Systolic blood pressure and (cardiac) mortality over 15 years after venous coronary bypass surgery

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Objective The aim of the present study was to determine the influence of pre-operative systolic blood pressure and systolic blood pressure 1 and 5 years after venous coronary bypass surgery on subsequent cardiac and non-cardiac mortality.

Design A prospective 15 years follow-up study.

Patients A series of 446 consecutive coronary bypass surgery patients, operated on between April 1976 and April 1977. According to their systolic blood pressure, patients were divided into five groups.

Main outcome measures Systolic blood pressure 5 years after surgery, but not pre-operative systolic blood pressure, was an independent predictor of cardiac mortality.

Results Multivariate Cox proportional hazards analysis revealed that pre-operative systolic blood pressure was not associated with cardiac mortality, while higher systolic blood pressure 1 year after surgery showed a trend towards increased cardiac mortality. Systolic blood pressure 5 years after surgery appeared to be a strong independent predictor of cardiac mortality during the subsequent follow-up period. Patients with a systolic blood pressure of 130-139 mmHg had the lowest risk. Compared to this group, the cardiac mortality risk in patients with a systolic blood pressure 5 years after surgery of 140-149 mmHg, 150-159 mmHg and ≥ 160 mmHg, was 2.3 (1.2 to 4.6), 3.4 (1.6 to 7.1) and 3.1 (1.4 to 6.5) times higher. Systolic blood pressure < 130 mmHg 5 years after surgery was also associated with a 2.3 times (1.1 to 4.7) times increased risk for cardiac mortality, compared to patients with a systolic blood pressure of 130-139 mmHg.

Conclusions These findings underline the importance of systolic blood pressure control in the initial years after coronary bypass surgery.

Key Words: Blood pressure, coronary bypass surgery.

Introduction

Although both systolic and diastolic blood pressure have been associated with cardiovascular mortality, systolic blood pressure is more strongly related to mortality from coronary heart disease than diastolic blood pressure[1]. Stamler et al.[3] found that for middle-aged and older persons, higher systolic blood pressure results in greater cardiovascular risk, at every diastolic blood pressure level. Similar effects were seen by Rutan et al.[3] who concluded that the level of systolic blood pressure appeared to be the major determinant of all-cause and coronary heart disease mortality, at any level of diastolic blood pressure. Accordingly, intervention studies showed that treatment of hypertension can reduce the risk of cardiovascular events in hypertensive patients[4-6]. Unfortunately, the cut-off points used for defining hypertension did not reflect a clear distinction between hypertension and normotension, but were merely used for their operational suitability[7]. Moreover, it has been suggested that an excessive lowering of blood pressure might affect organ perfusion, which can paradoxically increase cardiovascular mortality[8].

In patients who undergo coronary bypass surgery, pre-operative hypertension has been associated with long-term mortality after surgery[8,10]. However, the predictive value of blood pressure after coronary bypass surgery on long-term mortality is unknown. The aim of this study was to determine the independent influence of systolic blood pressure pre-operatively, and the influence of systolic blood pressure 1 and 5 years after surgery, on long-term mortality after venous coronary bypass surgery. The study population consisted of 446 consecutive
Follow-up and data collection

Several follow-up methods were used simultaneously in order for information to be as complete as possible. All patients were followed using the anniversary method at our outpatient clinic and/or the outpatient clinic of the referring cardiologists. All patients except one, who went abroad and was lost to follow-up 7 years after surgery, were traced at the common closing data of 1 April 1992.

Blood pressure measurements

Systolic blood pressure was measured at hospital admission before surgery, and 1 and 5 years after surgery. Measurements were performed by the examining physician, using a mercury sphygmomanometer. Patients were measured in the supine position. The mean of several recordings was taken as the final systolic blood pressure. Decisions about treatment for high blood pressure were made by the referring cardiologist.

