Cardio-thorac Surg 2001;20:1183-1187.
13. Pintor PP, Bobbio M, Colangelo S, Veglia F, Marras R, Diena M. Can EusoSCORE predict costs of cardiac surgery? Eur J Cardio-thorac Surg 2003; 23:595-598.
14. Sergeant P. Blackstone EH, Meyns B. Validation and interdependence with patient-variables of the influence of procedural variables on early and late survival after CABG. Eur J Cardio-thorac Surg 1997;12:1-19.

Chapter 8

Summary and conclusions

Samenvatting en conclusies

Summary and conclusions

Chapter 1

During the past years there is a trend towards surgically treating older and sicker patients, who have more complex and preexisting diseases. Prediction of postoperative morbidity of patients scheduled to undergo CABG surgery would facilitate decisions to operate, allocate resources and estimate costs. Furthermore, risk stratification of patients who undergo open-heart surgery makes it feasible to analyze operative results by risk groups and to compare results in similar groups between institutions. The focus of this thesis is to show how a simple database in set-up was growing over the past years and how the stored information, initially used in a more descriptive way, became gradually useful to support patient care in a more scientific way. For that purpose, several questions were formulated:

- Is the profile of our group of patients undergoing isolated myocardial revascularization comparable with other institutions and what is changing through the years (Chapter 2)?
- Because of the increasing number of patients with neurological and nephrological morbidity after CABG, a further analysis of postoperative morbidity was performed (Chapters 3 and 4). The following main questions were addressed:
    - Which of the variables measured pre-, and perioperatively could be considered as risk factors for postoperative neurological and nephrological morbidity?
    - Which of these factors contributed independently to an increased risk?
    - Which of these independent predictors changed over time?
- Are elderly patients undergoing CABG at higher risk now than ten years ago? (Chapter 5).
- Can patients, using our database information, be stratified according to their risk for prolonged stay in the intensive care unit (Chapter 6)?

- Is it meaningful to develop institution-specific scoring systems besides the international used predictive systems, for predicting prolonged hospital and intensive care stay after CABG (Chapter 7)?

Chapter 2

In this chapter our data were used in an observational study. It is a descriptive study of co-morbidity, postoperative morbidity, and mortality, observed in a group of 3834 patients undergoing isolated myocardial revascularization between January 1987 and December 1995 at the St Radboud University Medical Center Nijmegen. The total group was divided into three time cohorts. Group A: 1987–1989 (n = 1292); group B: 1990–1992 (n = 1130); and group C: 1993–1995 (n = 1412). Mean age increased significantly from 60.4±9.0 (S.D.) years in group A to 62.9±9.9 (S.D.) years in group C. Patients with preoperative existing insulin-dependent diabetes, nephrological, pulmonary, and neurological pathology increased significantly. Despite treating older patients with more coexisting diseases, hospital mortality remained stable (around 2.5%). However, there was a significant increase in major postoperative morbidity such as pulmonary, neurological, and nephrological problems.

Furthermore, this study confirmed that mortality and morbidity rates of myocardial revascularization performed during this time cohort at the St Radboud University Medical Center Nijmegen were in concordance with other series. Therefore, this study can also be interpreted as a quality control of performed surgery. It is remarked that this article was used in our discussion with health care providers and government in 1999, concerning the changing patient profile.

Chapter 3

Chapter 3 focused on the increased postoperative neurological morbidity, as was found in our cohort of patients during the time period 1987 until 1995. Postoperative neurological complications were divided into mild neurological complications and major complications. Neurological complications were defined as major if a new cerebrovascular accident and/or transient ischaemic attack occurred, and as mild in case of confusion for more than 12 hours or memory disturbances. Three main questions were addressed: a) which pre- and perioperative variables could be considered as risk factors, b) which of these risk factors contributed independently to an increased risk of postoperative neurological complications, and c) which of these independent predictors changed over time.

We found that the incidence of overall neurological complications increased from 1.4% to 3%. This increase was mainly due to an increase of mild neurological complications. Age > 75 years, hypertension, peripheral vascular atherosclerosis, preexisting neurological pathology, emergency operation, aorta-pathology, and perioperative myocardial infarction were identified as predictors for neurological complications. The following variables were identified as independent risk factors for *overall* neurological complications: peripheral vascular atherosclerosis, preexisting neurological pathology, aorta-pathology, perioperative myocardial infarction, and the time cohort 1993-1995. Independent risk factors for *mild* neurological problems were perioperative myocardial infarction and the time cohort 1993-1995. Independent risk factors for *major* neurological complications were: preexisting neurological pathology, aorta-pathology, and perioperative myocardial infarction. Furthermore, only the prevalence of preexisting neurological pathology was clearly increased in the time cohort 1993-1995.

