Management of mild to moderate aortic valve disease during coronary artery bypass grafting

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Received 20 September 2002; received in revised form 10 May 2003; accepted 18 May 2003

Abstract

Objective: The long term survival of patients with mild to moderate aortic valve disease who do not have valve replacement at the time of coronary artery bypass grafting (CABG) is unknown. Therefore we have reviewed our experience with such patients. Methods: We reviewed the medical records of consecutive patients between June 1978 and December 1996, and identified 40 patients with mild to moderate aortic valve disease, who underwent CABG, without valve replacement (study group). Mean preoperative aortic gradient was 34 mmHg and mean intraoperative gradient 20 mmHg. Eleven patients underwent valve inspection, and an equal number, underwent valve repair. The records of 61 other patients with severe aortic valve disease, who underwent concomitant aortic valve replacement (AVR) and CABG (control group), were also reviewed. Results: Survival was significantly better in the control group. Eleven patients (27.5%) in the study group underwent reoperation for AVR, with no operative mortality. Multivariate analysis confirmed valve replacement at initial CABG to be the only predictor of survival (β = 0.586, P = 0.038) Preoperative gradient < 40 mmHg, intraoperative gradient < 20 mmHg, age over 70, sex, aortic stenosis and valve pathology did not predict survival in the study group. Conclusion: Patients with mild to moderate aortic valve disease undergoing coronary artery bypass grafting may be best served by valve replacement, rather than repair, inspection or no procedure.

Keywords: Mild aortic valve disease; Coronary bypass surgery

1. Introduction

Cardiac surgeons are regularly presented with patients requiring coronary artery bypass grafting, but who also have mild to moderate aortic valve disease. The decision of whether to replace the valve or not is difficult and remains controversial. Some surgeons advocate aortic valve replacement (AVR) on the assumption that many of these patients will develop significant valve disease within a few years time [1–4]. Thus they would otherwise be exposed to the risks of a redo operation to replace the valve [5,6]. Others argue that previous CABG is not a risk factor for increased mortality following AVR [7–9] and combined AVR and CABG may not be required in many of these patients who would otherwise be subjected unnecessarily to the risks and possible complications of a major combined procedure, life long anticoagulation for those who receive a mechanical prosthesis, and the other short- and long-term complications of a prosthetic valve [10]. It is noteworthy that the mortality of isolated CABG in the UK was 2.2%, and that of CABG and AVR was 7.0% in the year 1999–2000 (Society of Cardiothoracic Surgeons of Great Britain and Ireland, http://www.scts.org/file/NACSDreport2000ukcsr.pdf). The decision to replace the valve or not is often not an easy one to make in these circumstances. While many patients have a slow progression of their aortic valve disease, others may have an accelerated course. Unfortunately, there are currently no randomised trials of AVR in these patients and decisions have to be guided by non-randomised observational studies. The aim of this study was to assess the long term survival of patients with ischaemic heart disease who present for myocardial revascularisation, but who are also known preoperatively to have a mild or moderate aortic valve disease, and in whom valve replacement was not carried out.
2. Material and methods

We reviewed the medical records of 40 patients with mild to moderate aortic valve disease, confirmed preoperatively, who underwent CABG without aortic valve replacement, between June 1978 and December 1996 (study group). Sixty-one other patients with significant aortic valve disease who underwent primary combined AVR and CABG were also reviewed (control group). The patients in the replacement or control group were a randomly selected sample of all patients undergoing AVR and CABG during the study period. Data were collected by reviewing the charts, and by telephone questionnaire, with the patients or their general practitioners. Dates of deaths and causes of deaths were obtained by contacting the Registrar General office of the government of the United Kingdom.

The inclusion criteria for the study group were:

1. patients undergoing coronary artery bypass grafting;
2. mild (gradient < 30 mmHg) to moderate (gradient < 45 mmHg), aortic stenosis confirmed pre-operatively; and
3. mild (grade 1) to moderate (grade 2) aortic regurgitation confirmed preoperatively.

The exclusion criteria were:

1. patients with left ventricular impairment; and
2. other associated cardiac pathology such as mitral valve disease.

Patients with impaired left ventricular function were excluded from the study, as the gradient over the aortic valve and the degree of the regurgitation are both usually underestimated when the ejection fraction is reduced, rendering assessment of the severity of these lesions unreliable [11]. The definition of left ventricular dysfunction in this study was any degree of impairment of the left ventricle detected on echocardiography and or angiography.

