Challenges in diabetic patients: EVOlving PCI’s clinical outcome through innovative technology

Clinical efficacy of PCI in diabetic patients is inferior to that in non-diabetic patients

Shmuel Banai, MD
Tel Aviv Medical Center
Israel
Disclosure Statement of Financial Interest

Speaker's name: Shmuel Banai

I have no conflicts of interest to report regarding the content of this presentation.
Diabetes: A global emergency

* IDF Diabetic Atlas 7th Ed. vs 3rd Ed.
** IDF Diabetic Atlas 7th Ed. estimation

2007: WORLD 246 M

2015: WORLD 415 M

2040: WORLD 642 M

+68%*

+55%**
### Percentage of undiagnosed diabetes

**Table 3.4** Proportion and number of people (20-79 years) living with diabetes who are undiagnosed, 2015

<table>
<thead>
<tr>
<th>IDF region</th>
<th>Proportion undiagnosed</th>
<th>Number of undiagnosed people with diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>66.7%</td>
<td>9.5 million</td>
</tr>
<tr>
<td>Europe</td>
<td>39.3%</td>
<td>23.5 million</td>
</tr>
<tr>
<td>Middle East and North Africa</td>
<td>40.6%</td>
<td>14.4 million</td>
</tr>
<tr>
<td>North America and Caribbean</td>
<td>29.9%</td>
<td>13.3 million</td>
</tr>
<tr>
<td>South and Central America</td>
<td>39.0%</td>
<td>11.5 million</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>52.1%</td>
<td>40.8 million</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>52.1%</td>
<td>79.8 million</td>
</tr>
</tbody>
</table>

**World**

| Proportion undiagnosed | 46.5% | 192.8 million |
Revascularization in Diabetic Patients

- More than 25% of patients referred for revascularization are diabetics.
- Their risk of complications from all types of revascularization procedures are higher than that in patients without diabetes, and their long-term prognosis is worse.

Patients with DM are at higher risk

<table>
<thead>
<tr>
<th>PCI</th>
<th>CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restenosis and TVR</td>
<td>Sternal wound infection</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Acute kidney injury</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>Post CABG angina</td>
</tr>
<tr>
<td>Death</td>
<td>Heart failure</td>
</tr>
<tr>
<td></td>
<td>Death</td>
</tr>
</tbody>
</table>

Stein B et al: Circulation 1995;91:979–89
Abizaid A et al: (ARTS) trial. Circulation 2001;104:533-8
Flaherty JD et al: JAMA 2005;293:1501-8
Randomized trials comparing DES to DES & DM

The latest generation DES (permanent or absorbable polymers) have not been able to improve outcome of diabetics compared to non diabetics.

ZES (Resolute) vs EES (Xience)

Orsiro (Biotronik) vs EES (Xience)
In Scanning Electron Microscopy (SEM) studies, inhomogeneous distribution of coating was recognized in all DES types examined.
Invasive Management of Coronary Artery Disease:

Recent studies indicate that:
1. Coronary angioplasty is less efficacious for patients with diabetes than for those without
2. Coronary artery bypass surgery is the preferred therapy in patients with diabetes when invasive management is required

Extensive data are not yet available with use of coronary stents in patients with diabetes, but regardless, bypass grafting seems to be preferred
What about more recent data?

In the era of 1st-generation DES:
1. the CARDIa (Coronary Artery Revascularization in Diabetes) study
2. subgroup analysis of the SYNTAX (Synergy between PCI with TAXUS and CABG)

Both showed higher rates of MACE in patients who underwent revascularization with PCI and DES compared with CABG surgery

Is the clinical outcome of **diabetic** patients better with CABG than PCI?

**Problems with these clinical trials:**

- Utilization of 1\textsuperscript{st} generation DES with inferior safety compared to 2\textsuperscript{nd} DES
- CARDIa trial was stopped early because of slow enrollment
- The SYNTAX trial was not designed to test differences in mortality in subgroups
Is the clinical outcome of diabetic patients better with CABG than PCI?

The FREEDOM trial was a prospective, open-label, randomized study comparing CABG versus PCI with DES in DM patients with multivessel CAD on a background of OMT.

Overall, the FREEDOM trial demonstrated the superiority of CABG over PCI with DES in patients with CAD and DM.

Limitations of the FREEDOM trial

1. It included only patients who were eligible for both CABG and PCI, therefore, it lacks validity of the entire DM population with CAD
2. Out of 33,000 patients screened only 1,900 (5.7%) were finally randomized
   • This observation provides critical evidence of the relatively poor validity of even well-designed randomized clinical trials
3. Low prevalence of patients with ejection fraction < 40% (2.5%)
4. Low prevalence of patients with a low SYNTAX score ≤ 22 (35.5%)
5. Among patients randomized to PCI, the predominant DES types used were the 1st-generation Cypher and Taxus stents
The same problem again....

Of the 6,678 patients with DM screened, only 207 (3%) were randomized
103 were assigned to surgery and 104 to PCI

"The clinical outcome of diabetic patients is better with CABG than PCI"...

This statement is based on the results of randomized controlled trials in which:

1. Only 1\textsuperscript{st} gen DES were used
2. Only diabetic patients with 3VD were enrolled
3. Only a very small fraction of the diabetic patients with 3VD were randomized (3\% in the VA CARDS, and 5.7\% in the FREEDOM)
4. Of the 3 major RCTs on which this statement is based, one was stopped prematurely (CARDIa), and the second was not designed to test differences in mortality in subgroups (SYNTAX)
A contemporary comparison of CABG surgery vs PCI in “all comers” diabetic patients is needed, with the use of:

1. Non-polymeric DES which induce less inflammatory reaction in the vessel wall
2. More potent DES addressing specifically restenosis in diabetic patients
3. High potency antiplatelet therapies, which demonstrated a superior antithrombotic efficacy compared to clopidogrel
Revascularization in Diabetic Patients

Improvements in stent technology and adjunctive therapies will have a favorable impact on the results, and will make PCI the preferred option for revascularization in most diabetic patients.
Thank You