Growth differentiation factor-15 correlates inversely with protease-activated receptor-1-mediated platelet reactivity in patients with left-ventricular assist devices

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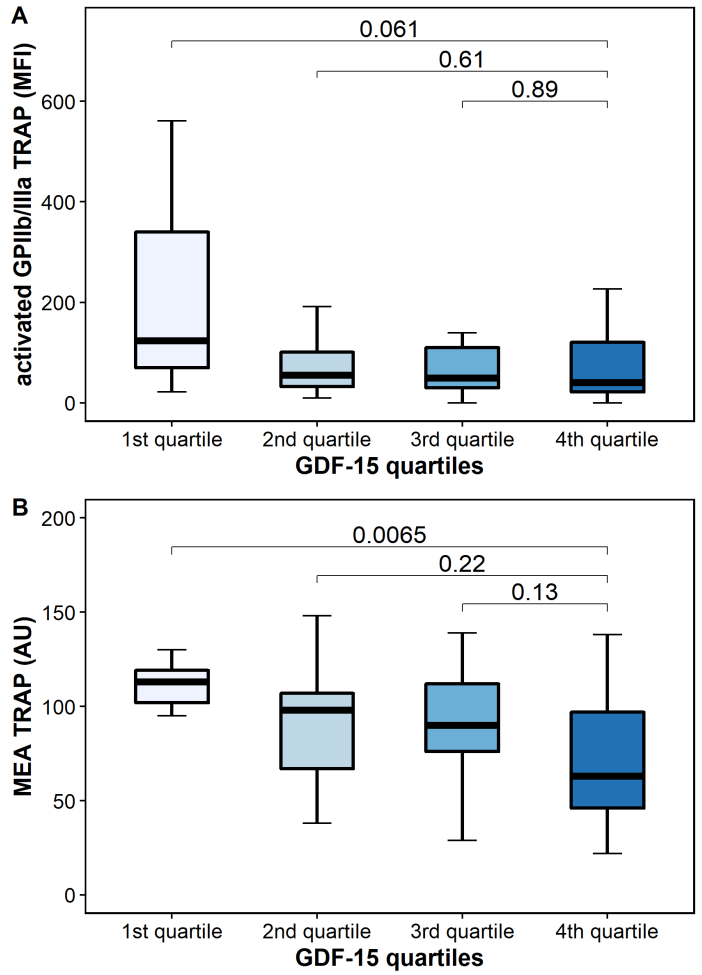
BACKGROUND

- **Growth differentiation factor-15 (GDF-15) has been demonstrated to partially inhibit platelet integrin activation and to prevent thrombus formation**.
- GDF-15 has been associated with bleeding events in acute coronary syndromes and atrial fibrillation.
- **Balancing the risk of bleeding events and thromboembolic complications remains a major challenge in the management of LVAD patients**

Methods and Results

- Prospective study including **51 stable LVAD (15 HVAD, 2 HM2, 34 HM3) patients on aspirin and phenprocoumon.**
- Platelet surface expression of activated glycoprotein (GP) IIb/IIIa was assessed by flow cytometry
- Platelet aggregation was measured by multiple electrode aggregometry (MEA) in response to arachidonic acid (AA), adenosine diphosphate (ADP), and thrombin receptor activating peptide (TRAP).
- GDF-15 was determined by a CE-marked commercially available assay (Roche)
- As a clinical endpoint, we assessed bleeding complications during six months of follow-up.

Central Figure



- There was a strong trend towards an inverse correlation of GDF-15 with platelet surface expression of activated GPIIb/IIIa in response to TRAP (r=-0.275, p=0.0532), but not in response to AA and ADP (both p>0.1).
- After excluding outliers, **GDF-15 correlated significantly with activated GPIIb/IIIa in response to TRAP (r=-0.291, p=0.0497).**
- Moreover, **GDF-15 correlated with MEA TRAP (r=-0.326, p=0.0194)**, whereas it did not correlate with MEA ADP and MEA AA (both p>0.05).
- Three patients (5.9%) experienced bleeding complications during follow-up. Two patients suffered from severe gastrointestinal bleeding requiring blood transfusions (GDF-15 levels: 2333 pg/ml and 8347 pg/ml) and one patient suffered from macrohematuria (GDF-15 level: 851 pg/ml).

Conclusions

- **GDF-15 was inversely correlated with residual platelet reactivity via PAR-1.**
- Further clinical trials are needed to investigate if GDF-15 might help to identify LVAD patients at risk of bleeding and to guide antithrombotic therapy.

Declaration of interest

DW is consultant and proctor for Abbott and Medtronic. DZ receives research grants from Abbott and Medtronic, is advisory board member for Abbott, Medtronic and Berlin Heart, and proctor for Abbott and Medtronic. The other authors have no conflict of interest to declare.