Health-related quality of life following off-pump versus on-pump coronary artery bypass grafting in elderly moderate to high-risk patients: a randomized trial

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Abstract

Objective: Previous trials comparing coronary artery bypass grafting (CABG) with or without extracorporeal circulation have mainly enrolled selected patients at younger age and low risk. Patient-reported health-related quality of life has not been significantly different. We compared health-related quality of life in elderly moderate to high-risk patients randomized to either off-pump or on-pump surgery.

Methods: The study is a sub-study of the randomized Best Bypass Surgery Trial that compares off-pump to on-pump treatment, with respect to peri- and postoperative mortality and morbidity in patients with a moderate to high-predicted preoperative risk. After randomization and before heart surgery, 120 consecutive patients were asked to fill in the Medical Outcomes Study Short Form 36 (SF-36) and Major Depression Inventory (MDI) diagnostic scale for self-report of health-related quality of life. Three months after surgery, the same questionnaires were mailed to the patients.

Results: The response rate was 96.5%. At baseline, the groups were comparable except for a difference in educational level. Both groups improved in all eight SF-36 domains from baseline to 3 months. No statistical differences were seen between the groups except for changes in mean difference of role limitation due to emotional problems, which was significantly (P = .04) improved in favour of the on-pump group. Depression scores remained unchanged within and between the two surgical groups.

Conclusions: Both on-pump and off-pump patients improved in health-related quality of life scores after CABG surgery. No clinically relevant difference between the groups could be demonstrated.

Keywords: Coronary artery bypass surgery; Off-pump; On-pump; Health-related quality of life; Quality of life; Depression

1. Introduction

Patients aged 70 years or older undergoing coronary artery bypass grafting (CABG) with the use of a heart-lung machine (on-pump) are at a higher risk of mortality and morbidity than younger patients, because they generally have more comorbidities and a decreased reserve capacity of most organ systems, making them more vulnerable to postoperative adverse effects on cardiac, pulmonary, renal and neurocognitive function [1]. Nevertheless, long-term survival and good functional improvement can be achieved in the elderly [2]. The success of cardiac surgery is not solely judged by its effects on mortality but also by its neuropsychological and emotional consequences, and by its influence on health-related quality of life (HRQoL) [2,3]. Changes in cognitive function have been associated with reduced HRQoL 1 year [3] and 5 years after cardiac surgery in terms of lower general health and a less productive working status [4]. A randomized study, using a post-test only design, compared medical treatment to invasive treatment in 113 patients with inducible ischemic heart disease. At an average follow-up of 36 months, more invasively treated patients had concentration difficulties but better HRQoL scores in the physical variables [5].

Depression is found to be an independent risk factor for cardiac events after CABG [6]. Patients suffering from depression before the operation are more often depressed after the surgery [7,8] and seem to have worse physical function and higher co-morbidity than patients with low depression score [9]. However, CABG appears to have a beneficial effect on psychological function and HRQoL for the
majority of patients [10]. Due to the lack of a common
definition and the dependence on subjective perception, it
has been difficult to assess an overall evaluation of HRQoL
among patients undergoing cardiac surgery [11]. Factors such
as increased age, female gender, persistent pain (more than 3
months), and poor quality of sleep have been associated with
reduced HRQoL outcomes [11]. As an alternative to on-pump
surgery, off-pump CABG may improve selected clinical
outcomes other than mortality in low to medium risk
patients, but no significant difference between surgical
groups in health status or HRQoL have been demonstrated in
these patients up to now [12]. Evidence for corresponding
statements is still lacking in elderly moderate to high-risk
patients [1]. We have recently compared cognitive function
in elderly moderate to high-risk patients at 3 months after
off-pump and on-pump surgery, respectively, and found no
significant difference between the groups for cognitive decline (unpublished data). In this study we compare HRQoL
of 120 patients who were randomized either to off-pump
or on-pump CABG surgery. HRQoL was measured by self-
reported information on functional capacity in daily living
including physical, emotional, social, mental, and psycho-
logical dimensions.

