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# Coronary revascularisation in diabetics: surgical aspects

## Summary

Recent advances in percutaneous coronary intervention (PCI) techniques and progress made with drug-eluted stents as well as with post-interventional anti-thrombotic management have increased the number of patients with three vessel coronary artery disease who are nowadays initially treated interventionally. However, coronary artery bypass grafting (CABG) has proven to be as effective as percutaneous methods, although these approaches are selected for different states of the disease. This is especially true for diabetic patients who generally demonstrate a greater mid- to long-term benefit following CABG than PCI. Nevertheless, surgery should also integrate the most recent advances like total arterial revascularisation and off-pump techniques in selected cases.

*Key words: percutaneous coronary intervention; drug-eluted stents; coronary artery bypass grafting; diabetes mellitus; arterial revascularisation; off-pump techniques; coronary artery disease*

## Zusammenfassung

Die Fortschritte, die durch interventionelle Techniken zur Dilatation der Koronararterien erzielt worden sind – mit beschichteten Stents und neuen antithrombotischen Medikamenten – haben zu einer Zunahme in der Behandlung von Patienten mit koronarer Dreifässerkrankung geführt; solche Patienten werden nicht selten initial nur kathetertechnisch angegangen. Nichtsdestotrotz ist die chirurgische Revaskularisation mindestens so effizient wie die perkutanen Verfahren, obwohl die Chirurgie meistens bei komplexeren Patienten zum tragen kommt. Dies gilt speziell für diabetische Patienten, die in der Regel mittel- und langfristig mehr von der Chirurgie als von den perkutanen Interventionen profitieren können. Die chirurgische Revaskularisation muss

aber zwingend die modernsten Verfahren integrieren, wie z.B. die Verwendung von multiplen arteriellen Bypass-Conduits und die Operationstechnik am schlagenden Herzen bei ausgewählten Fällen.

*Key words: perkutane koronare Intervention; beschichteter Stent; aortokoronare Bypass-Operation; Diabetes mellitus; arterielle Revaskularisation; Off-pump-Technik; koronare Herzkrankheit*

## Introduction

Recent medicamentous and technological advances in the field of cardiology have made percutaneous coronary revascularisation strategies increasingly performed even in patients with multivessel disease [1, 2]. Ongoing trials with drug-eluted stents and aggressive anti-thrombotic treatment show that the rate of restenosis may be favourably influenced, therefore decreasing the necessity for repeated revascularisation in these patients [3, 4]. However, in diabetic patients, there has been general agreement so far, that coronary artery bypass grafting (CABG) using arterial conduits should be the preferred initial revascularisation method; this is specially true for patients with left main involvement, coronary three vessel disease, reduced LV-function and diffuse coronary involvement.

Since the prevalence of diabetes mellitus in the western population seems to increase and accounts nowadays for 6 to 7% of the population, CABG surgery may still play an important role in the treatment of coronary ar-

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tery disease (CAD) in the next years. It is well known that the incidence of CAD is higher in patients with pathologic glucose tolerance and cardiovascular mortality is already more frequent in those individuals with asymptomatic hyperglycaemia than in normal subjects [5–7]. Finally, diabetic patients have a particularly high risk of cardiovascular mortality since diabetes alone is a major risk factor – even after adjustment of all other cardiovascular risk factors, because diabetics may suffer from accelerated atherosclerosis and a high proportion demonstrates an extensive form of CAD with diffuse peripheral involvement of the coronary circulation.

In most recent years, diabetes accounted for 15 to 25% of patients referred for coronary revascularisation in our institution and was one of the cardiovascular risk factor in up to 30% of the patients with acute coronary syndromes. In the actual population scheduled for CABG, diabetic patients constitute a substantial group which may be challenging from the technical point of view [8–10].