The patients were divided into five groups by means of group size, but mainly by mortality risk:
Group I: systolic blood pressure <130 mmHg; Group II: 130–139 mmHg; Group III: 140–149; Group IV: 150–159; Group V: ≥160 mmHg. Since only eight patients had a pre-operative systolic blood pressure of ≥160 mmHg, Groups IV and V were combined for the pre-operative analysis.

**Statistical analysis**

Clinical end-points were cardiac mortality and non-cardiac mortality. To establish the influence of both pre-and post-operative systolic blood pressure on cardiac and non-cardiac mortality, we used three prognostic models. For the first model, systolic blood pressure was measured pre-operatively, and patients were followed from surgery to 15 years thereafter. For the second model, systolic blood pressure was measured 1 year after surgery, and patients were followed from one to 15 years after surgery. For the third model, systolic blood pressure was measured 5 years after surgery, and patients were followed from 5 to 15 years after surgery.

To identify prognostic covariates that might have 'explained' a difference in survival time between different systolic blood pressure groups, we estimated survival curves by the method described by Kaplan and Meier\(^\text{[13]}\) from the following variables: age, sex, obesity (body-mass index: weight/height\(^2\)), diabetes mellitus, elevated levels of serum cholesterol and triglycerides, smoking, history of heart failure, history of hypertension, use of anticoagulants, persantin, aspirin, beta-blockers, diuretics, long- and short-acting nitrates, the use of low-salt diet, pre-operative angina pectoris, family history of coronary artery disease, number of vessels diseased, history of myocardial infarction, operation indication, left ventricular function, the presence of collateral arteries, left main coronary artery disease and proximal left anterior descending artery disease, completeness of revascularization, number of distal anastomoses.

The use of anticoagulants, persantin, aspirin, beta-blockers, diuretics, long- and short-acting nitrates, and the use of low-salt diet were recorded pre-operatively and 1 year after surgery. During analysis, the influence of blood pressure 1 and 5 years after surgery was adjusted for medication and low-salt diet 1 year after surgery. The following risk factors were measured 1 and 5 years after surgery: obesity, diabetes mellitus, serum cholesterol and triglycerides, and smoking. During analysis, the influence of blood pressure at 1 and 5 years after surgery was adjusted for these risk factors 1 and 5 years after surgery.

Differences in survival times between groups were calculated using the log-rank and the Wilcoxon test. All variables with a significance level of \(P<0.10\) in at least one of these univariate tests, were introduced in a multivariate model proposed by Cox\(^\text{[12]}\). Age and gender were always included. The inclusion level of the Cox model was \(P<0.10\). Systolic blood pressure, divided into five different groups, was finally added to the model. We checked the assumption of proportional hazards for each predictor variable by estimating the plots of the logarithm of the cumulative hazard. By using this analysis we could predict the independent influence of systolic blood pressure on (cardiac) death in this population. The mortality risk of one group in relation to the other group is reflected by the hazard ratio.

Correlations were performed using the Pearson and Spearman correlation tests where appropriate. A \(P\)-value of <0.05 was considered statistically significant.

**Results**

Follow-up was complete in 99.8% of the patients and averaged 15.4 years for the survivors. Thirteen patients (3%) died within 30 days of surgery. These patients were not included in the analysis. Twenty-seven patients (6%) suffered a peri-operative myocardial infarction. Long-term results of the complete study group (including the in-hospital deaths) have been described elsewhere\(^\text{[13]}\). Characteristic features of the patient group are presented in Table 1.

The mean pre-operative systolic blood pressure was 130 mmHg, and the mean systolic blood pressure 1 and 5 years after surgery was 137 mmHg and 138 mmHg, respectively. The increase in blood pressure after coronary bypass surgery is also presented in Table 2. This shows a substantially increased number of patients in the higher blood pressure groups 1 and 5 years after surgery compared to pre-operatively.

