

## PEER-REVIEW REPORT

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

**Manuscript NO:** 46221

**Title:** Could Brain Natriuretic Peptide Exacerbate Decompensated Heart Failure in humans? An In-Vitro Study

**Reviewer's code:** 03936425

**Reviewer's country:** Poland

**Science editor:** Ying Dou

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**Review time:** 14 Days and 11 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

In the present study authors examined the effects of ANP and BNP on isolated human pulmonary arteries collected during lung resection. It has been demonstrated that both ANP and BNP relaxed PGF2alpha-preconsticted rings but the latter was less potent. In

addition, BNP partially inhibited ANP-induced vasorelaxation. 1) The title of the paper should be modified. According to the results of in vitro study it is not possible to conclude that BNP exacerbates heart failure. Authors report only one effect of BNP in specific ex vivo preparation. 2) The results are interesting but partially predictable. It is well-known that BNP has lower affinity for natriuretic peptide A receptor and as such could partially antagonize the effect of ANP. 3) Page 9, line 3: I suppose that maximal relaxation rather than maximal contraction at 100 nM ANP should be mentioned. 4) It is suggested by the authors that BNP worsens the course of heart failure by attenuating the effect of ANP. However, several issues should be taken into consideration. First, only one effect (PA relaxation) was measured here. Second, are concentrations of ANP and BNP used to show these effects close to in vivo concentrations in patients with heart failure? Third, BNP still induces vasorelaxation and as such could exacerbate heart failure only if increasing AFTER the previous increase in ANP (compensated phase). Only in this case BNP could exacerbate heart failure previously compensated by ANP. 5) The major limitation of using natriuretic peptides in the treatment of heart failure is resistance to their activity partially mediated by enhanced metabolism of ANP and BNP. This issue should be discussed. 6) Increase in BNP predicts worse outcomes mostly because BNP is the marker of myocardial remodeling rather than the mediator of worse outcomes. This issue should be discussed as well. 7) The study was performed using PA samples obtained from patients with lung cancer but presumably without heart failure. Vascular effects of NPs may differ between these patients and patients with heart failure due to multiple factors such as receptor downregulation by chronically elevated NP level, altered expression of neutral endopeptidase, elevated levels of other vasoactive substances, etc. 8) It is suggested that BNP antagonist could be more beneficial than BNP itself in therapy. However, because both ANP and BNP bind to the same receptor (NPR-A), BNP antagonist should block the effects of ANP thus being even more



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detrimental than BNP itself (partial agonist).

#### INITIAL REVIEW OF THE MANUSCRIPT

##### *Google Search:*

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

##### *BPG Search:*

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No