### Characteristics of coronary heart disease (CHD) in diabetic patients

Clinical signs of coronary insufficiency may be less apparent or very atypical in diabetic patients: angina pectoris and myocardial infarction may present as dyspnea, congestive heart failure, arrhythmias or sudden cardiac death [11]. Patients suffering from diabetes have a higher mortality rate following myocardial infarction than those without diabetes [11–13]. Reasons for this may be multiple: changes in the vascular endothelium under elevated blood glucose induce an impairment of the endothelium-dependent vasodilatation [14–16], possibly due to a reduction of the synthesis or release of nitric oxide [17]. Other causes include accelerated inactivation of nitric oxide by high levels of free radicals [18], release of potent vasoconstrictors [19], increased activation of protein kinase C [20], and decrease expression of inhibitory proteins causing abnormalities in signal transduction [21]. All these mechanisms may be at least partially responsible for the observed reduced coronary flow reserve in diabetics and the diminished microvascular dilatation. Another major difference between diabetics and non-diabetic patients is the significantly poorer development of collateral vessels in the coronary circulation of diabetic patients [22].

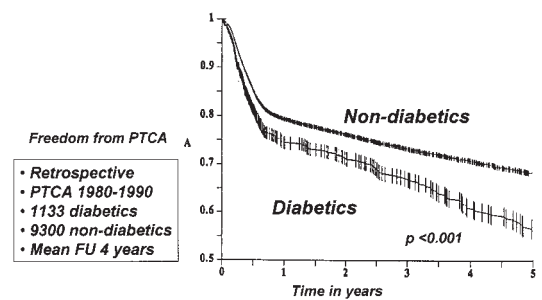


Figure 1

Diabetes and PTCA: repeat coronary intervention.

Figure 1–4 reprinted from: Stein B, Weintraub WS, Gebhart S, et al. Influence of diabetes mellitus on early and late outcome after percutaneous transluminal coronary angioplasty. *Circulation* 1995;91:979–89. With kind permission.

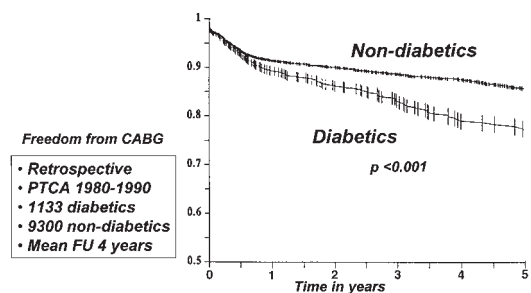


Figure 2

Diabetes and PTCA: Subsequent CABG.

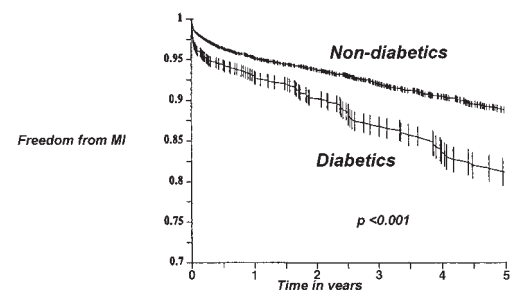


Figure 3

Diabetes and PTCA: freedom from myocardial Infarction.

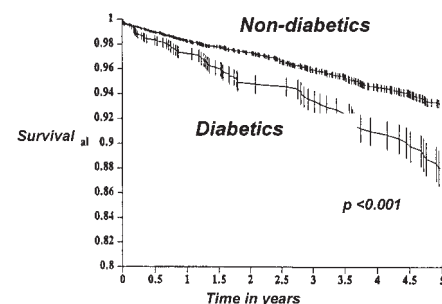


Figure 4

Diabetes and PTCA: survival.

### Options for myocardial revascularisation

It has been demonstrated by several trials that percutaneous transluminal coronary angioplasty (PTCA) in diabetic patients is followed by a higher rate of subsequent revascularisation than in non-diabetics because the rate of restenosis is higher [23, 24]. In the long-term, diabetics have a higher attrition rate both after PTCA and coronary stenting. Stein and co-authors demonstrated that following PTCA, diabetic patients had a higher rate of subsequent myocardial infarction as well as a higher rate of CABG than non-diabetics. As expected, overall survival was better in non-diabetic patients (fig. 1–4) [25].

