Hybrid approach for complex coronary artery and valve disease: a clinical follow-up study

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Background. For patients suffering from complex coronary artery disease (CAD) with or without concomitant valve disease, no evidence is available in the current guidelines to propose a predefined treatment regimen. We sought to assess the clinical impact of an unconventional or extended definition of the hybrid approach that combines percutaneous coronary intervention (PCI) and cardiac surgery in subjects suffering from severe solitary CAD or combined with valve disease.

Methods and results. Between July 2002 and August 2004, 18 consecutive patients with complex CAD with or without significant valve disease who qualified for a hybrid approach were enrolled in a clinical follow-up study. Four patients eventually did not complete the proposed interventions. One patient refused treatment after inclusion, one patient died before treatment could be undertaken and two patients died after surgery but before PCI. In the other 14 cases combined treatment was technically successful. After a mean follow-up period of 15 ± 5 months two patients had died, one due to sudden cardiac death and one of a non-cardiac cause. No other major adverse clinical

events were reported. A marked increase in quality of life was reported in those alive.

Conclusion. Hybrid approach had a favourable long-term outcome in patients with complex cardiovascular disease undergoing successful treatment; however, this was observed at the expense of significant periprocedural mortality in these high-risk subjects. Therefore we believe that hybrid approaches may provide an alternative for selected cases. (*Neth Heart J* 2007;15:329-34.)

Keywords: cardiac surgery, angioplasty, complex cases, hybrid

Most patients with either coronary artery disease (CAD) or valve disease can be treated according to the current guidelines. The presence of comorbidity, previous revascularisation, complex CAD or valve disease spurs physicians to customise treatment to the individual patients. For a small subgroup of patients with complex CAD, a tailored invasive approach by both cardiac surgery and percutaneous coronary intervention (PCI) may be an alternative.¹⁻⁵ With the advent of the minimally invasive direct coronary artery bypass operation in 1995 this hybrid concept was discussed for the first time.^{6,7} The traditional strategy for revascularisation of two-vessel disease combined surgery for one vessel with PCI for the other.⁸ However, the background for this strategy was especially based on the inferior results of PCI in the proximal left anterior descending coronary artery at that time, i.e. 1997.⁸ To date, technological and pharmacological innovations, such as new catheters, stents and anti-thrombotic drugs, enlarge the role of PCI in the clinical management of complex CAD. Still, for some patients the hybrid approach could be implemented to reduce the overall risk of either surgery or PCI.⁹ Data on outcome of the hybrid approach are available but sparse. We therefore sought to assess the feasibility of hybrid approaches customised to the individual patient and the effect on long-term outcome and quality of life.

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Methods

Hybrid strategy

We extended the traditional description of the hybrid approach to all combined percutaneous and surgical modalities. In these cases the procedural risk of surgery or PCI is considered to be higher than the cumulative risks of both types of intervention. The decision to perform a hybrid approach was made by consensus agreement between the cardiologists and cardiac surgeons of the heart team. Clinical argumentation was based on present guidelines for revascularisation, the comorbidity EuroSCORE and local clinical expertise.¹⁰

Because of the small number of patients that fulfil the precedents for the hybrid approach and the heterogeneity of this population, we decided not to study the effectiveness in a randomised fashion. There is no guideline on which part of the intervention should be carried out first. The time between the two modalities varied according to the clinical presentation (stable or unstable) and optimisation of the patient's condition in the second stage (improvement of ventricular function and pacification or regeneration of the endothelium), ranging from one day to 12 weeks. Procedural success was defined by the achievement of a successful clinical result following both treatment modalities without major cardiac complications.

Subjects

Patients were assessed according to an all-comer design. The protocol was approved by the local medical ethics committee and all patients gave written informed consent.

Left ventricular dysfunction

Left ventricular ejection fraction (LVEF) as assessed by two-dimensional transthoracic echocardiography was performed by observers who were unaware of the outcome and clinical data.

Percutaneous coronary intervention technique

PCI was performed by a standard percutaneous technique through the femoral artery or other access site as a second alternative. Each operator followed the most simple and effective method, in a procedural time as short as reasonably achievable. After lesion complexity was angiographically categorised, a direct stenting technique was implemented whenever possible. Insertion of an intra-aortic balloon pump was based on haemodynamic measures.

Surgical approach

The surgical approach did not have any specific preprocedural measures. Both on- and off-pump techniques were used. Mechanical pretreatment by intra-aortic balloon pump was implemented 24 hours prior to surgery in subjects with severe left ventricular dysfunction.

