Impact of coronary artery bypass grafting on various aspects of quality of life

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Abstract

Objective: To prospectively study the improvement in quality of life (QoL) after coronary artery bypass surgery (CABG). Patients and Methods: Consecutive patients (n = 2121) who underwent CABG at Sahlgrenska University Hospital between 1988 and 1991 received 3 questionnaires for the study of QoL: the Physical Activity Score, the Nottingham Health Profile and the Psychological General Well-being Index, which were responded both before surgery and at 3 months (n = 1059), 1 year (n = 1045) and 2 years (n = 1027) postoperatively. Results: All differences were tested against baseline. The Physical Activity Score improved (mean 4.3 before CABG, 3.1 3 months after (P < 0.0001), and 2.8 2 years postoperatively (P < 0.0001)). The Nottingham Health Profile score improved (mean 20.5 before CABG, 11.4 3 months (P < 0.0001), and 10.4, 2 years postoperatively (P < 0.0001)). The Psychological General Well-being Index improved (mean 91.1 before CABG, 103.8 3 months (P < 0.0001), and 105.8 (P < 0.0001) 2 years after CABG). The subscale analyses of the Nottingham Health Profile and the Psychological General Well-being Index 2 years after CABG showed the greatest improvement in areas reflecting physical capacity and pain, to be followed by mental qualities. At 2 years after CABG only sexual problems were still markedly frequent, and independent predictors for sexual problems after surgery were preoperative problems (P < 0.00001), male sex (P < 0.0001), and diabetes mellitus (P = 0.0008). Conclusion: QoL was markedly and significantly improved after CABG. The major improvement was seen already at 3 months, with further slight improvement observed 2 years after surgery. The major improvement was found in areas reflecting physical capacity and pain, which is consistent with symptomatic and objective measurements after CABG. In contrast to the overall improvement in QoL sexual problems were still markedly common 2 years after CABG. The mechanism for this is not fully understood and needs further investigation. © 1997 Elsevier Science B.V.

Keywords: Quality of life; Coronary artery bypass surgery

1. Introduction

Severe coronary artery disease can be successfully treated with coronary artery bypass grafting (CABG) with a considerable improvement in terms of the relief of angina pectoris [1–3]. Approximately 3 of 4 patients are free from ischemic events for 5 years [4]. However, increased survival is demonstrated only in selected subgroups with advanced coronary artery disease [5,6] and this effect has not been established in elderly patients [1,7]. The outcome of treatment in terms of quality of life is of major importance in severely symptomatic disease, and particularly if a prognostic gain cannot be expected. QoL constitutes the individual’s perception of symptoms, well-being and physical and mental functional capacity. Previous major evaluations after CABG have focused on physical improvement, such as
reduction in angina pectoris, reduction in nitrate medication and increase in exercise capacity [8,9] and large studies of QoL utilizing reliable and validated instruments are lacking. This study aims to describe the impact of CABG on a variety of aspects of QoL using a battery of standardized questionnaires.

2. Patients and methods

All patients from all 15 hospitals in western Sweden, who underwent CABG at Sahlgrenska University Hospital and the Scandinavian Heart Center in Göteborg between June 1988 and June 1991, received a questionnaire regarding QoL at the time of coronary angiography prior to the operation and 3 months, 1 year and 2 years after the operation. These hospitals constitute referral centers for CABG in western Sweden (1.6 million inhabitants). The preoperative questionnaires were administered prior to coronary angiography to all patients on waiting-list, scheduled for an elective angiography. Patients undergoing emergency coronary evaluation received the questionnaires on the ward prior to angiography.

The demographic data were collected through review of medical charts, interview, and physical examination of the patients by a physician of the research team, when the patient was hospitalized for CABG. The functional classification was made according to the Canadian Cardiovascular Society.

2.1. Quality of Life

The patients completed three self-administered questionnaires for the assessment of QoL: the Physical Activity Score, the Nottingham Health Profile and the Psychological General Well-being Index. These questionnaires have been carefully validated and tested for reliability [10–13].

The Physical Activity Score represents one dimension of an angina-specific questionnaire [10], the Angina Pectoris Quality of Life questionnaire, which contains six questions, for the self-estimation of physical abilities and limitations. Each response is graded from 1–6 and the mean value for all six questions is calculated. The higher the total value, the greater the degree of disability.