Chapter 4

This chapter focused on the significant increased postoperative nephrological morbidity between 1987 and 1995. The same questions as in the previous chapter were addressed. Postoperative nephrological morbidity was defined as renal dysfunction (creatinine $\geq$ 150 μmol/l) and/or requiring dialysis. The incidence of post-operative nephrological complications increased from 1.2% to 4%. The increase in the overall incidence was the result of an increase in the number of patients with postoperative renal dysfunction. The number of patients requiring postoperative dialysis remained stable. The variables age, diabetes, hypertension, preexisting renal disease, perfusion time > 100 minutes, aortic cross-clamp time > 60 minutes, emergency operation, and perioperative myocardial infarction were identified as risk factors for postoperative nephrological complications in the univariate analysis. Diabetes, hypertension, preexisting renal disease, perfusion time > 100 min, perioperative myocardial infarction, and the time cohorts 1990-1992 and 1993-1995 were identified as independent risk factors for renal dysfunction. The variables age, preexisting renal disease, and perioperative myocardial infarction were independent risk factors for those needing dialysis.

Chapter 5

In this study, we investigated whether elderly patients who were operated in 1995 and 1996, were at higher risk than approximately ten years before. In chapter 2, it was documented that the mean age and number of elderly patients undergoing a myocardial revascularization increased through the years. The preoperative morbidity of the whole patient group undergoing CABG increased also from 1987 until 1995. In this study, it was questioned whether the average elderly patient operated during the more recent years was at higher-risk, compared with patients operated in the beginning of our study. An analysis was performed of the outcome changes of 570 elderly patients, aged between 70 and 77 years, undergoing CABG between 1987 and 1996. Risk factors for postoperative morbidity and mortality in this particular group of patients were investigated. The patient group was divided into three time cohorts with comparable age distribution.

Over the studied time cohorts, the percentage of patients aged between 70 and 77 years increased from 12 to 23%. We found that preexisting neurological pathology and elective operations increased significantly, whereas emergency operations decreased. Furthermore, the use of arterial grafts increased significantly. Mortality decreased significantly in this patient population from 7.1% to 1.4%. The performance of an emergency operation was the only independent risk factor for mortality. Analyzing separately the group of patients who underwent an elective operation, there was a significant increase of patients with preexisting neurological pathology and diabetes, but no change in morbidity and mortality.

This study showed that an increasing number of elderly patients are undergoing CABG. It was suggested that patients aged between 70 and 77 years old, who were operated in more recent years, had a higher preoperative risk. Nevertheless, the mortality rate remained stable in the group of elderly patients who underwent an elective operation.

Chapter 6

An increased postoperative morbidity is a reason for obstruction of the patient flow and probably related to a longer postoperative stay in the intensive care unit (ICU) and hospital. In this study, data of 888 patients undergoing CABG were analyzed whether a prolonged stay in the ICU (defined as ≥ 3 days stay) can be predicted preoperatively. The data were not only analyzed, but also used to construct a predictive model for a prolonged stay.

The variables lung disease, absence of sinus rhythm, no-mild valve pathology, reoperation, non-elective operation, and on-pump procedure were identified as independent risk factors for a prolonged stay in the ICU. Patients were classified into low (5%), intermediate (15%), high (30%), and very high-risk groups (40%) for prolonged stay. A predicted probability P ≥ 40% (risk group very high) was used as cut-off point for constructing a prognostic test for prolonged stay (the PICUS score = Prolonged Intensive Care Unit Stay). The specificity of 99% and negative predictive value of 89% of this test were good. However, the sensitivity of only 9% and positive predictive value of 60% were disappointing. This study showed that with our risk model, patients presenting for CABG could be stratified according to their risk for prolonged stay in the ICU. Nevertheless, as the positive predictive value was only 60%, forty percent of the patients with a positive prognostic test will not suffer a prolonged stay in the ICU.

