Efficacy of aortic valve replacement on Heyde syndrome-related acquired von Willebrand syndrome and gastrointestinal bleeding: a systematic review and meta-analysis

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Background: Heyde syndrome is the co-occurrence of aortic stenosis, acquired von Willebrand syndrome, and gastrointestinal bleeding. Aortic valve replacement has been shown to resolve all three associated disorders.

Purpose: To assess the efficacy of aortic valve replacement (both surgical aortic valve replacement and transcatheter aortic valve implantation) on acquired von Willebrand syndrome recovery and gastrointestinal bleeding cessation.

Methods: A systematic review and meta-analysis using MEDLINE, Embase, and the Cochrane Library was performed to identify articles on Heyde syndrome and aortic valve replacement. Primary outcomes were the proportion of patients with recovery of acquired von Willebrand syndrome within 24 hours (T1), 24 to 72 hours (T2), 3 to 21 days (T3), and 4 weeks to 2 years (T4) after aortic valve replacement, and the proportion of patients with cessation of gastrointestinal bleeding. Pooled proportions and risk ratios (RR) were calculated using random-effects models.

Results: We identified 33 studies (32 observational studies and one randomized controlled trial) on acquired von Willebrand syndrome (n = 1,054), and 11 observational studies on gastrointestinal bleeding (n = 300). One study reported on both associated disorders (n = 6). The pooled proportion of Heyde patients with acquired von Willebrand syndrome recovery was 86% (95% CI, 79-91%) at T1, 90% (74-96%) at T2, 92% (84-96%) at T3, and 87% (67-96%) at T4. The pooled proportion of Heyde patients with cessation of gastrointestinal bleeding was 73% (62-81%). Residual aortic valve disease was associated with lower recovery rates of both acquired von Willebrand syndrome (RR 0.20; 0.05-0.72; p = 0.014) and gastrointestinal bleeding (RR 0.57; 0.40-0.81; p = 0.002).

Conclusion: Aortic valve replacement is associated with a rapid recovery of the bleeding diathesis in Heyde syndrome and cessation of gastrointestinal bleeding. Residual aortic valve disease negatively impacts clinical benefits of aortic valve replacement.
**Key question**
What is the effect of aortic valve replacement (AVR) on Acquired von Willebrand Syndrome (AVWS) and gastrointestinal bleeding (GIB) in patients with Heyde syndrome.

**Key findings**
The proportion of patients with AVWS recovery was 86% (95% CI, 79-91%) <24 hours, 90% (74-96%) 24-72 hours, 92% (84-96%) 3-21 days, and 87% (67-96%) >3 weeks after AVR. The proportion of patients with GIB cessation was 73% (62-81%).

**Take-home message**
AVR is associated with rapid recovery of the bleeding diathesis in Heyde syndrome and GIB cessation. Residual valve disease compromises clinical benefits.

**Heyde syndrome**
- Aortic stenosis
- Acquired von Willebrand syndrome
- Gastrointestinal bleeding

**Recovery**
- **Studies:** 33
  - **Patients:** 1054
  - 86% (79-91%) <24h
  - 90% (74-96%) 24-72h
  - 92% (84-96%) 3-21d
  - 87% (67-96%) >3w

- **Studies:** 11
  - **Patients:** 300
  - 73% (62-81%) 1-10y

Graphical Abstract