2. Materials and methods

2.1. Participants

The study is a sub-study of the randomized Best
Bypass Surgery (BBS) Trial (ClinicalTrials.gov identifier
NCT00120991) that aims to compare off-pump to on-pump
CABG with respect to per- and postoperative mortality and
morbidity, in patients with a moderate to high-predicted
preoperative risk. We screened consecutive patients with
known ischemic three-vessel heart disease who were >54
years of age, had a EuroSCORE more or equal to 5, and
admitted for elective or sub-acute CABG at the Heart Center,
Copenhagen University Hospital. We excluded patients with
previous heart surgery, ejection fraction less than 30%, those
with unstable preoperative condition, i.e., continuous
infusion of inotropics on the day of the operation, and
patients unable to give informed consent. For the present
sub-study, patients were recruited consecutively from the
BBS Trial but with the following additional exclusion criteria:
Mini Mental State Examination score below 24 points, as
a screening test for dementia after randomization and before
inclusion in the study, current severe psychiatric disease,
i.e., depression, psychosis or alcoholism (patients at referral
currently using either antipsychotic or antidepressive
medication, or drinking more than 5 units of alcohol per
day within the last 3 months), neuropsychological testing
within the last year, illiteracy, poor comprehension of Danish,
severe visual or auditory disorder, and unwillingness to return
to follow-up.

2.2. Procedure

The local Ethics Committee approved the study, subject to
journal no. 01-079/02, and all patients provided written
informed consent. The patients were centrally randomized to
one of the two groups by an external press button telephone
voice response system, stratified by the following character-
istics: gender, age (55—65 years; >65 years), diabetes
mellitus and EuroSCORE (5—8; >8). Patients were rando-
mized in a 1:1 ratio to off-pump or on-pump surgery. The
assessors of outcomes and the staff undertaking data analysis
were blinded for allocation.

In the off-pump group, the revascularization procedure
was performed on the beating heart with a stabilization of
the target coronary arteries. When access was needed for
posterior coronary arteries a suction device was used to lift
the heart. In the on-pump group, the revascularization
procedure was performed with the use of a heart-lung
machine in normothermia, with aortic cross clamp and cold
blood cardioplegic arrest. In both groups, the left internal
mammary artery in combination with saphenous vein grafts
were standard graft material. The same surgeons performed
both procedures. Outcome was assessed the day before
bypass surgery or on the day of operation and repeated 3
months after surgery. On both occasions, the patients
took the HRQOL questionnaire: the 36-item Medical Outcomes
Study Short Form (SF-36) and the Major Depression Inventory
(MDI). If a patient was unable to complete the questionaire, the
principal investigator did voice response system, stratified by the following character-
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months after surgery. On both occasions, the patients
took the HRQOL questionnaire: the 36-item Medical Outcomes
Study Short Form (SF-36) and the Major Depression Inventory
(MDI). If a patient was unable to complete the questionaire, the
principal investigator did interview administration. Three months after the operation
the same questionnaires were mailed to the patients.

2.3. Assessment of HRQoL

The SF-36 is a self-administered generic questionnaire,
which is widely used, reliable, and a valid tool that aims to
measure functioning, well-being, and general health status
[12]. SF-36 is one of the most commonly used questionnaires
for evaluating HRQoL in cardiac surgery and found sensitive
to changes within patients undergoing open-heart operation
[13]. Besides, it is available in Danish and previously applied
in a sample of the general population [14]. The age-matched
data are presented in Table 2 for comparison. The instrument
measures eight health domains using eight scales with 2—10
items per scale. It reflects the impact of both cardiac and
noncardiac diseases on: physical functioning, role limitations
due to physical health problems, bodily pain, general health
perceptions, vitality, social functioning, mental health, emotional
problems and mental health. The questions relating to each domain is scored on a scale from 0 to 100. The higher
the score, the higher the level of functioning, i.e., a
score of 100 indicates no impairment of functioning for a
given domain. Furthermore, the eight domains can be
divided into two distinct groupings summarizing a physical
health component and a mental health component. In the
current study, the scoring of data was done according to the
Danish manual to SF-36 [16] and findings are reported using
the eight domains.

