

**ESPS Peer-review Report**
**Name of Journal:** World Journal of Cardiology

**ESPS Manuscript NO:** 7861

**Title:** Is Reversal of Endothelial Dysfunction Still An Attractive Target in Modern Cardiology?

**Reviewer code:** 00225357

**Science editor:** Huan-Huan Zhai

**Date sent for review:** 2013-12-08 13:28

**Date reviewed:** 2013-12-13 21:14

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

The present manuscript reviews the potential role of endothelial function assessment in the routine clinical practice. Authors conclude that data are scant and its use to assess reversibility with therapeutic interventions remain an elusive clinical target. The review reports the main evidence collected so far, it is interesting but does not add a novel vision on the use of this parameter. 1. Authors forget to state that FMD never existed the research laboratories. There are several reasons to be listed, the main one being the low reproducibility of the method when not performed according to a standardized approach and an operator-independent system of measure. Please address. 2. It definitely remains an excellent research tool but it is hard to believe that it will become a routine method to assess endothelial dysfunction. 3. The most interesting part of the review is the final one where authors address the main limitation to this method (but it could be extended to many other clinical parameters) e.g. the proof that a normalization of FMD carries a prognostic benefit. This part should be extended because this is the real issue at task. Please discuss. 4. The manuscript would improve its readability with more tables and a real meta-analytic approach summarizing the major results available. 5. Data and survival curves in the prognosis sub-session should be reported. 6. It would be interesting to know how these authors use FMD in patient assessment.

# ESPS Peer-review Report

**Name of Journal:** World Journal of Cardiology

**ESPS Manuscript NO:** 7861

**Title:** Is Reversal of Endothelial Dysfunction Still An Attractive Target in Modern Cardiology?

**Reviewer code:** 00290396

**Science editor:** Huan-Huan Zhai

**Date sent for review:** 2013-12-08 13:28

**Date reviewed:** 2014-02-21 10:52

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Mordi and Tzemos

Is Reversal of Endothelial Dysfunction Still An Attractive Target in Modern Cardiology?

Mordi and Tzemos provide a brief and somewhat simplistic view of endothelial function and dysfunction and its measurement and apparent clinical role.

There are a number of issues with this manuscript that should be addressed.

1. (minor, p. 3, line 3 and following text). The authors state that Furchgott and Zawadzki (1980) made their observation in 'large arteries of rabbits'; with the actual observation being made after Jelliffe (1962, JPET, 135:349-353). However, on p. 376, 3rd paragraph of the 1980 paper, a role for their observation is also made with reference to large and small vessels from cat, dog, guinea pig and rat.

This issue is commonly overlooked but please correct this text.

2. (major, p. 3, latter half of 1st paragraph). The authors state that vasodilation in healthy human endothelium is due to nitric oxide (NO). Whilst this is in part correct, the text implies that this is the only mechanism involved and this potentially naive and misleading; and is obviously not correct. There are well described defects in other endothelium-dependent relaxation (EDR) pathways in studies of human artery function in health and disease; as well as defects in ED constricting factor (CF) mechanisms? The latter are alluded to in the 1st sentence of the 2nd paragraph, and elsewhere in the text (eg. p. 7, 1st and 3rd paragraphs; p. 8, 4th paragraph; XXX), but this contradicts the first paragraph at p. 3. Please expand the text at p. 3 to accurately reflect the literature. I believe that a simple fix is to add a paragraph mentioning the other mechanisms and then to state that this review will focus on NO.



## BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)

<http://www.wjgnet.com>

---

3. (minor, p. 4, line 8). Please insert 'apparently' before 'paradoxical'; and insert 'smooth muscle' after 'direct'; and at the end of this sentence add ', at comparatively high concentrations'. That is, the constrictor effects of Ach are due to smooth muscle M1 activation and occur at  $>[10^{-4} \text{ M}]$ , whilst the endothelial effects occur at M3 at  $<[10^{-4} \text{ M}]$ . The current text is not informative on this point.
4. (major, p. 4, line 16 and related to point 2, above). Please correct the implication that endothelial function is analogous to NO bioactivity, as, although it can be in some vessels, it is not in all beds. Again, as per point 2, above, please avoid use of generalizations that are incorrect.
5. (minor, p. 6, line 15). Please cite references referred to after 'FMD'.
6. (minor). A Figure illustrating the aim/s / summary / conclusion of the review would be helpful