Chapter 7

Analysis of patient outcome has gained increased importance, as institutions, healthcare providers and patients ask for data on risk and prognosis for specific procedures and therapies. In this study we compared the EuroSCORE, as an international developed and used predictive system, with our own institution-specific scoring systems for prolonged hospital stay (CORRAD morbidity score) and intensive care stay (PICUS score). For the evaluation of prolonged hospital stay, 3359 patients undergoing CABG in our hospital between January 1997 and December 2003 were included in the analysis concerning the usefulness of the EuroSCORE versus the CORRAD morbidity score. For a prolonged ICU stay, 1638 patients operated between 2000 and 2003 were included in the analysis concerning the EuroSCORE versus the PICUS score.

We found no significant difference in postoperative hospital stay between the three different risk groups identified by the EuroSCORE. However, a statistically significant difference was found in hospital stay between the low and high-risk groups, as identified by the CORRAD morbidity score. For a prolonged ICU stay, the EuroSCORE as well as the PICUS score identified a high-risk group of patients for prolonged ICU stay. However, the discriminatory power of both scoring systems was low (ROC curve 0.62).

Samenvatting en conclusies

Hoofdstuk 1

Gedurende de afgelopen jaren bestaat er een trend om meer oudere patiënten met een hogere co-morbiditeit te opereren. Deze trend wordt ook waargenomen in de coronair chirurgie. Meer inzicht in de risicofactoren kan mogelijk leiden tot een vermindering van de morbiditeit en mortaliteit bij de patiënt die een CABG moet ondergaan. Dit kan van invloed zijn op het maken van keuzes betreffende wel of niet opereren, de operatieve procedure en benodigde postoperatieve zorg. Hierdoor wordt meer inzicht verkregen in de kwaliteit van de coronair chirurgie en de risicofactoren die een rol kunnen spelen bij het maken van keuzes. Het is mogelijk dat deze kennis van belang kan zijn bij toekomstige ontwikkelingen op het gebied van de coronair chirurgie en behoefte aan postoperatieve zorg. Verder biedt het indelen van patiënten in risicogroepen de mogelijkheid om operatieve resultaten te vergelijken tussen de verschillende risicogroepen en tussen operatieve centra onderling.

In dit proefschrift wordt beschreven hoe een in opzet eenvoudige database verandert in de loop van de tijd. De opgeslagen data-informatie (CORRAD database) werd in opzet meer descriptief gebruikt, maar werd geleidelijk bruikbaar om patiëntenzorg op een meer wetenschappelijke wijze te ondersteunen. Met betrekking tot deze doelstelling werden een aantal vraagstellingen geformuleerd:

- Is onze database registratie een goede weergave van het profiel van de patiënten die een CABG ondergaan. Wat zijn de veranderingen wat betreft risicoprofiel, morbiditeit en mortaliteit gedurende de afgelopen jaren (Hoofdstuk 2)?
- Omdat er een toename is van het aantal patiënten met neurologische en nefrologische complicaties na een CABG, werd een nadere analyse verricht van dit probleem (Hoofdstukken 3 en 4). Hierbij werden de volgende vraagstellingen geformuleerd:

- Welke pre- en peri-operatieve variabelen geven een verhoogd risico op postoperatieve neurologische en nefrologische complicaties?
- Welke van deze variabelen dragen onafhankelijk bij tot een verhoogd risico op deze complicaties?
- Wat zijn de veranderingen van deze onafhankelijke risicofactoren in de loop van de tijd?

- Hebben oudere patiënten die een CABG ondergaan tegenwoordig een hoger risicoprofiel en een hoger risico op postoperatieve morbiditeit en mortaliteit (Hoofdstuk 5)?
- Kunnen patiënten, gebruikmakend van onze database informatie, preoperatief worden gestratificeerd op basis van hun risico op een verlengde opnameduur op de Intensive Care (Hoofdstuk 6)?
- Is het zinvol om ziekenhuis-afhankelijke scoringssystemen te hanteren, naast de international gebruikelijke scoringssystemen, om de kans op een verlengde opnameduur op de Intensive Care of ziekenhuisopname te voorspellen (Hoofdstuk 7)?