The Major Depression Inventory diagnostic scale is a
validated 10-item self-rating list containing the 10 ICD-10
symptoms of depression [17]. It can be used both as an
instrument measuring the severity of depressive states, and
as a screening instrument for the diagnosis of clinical
depression. The instrument is available in Danish and
previously applied in a sample of the general population
[18]. Symptoms are measured on a six-point Likert scale,
indicating whether the symptom has not been present at all (score = 0) to symptom being present all the time (score = 5). Two of the items (8 and 10) are divided into two sub-items (a and b). Only the maximum score for these items were included in the statistical analysis. For this study, we used the MDI as a screening instrument. A mean score for the replied 10 items was calculated in a score range from 0 to 5 with a mean score > 2.5 indicating depression.

2.4. Statistical analysis

All data were analyzed according to randomization on an intention to treat basis. The primary end point was the change in SF-36 score. Differences are presented with 95% confidence intervals (95% CI). The SF-36 and MDI scores are presented with mean and standard deviation (SD) or number and percentage (%). Categorical variables were compared using Pearson’s chi-square test or Fisher’s exact test as appropriate. For continuous data, changes within the groups were analyzed using paired t-test. Groups were compared using unpaired t-test (for normally distributed data) or Mann–Whitney’s rank sum test (for data not normally distributed). A P-value less than .05 were considered statistically significant. No correction for multiple comparisons was applied. All data management and analyzes were performed with Statistical Package for Social Sciences (SPSS) 12.0 software.

3. Results

Between July 2002 and December 2004, 206 consecutive patients who were included for the BBS Trial were evaluated for eligibility. Of these, 56 patients were excluded due to: logistic reasons (35 patients), not meeting inclusion criteria for cognitive testing (13 patients), and refusing to participate (8 patients). As patients were included consecutively, the logistic reasons for the exclusion of 17% can be explained by the absence of a trained surgeon in off-pump technique, the staff collecting data having vacation or day off, or patients not available for baseline information due to inclusion late in the evening or just before operation. Furthermore, 30 of the eligible patients were excluded due to Mini Mental State Examination score of less than 24. Thus, 120 randomized patients were included in the present study. At 30 days, one patient in the off-pump group and three patients in the on-pump group had died. Furthermore, 3 patients in the off-pump group had died beyond 30 days, thus 7 patients (5.8%) were dead by the time of follow-up. Of the remaining 113 patients, response was obtained from 109 (96.5%), i.e., HRQoL could be determined by 54 in the off-pump group and 55 in the on-pump group (Fig. 1). At baseline there were no differences between the groups except for level of education (Table 1).
Mean duration of operation was 159 (±40) min in the off-pump group and 152 (±30) min in the on-pump group. Duration of cardiopulmonary bypass was 60 (±19) min with 36 (±13) min cross-clamp time. The incidence of postoperative atrial fibrillation was 57% (CI: 43.2—69.4) in the off-pump group and 55% (CI: 41.5—68.3) in the on-pump group. At 3 months, one nonfatal stroke was seen in the off-pump group and two nonfatal strokes occurred in the on-pump group.

### 3.1. HRQoL

In both groups there was an improvement in HRQoL at 3 months (Table 2). Except for RE favoring on-pump surgery ($P = .04$), no significant difference was found in the change of SF-36 scores between the two groups (Table 3).

The number of patients with depressive symptoms remained unchanged in both groups from baseline to 3 months (Table 4). No significant difference between the groups was found in the change of depressive symptoms (Tables 5 and 6).

#### Table 2
Changes in health-related quality of life (SF-36 scores) in patients undergoing coronary artery bypass grafting with or without cardiopulmonary bypass (off-pump vs on-pump)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Off-pump</th>
<th>On-pump</th>
<th>National norms $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>3 months</td>
<td>Difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PF</td>
<td>54.9 (27)</td>
<td>68.4 (23)</td>
<td>11.5 (30)$^b$</td>
</tr>
<tr>
<td>RP</td>
<td>21.2 (34)</td>
<td>43.5 (43)</td>
<td>22.3 (41)$^b$</td>
</tr>
<tr>
<td>BP</td>
<td>62.9 (28)</td>
<td>78.3 (21)</td>
<td>15.4 (29)$^b$</td>
</tr>
<tr>
<td>GH</td>
<td>63.0 (18)</td>
<td>62.7 (21)</td>
<td>0.4 (21)</td>
</tr>
<tr>
<td>VT</td>
<td>47.0 (23)</td>
<td>57.5 (26)</td>
<td>10.5 (31)$^b$</td>
</tr>
<tr>
<td>SF</td>
<td>74.8 (28)</td>
<td>88.0 (19)</td>
<td>11.1 (33)$^b$</td>
</tr>
<tr>
<td>RE</td>
<td>44.8 (43)</td>
<td>54.6 (41)</td>
<td>10.8 (57)</td>
</tr>
<tr>
<td>MH</td>
<td>63.0 (19)</td>
<td>75.7 (22)</td>
<td>11.1 (29)$^b$</td>
</tr>
</tbody>
</table>

