Five-year follow-up of drug-eluting stents implantation vs minimally invasive direct coronary artery bypass for left anterior descending artery disease: a propensity score analysis

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Abstract

OBJECTIVES: The spread of drug-eluting stents (DES) has reduced the incidence of early restenosis following percutaneous coronary interventions (PCI). Meanwhile, development of minimally invasive coronary artery bypass surgery (MIDCAB) has offered a valuable alternative to conventional sternotomy with preservation of the benefit of the internal mammary artery use. Therefore, the revascularization of the left anterior descending (LAD) artery is suitable for both techniques. However, few data with long-term comparison of these two techniques exist.

METHODS: Prospective data were collected for 456 patients undergoing isolated LAD revascularization between 1997 and 2011. Two hundred and sixty patients were treated with MIDCAB and 196 with first-generation DES implantation. A propensity score model was created to adjust for 19 relevant confounding variables. Primary and secondary end-points were, respectively, 5-year survival and freedom from major adverse cerebro-cardiovascular events (MACCE).

RESULTS: Both groups were similar in age, EuroSCORE and mean duration of follow-up. Five-year survival was similar after MIDCAB or DES (hazard ratio (HR): 0.95; \( P = 0.89 \)). Freedom from MACCE was significantly in favour of the MIDCAB group (HR: 0.32, \( P < 0.0001 \)), mainly triggered by high subsequent need for revascularization of the targeted vessel in the DES group (HR: 0.17, \( P < 0.0001 \)).

CONCLUSIONS: MIDCAB and DES implantation showed similar rates of survival but despite an expected lower rate of reintervention on the targeted vessel with DES use, a highly significant higher MACCE rate was observed in the PCI group at 5-year follow-up.

Keywords: Surgery • Bypass • Coronary disease • Internal thoracic artery • Stent

INTRODUCTION

Coronary artery bypass surgery (CABG) and percutaneous coronary interventions (PCI) have experienced major improvements in the last few years. Development of minimally invasive direct coronary artery bypass (MIDCAB) for the treatment of left anterior descending (LAD) coronary artery disease has allowed an approach less invasive than conventional sternotomy procedure. Meanwhile, recent spreading of drug-eluting stents (DES) has led to the hope of reduced incidence of subsequent restenosis after PCI. However, few studies compared those two techniques. A meta-analysis of MIDCAB [1] procedures has shown some disappointing patency rates of the left internal mammary artery. Other studies have raised [2] some doubts concerning promises of sustained advantages of DES when compared with bare metal stents (BMS). Moreover, lack of long-term data does not allow definite validation of the potential advantages of one of those two techniques. Therefore, we conducted a multicentre study with prospective collection of data from all patients undergoing single-vessel LAD revascularization with those two techniques in our institutions and a propensity score model was created to adjust for 19 confounding variables. Primary and secondary end-points were, respectively, 5-year survival and freedom from major adverse cerebro-cardiovascular events (MACCE).

METHODS

Prospective data from two cardiac centres were collected to obtain two groups of patients who benefited from single-vessel
LAD revascularization. Group 1 included 260 consecutive patients operated by the MIDCAB technique (from April 1997 to February 2011). Group 2 included 196 consecutive patients who benefited from PCI with DES (from June 2002 to October 2005). The inclusion and the exclusion criteria are defined in Table 1. Emergent patients who underwent rescue PTCA because of cardiogenic shock during this period were excluded (10 patients), as were also excluded patients who underwent LIMA to LAD by sternotomy because of preoperative severe instability (3 patients).

Patient characteristics are listed in Table 2 and angiographic characteristics in Table 3. A larger proportion of diabetic patients were found in the DES group. Also, more patients with previous or recent myocardial infarction were found in the DES group but the proportion of unstable patients was not statistically different between the two groups. More patients with peripheral vascular disease were present in the MIDCAB group. A similar proportion of patients had a past history of PCI of the LAD. Risk factors were evaluated using the EuroSCORE additive model and predicted mortality was similar between the two groups (3.27 vs 3.26, P = 0.8). Angiographic characteristics of the LAD lesions differed among both groups with more patients with an occlusion of the LAD or with involvement of a major diagonal branch being found in the MIDCAB group while more mid-LAD lesions were encountered in the DES group.