Hoofdstuk 2

Dit hoofdstuk betreft een observationele studie van een groot aantal pre-, per- en postoperatieve variabelen, vastgelegd in de CORRAD database, betreffende 3834 patiënten die een CABG operatie ondergingen in de periode tussen januari 1987 en december 1995 in het St. Radboud Universitair Medisch Centrum Nijmegen (UMCN). De groep werd ingedeeld in 3 tijdscohorten: groep A: 1987-1989 (n = 1292), groep B: 1990-1992 (n = 1130), groep C: 1993-1995 (n = 1412). De gemiddelde leeftijd van de patiënten steeg van 60,4 ± 9,0 (S.D.) in groep A naar 62,9 ± 9,9 (S.D.) jaren in groep C (*P* < 0,0005). Tevens was er een significante toename van het aantal patiënten met preoperatief bestaande insuline-afhankelijke diabetes, nefrologische-, long- en neurologische pathologie. Ondanks het feit dat er meer oudere patiënten werden geopereerd in de loop der jaren, waarbij er sprake was van een toegenomen preoperatieve morbiditeit, bleef de postoperatieve mortaliteit gelijk in de loop der tijd (circa 2,5%). Er was echter wel een significante toename van de postoperatieve morbiditeit zoals, long-, neurologische-, en nefrologische complicaties.

Deze studie bevestigde tevens dat de morbiditeit en mortaliteit bij patiënten die een CABG in het UMCN ondergingen, vergelijkbaar was met andere literatuur studies. Dat betekent, dat deze studie beschouwd kan worden als een kwaliteitscontrole voor de verrichte operaties. Opgemerkt wordt nog dat de gegevens die beschreven werden in deze studie, gebruikt werden in de discussie met zorgverzekeraars en de regering in 1999, betreffende het weergeven van het veranderde risicoprofiel van patiënten die een CABG operatie ondergingen in de afgelopen jaren.

Hoofdstuk 3

Doel was een nadere analyse verrichten van de postoperatieve neurologische complicaties na een CABG en welke risicofactoren hierop van invloed waren. Dezelfde groep patiënten als in de eerder genoemde studie, geopereerd gedurende de tijdsperiode 1987 tot en met 1995, werd geanalyseerd. De postoperatieve neurologische complicaties (A) werden onderverdeeld in milde complicaties (B) en ernstige complicaties (C). B werd gedefinieerd als postoperatief verwardheid gedurende een periode van > 12 uren of geheugenstoornissen. C werd gedefinieerd als het optreden van een nieuw CVA of TIA. Drie vragen werden gesteld in deze studie: a) welke pre- en perioperatieve variabelen waren een risicofactor voor het optreden van neurologische complicaties, b) welke van deze risicofactoren waren statistisch onafhankelijk, c) hoe veranderden deze onafhankelijke variabelen in de loop der tijd.

De incidentie van neurologische complicaties (A) nam toe in de loop der tijd van 1,4% tot 3%, dit betrof met name een toename van de milde complicaties. De volgende variabelen waren een risicofactor voor het optreden van neurologische complicaties (A) na een CABG: leeftijd > 75 jaar, hypertensie, atherosclerose, preoperatief bestaande neurologische pathologie, spoedoperatie, aorta-pathologie en het optreden van een perioperatief myocardinfarct. In de multivariate analyse werden alleen de preoperatieve variabelen arteriosclerose, neurologische pathologie, aortapathologie, het tijdscohort 1993-1995 en de peri-operatieve variabele myocardinfarct, geïdentificeerd als onafhankelijke risicofactoren voor het optreden van postoperatieve neurologische complicaties (A). De variabelen perioperatief myocardinfarct en tijdcohort 1993-1995 waren onafhankelijke risicofactoren voor het optreden van *milde* neurologische complicaties (B). De variabelen preoperatief bestaande neurologische pathologie, aortapathologie en peri-operatief myocardinfarct waren onafhankelijke risicofactoren voor het optreden van *ernstige* postoperatieve neurologische complicaties (C). Op te merken is dat er in het tijdcohort 1993-1995 sprake was van een duidelijk toegenomen prevalentie preoperatief bestaande neurologische pathologie (11,6%).