Peak preoperative aortic gradient in both groups was measured either by echocardiography or by cardiac catheterisation. Unfortunately the aortic valve area was not available for the majority of these patients, so we relied on the aortic gradient as a measure of the severity of the aortic stenosis, and on the degree of the regurgitation as detected on echocardiography or angiography. Intraoperative aortic gradient was measured, just before going on bypass by inserting a long manometer needle tangentially through the wall of the ascending aorta to record the intra-aortic pressure. The left ventricular pressure was measured by inserting the needle through the right ventricular outflow tract, across the interventricular septum into the left ventricular cavity. The mean intra operative aortic gradient was 20 mmHg (range 10–35 mmHg). All patients in the control group had severe aortic valve disease, i.e. aortic gradient of more than 50 mmHg, or grade 3 or 4 aortic regurgitation. Follow-up was 100% complete.

2.1. Operative data

All operations were performed through a median sternotomy. Cardiopulmonary bypass was instituted by cannulation of the ascending aorta, and right atrial cannulation. Intermittent antegrade cold crystalloid cardioplegia was initially infused into the aortic route in patients with aortic stenosis, and by direct cannulation of the coronary ostia in cases of aortic incompetence. Topical ice slush was used and the myocardial temperature was monitored by using a temperature probe inserted into the inferior surface of the heart. Cardioplegia was infused every 20 min or if the heart temperature rose above 10 °C. Table 1 shows the clinical and operative details of the patients in the study and the control groups.

2.2. Study group

Thirteen patients had left internal mammary artery (LIMA) graft to the LAD, and four patients had bilateral internal mammary artery grafts; LIMA graft to the marginal circumflex, and right internal mammary artery (RIMA) graft to the LAD. The rest of the patients in this group all had vein grafts (Fig. 1). In 18 patients the aortic valve was not opened and only CABG was performed. In 11 patients the aorta was opened, and the aortic valve was inspected. Valve repair was carried out in an equal number of patients. Repair was in the form of valvotomy and decalcification for aortic stenosis, or approximation of leaflets and resuspension of the aortic valve for aortic regurgitation.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Study group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>67.4 (S.D. 7.7)</td>
<td>65.6 (SD 8.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic stenosis present</td>
<td>30 (75%)</td>
<td>55 (90%)</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic incompetence present</td>
<td>14 (35%)</td>
<td>15 (24.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Female sex</td>
<td>16 (40%)</td>
<td>14 (23%)</td>
<td>NS</td>
</tr>
<tr>
<td>LIMA used</td>
<td>17 (42.5%)</td>
<td>26 (42.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean number of grafts</td>
<td>2.0 (S.D. 0.8)</td>
<td>1.6 (SD 0.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean × clamp time (min)</td>
<td>65.5 (S.D. 21.4)</td>
<td>86.9 (SD 26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean CPB time (min)</td>
<td>95.3 (S.D. 27.6)</td>
<td>116.5 (SD 26.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Valve pathology</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Degenerative</td>
<td>31 (77.5%)</td>
<td>37 (60.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Bicuspid</td>
<td>1 (2.5%)</td>
<td>21 (34.4%)</td>
<td>0.0001a</td>
</tr>
<tr>
<td>Rheumatic</td>
<td>8 (20%)</td>
<td>2 (3.28%)</td>
<td>0.006a</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>0</td>
<td>1 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>Mean hospital stay (days)</td>
<td>11.6 (S.D. 3.6)</td>
<td>17.0 (S.D. 12.5)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

a Compared to the rest (Fisher’s exact test).
2.3. Control group

All patients in this group underwent combined AVR and CABG. Twenty-six patients received an internal mammary artery graft. Twenty-two patients had LIMA to LAD, two had RIMA to the LAD and LIMA to the circumflex, one patient had RIMA to the LAD and one had RIMA to the right coronary artery (Fig. 2).

2.4. Statistical analysis

Statistical analysis was performed using Statistica software (Statsoft Inc., Tulsa, OK, USA). The Kaplan–Meier method was used for survival analysis. Fisher’s exact test and Student’s t-test were used. Multivariate analysis was performed using Cox’s proportional hazard regression method. A P value of less than 0.05 was considered statistically significant.