In addition to the IMA-to-LAD anastomosis, 87 patients received a sequential graft to the diagonal branch and 1 patient to two diagonal branches. Three hundred and forty-nine anastomoses were thus performed in the LAD territory (1.34 per patient) in the MIDCAB group. In the DES group, 219 sites were stented including 196 procedures on the LAD, 10 procedures on diagonal branches and 13 procedures on a second site on the LAD.

Operative technique

In the MIDCAB group, the left internal mammary artery was completely harvested through a true thoracoscopic approach without help of robotics. A 5-cm incision was secondarily made in the fourth intercostal space, and the chest was opened through a soft tissue retractor (Edwards Lifesciences, Irvine, CA, USA) without any rib retraction to minimize postoperative pain. Anastomosis between the internal mammary artery and the LAD was performed through this incision on the beating heart using endoscopic stabilization devices. Complex procedures included sequential grafting on the diagonal branch and the LAD in 87 patients. In the DES group, paclitaxel-eluting stents were used in 59% of the patients and sirolimus-eluting stents in 41%. Complex procedures included diagonal branch PCI in 10 patients and second-site LAD PCI in 13 patients.

Clinical follow-up

Patients were controlled at 3 months after the procedure and then yearly thereafter. We used the anniversary method for the follow-up. Records from subsequent hospitalizations were obtained while patients underwent a systematic stress test on a cyclo-ergometer performed under the supervision of their referring cardiologist whenever technically feasible. General practitioners were directly contacted by phone call to obtain last clinical evaluation or eventual cause of death of the patients. All the patients were followed up to the latest contact information available.

Myocardial infarction was defined as the apparition of a new Q-wave, a rise of >10 ng/ml of troponin in the early postoperative period or any episode of chest pain with typical rise and fall of cardiac enzymes thereafter.

### Table 1: Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-vessel LAD disease</td>
<td>Two- to three-vessel disease</td>
</tr>
<tr>
<td>Significant LAD disease</td>
<td>Emergent procedure</td>
</tr>
</tbody>
</table>

LAD: left anterior descending.

### Table 2: Patients characteristics

<table>
<thead>
<tr>
<th></th>
<th>MIDCABG</th>
<th>DES</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>63.4 ±12</td>
<td>62.4 ±12</td>
<td>0.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>57 (155)</td>
<td>67 (131)</td>
<td>0.1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21 (56)</td>
<td>60 (117)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking habits</td>
<td>54 (141)</td>
<td>46 (90)</td>
<td>0.1</td>
</tr>
<tr>
<td>Family history</td>
<td>47 (122)</td>
<td>48 (95)</td>
<td>0.8</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>71 (186)</td>
<td>70 (137)</td>
<td>0.7</td>
</tr>
<tr>
<td>EF &lt;30%</td>
<td>3 (8)</td>
<td>1 (3)</td>
<td>0.7</td>
</tr>
<tr>
<td>EF 30–50%</td>
<td>12 (32)</td>
<td>10 (19)</td>
<td>0.4</td>
</tr>
<tr>
<td>EF &gt;50%</td>
<td>85 (220)</td>
<td>90 (174)</td>
<td>0.2</td>
</tr>
<tr>
<td>Mean EuroSCORE</td>
<td>3.27</td>
<td>3.26</td>
<td>0.4</td>
</tr>
</tbody>
</table>

### Table 3: Angiographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>MIDCAB, % (n)</th>
<th>DES, % (n)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal LAD</td>
<td>24 (63)</td>
<td>33 (65)</td>
<td>0.05</td>
</tr>
<tr>
<td>Mid- or distal LAD</td>
<td>28 (74)</td>
<td>59 (115)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diagonal-LAD bifurcation</td>
<td>33 (88)</td>
<td>5 (10)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Occluded LAD</td>
<td>13 (35)</td>
<td>3 (6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Previous PCI of the LAD</td>
<td>11 (31)</td>
<td>12 (23)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

LAD: left anterior descending; PCI: percutaneous coronary intervention.
Statistical analysis

Data are presented as the mean ± standard deviation. Chi-square test was used to compare proportions. Student’s t-test for independent samples was used to compare means.

To deal with non-comparability of groups of patients receiving either MIDCAB or DES in this observational study, we used a two-step analytical strategy.