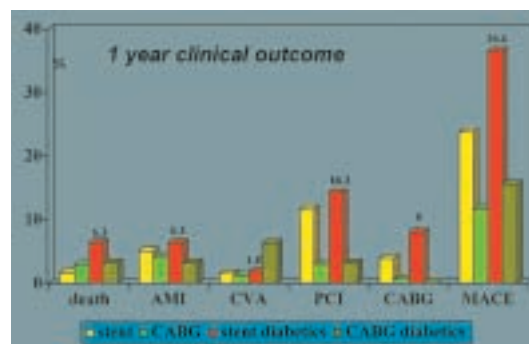
Within the global CABG population, diabetic patients demonstrated the following particular characteristics: they are older, the proportion of females is higher, and the coronary circulation is more severely involved: a higher number of stenoses, a higher rate of prior myocardial infarction, a higher incidence of decreased left ventricular contractility and their overall cardiovascular risk profile is significantly worse than in non-diabetic patients [26].

Several previously published trials and meta-analyses of randomized studies of PTCA versus CABG have suggested a lower death/myocardial infarction rate in patients randomised to CABG with an increased rate of repeat revascularisation procedures in patients treated with PTCA. One important concern about these published trials is the selection procedure. Due to restrictive inclusion criteria, the number of patients enrolled in the trials following screening was rather low and therefore, the population analysed in those trials may not be representative of the overall population requiring PCI or CABG in the daily practice. In a recently published “real-world” analysis, Brener and co-authors analysed more than 6000 patients who received myocardial revascularisation. They used propensity score analysis to adjust for differences in baseline characteristics and risk profile between patients with multivessel CAD. Following risk adjustment, a significantly higher mortality rate was observed in patients treated with PCI (adjusted hazard ration 2.1, 95% confidence interval 1.7–2.6;  $p < 0.0001$ ). The rate of complete revascularisation was also higher in the CABG group than in the PCI group. The increased risk of death was particularly pronounced in diabetic patients who underwent PCI [27].

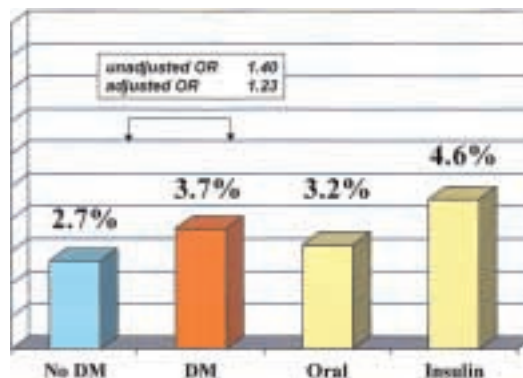
### Special surgical aspects

Many trials have addressed the question of which type of revascularisation will provide the best short- and long-term results. One of the study with the highest citation index is the Bypass Angioplasty Revascularisation Investigation (BARI), which aimed to compare the efficacy of PTCA and CABG in patients with multivessel CAD [2, 23]. No difference was found in the five-year survival rate between both treatment options but in diabetic patients, early and late mortality was significantly smaller following CABG than PTCA (19% versus 35%;  $p = 0.003$ ) [28]. Subsequent studies demonstrated that this initial advantage went even stronger in the long-term follow-up [29]. Most recently, a similar advantage of CABG over PTCA in diabetic patients was shown in the Arterial Revascularisation Therapy Study (ARTS trial) [1, 30]. The most important characteristics of the results of the ARTS trial are summarised on figure 5.