**Cardiac mortality (Fig. 1)**

Of the 158 patients who died within 15 years of venous coronary bypass surgery, 96 (61%) were due to cardiac causes. From surgery to 7 years after, cardiac mortality remained low, while from 7 to 15 years cardiac mortality increased significantly. Pre-operative systolic blood pressure did not appear to be a good predictor of cardiac death during the entire follow-up period. Both in univariate and multivariate analysis, we found no
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Figure 1 Schematic presentation of multivariate hazard ratios (95% confidence intervals) of cardiac mortality in patients in different systolic blood pressure groups, compared to patients with a systolic blood pressure of 130–139 mmHg. Blood pressure was measured at baseline, 1 year and 5 years after surgery, and patients were followed from 0–15 years, 1–15 years and 5–15 years after venous coronary bypass surgery, respectively.

The only statistically significant predictor of non-cardiac mortality during the 15 years follow-up period was increased age (Table 3).

Correlation of systolic blood pressure with other risk factors

The above results were adjusted for a large number of other factors which could have biased the outcome. Factors which were significantly correlated with both pre-operative systolic blood pressure and systolic blood pressure 1 and 5 years after surgery are age (r≈0.21, P=0.0001), female sex (r≈0.10, P<0.05) and diabetes mellitus (r≈0.11, P<0.05). It is important to realize that these factors are also intercorrelated. In our study population, mean female age was 57-1 years, compared to a mean male age of 52-0 years (P<0.0001, t-test). Five years after surgery, patients with diabetes mellitus were 55-8 years, compared to 52-4 years in the non-diabetic patients (P=0.01, t-test), and 58-8% of the female patients were diabetic, compared to only 8-3% of the males (P<0.0001, chi-square test). To separately analyse the predictive value of these three confounders, we entered age, diabetes mellitus and sex in a multiple regression model. Of these three highly inter correlated factors, age was the best predictor of systolic blood pressure at 5 years (P=0.0001), followed by diabetes...
Table 3 Other independent risk factors (besides systolic blood pressure) of cardiac and all-cause mortality after coronary bypass surgery

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Follow-up 0 to 15 years after surgery</th>
<th>Follow-up 1 to 15 years after surgery</th>
<th>Follow-up 5-15 years after surgery</th>
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<tbody>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>P</td>
<td>Hazard ratio (95% CI)</td>
<td>P</td>
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<tr>
<td>Cardiac mortality</td>
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<tr>
<td>Left ventricular dysfunction (CASS wall motion score &gt; 0)</td>
<td>3.14 (1.95 to 5.05) &lt; 0.0001</td>
<td>3.22 (1.97 to 5.26) 0.026</td>
<td>3.07 (1.97 to 5.05) &lt; 0.0001</td>
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<td>Three vessel disease compared to one vessel disease</td>
<td>2.47 (1.11 to 5.4) ns</td>
<td>1.63 (1.05 to 2.54) 0.03</td>
<td>0.97 (0.54 to 1.77) ns</td>
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<td>Use of beta-blocker one year after surgery</td>
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<tr>
<td>Cardiac mortality</td>
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<tr>
<td>Non-cardiac mortality</td>
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<tr>
<td>Age (increase per year)</td>
<td>1.08 (1.04 to 1.12) &lt; 0.0001</td>
<td>1.09 (1.05 to 1.13) &lt; 0.0001</td>
<td>1.09 (1.05 to 1.13) &lt; 0.0001</td>
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CASS = Coronary Artery Surgery Study; CI = Confidence Interval; na = not applicable; ns = not statistically significant.
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mellitus (P=0.02); it appeared that female sex was no independent predictor of systolic blood pressure 5 years after surgery (P=0.5).