3. Results

Eleven patients in the study group (27.5%) were re-operated upon for aortic valve disease, nine of whom had developed severe aortic stenosis and two patients had significant regurgitation. There was no operative mortality after redo surgery in these patients. The mean interval to repeat AVR was 7.6 years (range 5 months to 17 years). The mean rate of progression of aortic stenosis was 7.6 mmHg per year. This was calculated for each individual patient by dividing the difference between the aortic gradient at the initial presentation and the gradient at the second operation by the interval between the two operations in years. Three patients in the re-operation subgroup (27.2%), had had their valves inspected in the initial presentation, four patients (36.4%) underwent initial repair of their aortic valve and four others (36.4%) underwent no procedure.

There was no operative mortality in the control group, and none was re-operated upon. Overall survival was significantly better in the replacement or the control group (P = 0.036, log rank) (Fig. 3). Multivariate analysis was performed by using Cox’s proportional hazard regression analysis, and including all the patients in the study and the control groups (n = 101), with survival times as the dependent variable; the independent variables are: age, sex, valve replacement at the first operation or not, the use of the internal mammary artery and the number of grafts performed per patient.

The only significant predictor of survival was aortic valve replacement (β = 0.586, P = 0.038).

Multivariate analysis including only patients in the study group (n = 40) was done with the independent variables being: age, sex, valve procedure (none, inspection or repair), valve pathology, presence of aortic stenosis, use of LIMA and the number of grafts. The only significant variables predicting survival were sex (P = 0.033, see Fig. 4) and valve procedure (P = 0.045). Survival without re-operation is shown in Fig. 5. Preoperative aortic gradient of 40 mmHg or less, age 70 years or less and valve pathology did not help predict survival. For reasons that are not clear, survival was worst in the inspection subgroup (Fig. 6). Intra-operative gradient was unhelpful in predicting the progression of valve pathology (Fig. 7). The use of left internal mammary artery graft did not influence survival (P = 0.811, log-rank).
4. Discussion

The management of coexisting coronary artery and mild to moderate aortic valve disease is a very controversial subject. The advocates of aortic valve replacement at the time of CABG argue that patients with mild aortic valve disease invariably develop worsening symptoms due to the progression of valve disease in a few years’ time [2,3,12], and they recommend simultaneous AVR for mild aortic valve disease on the basis of the high operative risks of repeat surgery for aortic valve disease following initial CABG. Fiore et al. [5] reported an 18% operative mortality in 28 patients who underwent AVR following initial CABG as opposed to 9.1% in a group that underwent combined AVR and CABG. Odell et al. [6] reported a 16.6% mortality in 145 patients who had AVR after previous CABG. Valve replacement minimizes the occurrence of sudden death in patients with aortic stenosis which is reported to be 3–5% [13]. Others hold the view that only a proportion of these patients develop haemodynamically significant aortic valve disease and it is unfair to subject those in whom valve replacement might not be indicated, to a major operation such as concomitant CABG and AVR with a higher operative morbidity and mortality, in addition to the added unnecessary risks of a prosthetic valve with its attendant anticoagulation (in those with mechanical implants) and valve related complications. The natural history of aortic stenosis suggests an accelerated progression in elderly patients [12], in patients with degenerative pathology and in patients with associated coronary artery disease. In patients with aortic stenosis who become symptomatic, the rate of progression per year is faster than in those who are asymptomatic [14]. Some authors recommend valve repair as an option to deal with mild aortic valve disease at the time of CABG [15]. Decalcification of the aortic valve, either manually or by using ultrasonic surgical devices has been recommended by some [16,17], but the outcome was disappointing [18,19]. In our series, aortic valve repair was carried out in 11 patients in the study group, but this did not stop disease progression, and more than 36% of them underwent reoperation for AVR. Aortoscopy has recently been described as a means to inspect the aortic valve at the time of coronary bypass surgery.
grafting [20] in order to avoid opening the aorta, but in our experience, the subgroup of patients who had their valve inspected did worse than those who had aortic valve repair or those who had no procedure to the valve at all. We measured the intraoperative aortic gradient in 25 of the 40 patients in the study group, all of whom had mild to moderate aortic stenosis. Neither the preoperative nor the intraoperative gradient was able to predict the progression of the aortic valve disease. Subsequent valve replacement was carried out in 11 patients in the study group with no operative mortality, but a significant percentage of the remaining patients in this group were deemed to be high risk patients at their second presentation, either on the grounds of age, impairment of the left ventricular function or both. In our opinion, those patients could have had a better outcome had they been operated upon when they first presented. It is difficult to set a certain gradient limit, beyond which to recommend valve replacement or non-replacement, because as mentioned earlier, preoperative or intraoperative aortic gradient could not help predict disease progression, and that there was no uniform relationship between the aortic gradient and disease progression. Long term survival according to our data is significantly better in the control group, in whom concomitant valve replacement was carried out along with CABG, compared to the study group where only CABG was performed, despite the presence of a more severe aortic disease in the control group. One of the drawbacks of this study is that the AVR and CABG group is not a true control group, because all patients in this group presented with significant aortic valve disease as opposed to the other group where the disease is either mild or moderate. But even so, their survival was superior to those with milder disease who were observed. It may be argued that patients with mild aortic disease have a higher gradient than the actual gradient measured at initial presentation, and that the severity of the aortic valve disease may be masked by the depression of the ventricular function caused by the associated coronary artery disease, therefore we excluded these patients from this study. We conclude from these data that valve replacement as opposed to non-replacement, is associated with a better overall long term survival and that valve replacement at the time of CABG in the patient with associated mild or moderate aortic valve disease may be a better option than inspection only, repair or no procedure.