(i) Univariate analyses were performed for the analysis of late mortality (Table 4) and cardiac events. Survival and event-free survival curves were estimated using the Kaplan–Meier method and differences between groups were compared using the log-rank test. Calculated P-values of <0.05 were considered significant.

(ii) We then calculated a propensity score to model the probability of experiencing MIDCABG vs DES in order to create relatively homogeneous subgroups of patients. Subgroups have a similar probability of getting MIDCAB and similar clinical characteristics. Stepwise logistic regression was performed to calculate the propensity score, using preoperative factors: age, male sex, history of infarction, hypertension, diabetes mellitus, hyperlipidaemia, history of smoking, family history, chronic obstructive pulmonary disease, chronic renal failure (preoperative creatinine >2 mg/dl), peripheral vascular disease and status of the patient, presence of a long LAD lesion, proximal LAD lesion, bifurcation lesion, LAD occlusion and previous LAD PTCA. Model fit was assessed with the likelihood ratio statistic and the Hosmer–Lemeshow statistic. The C-statistic was calculated to assess the discriminatory ability of the model. Owing to sample limitation and to ensure adequate fit, the final logistic regression model was parsimonious and included six variables (age, gender, current smoking, diabetes mellitus, peripheral vascular disease and instable angina).

Five strata corresponding to the quintiles of the distribution of propensity score were created as described by Blackstone [3].

Cox regression, stratified for the quintiles of the propensity score, was then used to estimate the hazard ratio of MIDCAB vs DES. The same models were used to output adjusted survival curves. However, for the sake of parsimony, curves displayed in this article are adjusted for the propensity score with no stratification (Fig. 1). This simplification has no incidence on the interpretation of results.

Data were analysed using the PHREG procedure of SAS (9.3 release). SPSS Statistics 20 (IBM Corporation, 2011) for Windows (Microsoft Corp., Redmond, WA, USA) was used to output graphics. In-hospital mortality was included in the survival analysis. Cardiac death included in-hospital mortality, cardiogenic death and sudden death or death for unexplained cause.

RESULTS

Hospital mortality

There were no differences in hospital mortality between the two groups (MIDCABG: 0.4% vs DES 1%, P = 0.7). In the MIDCAB group, an 80-year old patient with 30% preoperative ejection fraction developed postoperative low cardiac output and died on day 4 from intestinal ischaemia. In the DES group, 2 patients died from cerebral haemorrhagic complications.

Hospital morbidity

Five patients (1 in the MIDCAB group and 4 in the DES group) developed postoperative infarction in the LAD territory during the hospital stay but none of them developed new Q waves. One patient in the MIDCAB group was reoperated after 24 h for persisting ischaemia caused by a kinking of a sequential graft between the diagonal branch and the LAD.

Two patients in the MIDCAB group suffered from a transient ischaemic cerebrovascular accident attributed to atrial fibrillation on the 7th and the 14th postoperative days.

No patient developed cerebrovascular accident in the DES group but cerebral haemorrhages occurred in 2 patients who died during hospital stay on the 4th and the 21st days.

Late clinical outcome

The mean follow-up was 70.6 months (range: 3–183 months) and was complete for 99.6% of the MIDCAB group. For the DES group, the mean follow-up was 67.5 months (range: 27–100 months) and was complete for 98.1% of the patients.

(i) First-step analysis: univariate analysis:

Major cardiovascular and cerebrovascular events occurred in 40.1% of DES patients and in 14.2% of MIDCAB patients over the follow-up period. Freedom from MACCE at 5 years was significantly higher in MIDCAB (85 ± 4%) vs DES (60 ± 6%) patients (P < 0.0001). Overall 5-year survival was similar after MIDCAB and after DES (92 ± 3%) and (92 ± 3%), respectively (P = 0.6). During follow-up, 6 patients in the MIDCAB group died from cardiovascular cause: 1 patient from persistent cardiac

Table 4: Cause of late mortality

<table>
<thead>
<tr>
<th>Causes of late deaths</th>
<th>MIDCAB 27 patients (n)</th>
<th>DES 23 patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarct</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Colic haemorrhage</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sudden death</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Psoas haemorrhage</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Suicide</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Alzheimer disease</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cachexia</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