Hoofdstuk 4

Doel van deze studie was een analyse van de postoperatieve nefrologische morbiditeit na een CABG. De analyse betrof dezelfde groep patiënten (1987-1995) als genoemd in de 2 eerdere studies. Postoperatief optredende nefrologische complicaties werden onderverdeeld in gestoorde nierfunctie (creatinine ≥ 150 umol/l) en dialyse behoefte. Over de 3 tijdscohorten nam de incidentie van nefrologische complicaties toe van 1,2% naar 4%. Deze toename betrof een toename van patiënten met gestoorde nierfunctie, de dialyse behoefte nam niet toe in de loop der tijd. De volgende variabelen waren significant voor het optreden van nefrologische complicaties in de univariate analyse: leeftijd, diabetes, hypertensie, vooraf bestaande nefrologische pathologie, perfusietijd > 100 minuten, aorta-klemtijd > 60 minuten, spoedoperatie en perioperatief optreden myocardinfarct. In de multivariate analyse waren diabetes, hypertensie, vooraf bestaande nefrologische pathologie, perfusietijd > 100 minuten, perioperatief myocardinfarct en de tijdscohorten 1990-1992 en 1993-1995 onafhankelijke risicofactoren voor postoperatief gestoorde nierfunctie. De variabelen leeftijd, vooraf bestaande nefrologische pathologie en perioperatief myocardinfarct waren onafhankelijke risicofactoren voor postoperatieve dialyse behoefte.

Hoofdstuk 5

In hoofdstuk 2 werd beschreven dat de gemiddelde leeftijd en het aantal oudere patiënten die een CABG ondergingen toenam in de afgelopen jaren. Ook werd gevonden dat de preoperatief bestaande co-morbiditeit van de patiënten die een CABG ondergingen gedurende de tijdcohort 1987 tot en met 1995 toenam in de loop van de tijd. Men kan zich afvragen of de oudere patiënt tegenwoordig ook een hoger operatierisico heeft. De huidige studie betrof een analyse van 570 oudere patiënten (leeftijd 70-77 jaar) die een CABG ondergingen gedurende de tijdcohorten 1987-1988, 1990-1991 en 1995-1996. Deze cohorten werden iets anders gekozen dan in de vorige 3 studies om een gelijke leeftijdsverdeling per cohort na te streven. Het percentage oudere patiënten in deze leeftijdscategorie nam toe van 12% tot 23% in de loop van de tijd. Over de 3 cohorten nam het aantal patiënten met preoperatief bestaande neurologische morbiditeit en het aantal electieve ingrepen significant toe. Tevens was er een toename van het gebruik van arteriële grafts. De mortaliteit van de geopereerde patiënten nam af in de loop van de tijd van 7,1% naar 1,4%. Het verrichten van een spoedoperatie was de enige onafhankelijke risicofactor voor mortaliteit. Omdat het aantal spoedoperaties afnam in de loop der tijd, werd de groep patiënten die een electieve ingreep ondergingen apart geanalyseerd. In deze laatste groep patiënten was er een significante toename van het aantal patiënten met vooraf bestaande neurologische pathologie en diabetes. Desondanks was er in deze specifieke groep patiënten geen significante toename van postoperatieve mortaliteit of morbiditeit.

Hoofdstuk 6

Gedurende de laatste jaren is er een toename van oudere patiënten waarbij een CABG verricht wordt met een hoger percentage co-morbiditeit. Alhoewel de mortaliteit na CABG niet leek toe te nemen gedurende de laatste jaren (periode 1987- 1995), nam de de postoperatieve morbiditeit wel toe (Hoofdstuk 2). Een toegenomen postoperatieve morbiditeit verhindert de doorstroming van patiënten en is waarschijnlijk geassocieerd met een langduriger opname op de intensive care (IC), en daarmee met totaal hogere kosten. In deze studie werd onderzocht welke risicofactoren geassocieerd zijn met een verlengde opname op de IC ≥ 3 dagen. Er werd een analyse verricht van 888 patiënten die een geïsoleerde CABG procedure ondergingen van januari 2000 tot en met december 2001.

