Author's response to reviews

Title: Coronary artery occlusions diagnosed by transthoracic Doppler

Authors:

Johnny Vegsundvag (johnnyvegsundvag@mimer.no)
Espen Holte (es-holte@online.no)
Rune Wiseth (rune.wiseth@stolav.no)
Knut Hegbom (knut.hegbom@stolav.no)
Torstein Hole (torstein.hole@mimer.no)

Version: 2 Date: 4 March 2014

Author's response to reviews: see over
Editors-in-Chief
Cardiovascular Ultrasound

Dear Editors-in-Chief

We are most grateful for the valuable comments concerning our manuscript
MS: 1116823942115487 – Coronary artery occlusions diagnosed by transthoracic Doppler.

The comments and questions raised by the reviewers are addressed below. The corresponding additions/changes in the revised manuscript are shown by red font.

**Reviewer #1 (Antti Saraste):**

1. **Comment:** “It appears that the patient recruitment is prospective that is a merit. The patient inclusion could be described more specifically: Prospective? Consecutive patients? Selected from what population (angiography referrals?)? Time frame? Hospital?”

1. **Response:** Patient recruitment was prospective during the period 2006 – 2007 and all patients were from the local area of Ålesund Hospital. All patients fulfilling the inclusion criteria and not meeting the exclusion criteria were eligible for inclusion in the study. However, because of administrative reasons (summer vacations, weekends, holidays, other hospital tasks interfering) we could not include several eligible patients in the study. Extended study information is included in the Study population section (page 4) of the revised manuscript.

2. **Comment:** “One main finding is cut-off > 0.57 m/sec in septal branches for the detection of occlusion. Absolute flow values are problematic due to angle dependency, physiological variation etc. as discussed. It is stated that angle correction was used, but can you give an estimate how large was the angle (appears from the images that the flow is relatively perpendicular to the beam that is good).”
2. Response: Using modified short-axis views, the angle between the interventricular septum with its septal branches and the ultrasound beam was small and usually below 20°. Therefore, the angle correction used during measurements of anterograde flow velocities in septal vessels was small.

3. Comment: “Feasibility to differentiate epicardial collaterals from pericardial fluid?”

3. Response: Epicardial collaterals were differentiated from pericardial fluid by colour Doppler showing the tubular collateral vessel(s) with enhanced, mosaic-patterned flow (Figure 5A in the revised manuscript). Additionally, epicardial collateral vessels showed the coronary artery velocity waveform of a smaller wave in systole and a larger wave in diastole when examined with pulsed Doppler.

4. Comment: “Results, page 8, 1st para: groups A – D not defined in text.”

4. Response: Groups A – D are defined in the text of the revised manuscript (page 8)

5. Comment: “Numbering of panels with “subcodes” (A1, A2 etc) is difficult, please consider just letters for each panel.”

5. Response: Numbering of panels with “subcodes” is changed to letters in the revised manuscript (with figures).

Reviewer #2 (Maurizio Galderisi):

1. Comment: “The protocol of the study appears to be time-consuming. Accordingly, it could be very useful to know the time of execution of each examination as well as the learning curve to achieve an acceptable level of technical skills in this field.”

1. Response: In advance of the study, we had the experience of examining the three major coronary arteries by transthoracic Doppler (TTE) for assessing coronary flow velocity reserve. During these examinations we soon learned that coronary arteries likely showed retrograde flow downstream to an occlusion. Furthermore, we experienced that septal branches could demonstrate retrograde flow to an occluded or severely stenosed major artery, and that anterograde flow velocities in septal branches often showed high flow velocities when the contralateral coronary artery was occluded. Finally, we had seen some examples of epicardial collateral vessels with enhanced, mosaic-patterned flow to occluded coronary arteries. We decided to investigate this in the present study, measuring anterograde septal flow velocities for identifying a possible cutoff value for predicting an occluded contralateral coronary artery, as well as using several parameters for the detection of occluded major coronary arteries. However, when planning the study, we decided to investigate more than just parameters indicating coronary occlusions, such as the feasibility of visualizing the various coronary segments. Thus, the patients in the study cohort had a comprehensive examination and the time used for each study component was not measured. However, after ending the study we have examined patients for coronary occlusions investigating the various parameters described. Each full examination takes 15 to 20 minutes. This information is added in the revised manuscript (Clinical implications, page 11).
2. Comment: “The feasibility of the overall procedure (comprehensive of all the chosen parameters is another critical issue. The authors should calculate it including also the three patients with “presumed insufficient acoustic windows.”

2. Response: Unfortunately, the three patients mentioned were included in the study before we had seen the patients. Those patients were actually protocol violators because of severe emphysema or severe overweight and the patients were excluded from the study without having a TTE examination. Therefore, in our opinion, it will be incorrect to include those three patients in the study.

3. Comment: “A multiple regression analysis including all the suggested variables could be very useful to understand which variables predict independently the coronary occlusion.”

3. Response: Logistic regression analyses have not revealed any relationships between demographic variables and occlusions. Retrograde flow and high velocity findings were significantly related to occlusions in multiple regression analyses, but due to limited numbers of events the estimates OR of the multiple regression analysis showed too high uncertainty to be meaningful in rating the impact of the individual method. The significant relation of the findings of anterograde pDV ≥ 0.57 m/sec in septal branches, retrograde flow in a coronary artery or septal branch, or demonstration of other collaterals to occlusions, was, however, confirmed by exact tests (p < 0.001 for all parameters). This information is added in the revised manuscript (pages 6 and 9).

4. Comment: “The discussion is too long and should better point out comment on the main findings of the study.”

4. Response: As recommended, the “Discussion” section is rearranged to better point out the main findings of the study. Additionally, we have shortened the manuscript by omitting unnecessary words in the “Introduction”, “Results”, and “Discussion” sections. Borderline and high-grade stenoses have been defined in relation to degree of diameter stenosis once and for all in the “Coronary angiography” part of the manuscript, without repeating the stenosis definitions later in the manuscript text.

5. Comment: “Some observations (reasons for measuring only peak diastolic velocities and other) shall be moved from the “Results” to the “Methods” section.”

5. Response: As suggested, we have moved the text describing the reasons for measuring only septal branches’ peak anterograde diastolic flow velocities from “Results” to the “Methods” section (page 5), with corresponding changes in the order of references.

6. Comment: “In the “Methods” section what it is the meaning of “administrative reasons” among the exclusion criteria?”

6. Response: The term “administrative reasons” refers to reasons for precluding study inclusion of eligible patients because of investigators’ summer vacations, weekends, holidays, or because of other hospital tasks interfering.

We hope by this to have addressed all major and minor comments by the reviewers, and that the manuscript may be considered for publication.
Enclosed: abstract and manuscript files, 6 figure files.

Yours sincerely,

Johnny Vegsundvåg   Espen Holte   Rune Wiseth   Knut Hegbom   Torstein Hole