The Nottingham Health Profile is divided into 2 parts. Part I consists of 38 statements which convey limitations of activity or aspects of distress in 6 dimensions: physical mobility, pain, sleep, energy, social isolation and emotional reactions. Patients are required to indicate by a yes/no answer which of the problems they are experiencing at the time they complete the questionnaire. A score ranging from 0 to 100 can be calculated for each dimension of this part of the profile; the higher the score, the greater the limitations in activity or the distressing social and emotional problems. Part II lists the seven aspects of life which are found to be most affected by a person’s state of health: occupation, ability to perform jobs around the house, social life, home relationships, sexual life, hobbies and holidays; a yes/no answer indicates which areas are affected by the respondent’s present state of health.

The Psychological General Well-being Index contains 22 questions, dealing with six sections of well-being: anxiety, depressed mood, vitality, general health, self-control and well-being [13]. The response format is graded from 1 to 6 (range 22–132), with the highest value corresponding to superior well-being.

2.2. Choice of questionnaires

The symptomatic response to myocardial ischemia in angina pectoris is chest discomfort, brought about by physical or mental stress, thereby limiting physical performance. However, angina pectoris affects various aspects of personality with increased anxiety and limitations of leisure activity, work capacity and social and sexual function as a result [14–16].

The Physical Activity Score represents one dimension of a disease-specific questionnaire for the estimation of physical capacity in angina pectoris [10]. The Nottingham Health Profile and the Psychological General Well-being Index constitute general questionnaires. The Nottingham Health Profile is most useful among patients with chronic and pronounced symptoms [17] and in the detection of treatment effects [18]. The Psychological General Well-being Index is suitable for addressing the impact of symptoms on well-being and is applicable for healthy and patient populations. The purpose of this choice of questionnaires was to capture the whole range of outcomes, from symptomatic limitations of physical abilities due to angina pectoris to overall well-being and health-related QoL. These questionnaires were chosen rather than other estimates, observed to have a lesser ability to reflect subjective results after CABG; such as NYHA classification [19], and return to work [20].

2.3. Statistical Methods

To test for differences between group A and group B Fischer’s exact test was used for dichotomous variables and Mantel-Haenszel $\chi^2$ for functional class. The log rank test was used for 2-year mortality and morbidity. Wilcoxon’s signed rank test for continuous variables and the sign test for proportions were used for paired observations to test changes over time. We did not use the normal repeated measurements model because of the substantial loss of information this would entail, as almost one-third of the responders had incomplete data
Table 1
Clinical characteristics at operation among patients who answered the questionnaire both prior to and at some time after the operation (Group A) and those who did not (Group B)

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th></th>
<th></th>
<th>Group B</th>
<th></th>
<th></th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (n = 1160)</td>
<td>%</td>
<td></td>
<td>n (n = 961)</td>
<td>%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>964</td>
<td>83</td>
<td></td>
<td>756</td>
<td>79</td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Age ≥ 65 years</td>
<td>546</td>
<td>47</td>
<td></td>
<td>453</td>
<td>47</td>
<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>3-vessel disease (92)</td>
<td>752</td>
<td>67</td>
<td></td>
<td>584</td>
<td>65</td>
<td></td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>Preoperative functional class (10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.003b</td>
</tr>
<tr>
<td>1</td>
<td>21</td>
<td>2</td>
<td></td>
<td>33</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>138</td>
<td>12</td>
<td></td>
<td>113</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>731</td>
<td>63</td>
<td></td>
<td>476</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>263</td>
<td>23</td>
<td></td>
<td>336</td>
<td>35</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous history of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction (1)</td>
<td>676</td>
<td>58</td>
<td></td>
<td>620</td>
<td>65</td>
<td></td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Congestive heart failure (2)</td>
<td>155</td>
<td>13</td>
<td></td>
<td>167</td>
<td>17</td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Hypertension (4)</td>
<td>413</td>
<td>36</td>
<td></td>
<td>360</td>
<td>38</td>
<td></td>
<td></td>
<td>0.34</td>
</tr>
<tr>
<td>Diabetes mellitus (2)</td>
<td>136</td>
<td>12</td>
<td></td>
<td>130</td>
<td>14</td>
<td></td>
<td></td>
<td>0.21</td>
</tr>
<tr>
<td>Claudication (3)</td>
<td>133</td>
<td>11</td>
<td></td>
<td>127</td>
<td>13</td>
<td></td>
<td></td>
<td>0.23</td>
</tr>
<tr>
<td>Cerebrovascular disease (1)</td>
<td>93</td>
<td>8</td>
<td></td>
<td>84</td>
<td>9</td>
<td></td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>Smoking (13)</td>
<td>134</td>
<td>12</td>
<td></td>
<td>141</td>
<td>15</td>
<td></td>
<td></td>
<td>0.03</td>
</tr>
</tbody>
</table>

*a Numbers in parentheses denote patients where information is missing.
*b Refers to the overall ordered distribution of patients.

during follow-up. The multivariate analysis was performed using a stepwise logistic regression model. All P values are two-sided.