Discussion

Several studies have been designed to define factors influencing late survival after coronary bypass surgery. Cosgrove et al.\(^\text{[10]}\) reported that pre-operative hypertension was an independent positive predictor of mortality in 1000 patients after primary coronary artery bypass surgery, although these findings were not supported by other long-term follow-up studies\(^\text{[14–16]}\). Smith et al.\(^\text{[9]}\) concluded that a history of hypertension was associated with an elevated risk of dying both early and late after a first coronary bypass operation in 2967 patients. We found that, in particular, systolic blood pressure 5 years after surgery was an important predictor of cardiac mortality during the subsequent 10 years of follow-up, while neither pre-operative systolic blood pressure nor a history of hypertension were significant predictors. Our findings might be explained by the fact that the deleterious effects of high blood pressure on the venous bypass grafts started from the time of surgery. Blood pressure before and after surgery differ considerably, partly due to differences in pre- and post-operative medication. Therefore, blood pressure 1 and 5 years after surgery probably provide a much better reflection of the blood pressure to which the venous grafts are exposed. It should be noted that it was the treated systolic blood pressure that had this important predictive value for cardiac mortality. Additionally, the results were adjusted for the use of blood pressure lowering medication and the use of a low-salt diet.

Comparable results were found by Cruickshank et al.\(^\text{[17]}\), although they described a group of newly diagnosed hypertensive patients with or without previous cardiovascular events. They concluded that initial blood pressure (both systolic and diastolic) was a poor predictor of mortality from myocardial infarction after 10 years, whereas treated systolic blood pressure was a strong predictor.

Another interesting finding of this study was that a systolic blood pressure <130 mmHg 5 years after surgery was also associated with increased cardiac mortality. Although several studies have shown a relationship between low blood pressure and increased mortality, this J-shaped relationship still remains controversial. In the EWPHE trial, hypertensive patients were double blind, randomly allocated to treatment or placebo\(^\text{[18]}\). In the actively treated group, there was a significant increase in mortality in patients with a systolic blood pressure <140 mmHg. The same trends were found for cardiovascular mortality. Samuelsson et al.\(^\text{[19]}\) found an increase in the incidence of coronary heart disease in patients with a treated systolic blood pressure <150 mmHg. In a follow-up study of 10 732 patients screened for the HEP trial, Coope and colleagues\(^\text{[20,21]}\) reported that death from stroke was increased in subjects with a systolic blood pressure below 120 mmHg, and cardiovascular mortality was increased if systolic blood pressure was below 160 mmHg. It must be taken into consideration, however, that our study population was different from the previously described studies, since they underwent coronary bypass surgery. The patients who had lower systolic blood pressure after surgery may have reflected a patient group with a diminished left ventricular function, which appeared to be one of the main predictors of cardiac mortality after coronary bypass surgery\(^\text{[22]}\). However, we found no correlation between systolic blood pressure, left ventricular function, a history of myocardial infarction, or heart failure.

Factors which did show a statistically significant positive correlation with systolic blood pressure were increasing age, female gender and diabetes mellitus. After adjustment for intercorrelation, only age and...
diabetes mellitus remained statistically significant. In several studies, all three factors have been associated with blood pressure. Obviously, in the present study, the influence of systolic blood pressure on (cardiac) mortality was adjusted for these confounders. Unfortunately, we were not able to adjust for alcohol consumption and social class, although these factors have also been associated with blood pressure. However, social class differences are small in the Netherlands. We also found that the use of beta-blockers 1 year after surgery was a strong predictor of cardiac mortality, clearly representing a group of patients with an early return of complaints.

Non-cardiac mortality comprised about 40% of the total mortality, but showed the same tendency as cardiac mortality. Both for all-cause mortality and for cardiac mortality, systolic blood pressure 5 years after surgery was the best predictor, although the influence on cardiac mortality was larger, reflected by the higher hazard ratios. Moreover, non-cardiac mortality results were not statistically significant. Causes of death were the total mortality, but showed the same tendency as in the Netherlands. We also found that the use of beta-blockers 1 year after surgery was a strong predictor of cardiac mortality, clearly representing a group of patients with an early return of complaints.

In conclusion, this prospective, multivariate analysis, in a consecutive patient group operated on during one year, showed that (treated) systolic blood pressure 5 years after surgery was an important predictor of cardiac mortality, whereas pre-operative systolic blood pressure was not. These findings underline the importance of monitoring and controlling blood pressure in patients after coronary bypass surgery.

References