Significante risicofactoren voor verlengde opname ≥ 3 dagen op de IC waren; aanwezigheid longziekte, afwezig sinusritme, reoperatie en niet-electieve ingreep. De aanwezigheid van mild kleplijden (versus afwezigheid mild kleplijden) en off-pomp procedure waren onafhankelijke risicofactoren juist geassocieerd met een lager risico op verlengde opname op de IC. Op basis van deze risicofactoren kon voor iedere patiënt een prognostische *S* score en waarschijnlijkheid *P* worden berekend voor verlengde opname op de IC (PICUS score = Prolonged Intensive Care Unit Stay). Op basis hiervan werden de patiënten onderverdeeld in een lage (5%), medium (15%), hoogrisico (30%) en extreem-hoog risico groep (40%) voor verlengde opname. De geobserveerde verlengde IC opname kwam goed overeen met de voorspelde IC opname op basis van deze risicofactoren. Een voorspelde verlengde opname van ≥ 40% werd gebruikt als cut-off voor de prognostische test. De specificiteit (99%) en negatief voorspellende waarde (89%) van deze test was goed. Echter, de sensitiviteit van deze test was slechts 9% en de positief voorspellende waarde was 60%. Dat betekent dat een patiënt met afwezigheid van alle risicofactoren een risico heeft van 11% op een verlengde opname op de IC. Echter indien alle risicofactoren wel aanwezig zijn, heeft de patiënt een risico van 60% op verlengde opname. Alhoewel dit risicomodel (prognostische test) niet de uitkomst voor de individuele patiënt kan voorspellen, geeft dit model wel meer inzicht in welke variabelen een verhoogd risico geven op een verlengde IC opname.

Hoofdstuk 7

Het analyseren van pre, peri- en postoperatieve gegevens wordt steeds belangrijker, aangezien men meer inzicht wil krijgen omtrent de risico's en prognose van verschillende behandelingen, onder andere CABG operaties. Gegevens omtrent de uitkomst van coronair chirurgie zijn interessant voor de zorgverzekeraars en patiënten en bieden tevens de mogelijkheid om resultaten van centra onderling te kunnen vergelijken. In de huidige studie werd de EuroSCORE, een internationaal gebruikt risicomodel, vergeleken met de CORRADscore, een risicomodel dat ontwikkeld werd in ons eigen centrum, wat betreft de kans op een verlengde postoperatieve ziekenhuis opname. Voor de risico-inschatting op een verlengde IC opname werd de EuroSCORE vergeleken met de PICUSscore, zoals beschreven werd in het vorige hoofdstuk. Voor de evaluatie van de EuroSCORE versus de CORRADscore werden 3359 patiënten geincludeerd die tussen 1997 en 2003 een CABG ondergingen. Voor de evaluatie van de EuroSCORE versus de PICUSscore werden 1638 patiënten geincludeerd die tussen 2000 en 2003 geopereerd werden. Er konden minder patiënten in dit 2^{e} deel van de studie geincludeerd worden, omdat de variabele IC opnameduur pas sedert 2000 in de CORRADdatabase werd geregistreerd.

Er werd geen significant verschil gevonden wat betreft de duur van de ziekenhuisopname, tussen de 3 verschillende risicogroepen die door de EuroSCORE werden geïdentificeerd. Daarentegen werd er wel een significant verschil gevonden wat betreft de duur van de ziekenhuisopname tussen de laagrisico groep (6,9 dagen) en de hoogrisico groep (11,2 dagen) met de CORRAD-morbiditeit score. Zowel met de EuroSCORE als met de PICUSscore kon een hoogrisico groep geïdentificeerd worden wat betreft verlengde opname op de IC $\geq$ 3 dagen. Het onderscheidend vermogen van beide testen om patiënten te onderscheiden die wel of geen verlengde opname duur op de IC hadden, was echter gering (ROC curve 0.62).

Publicaties

1. Noyez L, Van der Werf T, *Janssen DPB*, Klinkenberg TJ, Kaan GL, Van Asten WNJC, Lacquet LK. Early results with bilateral internal mammary artery grafting in coronary reoperations. Am J Cardiol 1992;70:1113-1136.

2. *Janssen DPB*, Van de Kaa CA, Noyez L, Van Haelst UJGM, Lacquet LK. A solitary metastasis in the heart from Ewing's sarcoma. Eur J Cardio-thorac Surg 1994;8:51-53.

3. Noyez, L, Van der Werf T, Klinkenberg TJ, *Janssen DPB*, Kaan GL, Lacquet LK. Experience and early results of second reoperations for coronary artery disease. Should patent vein grafts be replaced during operation ? J Thorac Cardiovasc Surg 1994;107:684-689.

4. *Janssen DPB*, Schilte PPM, De Graaff CS, Van Dijk HA. Bronchopulmonary sequestration associated with an aneurysm of the aberrant artery. Ann Thorac Surg 1995;60:193-194.

5. *Janssen DPB*, Snijders AET, Zegers H, Noyez L. De Intra Aortale Ballonpomp. De verfijning van een techniek en de complicaties ervan. Cordiaal 1996;4:23-26.