Recent advances in the percutaneous approach with optimised anti-thrombotic strate-



**Figure 5**  
Diabetics in the ARTS trial [30].  
MACE = major advance cardiac events  
AMI = acute myocardial infarction  
CVA = cerebrovascular accident  
PCI = percutaneous coronary intervention  
CABG = coronary artery bypass grafting



**Figure 6**  
CABG: diabetes and 30-day mortality [33].

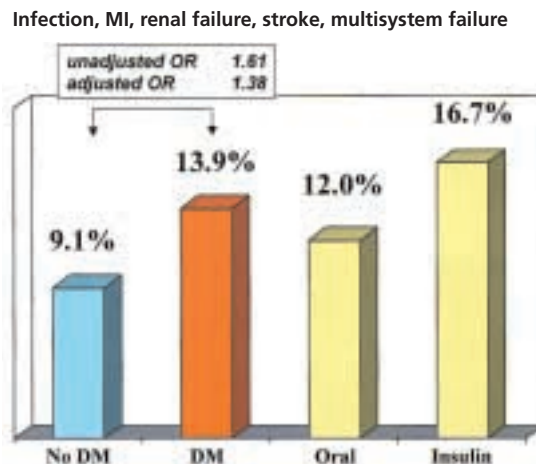
gies (eg abciximab), a liberal use of drug-eluted stents and radiation therapy in selected cases may show a promising reduction of restenosis and instent restenosis even in these most vulnerable patients [31]. Interestingly, bypass surgery has the additional advantage because it provides an alternative pathway beyond the most vulnerable coronary artery segment for late atherosclerosis (proximal 6 cm from the coronary ostia) [32]. However, Carson demonstrated that compared to patients without diabetes, diabetics have a higher early postoperative mortality – which correlated directly

with the severity of the diabetes – as well as a higher morbidity in terms of myocardial infarction, stroke, renal failure, wound infection and multiorgan failure (fig. 6–8) [33]. Sprecher and co-authors showed in a large collective of 6428 patients from the Cleveland Clinic Database, that every additional cardiovascular risk factor increases the mortality following CABG (table 1) [34].

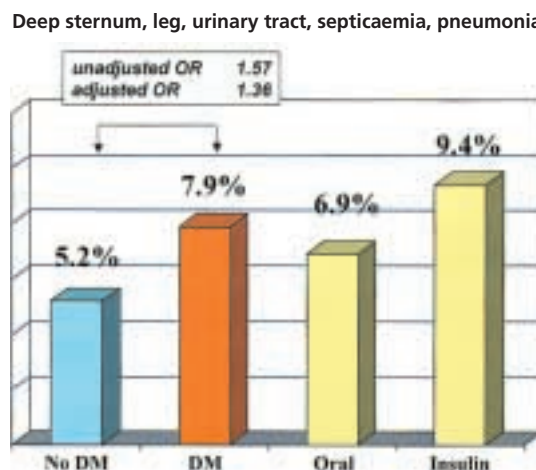
During the long-term follow-up of CABG patients, a major proportion of venous grafts will be diseased or occluded within 6 to 8 years; these results may considerably be improved with the exclusive use of arterial conduits [35]. In fact, this is particularly true for diabetic patients. Therefore an aggressive use of the internal thoracic arteries (ITA) is necessary in these patients. Results of the BARI trial showed a cardiac mortality of 2.9% within 5 years following CABG with at least one ITA, compared to 18.2% if only venous conduits were used [36]. The majority of comparative trials (CABG versus PTCA) have been able to demonstrate a greater benefit over PTCA following CABG with one or more arterial bypass grafts. In fact the ITA is less susceptible to atherosclerosis progression and its long-term patency rate approaches 95% after 10 to 15 years, even in diabetic patients. However, there has been some reluctance among surgeons to use bilateral ITA in diabetic patients because of the risk of sternotomy infection. Procurement of ITA in the skeletonized technique leads to reduction of sternal wound infection and the use of radial artery allows to perform total arterial revascularisation with excellent results, even in these more complicated patients [37–39]. In analogy to non-diabetic patients, the percentage of redo is directly correlated to the age of the patients at the initial operation and the use or not of more than one arterial bypass conduit [40].

Numerous studies have shown that diabetic patients may have sub-clinical, but objectively demonstrable impairments of the neuro-cognitive function postoperatively [41, 42]. Another frequent complication is acute renal failure, which occur in up to 16% of the patients with an elevated preoperative creatinine value [43]. There are several reasons for this, but the major risk may probably be due to the negative effects of the cardio-pulmonary bypass (CPB) circuit. According to these observations, revascularisation strategies without CPB should be used preferentially in diabetic patients, providing the fact that an adequate revascularisation – in terms of number and quality of anastomoses – will be performed.