Five strata corresponding to the quintiles of the distribution of propensity score were created as described by Blackstone [3].
Figure 1: Propensity score-adjusted survival curves output by Cox regression. (A) Survival, (B) freedom from MACCE, (C) freedom from all PCI, (D) freedom from target vessels revascularization, (E) freedom from stroke, (F) freedom from none target vessels revascularization.
insufficiency, 1 from an infarction, 2 from haemorrhagic complications non-related to the operation, 1 from CVA and 1 from sudden death. In the DES group, 7 patients died from cardiovascular cause: 2 patients died from cerebral haemorrhage, 2 from CVA, 1 from an inferior infarction, 1 from aortic dissection and 1 from cardiac insufficiency. Other causes of death are listed in Table 3. Four patients of the MIDCAB group and 3 of the DES group suffered from stroke during the follow-up period. Stress test was done in 216 patients (83%) in the MIDCAB group and in 80% of the DES group. Angiographic patency of the LIMA was attested in 75.4% of the patients either by conventional coronary angiography (24%) or by fast scan computed tomography (76%) in the MIDCAB group. Conventional angiographic controls were obtained in 57.7% of patients of the DES group, mostly triggered by suspicion of recurrent ischaemia.

Ten patients (3.85%) in the MIDCAB group needed subsequent revascularization on the target vessel during the 5-year follow-up (PCI in 8 patients, redo surgery in 2 patients). The majority of these TVR (7 of 10) occurred during the first 12 months after the intervention and were triggered by a stenosis of the anastomosis on the LAD in 3 patients and by an occlusion of the segment of the LIMA between the diagonal branch and the LAD in sequential grafts in 4 patients. One internal mammary artery was found to be non-functional after 2 years, 1 was found to be occluded after 65 months and 1 patient needed PTCA of a diagonal artery after 4 years. In the DES group, 42 patients (21.4%; P < 0.001 vs MIDCAB group) needed additive procedures on the target vessel mainly by secondary PCI. Causes of recurrences were in-stent or in-segment restenosis for the huge majority of the patients, while acute stent thrombosis occurred in 4 patients. Those secondary revascularization procedures were distributed during the 67 follow-up months. Non-target vessel subsequent PCI were performed in 30 patients of the MIDCAB group and in 37 patients of the DES group.

In the diabetic patients, the percentages of TVR in the PCI group as well as in the MIDCAB group were similar compared with non-diabetic patients (MIDCAB: 3.5 vs 3.4%, P = 0.8; DES 21 vs 25%, P = 0.6).

(ii) Second-step analysis: Cox proportional hazard regression analysis using propensity score strata:

MIDCABG did not significantly influence the overall survival (HR: 0.88, 95% CI 0.13–5.5, P = 0.89) as well as the NTVR rate (HR: 0.64, 95% CI 0.38–1.09, P = 0.1) and the stroke rate (HR: 0.56, 95% CI 0.15–2.1, P = 0.39). Unlike, MIDCABG did significantly influence the MACCE rate (HR: 0.32, 95% CI 0.2–0.5, P < 0.0001) as well as the overall PCI rate (HR: 0.37, 95% CI 0.23–0.57, P < 0.0001) and TVR rate (HR: 0.17, 95% CI 0.08–0.35, P < 0.0001). The number of infarction events was too small to calculate any statistics or draw any conclusion.

**DISCUSSION**

The present study shows that in patients with isolated LAD stenosis, revascularization with either DES implantation or MIDCAB is associated with a similarly low mortality rate after 5 years. However, despite the proven efficacy of DES to reduce restenosis [4], reinterventions remain significantly higher and continuous over time after PCI.

The selection of the appropriate LAD revascularization procedure is usually guided by the angiographic characteristics of the stenosis (ostial stenosis, complex anatomic lesion, bifurcation, LAD occlusions), but also by the respective expertise of the interventional and surgical teams and preferences of the patient, once given his/her informed consent. Recent technical progresses in stents as well as in surgical approach techniques are additional factors that can influence the decision. However, few data comparing the most recent techniques [5–7] are currently available, and lack of long-term follow-up remains a crucial point of these studies [8]. Moreover, even if target vessel revascularization is usually in favour of MIDCAB, these trials have usually shown similar survival outcomes in patients assigned to MIDCAB or to PCI and expected diminution of restenosis with DES [9] has led to even more widespread diffusion of percutaneous techniques.