3. Results

In all during the 3 years, 2121 patients underwent CABG without simultaneous valve surgery, of whom 2030 survived after 3 months, 2002 after 1 year and 1964 survived after 2 years. Information on QoL was available in 1290 of these patients (61%) prior to operation. Among the survivors 1659 patients (82%) responded to the questionnaire at 3 months, 1631 patients (81%) at 1 year and 1605 patients (82%) 2 years after CABG. The total 30-day mortality in the population was 3.6% and the total 2-year mortality was 7.4%. The median time from coronary angiography, i.e. preoperative assessment of QoL, to CABG, was 105 days (range 0–365, mean 120). Table 1 shows group A as those patients who answered the questionnaire both prior to and at some time after surgery and group B (n = 961) as those who did not. The patients in group B were more often female (P = 0.01), suffered from more severe angina (P = 0.003) and had a more frequent history of myocardial infarction (P = 0.004) and congestive heart failure (P = 0.01) than patients in group A.

Table 2 shows that the patients in group B signifi-
cantly more often suffered a new cardiovascular event or were dead 2 years after CABG, than patients in group A. Functional classification did not differ between the groups 2 years after CABG.

3.1. Measurements of Quality of Life

The Physical Activity Score (Table 3) improved significantly after the operation. Improvement was slightly more marked 1 year and 2 years after CABG as compared with the situation at the 3-month control (P < 0.0001 for improvement between 3 months and 2 years). Total scores for the Nottingham Health Profile were significantly improved at 3 months after CABG, with further slight improvements at 1 and 2 years (P = 0.02 for the improvement between 3 months and 2 years). As seen in Table 3 and Fig. 1, the mean scores for all aspects of QoL measured in the Nottingham Health Profile part I were significantly reduced after the operation. The major improvement was seen in terms of lesser pain and increased energy. Physical mobility and emotional status also appeared to be markedly improved. Overall results appeared similar at 3 months, 1 year and 2 years after the operation. The Nottingham Health Profile part II (Fig. 2) showed significant and pronounced reductions in the presence of all health-related problems included in the scale. The proportion of patients with complaints on sexual life 2 years after CABG were still markedly high.

Overall and subscale scores for the Psychological General Well-being Index (Table 3 and Fig. 3) all
Table 2
Clinical characteristics 2 years after coronary artery bypass surgery among patients who answered the questionnaire both prior to and at some time after the operation (group A) and those who did not (group B)

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th></th>
<th>Group B</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Functional class at 2 years*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>608</td>
<td>76</td>
<td>384</td>
<td>77</td>
<td>0.50b</td>
</tr>
<tr>
<td>2</td>
<td>464</td>
<td>16</td>
<td>297</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>97</td>
<td>7</td>
<td>48</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>7</td>
<td>32</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0</td>
<td>7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Mortality and morbidity at 2 years after coronary bypass</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>1160</td>
<td></td>
<td>961</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2.6</td>
<td>13.3</td>
<td>1.3</td>
<td>3.4</td>
<td>0.006</td>
</tr>
<tr>
<td>Transitory ischemic attack</td>
<td>0.6</td>
<td>1.5</td>
<td>1.5</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1.7</td>
<td>4.5</td>
<td>4.5</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Any of the 4 above</td>
<td>5.7</td>
<td>19.2</td>
<td>19.2</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

* Postoperative functional class was registered in a total of 992 patients. b Refers to the overall ordered distribution.

Fig. 1. Mean scores for Nottingham Health Profile part I subscales before and 2 years after coronary bypass surgery in relation to normal values for men aged 60–64 years (n = 1027). A lower score represents superior QoL. The social dimension differed at 2 years from preoperative values with \( P = 0.0008 \), for all other dimensions \( P < 0.0001 \).

Fig. 2. Scores for Nottingham Health Profile part II before and 2 years after coronary bypass surgery in relation to normal values for men aged 60–64 years (%). The percentage presented represents the percentage of study subjects who reported their health to affect the respective areas of life. All dimensions differed at 2 years from preoperative values with \( P < 0.0001 \).