**Figure 7**  
CABG: diabetes and 30-day morbidity [33].



**Figure 8**  
CABG: diabetes and 30-day infection [33].

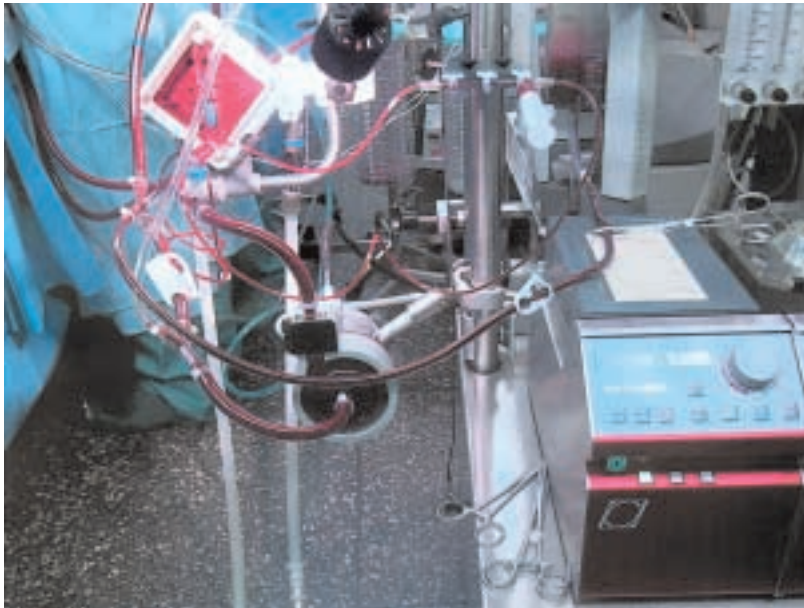


**Table 1**  
CABG and “the deadly quartett” [34].

risk factors (RF)	1-Y adjusted* mortality hazard ratio
0	1
1	1.6
2	2.0
3	2.5
4	4.0

Cleveland Clinic Database, 6428 CABG  
RF = obesity, diabetes, hypertension, hypertriglyceridaemia  
\* for age and surgical variables





**Figure 9**  
Alternative methods for extracorporeal circulation (minimal CPB without cardiomy reservoir and with opto-electrical suction system).

When this last issue is critical, alternative methods of perfusion (minimal CPB without cardiomy reservoir and with opto-electrical suction system (fig. 9), as well as other minimised circulatory support devices) may improve the perioperative outcome even in those patients who cannot be operated safely enough off-pump.

### Postoperative care and long-term follow-up

Diabetic patients are known to be exposed to a significantly higher risk of wound infections following cardiac surgery; the latter are associated with prolonged hospitalisation time and a higher incidence of re-admissions. In some subset of patients, there is a close relationship between the preoperative blood glucose level and the rate of infection [44], while in others, a correlation was found between the overall rate of complications and the preoperative HbA<sub>1c</sub> value [45, 46].

In general, an aggressive secondary prophylaxis which is directed to correct all cardiovascular risk factors is recommended in all patients, especially in diabetics. There are no difference to make in recommendations for long-term follow-up after PCI or CABG surgery.

### Conclusions

Based on the daily clinical observation, percutaneous treatment of diabetes associated coronary artery disease seems to remain challenging, despite advances in the stent technology and anti-thrombotic treatment. Although acute results of PCI are comparable to those obtained in non-diabetic patients, the long-term results are in the majority of trials still worse [46–50]. There is great hope among cardiologists, that systematic use of clopidogrel preloading, drug-eluted stents and treatment with GP IIb/IIIa inhibitors will improve the results [51]. This may be partially true in the future, but nevertheless, all these strategies will never compete with exclusive arterial surgical revascularisation techniques with or without cardiopulmonary bypass [35].

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