The present study compares two consecutive groups of patients treated in our institution and representing our daily practice. In-hospital and 5-year mortality were similar between the two groups.

Some preoperative variables differ between the two groups (reoperation, renal insufficiency, recent infarction). Even if those small groups of patients were more preferentially treated with PCI, propensity score analysis did not show any significant influence of those variables on long-term results.

**Angiographic characteristics**

As this study is not randomized, patients sent to surgery are in many ways different from patients that are usually considered for PCI especially in terms of anatomic characteristics of the stenosis. Recurrence of stenosis after PCI of bifurcations is known to be more common than with isolated lesions but sequential grafting of the diagonal branch and of the LAD is also more technically challenging during MIDCAB procedures. Occluded LAD are more often found in the MIDCAB group and failure of des- occlusion is frequently encountered with chronic or more severe disease of the vessel. Even if these facts should be to the detriment of MIDCAB, patency results remain highly in favour of surgery.

**Anticoagulation**

The number of neurological complications was also similar between the two groups but it must be emphasized that the 3 patients in the DES group who underwent cerebral haemorrhage died in the 24 h following appearance of this pathology; on the other hand, the stent thromboses that occurred after interruption of antiplatelet medications in 4 patients underline the strategic importance of anticoagulation management of those patients. Recommendations in antiplatelet therapy associated with DES use have been modified over time, and management of anticoagulation remains of major importance in the occurrence of DES-associated complications.
Risk factors

A higher incidence of diabetic patients was found in the DES group, mainly due to the Belgian government policy of reimbursement of these stents. While the incidence of TVR in our study was perfectly similar among diabetic or non-diabetic patients in both groups, a propensity score analysis was conducted to validate our results; same results were obtained for peripheral vascular disease.

Patency rate

Despite the proven efficacy of DES to reduce restenosis and reintervention rates, target vessel-related recurrence of angina was significantly higher in the DES group than in the MIDCAB group, even without taking into account the secondary stent occlusions that occurred in patients who stopped their antiplatelet medications. In-stent or in-segment restenosis rate reached 10% at 2 years, which is in accordance with published data [10, 11]. Moreover, sustained occurrence of TVR was observed even after 5 years. These stents have now been replaced by new-era devices using different coating surfaces; long-term follow-up will be absolutely mandatory to find the place of these new devices between BMS and first-generation DES.

On the other hand, left internal mammary artery patency achieved in this study equally compared with the immediate postoperative expected permeability of 97–98% reported in large angiographic studies of patients operated on-pump by sternotomy [12, 13].

As in the Syntax trial [14], large numbers of patients and long-term follow-up are usually necessary to show statistically significant differences in survival between surgery and PCI. Anyway, quality of life of the patients is also triggered by freedom from iterative PCI procedures, subsequent hospital stays or necessity to maintain long-time hazardous anticoagulation regimen. More than 30% of the DES patients needing subsequent PCI underwent 2, 3 or 4 additional procedures. Unpredictable MID-term stent thromboses or acute haemorrhagic events depicted in this study also underline a possible continuous exposure to life-threatening risks in the DES group.

Study limitations

This multicentre study compared the daily practice of two cardiac units using recent technologies in two parallel groups of consecutive patients. Despite propensity score analysis used to avoid biases related to preoperative risk factors, the two groups of patients had obviously different angiographic lesion characteristics. As this study was not a randomized study, patients were always referred to surgery as they presented more complex lesions involving a risk of technical failure during PCI, an higher expected incidence of restenosis or were immediate or secondary failures of PCI.

First generations of DES are nowadays obsolete and technical improvements have been made to achieve lower secondary complications rate especially in terms of late thrombosis; further studies will have to prove efficacy and security of those new devices.

CONCLUSIONS

The present study found a higher freedom from target vessel revascularization in the MIDCAB group when compared with the DES group for the treatment of isolated LAD disease. While late patency of internal mammary anastomoses remains perfectly stable, late results of first-generation DES have been disappointing; occurrence of complications related to unexpected stent thrombosis, late recurrence of restenosis or anticoagulation management has led to virtual withdrawal of these stents. Further studies with long-term follow-up will be mandatory to ensure clinical efficacy of next-generation devices.