References


Appendix A. Conference discussion

Dr R. Dion (Leiden, The Netherlands): You bring up a question about what to do for moderate aortic stenosis when CABG is indicated. So you are clear, better replace than leave?

Dr Graham: Well, like a lot of things, the more you look at it, the less clear it becomes.
Dr T. Sundt (Rochester, Minnesota): Did I miss the perioperative mortality in your study group?

Dr Graham: None of the patients in the study group died. There was one patient in the control group that died.

Dr Sundt: Does the study group include all of patients in your unit who underwent either of the two procedures?

Dr Graham: No. There was only 62. The control was selected over the same time period. Obviously, it was a small proportion of the patients undergoing combined aortic valve replacement and bypass grafting. Our current mortality as shown in the UK cardiac surgical register on the Internet is 3% in that group of patients.

Dr Sundt: For which, for combined CABG/AVR?

Dr Graham: For CABG and AVR.

Dr Sundt: And for CABG alone in a comparable group of patients, what would you say the perioperative risk is?

Dr Graham: Well, I can’t give you for a comparable group. Our mortality is 1.9 for CABG alone. It’s probably similar because there are going to be more older patients in that group.

I think focusing on the mortalities is quite difficult, because most people’s results are getting better. The 11 patients that we had that underwent a redo procedure, none of them died. We looked at the other patients we had, not in this series, that had aortic valve replacement after previous CABG, but weren’t known to have aortic valve disease at the time of the previous CABG, they did well with the redo procedure. So I would caution against placing a rigid rule that one must replace the valve. I think all we have shown in this retrospective study is that these patients will come back with further problems.

Now, a lot of the patients, and it’s hard to bring it out in analysis, were felt to be inoperable on the second occasion they presented, perhaps due to advanced age, perhaps due to the physiology at the time, or perhaps deterioration of left ventricular function. We cannot answer that. But I get the strong feeling that’s that part of the reasons why they did not do so well, they weren’t able to undergo a redo procedure in some cases.

Dr Sundt: Clearly the patients who do not have a valve procedure are at risk of coming back for AVR, but I disagree about focus on operative risk. I do think that the perioperative risk is a relevant issue. With regard to patients felt inoperable on the second occasion, it may well be that some of them were felt at the time of initial CABG to be of too great risk to undergo the combined procedure.

Dr Graham: Sure, I’ll accept that.

Dr Sundt: I believe that it is the cumulative mortality rate over time that’s critical; the added risk of the additional procedure at the first operation applied to the group as a whole versus the combined risk of the first plus risk of the second in the subset requiring AVR.

It’s interesting that you had no deaths in the redo group. Ten years ago the arguments concerning this entity were centered on the notion that the operative risk of the redo procedure was prohibitive. You’ve shown again that this is not the case.

Dr Graham: That’s right. And there’s some other recent publications I think that would back that up.

