REFERENCES


Table 1 Baseline Characteristics Comparison

<table>
<thead>
<tr>
<th></th>
<th>SYNTAX (n = 1,800)</th>
<th>Asan Registry (n = 3,042)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DES</td>
<td>CABG</td>
</tr>
<tr>
<td>Age, yrs*</td>
<td>65.2</td>
<td>65.0</td>
</tr>
<tr>
<td>Male, %*</td>
<td>76.4</td>
<td>78.9</td>
</tr>
<tr>
<td>Mean body mass index, kg/m²*</td>
<td>28.1</td>
<td>27.9</td>
</tr>
<tr>
<td>Current smoker, %†</td>
<td>18.5</td>
<td>22.0</td>
</tr>
<tr>
<td>Hypertension, %*</td>
<td>68.9</td>
<td>64.0</td>
</tr>
<tr>
<td>Hyperlipidemia, %*</td>
<td>78.7</td>
<td>77.2</td>
</tr>
<tr>
<td>Medically treated diabetes Any, %†</td>
<td>25.6</td>
<td>24.6</td>
</tr>
<tr>
<td>Requiring insulin, %*</td>
<td>9.9</td>
<td>10.4</td>
</tr>
<tr>
<td>Ejection fraction &lt;30%, %</td>
<td>1.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Congestive heart failure, %*</td>
<td>4.0</td>
<td>5.3</td>
</tr>
<tr>
<td>Prior myocardial infarction, %*</td>
<td>31.9</td>
<td>33.8</td>
</tr>
<tr>
<td>Left main lesion, %*</td>
<td>39.5</td>
<td>38.8</td>
</tr>
<tr>
<td>Total occlusion, %</td>
<td>24.2</td>
<td>22.2</td>
</tr>
<tr>
<td>SYNTAX score, %*</td>
<td>28.4</td>
<td>29.1</td>
</tr>
</tbody>
</table>

*Higher risk profile patients in SYNTAX (Synergy Between PCI With TAXUS and Cardiac Surgery).
†Higher risk profile patients in Asan-Multivessel Registry.
CABG = coronary artery bypass grafting; DES = drug-eluting stent(s).

Reply

We thank Dr. Head and colleagues for their remarks concerning our paper (1). Although a randomized clinical trial (RCT) is the ideal method for measuring true treatment effects, the RCT does not necessarily provide the final answer to treatment effectiveness, as there are many restrictions that limit generalizability of study findings (2).

There are many considerations when one is choosing a treatment strategy for coronary revascularization (3). In real practice, it is mostly likely that patients with less complex anatomy of atherosclerotic coronary artery disease (CAD) and less comorbidity tend to be more often referred for percutaneous coronary intervention (PCI), whereas those with more severe anatomic complexity and coexisting conditions tend to be preferentially considered for coronary artery bypass grafting (CABG). These factors, therefore, may cause potential bias due to confounding by indication in comparative clinical strategies studies (4).

Several comparisons of CABG with PCI suggest a strong relation between the extent of coronary disease and the relative effectiveness of these procedures on survival (5,6). In particular, clinical registry studies have reported that patients with the least extensive coronary disease (i.e., 2-vessel disease) have better survival after PCI, whereas patients with the most extensive disease (i.e., 3-vessel disease) have better survival after CABG. Our registry data collected consecutive “real world” patients who received multivessel revascularization with minimal exclusion criteria. Therefore, the major difference in patient inclusion of our study and the SYNTAX (Synergy Between PCI With TAXUS and Cardiac Surgery) trial was the enrollment of patients with 2-vessel disease. A more beneficial effect of PCI with drug-eluting stents relative to CABG for patients with less severe, 2-vessel disease is the most likely explanation for our contradicting results compared with the SYNTAX trial. Referring patients with 2-vessel disease for CABG is common in clinical situations, but this subset was not included in the SYNTAX trial.

Although findings of observational studies should be interpreted with caution due to selection bias and unmeasured, multiple confounders, well-conducted observational studies can address long-term effectiveness and safety problems of revascularization procedures in a broader array of patients by the optimal judgment of the treating physician in routine practice, and may more accurately reflect “real world” experience.