Conflict of interest: none declared.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr P. Sergeant (Leuven, Belgium): The UCL group have created an interesting manuscript on a rather long follow-up of single vessel disease therapy. They have used propensity scoring to correct for variability. Propensity scoring transforms variability into a continuous number. So this process was made somewhat difficult since most of their variables are nominal variables and not continuous, and it is difficult to transform nominal variables into a continuous number. They reach just borderline statistical significance and saturation of the model in having an area under the curve of 0.8. This is the minimum criterion for saturation. They then used one of the three acceptable methods of propensity scoring, namely strata matching or group matching. So they have definitely tried to correct for variability and simulate a randomized controlled trial. But the problem is that in multivariable analysis and to be able to correct for variability, it demands sufficient events.

So my question concerns four observations of non-significant differences after this process of correction. The first one is the overall survival, the second one is the infarction rate, the third one is stroke, and the fourth one is non-target vessel revascularization. Could it be that the data set is not powered enough for significance and can you criticize each of the four events?

Dr Glineur: Yes, we had four follow-up end points that were not significant, and let’s look at them. First, we had three unbiased variables, the survival, the stroke rate, and the infarction rate. If we look at the survival, we had a hazard ratio of 0.88, so there was a 12% added value of the MIDCAB compared to the drug-eluting stents, and the P value was 0.2. So if we wanted to have a significant impact on this follow-up variable, we should have included at least 10,000 patients. So, yes, of course, it is underpowered. Concerning the infarction rate, unfortunately, and you are completely right, the event rate was very small. So, once again, it could not be powered enough.

Concerning the stroke rate, and I definitely agree with you, the hazard ratio was 0.56, so there was 44% benefit for the MIDCAB, and the P value was 0.08, meaning that if we had added just, let’s say, 50 patients, I definitely think that we would have a significant benefit for the MIDCAB.

Now, for the last follow-up variable, the non-target vessel revascularization, this is classically what we could call a biased variable, because it all depends on the medical judgement of the physician and it is just human decision. And so for this variable I think it is very difficult to conclude anything, because it would be different from one physician to another.

Dr F. Mohr (Leipzig, Germany): You mentioned stent occlusions several times. Do you have a number for stent occlusions, how often and when did they occur, and did they occur with myocardial infarction in all cases?

Dr Glineur: We thought, as described in the literature, when we reviewed the follow-up that we would have mainly stent occlusion within the first year, but we saw that stent occlusion also happened after two, three and four and five years. So definitely all these patients have to be kept under dual antiplatelet therapy for the long term, and when it happened, of course, it was an infarction, yes.

Dr Mohr: And what was the rate of stent occlusion? I didn’t see that number.

Dr Glineur: I would have to read the manuscript. I don’t remember exactly the stent occlusion rate versus the restenosis rate.

Dr Mohr: Another question. If you are looking to other studies comparing, can we really expect a mortality difference in one-vessel disease?

Dr Glineur: Well, that was Paul’s question. I think if you want to have a significant difference, you have to enrol 10,000 to 20,000 patients.

Dr M. Zembala (Zabrze, Poland): From this experience with long terms, what is your opinion about hybrid, especially in two-vessel disease; where is the place - having this experience - for surgeons?

Dr Glineur: Well, I definitely think that the hybrid procedure could be a possibility, but for me, the use of two mammaries (and we discussed that yesterday in the postgraduate course), will always be better than drug-eluting stents targeted to the left system. Now, concerning the right coronary system, yes, I don’t see any problem of stenting versus the vein on the right. So for the right coronary system, I have no problem about that, but for the left coronary system, I think that two mammaries will always be better than a stent.

Dr Zembala: That means you see a place for the right?

Dr Glineur: Yes.

Dr P.Y. Etienne (Namur-Bouge, Belgium): Just to give a response to Professor Mohr, six patients in the follow-up group developed a stent thrombosis, half of them after discontinuation of the antiplatelet therapy, but on the other hand, three patients died from cerebral haemorrhage being on Plavix.

Dr Sergeant: In multivariable analysis there is a rule of thumb that you need 15 events for each variable you bring into the final model. So if you want to correct for three or four different variables and then bring in your analysis variables, you need at least 45, 50, 60 events. So with five stent events, you cannot really do a multivariable analysis. Some of the event rates become nearly at random.