Dr M. Turina (Zurich, Switzerland): This is a very timely paper. It addresses the problem, which is really not easy to resolve, and this is unpredictability of the development of the aortic valve disease, especially the degenerative aortic valve disease presenting as aortic stenosis. There is a huge variability in the rate of progression of aortic stenosis.

And that is my question. Do you have any data to show which kind of a patient will more quickly progress, who should be exposed to additional risk of revascularization plus aortic valve replacement, and in whom you could wait? For many years my policy was to replace the valve when it has more than 10 mm average gradient. But the situation is now changing with the off-pump coronary surgery: you can revascularize these patients but you cannot replace the valve when using this strategy.

So in which subgroup of patients you will now perform off-pump coronary surgery and in whom will you replace the valve and do revascularization the conventional way?

Dr Graham: That was certainly one of our aims was to try and identify the patients in whom we could then recommend should have the valve replacement. But on multivariate assessment in this group of patients in a retrospective setting, we were unable to identify that. Female patients did particularly poorly. And it’s hard to be entirely sure why that was. They had a higher proportion of rheumatic valves, but on multivariate analysis we could not tell you which ones to do. And as I say, I still get the strong feeling that it’s not so much that you make a rigid rule. Many of these patients will come back. And if you’re prepared to take on the redo in the 80-year-olds, good results can still be achieved. I think some of them just didn’t get a second bite at the cherry.

The other factor, of course, as you mentioned, is that the situation is changing and some evidence or suggestion that better control of cholesterol will limit the progression of the disease, particularly in degenerative valves. And it will be hard to make any rigid rule that will remain in the future.

Dr M. Antunes (Coimbra, Portugal): I think you cited me early in your talk, because I wrote an editorial in one of the Scientific Journals which was triggered by two related papers, one not published in the same issue. Most of the papers written recently deal with patients who came for a second operation. And we don’t know exactly what is the percentage of patients with moderate disease initially who later came for a reoperation. You give your figures, but figures vary widely.

I was interested to see that you had a fair number of repairs. One of the things that I have said is that in some occasions one should, perhaps, attempt to decalcify the evolution of the severe aortic valve disease, which requires replacement. You did mention in your presentation that most likely those were cases with regurgitation, but did you compare exactly regurgitation with stenosis? That’s the first point.

The second point is that there appears to be some evidence that we can retard the evolution of calcification of these valves by antiplatelet therapy, for example. Did you do that in your patients? The third point, and the burning question, are you going to change your policy now? Are you going to operate on these patients? Because one thing is to say "maybe we should" and another is to say "from now on we’re going to do it." Because that’s the message we’re all waiting for.

Dr Graham: Credit to the good results goes to Mr. O’Kane, senior author of the paper, who performed most of the operations. He was certainly very interested in valve repair and decalcification. One of my findings was that there was no patient, who had valve repair which was either resuspension or decalcification, alive without a reoperation by 8 years. Now, there’s still some of them did well, but they required something further to be done by 8 years or they died. That was the first question.

The second question. No, we didn’t have a policy. And as I say, this was over an 18-year time period starting 1978. I would love to see the results of a study starting now with the incidence of statins and better cholesterol control. I think it must have an effect in the future, but I can’t answer that.

And as I said, the third, as I indicated in one of the other questions, I would hesitate before I make any recommendation, a rigid rule, based on this data. The one message we have, the only strength I think really of our data is that we captured patients at the start with mild to moderate disease at the time of surgery. If they weren’t known to have mild to moderate disease at the time of the initial operation, we excluded them. So this is where you had some knowledge. And we followed those three.

And all I can say is they’ll be back. They’ll either come back and die without an operation or they’ll come back and need an operation. But I think the results for redo surgery in that category of patients are improving. And I wouldn’t hesitate. I’d say perhaps the next 75-year-old I see that has mild disease, they’ll get the graft. With a 60-year-old, I think it’s reasonable to leave it and the redo, but I can’t make a rigid rule.

Dr A. Youhana (Swansea, United Kingdom): We had a similar study when I was a trainee at the previous institution, at the London Chest Hospital, where the cardiologists looked at this group of patients. And they looked at a 10-year period. And there was an indicator that in a certain group of patients the progression of aortic stenosis was much faster than the rest. And that indicator was if there was calcification on the leaflets, then we found that majority of those patients came for valve replacement within 5 years. So I think calcification on the leaflets is one of the predictors of quick progression of disease there.

Dr Graham: I agree entirely.