Table 3
Mean total quality of life scores for the 3 questionnaires at various times before and after coronary bypass surgery for patients who responded prior to and at the respective time points after surgery

<table>
<thead>
<tr>
<th></th>
<th>Preop (n = 1160)</th>
<th>3 Months postop (n = 1059)</th>
<th>1 Year postop (n = 1045)</th>
<th>2 Years postop (n = 1027)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity score*</td>
<td>4.3</td>
<td>3.1*</td>
<td>2.8*</td>
<td>2.8*</td>
</tr>
<tr>
<td>Nottingham health profile I totalb</td>
<td>20.5</td>
<td>11.4*</td>
<td>11.9*</td>
<td>10.4*</td>
</tr>
<tr>
<td>Psychological general well-being index totalc</td>
<td>91.1</td>
<td>103.8*</td>
<td>104.7*</td>
<td>105.8*</td>
</tr>
</tbody>
</table>

* \( P < 0.0001 \) (refers to changes from preoperative values).

* A lower score represents a higher estimation of physical abilities.

* A lower score represents superior QoL. A higher score represents superior general well-being.
improved significantly after the operation. Beneficial results were observed as early as 3 months after surgery and increased additionally throughout the postoperative long-term follow-up ($P = 0.001$ for the improvement between 3 months and 2 years). The major improvement appeared for health, followed by anxiety and vitality.

A multivariate analysis (Table 4) of preoperative characteristics showed that preoperative sexual problems, male sex, and diabetes mellitus were independent predictors for postoperative sexual problems in the Nottingham Health Profile.

### 4. Discussion

This is a unique study as it is the largest consecutive patient series evaluating the impact of CABG on QoL, utilizing a set of reliable and validated instruments. Furthermore, both men and women from a well-defined area are included. A large proportion of all the patients undergoing surgery due to angina pectoris cannot expect any prognostic gain, but the greatest benefit is to be derived in terms of symptomatic relief. The subjective overall outcome regarding QoL is therefore of major importance.

#### 4.1. General results of all QoL questionnaires

The patients who did not respond to both pre- and postoperative QoL questionnaires (Table 1 and Table 2) generally suffered from more cardiovascular disease, and had a higher mortality, which may affect the generalizability of our findings.

The overall results were similar for all the questionnaires with a dramatic and highly significant improvement in various measurements at 3 months postoperatively, with further significant improvements observed at the end of the study.

Thus, the Physical Activity Score show a significant improvement in self-estimated physical abilities at just 3 months postoperatively, with further slight improvements seen 1 and 2 years after CABG. The results of this instrument has been observed to correlate with angina severity, treadmill time and time until onset of chest pain [21].

The global results for the Nottingham Health Profile and the Psychological General Well-being Index show the same patterns of initial dramatic improvement and smaller adjustments at 1 and 2 years after surgery. When compared with a male population of approximately the same age, the postoperative scores for both these instruments were close to normal values [13,22]. Previously, Jenkins et al. found normal social function and physical improvement 6 months after CABG [23], whereas Papadantonaki et al. found no change in QoL and only partial recovery of physical function 3 weeks after surgery [24]. Our interpretation of the overall results is that both in terms of physical abilities, health-related QoL and general well-being, QoL is to its major part restored 3 months after surgery. This may serve as a guideline for rehabilitatory measures and work resumption targets. It is important to identify potential treatment failures as early as possible since a number of rehabilitation programs have had positive effects on QoL [25,26]. Our findings indicate that unsuccessful results in terms of QoL are likely to be detectable after just 3 months.

#### Table 4

<table>
<thead>
<tr>
<th>Independent factors</th>
<th>$P$ value</th>
<th>Odds ratio</th>
<th>95% Confidence interval for odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative problems</td>
<td>$&lt;0.0001$</td>
<td>4.80</td>
<td>(3.51–6.57)</td>
</tr>
<tr>
<td>Male sex</td>
<td>$&lt;0.0001$</td>
<td>2.94</td>
<td>(1.72–5.01)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.0008</td>
<td>2.12</td>
<td>(1.37–3.30)</td>
</tr>
</tbody>
</table>
4.2. Improvement in subscales

The greatest improvement in the Nottingham Health Profile part I subscales after CABG was seen in the energy, pain, emotion and mobility dimensions in our study. We consider this to be an important confirmation of the objective observation of disappearing or improving symptoms of angina pectoris and the increased physical performance at exercise test after CABG [8,9]. The improvement in Nottingham Health Profile part I corresponded well with that observed by Caine et al., using the same instrument, in a bypass-operated population under 60 years of age, one year after surgery [27]. One may speculate about the physical basis for the improvement in the energy dimension. Significant correlations have been observed between NYHA angina classification and the dimensions of pain, mobility and energy in the Nottingham Health Profile I [28,29]. It is possible that the preoperative experience of a lack of energy was the equivalent of myocardial ischemia.