6. Noyez L, Van Eck FM, *Janssen DPB*, Skotnicki SH, Lacquet LK. Myocardial revascularisation in octogenarians: evaluation by the Barthel index. Cardiologie1997;4:378-381.

7. Noyez L, *Janssen DPB*, Van Druten JAM, Skotnicki SH, Lacquet LK. Coronary bypass surgery: what is changing ? Analysis of 3834 patients undergoing primary isolated myocardial revascularization. Eur J Cardiothorac Surg 1998;13:365-369.

8. Noyez L, *Janssen DPB*, Van Druten JAM, Skotnicki SH, Lacquet LK. Wat brengt de toekomst? Analyse van 3834 patiënten die een primaire geïsoleerde myocard revascularisatie ondergingen. Cardiologie 1998;6:375-379.

9. *Janssen DPB*, Noyez L, Van Druten JAM, Skotnicki SH, Lacquet LK. Predictors of neurological morbidity after coronary artery bypass surgery. Eur J Cardiothorac Surg 1999;15:166-172.

10. Noyez L, Onundu JW*, Janssen DPB,* Skotnicki SH, Lacquet LK. Myocardial revascularization in patients ≤ 45 years old: evaluation of cardial and functional capacity, and return to work. Cardiovasc Surg 1999;7:128-133.

11. *Janssen DPB*, Noyez L, Skotnicki SH, Lacquet LK. Coronary artery bypass grafting in elderly patients: analysis of the outcome changes in patients aged between 70 and 77 years. Cardiologie 1999;6:297-302.

12. *Janssen DPB*, Noyez L, Van Druten JAM, Skotnicki SH, Lacquet LK. Predictors of nephrological morbidity after coronary artery bypass surgery. Cardiovasc Surgery 2002;10:222-227.

13. *Janssen DPB*, Noyez L, Wouters C, Brouwer RMHJ. Preoperative prediction of prolonged stay in the intensive care unit for coronary bypass surgery. Eur J Cardiothorac Surg 2004;25:203-207.

14. Van der Wal RAB, Noyez L, *Janssen DPB*, Wouters CW, Brouwer RMHJ. Quality of life and survival in cardiac patients with a prolonged intensive care unit length of stay. Neth J Cti Care 2004;8:123-125.

15. Noyez L, *Janssen DPB*, Wouters CW, Brouwer RMHJ. The EuroSCORE as predictor for prolonged hospital and intensive care stay after cardiac surgery ? Neth Heart J 2005;13:170-174.

Dankwoord

Het tot stand komen van dit proefschrift is mede mogelijk gemaakt door de ondersteuning van vele anderen.

Dr. Luc Noyez, co-promotor, oprichter en stuwende kracht achter de CORRAD databank, wil ik in het bijzonder bedanken. Zijn niet aflatende enthousiasme, geloof in de databank en het belang van het registreren van gegevens, heeft vele publicaties voortgebracht en onder andere tot dit proefschrift geleid. Met plezier denk ik nog terug aan de vele ochtenden die om 7.00 uur begonnen met een kop koffie na een lange autorit, een voorbespreking van het ochtend rapport, het doornemen van de dag en waar een basis werd gelegd voor dit proefschrift.

Daarnaast wil ik de professoren L.K. Lacquet en S.H. Skotnicki, mijn leermeesters in de cardiothoracale chirurgie bedanken voor de goede leerschool. Professor René Brouwer, die de taak als promotor op zich nam. De professoren Dr. F.W.A. Verheugt, Dr. J.G. van der Hoeven, Dr. G.J. van der Wilt, Dr. G.J. Scheffer en Dr. B. Mochtar voor het beoordelen van het manuscript. Verder Dr. Hans van Druten, maar ook Stijn Wouters voor de statistische analyses.

Tevens wil ik mijn collegae Rien Huybregts, hoofd van de afdeling cardiothoracale chirurgie in het VU Medisch Centrum, Evert Jansen, Stefan Spiegelenberg en Alexander Vonk bedanken voor de hechte samenwerking en de gelegenheid om dit proefschrift te voltooien. Verder wil ik collegae Stefan Spiegelenberg en John Bolraap bedanken voor hun optreden als paranymph.