Change in groups, with age-matched normative scores included for comparison. PF: physical functioning; RP: role limitations due to physical health problems; BP: bodily pain; GH: general health perceptions; VT: vitality; SF: social functioning; RE: role limitations due to emotional problems; MH: mental health. Values are mean (SD).

$^a$ General Danish population aged 75+ years ($n = 229$).

$^b$ Significant difference ($P < .05$) compared with baseline.

#### Table 3
Changes in health-related quality of life (SF-36 scores) in patients undergoing coronary artery bypass grafting with or without cardiopulmonary bypass (off-pump vs on-pump) at 3 months

<table>
<thead>
<tr>
<th>Domain</th>
<th>Off-pump</th>
<th>On-pump</th>
<th>National norms $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>3 months</td>
<td>Difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PF</td>
<td>55.5 (24)</td>
<td>64.4 (25)</td>
<td>8.9 (31)</td>
</tr>
<tr>
<td>RP</td>
<td>15.1 (29)</td>
<td>42.5 (45)</td>
<td>27.4 (26)</td>
</tr>
<tr>
<td>BP</td>
<td>65.0 (26)</td>
<td>75.2 (23)</td>
<td>10.2 (31)$^b$</td>
</tr>
<tr>
<td>GH</td>
<td>64.3 (19)</td>
<td>64.2 (18)</td>
<td>0.1 (24)</td>
</tr>
<tr>
<td>VT</td>
<td>51.5 (25)</td>
<td>54.9 (24)</td>
<td>3.4 (27)</td>
</tr>
<tr>
<td>SF</td>
<td>79.6 (22)</td>
<td>81.1 (26)</td>
<td>1.5 (30)</td>
</tr>
<tr>
<td>RE</td>
<td>36.4 (38)</td>
<td>59.8 (40)</td>
<td>23.4 (51)$^b$</td>
</tr>
<tr>
<td>MH</td>
<td>68.8 (24)</td>
<td>76.7 (22)</td>
<td>7.9 (24)</td>
</tr>
</tbody>
</table>

#### Table 4
Changes in depression (based on MDI questionnaire) in patients undergoing coronary artery bypass grafting with or without cardiopulmonary bypass (off-pump vs on-pump)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Baseline 3 months Difference 95% CI of the difference</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPCAB</td>
<td>1.10 (.90) 1.03 (.87) -.07 (.76)</td>
<td>-.16</td>
<td>.26</td>
</tr>
<tr>
<td>CCAB</td>
<td>1.03 (.81)  .96 (.91) -.07 (.92)</td>
<td>-.37</td>
<td>.14</td>
</tr>
</tbody>
</table>

Change in groups. CI: confidence interval.

#### Table 5
Changes in depression (based on MDI questionnaire) in patients undergoing coronary artery bypass grafting with or without cardiopulmonary bypass (off-pump vs on-pump)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Baseline 3 months Difference 95% CI of the difference</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPCAB</td>
<td>.08</td>
<td>.24</td>
<td>.39</td>
</tr>
<tr>
<td>CCAB</td>
<td>.16</td>
<td>.16</td>
<td>.49</td>
</tr>
</tbody>
</table>

Difference between groups. CI: confidence interval.