Medical therapy

In all angioplasty cases, clopidogrel was given once in a loading dose of 300 mg, followed by a daily dose of 75 mg for one year. Furthermore, abciximab was administered in all percutaneous coronary intervention procedures in a weight-adjusted loading dose of 0.25 mg/kg, followed by a 24-hour continuous intravenous infusion of 0.125 µg/kg/min. When patients were on acenocoumarol or phenprocoumon, this was withheld two and four days before PCI, respectively, in elective procedures.

Follow-up

Data were obtained from clinical records and an electronic data system Infocop (Attachmate Corporation, Bellevue, Washington, USA). In addition, all patients also underwent a telephone follow-up interview to obtain their current clinical status. Key clinical variables such as cardiac symptoms, New York Heart Association (NYHA) class, hospital admissions, major adverse cardiac events (MACE), risk factors for heart disease and medication were registered. The presence of a first-degree relative with documented CAD before the age of 60 was defined as a positive family history. A current smoker was characterised by a chronic smoking habit of at least three cigarettes a day within the last three years. MACE was defined by the occurrence of all cardiac death, nonfatal myocardial infarction and coronary revascularisation. The causes and circumstances of all adverse cardiac events were registered. Deaths were classified as either cardiac or noncardiac. Follow-up was performed after 3, 12 and 24 months. Quality-of-life assessment was performed using the Nottingham Health Profile (NHP) I questionnaire for the items mobility (range 1-100).¹¹ For the assessment of pain a visual analogue scale was implemented, ranging from 0 (no pain) to 10 (worst possible pain). The assessment forms were completed by the patients and returned by mail.

Results

From July 2002 to August 2004, 18 patients with complex CAD such as with multivessel, left main CAD and valve disease qualified as candidates for a hybrid approach and were enrolled in a clinical follow-up study. The patient characteristics are shown in table 1. Four patients were female. Average age at the time of the first intervention was 65.2±10.2 years, ranging from 43 to 78 years. Medical history, in particular cardiac history, was comprehensive in all patients. One patient had been found unsuitable for surgery three years prior to the hybrid approach. This was based on technical limitations related to anatomical findings and an unacceptably high intervention risk. Seven patients had undergone prior cardiac surgery. Traditional cardiac risk factors were present in all patients. Both hypertension and hypercholesterolaemia were present in 16 patients (89%). Nine had a positive family history for CAD. Only two patients suffered from diabetes and seven subjects were current smokers.

Table 1. Patient characteristics of all patients with proposed hybrid approach (n=18).

Age, years $\pm$ SD	65.2 $\pm$ 10.2
Male/female	13/5
Ejection fraction, % $\pm$ SD	32 $\pm$ 9
NYHA classification $\pm$ SD	2.4 $\pm$ 0.3
Hypercholesterolaemia	16
Hypertension	16
Diabetes	2
Current smoking	7
Previous MI	8
Previous PCI	12
Previous CABG	7
One-vessel disease	1
Two-vessel disease	7
Three-vessel disease	10
Lesion in LAD	16
Lesion in CX	17
Lesion in RCA	11
Calcium antagonists	6
Beta-blockers	7
ACE inhibitors	14
Statins	10
Diuretics	5
Aspirin	12
Coumarins	1

Data are numbers unless otherwise indicated. NYHA=New York Heart Association, MI=myocardial infarction, PCI=percutaneous coronary intervention, CABG=coronary artery bypass grafting, LAD=left anterior descending coronary artery, CX=circumflex coronary artery, RCA=right coronary artery.

Lesion characteristics

At baseline, ten patients were suffering from three-vessel disease. The majority of patients had a lesion in the left anterior descending coronary artery. The only two patients without a lesion in the left anterior descending coronary artery had a significant stenosis in the main stem of the left coronary artery. Lesions of the circumflex coronary artery were present in 17 patients. One patient had a significant stenosis in a venous graft after previous cardiac surgery. Each individual patient had at least one type B2/C lesion.

Planned strategy

In 11 of the proposed hybrid revascularisation approaches, cardiac surgery was planned prior to PCI. In 16 cases the surgical intervention consisted of coronary artery bypass grafting. In 11 cases of coronary artery bypass grafting, the left internal mammary artery was to be used. One patient underwent aortic valve replacement and another had a mitral valve repair for papillary muscle rupture. In 11 subjects PCI was targeted at lesions in the circumflex coronary artery.

Table 2. Overview of performed interventions.