Ook wil ik nadrukkelijk mijn moeder bedanken voor de steun en mogelijkheden die zij mij altijd geboden heeft. In mijn jeugd de gelegenheid gaf om dagenlang te sporten en mij daarnaast nog duidelijk wist te maken hoe belangrijk het is om een goede opleiding te genieten en door te zetten. En ook nu nog de liefde die zij besteedt aan onze dochter Lisa. Als laatste, maar meest belangrijke in mijn leven wil ik mijn vrouw Katja Gaarenstroom bedanken, zonder wie ik dit niet allemaal zou kunnen.

Curriculum vitae

Douglas Janssen werd geboren op 7 augustus 1960 te Amsterdam. In 1980 behaalde hij het Atheneum B diploma aan het Nobelweg Lyceum te Amsterdam. Hierna werd aangevangen met studie lichamelijke opvoeding aan de Vrije Universiteit te Amsterdam in verband met uitloting voor de studie geneeskunde. In 1981 kon toch worden aangevangen met de studie geneeskunde aan de Vrije Universiteit te Amsterdam. Gedurende het laatste kwartaal van 1986 werkte hij als vakantie assistent op de afdeling interne geneeskunde van het Onze Lieve Vrouwe Gasthuis te Amsterdam. In 1988 werd het artsexamen behaald aan de Vrije Universiteit van Amsterdam.

Hierna werkte hij als arts in militaire dienst gedurende anderhalf jaar op de afdeling anesthesiologie van het St. Radboud Universitair Medisch Centrum Nijmegen (UMCN). Van 1990 tot 1991 was hij werkzaam als arts-assistent op de afdeling intensieve zorg van het St. Radboud UMCN, waarna hij gedurende twee jaren een assistentschap volgde op de afdeling cardiothoracale chirurgie van dit ziekenhuis. In oktober 1993 werd aangevangen met de opleiding voor het specialisme cardiothoracale chirurgie. De eerste twee jaren van zijn specialistische opleiding werden doorlopen op de afdeling chirurgie in het Medisch Centrum Alkmaar (opleider: Dr. B. Beijnen), gevolgd door vier jaren op de afdeling cardiothoracale chirurgie in het St. Radboud UMCN (opleiders: Prof. Dr. L.K. Lacquet en Prof. Dr. S.H. Skotnicki). Hier werd een aanvang gemaakt met het onderzoek dat tot dit proefschrift heeft geleid. In oktober 1999 volgde zijn inschrijving als cardiothoracaal chirurg in het specialistenregister, waarna hij nog gedurende enige tijd werkzaam was als specialist in het St. Radboud UMCN. In 2001 was hij gedurende 2 maanden werkzaam als waarnemend cardiothoracaal chirurg in het Ignatius Ziekenhuis te Breda. Sedert april 2001 is hij werkzaam als stafarts op de afdeling cardiothoracale chirurgie van het Universitair Medisch Centrum VU te Amsterdam. Douglas is getrouwd met Katja Gaarenstroom en samen hebben zij een dochter Lisa.

Stellingen

behorende bij het proefschrift

The development of a CABG database, a never ending story

A risk analysis of morbidity and mortality in CABG surgery

Douglas P. B. Janssen

I.

Dataregistratie is een cyclisch proces dat start bij patiëntenzorg, en via registreren en evalueren opnieuw eindigt bij patiëntenzorg.

II.

De waarde van kleinere publicaties ligt soms meer in de evaluatie van de data dan in de wetenschappelijke waarde.

III.

In de snel veranderende medische wereld zijn databanken die niet regelmatig worden gereorganiseerd, snel verouderd en waardeloos.

IV.

Georganiseerde follow-up na hartchirurgie is een noodzaak en een verplichting van de hartchirurg.

V.

Omdat steeds oudere en hoger risicopatiënten voor een myocardrevascularisatie worden aangeboden, is onderzoek naar de kwaliteit van leven een noodzaak.

VI.

“Als we niets doen gaat patiënt dood” is geen indicatie voor een hartoperatie.

(naar analogie van F.M. van Eck, proefschrift 18 februari 2004)

VII.

Het bevolkingsonderzoek maakt deel uit van het proces van toenemende medicalisering van de westerse samenleving en is gebaseerd op de gekoesterde illusie van de beheersbaarheid van het menselijk bestaan.

(Medisch Contact 2002;57:1014)

VIII.

De overeenkomst tussen hartchirurgie en stroke-play is dat elke steek c.q. slag meetelt voor het eindresultaat.

6 november 2006