#### Table 6
Number of patients with depression (based on MDI questionnaire) before and after coronary artery bypass grafting with or without cardiopulmonary bypass (off-pump vs on-pump)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Baseline 3 months Changes from baseline to 3 months</th>
<th>No — yes</th>
<th>Unchanged</th>
<th>Yes — no</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPCAB</td>
<td>4 (6.9) 4 (7.5) 3 (5.8) 48 (92.3) 1 (1.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCAB</td>
<td>4 (6.9) 4 (7.5) 4 (7.7) 44 (84.6) 4 (7.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values in percentages are shown in parentheses.
4. Discussion

Our objective was to evaluate the effect of off-pump versus on-pump CABG on changes in various aspects of HRQoL in elderly moderate to high-risk patients during the first 3 months after the operation. To our knowledge, this is the first randomized study focusing on that specific topic and, in addition, we assessed depression scores. Generalizations of the findings are further limited by the single-center experience, and should therefore be replicated in larger multi-center trials in order to finally verify whether or not there is an improvement in health-related quality of life among off-pump patients compared to patients undergoing on-pump CABG surgery. This study is characterized by a high degree of internal validity in terms of accounting for patient selection, and a large number of the patients were available for 3 months follow-up, as only 4 out of 113 refused to participate. The study was randomized with a negligible crossover between the groups and the instruments used are based on well-documented valid and reliable questionnaires. The two treatment groups were similar regarding demographic variables at baseline except for education level.

The two treatment groups were similar regarding demographic variables at baseline except for education level which is considered to be incidental (Table 2). We have previously found to be 7% in the off-pump group and 10% in the on-pump group, it was not possible to make any reasonable analysis for this study, examining the impact of cognitive dysfunction on specific domains of SF-36 within and between the groups.

In both groups, there was an improvement in SF-36 scores. Baseline scores were clearly below the values in the background population but after surgery, several domains improved to a level equal to or even better than those of a comparable background population. We expected that the improvement would be greater in the off-pump group but, in contrast, a small but significant difference in one SF-36 domain (RE) (P = .04) was seen at 3 months, favoring treatment with on-pump. It should, however, be taken into account that we did not correct for multiple comparisons, so we must conclude that no difference could be detected. We are aware that limited statistical power may be important but, on the other hand, the differences in the individual scores between the groups are very small and in different directions. The detection of a difference between scores of RE at 54.6 and 59.8 would require approximately 2000 patients if a type 2 error of 20% is accepted. Besides, the variation in scores of HRQoL may not only reflect variation of the individual person, but suggests consideration of the total surgical treatment and care from admission to completed outpatient rehabilitation. The use of extracorporeal circulation is only one element of this course of the disease [19].

Previously published measurements of HRQoL at 1, 3, 6, and 12 months have been reported in four randomized trials mainly including younger patients at lower risk [19–23]. Additionally, one study obtained data from 328 of 401 randomized patients using a post-test only design with a median follow-up at 3 years [24]. Different instruments such as EuroQOL-6, EuroQOL (original version), EuroQOL-5, SF-36, and the 16-item Quality of Life Scale-Norwegian were used, all showing that HRQoL improved in off-pump and on-pump groups over time, but there were no significant differences between the surgical groups regardless of the instruments used or the design of the study.

It is remarkable that only 6.9% and 7.5% of the patients scored more than 2.5 at the MDI diagnostic scale. For this study, we used the MDI as a screening instrument. A mean score for the replied 10 items was calculated in a score range from 0 to 5 with a mean score > 2.5 indicating symptoms of depression. This is in accordance with the reported prevalence of MDI score ≥ 20 that was 7.1% in the Danish population [18]. In contrast, the prevalence of depression is estimated to be between 27% and 47% of patients scheduled for heart surgery, and between 19% and 61% of patients after the intervention [25]. A plausible explanation might be that the studies up to now, mainly were completed in the mid 90s as criteria for operation were more restrictive and the course of disease from the first signs of symptoms until discharge from hospital has become much shorter now. Another possible explanation could be the age of the study population as younger persons might have a higher degree of anxiety when they are confronted with a life-threatening disease and its emotional consequences.

In conclusion, this is the first randomized trial of self-reported outcomes after on-pump versus off-pump coronary artery bypass surgery in elderly moderate to high-risk patients. We revealed improvement in HRQoL within both surgical groups to the same level as a comparable healthy background population. Depression scores remained unchanged within and between the two surgical groups. No clinically relevant difference between off-pump and on-pump bypass surgery could be demonstrated. Therefore, the method of choice at our center still depends on which of the techniques the individual surgeon prefers and feels most comfortable with.

Acknowledgements

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References