First intervention surgery/PCI	11/7
Therapy completed	14
Therapy uncompleted	4
- Refusal by patient	1
- Death before start	1
- Death after surgery and before PCI	2
Use of intra-aortic balloon pump	5
CABG	12
LIMA	8
LIMA + RIMA	1
Free radial	1
LIMA + free radial	1
Vein	1
Valve repair	2
Aortic valve	1
Mitral valve	1
PCI	14
Left main	1
LAD	1
CX	13
RCA	3
Venous graft	2

PCI=percutaneous coronary intervention, CABG=coronary artery bypass grafting, LIMA=left internal mammary artery, RIMA=right internal mammary artery, LAD=left anterior descending coronary artery, CX=circumflex coronary artery, RCA=right coronary artery.

Success rate

In 14 cases the proposed hybrid therapy was performed entirely as planned. One patient chose to withdraw from further treatment. There was one sudden death before the first intervention. Of the remaining patients two died after persistent postoperative bleeding as a result of severe underlying coagulopathy, despite appropriate treatment measures, with secondary cardiac arrest. In one patient who underwent cardiac surgery for the second step, the decision was made to change the target vessel according to operative anatomical findings. Table 2 shows all lesion and intervention characteristics.

Follow-up

The mean follow-up period was 15 $\pm$ 5 months. During this period two patients died. One patient suffered a cardiac arrest three months after the hybrid therapy and initial clinical improvement. The other was reported to have shown significant benefit from the hybrid therapy before his death caused by pancreatic malignancy, without symptoms at inclusion. Tables 3 and 4 show the follow-up results. During follow-up there were no readmissions for cardiac events or other MACE reported by patients. Furthermore, overall immobility and exercise tolerance improved (figure 1).

Table 3. Follow-up.

Follow-up time, months $\pm$ SD	15 $\pm$ 5
LVEF in patients completing therapy (n=14), % $\pm$ SD	41 $\pm$ 10
NYHA classification after completing therapy (n=14), $\pm$ SD	1.7 $\pm$ 0.6
MACE in patients completing therapy (n=14)	
- Cardiac death	1
- Noncardiac death	1
- Myocardial infarction	0
- Other readmission to hospital	0
MACE in patients not completing therapy (n=4)	
- Cardiac death before CABG	1
- Cardiac death after CABG, before PCI	2
- Noncardiac death	0
- Myocardial infarction	1
- Other readmission to hospital	1

Data are numbers unless otherwise indicated. LVEF=left ventricular ejection fraction, NYHA=New York Heart Association, MACE=major adverse cardiac events, PCI=percutaneous coronary intervention, CABG=coronary artery bypass grafting.

Table 4. Quality-of-life scores at baseline and follow-up.

Mobility at baseline in all patients*	49 $\pm$ 17
Mobility at baseline in patients completing therapy (n=14) *	47 $\pm$ 14
Pain at baseline in all patients **	4.0 $\pm$ 0.9
Pain at baseline in patients completing therapy (n=14)**	4.2 $\pm$ 0.8
Mobility in patients after completing therapy (n=14) *	77 $\pm$ 10
Pain in patients after completing therapy (n=14) **	2.2 $\pm$ 0.5

* scale 1-100 $\pm$ SD, ** scale 1-10 $\pm$ SD.

Discussion

In selected high-risk patients with ischaemic left ventricular dysfunction, a hybrid approach seems feasible although four of our 18 patients died. The results of this study should be interpreted from the perspective of the underlying complexity of the CAD or valve disease. One patient died before invasive treatment and two other patients died of persistent bleeding following first-step surgery. Both subjects were referred for surgery in an unstable condition. In these two patients it could be debated whether they would have benefited from a conservative noninvasive approach. Significant blood loss that required blood transfusions in 22 out of 24 patients was observed in a study of combined PCI and cardiac surgery for complex CAD and valve disease.^{12,13} In our study all subjects with successful interventions reported an improvement in their quality of life.