*Seung-Jung Park, MD, PhD
Duk-Woo Park, MD, PhD
*Asan Medical Center
Department of Cardiology
University of Ulsan College of Medicine
388-1 Poongnap-dong, Songpa-gu
Seoul
Republic of South Korea
E-mail: sjpark@amc.seoul.kr
doi:10.1016/j.jacc.2011.03.016

Stuart J. Head, BSc
Ad J. J. C. Bogers, MD, PhD
*A. Pieter Kappetein, MD, PhD

*Department of Cardio-thoracic Surgery
Erasmus Medical Center, Room Bd 569
P.O. Box 2040
3000 CA Rotterdam
the Netherlands
E-mail: a.kappetein@erasmusmc.nl

lesion; these patients have been identified as having the worst prognosis (3). Furthermore, CABG has always shown a better prognosis in patients with more extensive coronary artery disease. Outcomes in the study by Parks et al. (1), therefore, represent results from a patient cohort in whom it is unlikely that an advantage of surgery could be demonstrated.

To conclude, the recently published results show interesting data on patients treated with DES in perspective to CABG in a real-world design, but this should not lead to treatment preferences for patients with multivessel coronary artery disease. SYNTAX remains the only randomized trial addressing this issue, and although we anticipate the stronger long-term results from this trial, conclusions from the Asan-Multivessel Registry can only be drawn with caution.
Clinical, Molecular, and Genomic Changes After Left Ventricular Assist Device Implantation

We read with interest the state-of-the-art paper by Hall et al. (1) that was recently published in the Journal. The paper summarizes the main molecular and genomic changes in response to mechanical unloading by left ventricular assist devices (LVADs). However, we consider that, as suggested by the title of the review, the clinical changes induced by left ventricular (LV) unloading deserve the same attention because to date, the decisions to remove LVADs after detection of unloading-induced cardiac recovery have all been ultimately based on clinical parameters (2–8).

Unfortunately, Hall et al. (1) provide neither data on clinical parameters that can predict weaning success nor data on long-term cardiac function and transplantation-free outcome after weaning from LVADs, although such information already exists (2–7). Since 1995, we have weaned 78 patients from LVADs, and echocardiographic data obtained during "off-pump" trials were the cornerstone of weaning decisions. We found that LVAD removal is a feasible therapeutic option with potentially successful results for >15 years even with incomplete unloading-promoted cardiac recovery (LV ejection fraction: 45% to 50%) (7). In patients with dilated cardiomyopathy (DCM) as the underlying cause for heart failure (HF), the post-weaning 5-year freedom from HF recurrence reached 66% (7). Kaplan-Meier estimates of overall survival after weaning revealed probabilities of 71.4 ± 7.1% and 65.7 ± 7.6% for 5- and 10-year survival, respectively (7). We also showed that parameters of pre-explantation cardiac function, LV size and geometry, their stability during final "off-pump" trials, and HF duration before LVAD implantation allow detection of patients with the potential to remain stable for >5 post-weaning years (4,6,7).

Data on beta-adrenergic signaling and calcium handling in recovery patients presented by Hall et al. show that the assessment of molecular and genomic changes in response to unloading by LVADs can indeed be potentially helpful for future improvement of weaning protocols. The review discusses a study recently published by Ogletree et al. (9), who found that the favorable effects of unloading on calcium handling and contractility are time dependent (highest during the first 4 months of unloading; thereafter, with longer duration of LVAD support, there is a reversal to failing levels). These observations concur with our clinical observations in DCM patients weaned from LVADs. Thus, the patients with long-term post-weaning cardiac stability had required a significantly shorter time of mechanical unloading (4.3 ± 0.7 months) until maximal myocardial improvement was reached than those with heart failure recurrence during the first 5 years after LVAD removal (6.9 ± 1.7 months). Moreover, the necessity of more than 6 months of unloading until recovery appeared to be a risk factor for HF recurrence after weaning (4,6).

As mentioned by Hall et al. (1), reversal of the proinflammatory state is also an important change induced by ventricular unloading. However, the authors omit to mention the autoantibodies, especially the beta1-adrenoreceptor autoantibodies (AABs), which appear particularly relevant from a pathophysiological point of view in DCM patients (10). Before LVAD implantation, 97.1% of our weaned DCM patients tested positive for beta1-AABs, whereas after 3 to 31 weeks of LV unloading, the beta1-AABs disappeared in 97% of those patients (6). At LVAD explantation, only 3% of DCM patients with cardiac recovery remained positive for beta1-AABs.

Roland Hetzer, MD, PhD
*Michael Dandel, MD, PhD
Christoph Knosalla, MD, PhD

*Department of Cardiothoracic and Vascular Surgery
Deutsches Herzzentrum Berlin
Augustenburger Platz 1
13353 Berlin
Germany
E-mail: dandel@dhzb.de

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