Angina pectoris is known to confer increased anxiety and neuroticism [14] and it is interesting that the symptomatic improvement confers such a marked change in emotional state.

The preoperative problems due to state of health in the Nottingham Health Profile part II were generally most apparent in activities involving considerable physical effort; hobbies, holidays and housekeeping. As expected, according to the outcome in part I, the postoperative improvement was also most apparent in these areas. With the exception of sexual problems all areas in the Nottingham Health Profile part I and II came close to the prevalence reported in a healthy population [23]. Sexual problems were markedly frequent before surgery. This was also the only area where postoperative improvement was also most apparent in these areas. With the exception of sexual problems all areas in the Nottingham Health Profile part I and II came close to the prevalence reported in a healthy population [23]. Sexual problems were markedly frequent before surgery. This was also the only area where postoperative improvement was also most apparent in these areas. With the exception of sexual problems all areas in the Nottingham Health Profile part I and II came close to the prevalence reported in a healthy population [23]. Sexual problems were markedly frequent before surgery. This was also the only area where postoperative improvement was also most apparent in these areas. With the exception of sexual problems all areas in the Nottingham Health Profile part I and II came close to the prevalence reported in a healthy population [23]. Sexual problems were markedly frequent before surgery. This was also the only area where postoperative improvement was also most apparent in these areas. With the exception of sexual problems all areas in the Nottingham Health Profile part I and II came close to the prevalence reported in a healthy population [23]. Sexual problems were markedly frequent before surgery. This was also the only area where postoperative improvement was also most apparent in these areas. With the exception of sexual problems all areas in

The values for the Psychological General Well-being Index after just 3 months were close to normal. The main improvement was seen in the health, vitality and anxiety dimensions, but the depression, well-being and self-control domains also improved significantly. These subscales are not strictly comparable to the Nottingham Health Profile, although the impression that the physical improvement is dominant, and the mental recovery slightly less marked, is consistent.

When the clinical significance of these results is evaluated one must keep in mind that comparisons between healthy populations and patients with serious illness do not account for the psychological and physical adaptive mechanisms occurring with disease and disability. The most important results are therefore the comparative results before and after intervention.

4.3. Limitations

We were unable to administer reminders and this might have reduced the response rate in our study.

The results of the patients who did not respond to the questionnaires can not be accounted for, and those patients appeared to suffer from more severe heart disease than the responders. Thus, we do not know if our results are applicable in a non-selected population undergoing CABG. Two major explanations for the low response rate prior to CABG could be identified and estimated: First, the fact that emergency surgery was performed, precluded the possibility to make an assessment at short notice in many cases (n = 129). We have previously observed that patients with more severe anginal symptoms demonstrate the greatest improvement in QoL [34], and the lower response rate among these patients makes an overestimation of improvement unlikely. Second, of all patients operated on during the time period 128 had already undergone coronary angiography before the start of the study, and had not received a preoperative QoL questionnaire. These non-responders were unlikely to have systematically affected the outcome. These two explanations accounted for 31% of the preoperative non-responders.

In Fig. 1 and Fig. 2, we present normal values for a male population aged 60–64 years for comparative reasons [22]. We are aware that, although the median age in our material is 64 years, the age span is much greater (32–86 years) and our responders also include 17% women who generally obtain lower QoL than men in a normal population [22]. One may argue that admission to this study was biased since all patients underwent CABG, and that QoL in angina pectoris would increase also on medical therapy alone. However, based on the large randomized studies, which have established the efficacy of pain control and reduction of mortality through CABG [1–3,5,6], medical treatment alone would not have been an option in these patients at the beginning of the study.
5. Conclusion

This study confirms significant improvements in various aspects of QoL after CABG, measured using a set of questionnaires in a large consecutive number of men and women of a wide range of ages, reported from one surgical center. The improvements are clear and considerable just 3 months after surgery, with further slight improvements observed 1 and 2 years after CABG. The major improvement takes place in dimensions reflecting health, physical capacity, and pain, but mental qualities also improve considerably. After evaluation of various subscales and areas of life, only sexual problems are still considerable 2 years after surgery, and the cause or appropriate treatment for this is not known.

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References