The results from other groups show that in their cases good to very favourable results were obtained. De Canniere and colleagues from Brussels, Belgium matched two groups of 20 patients and observed a shorter stay on the intensive care unit, fewer blood products transfused, less pain, better early quality of life, and faster return to work in patients treated with

the hybrid approach.¹⁴ After two years all patients were alive. In Katowice, Poland, Cisowski and colleagues showed that in 50 patients treated with a hybrid myocardial revascularisation procedure combining surgery of the LAD with interventional procedures for additional coronary lesions there were no major acute in-hospital cardiac events.¹⁵ Angiographic studies showed patent graft in all patients (100%) and long-term MACE was only 12%. Wittwer and colleagues performed a multicentre study in Germany and the Netherlands and found that hybrid treatment of 47 lesions in 35 patients was successful during hospital admission.¹⁶ Cohen and colleagues in Pittsburgh, USA found that after seven months none of 31 patients undergoing hybrid therapy had complaints of pain and only two adverse events occurred after PCI.¹⁷ Byrne and colleagues from Boston, USA treated 26 consecutive patients first with PCI followed by valve surgery.¹² Only one patient died due to the operation. Survival after five years was 44%. Stahl and colleagues from Cleveland Clinic, Florida, USA observed that after 11.7 months event-free survival was 87.1% in 54 consecutive patients.¹³ And Riess and colleagues from Hamburg, Germany followed their patients for approximately 100 weeks.¹⁸ One patient died within

Figure 1. Effect of hybrid approach on New York Heart Association (NYHA) class, left ventricular ejection fraction (LVEF), mobility and pain in patients undergoing successful interventions (n=14).

follow-up due to intracerebral haemorrhage. Presbitero and colleagues in Rozzano, Italy showed that in 12 patients the hybrid approach was related to in-hospital adverse events in three patients and one death occurred after approximately 160 days.¹⁹ As in our study, they also used a combination of PCI and cardiac surgery including both valve surgery and coronary bypass grafting. From Bristol, UK, Lloyd et al. reported on the results of 18 patients.²⁰ After 18 months these patients were alive and symptom-free. The first cases of a combination of robotic technology-enabled totally endoscopic coronary artery bypass grafting and PCI came from Farhat and colleagues of Aalst, Belgium.²¹ The same group found that this technique was feasible in 20 patients with multivessel disease and they observed no deaths, myocardial infarctions, or need for repeat revascularisations within 19±10 months follow-up.²² From Richmond, USA, Katz et al. reported that in a multicentre study of 27 patients, robotic intervention and PCI resulted in only one myocardial infarction and no deaths within three months.²³ Earlier concerns related to the limiting role of PCI on the long-term results of hybrid approaches might now have been addressed by the use of optimal hardware

new delivery techniques and drug-eluting stents. Vassiliades and colleagues from Atlanta, USA, showed that combined cardiac surgery and PCI with drug-eluting stents in 47 consecutive patients resulted in less than 10% repeat revascularisations after approximately seven months follow-up.²⁴ Recently, Us and colleagues from Istanbul, Turkey treated 17 patients (2% of all coronary cases) with off-pump CABG combined with PCI. First significant lesions in the circumflex and right coronary arteries were treated with PCI, followed by beating-heart CABG in the remaining obstructed vessels. After one year three patients had restenosis, which did not need any intervention.²⁵ In summary, the hybrid approach appears to generate less perioperative morbidity associated with minimal surgical aggression than classic multiple bypass grafting does. Especially subjects with severe concomitant disease may benefit from avoiding the hazards of cardiopulmonary bypass. Combination of new surgical and percutaneous techniques could result in the most favourable outcome.

Whether to perform PCI or (minimally invasive) surgery as the first step remains an issue that needs careful consideration in each individual patient.^{9,12}

Choosing PCI as the first option may be logical as an unsuccessful attempt may allow reconsideration of a complete surgical intervention and after PCI ventricular dysfunction could improve. However, adjunctive pharmacotherapy such as glycoprotein IIb/IIIa receptor inhibitors may delay surgery, especially in the presence of periprocedural adverse events. If the surgical step is applied first, it will be possible to assess patency of the grafts and anastomosis at the time of the planned PCI. In our study, the type of intervention for the first stage was chosen by mutual agreement that the first step was the safest accessible alternative or a predefined bridge to a high-risk second stage. It was assumed that the first-step strategy chosen would improve the second stage procedural outcome.

Several limitations have to be mentioned. This was a single-centre study of a heterogeneous group of patients with mixed CAD and valve disease and the observations can not easily be translated to other individuals.¹⁰ However, we think that our results and observations of other groups can guide treatment of new cases with complex CAD or valve disease. We observed more complications than reported by other groups. Possibly our results reflect daily practice rather than the investigation of a new approach. New minimally invasive surgical techniques such as robotic technology-enabled totally endoscopic coronary artery bypass grafting were not used in this study.

In conclusion, our findings suggest that hybrid approaches are feasible in individual complex cases of CAD or valve disease. ■

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