The version of QUADAS-2 used in this assessment included only the risk of bias components, as it was considered that the inclusion criteria matched the review question and that questions of applicability were, therefore, not relevant.

Before starting the risk of bias assessment, we considered the relevance of each signalling question to our review, as well as the potential need for additional questions. Further criteria were then defined, as needed, to ensure consistent application of signalling questions and to help in the judgement of the risk of bias. Many signalling questions were not further specified and the answer was judged to be 'yes' if it was clearly reported in the study. If the answer to a signalling question was not clearly reported the question was judged as 'unclear' unless specified differently. 'No' was answered if it was clear from the reporting that an aspect was not fulfilled. An additional question (question 3) was added to domain 2 'index test' to record the potential bias introduced where studies include multiple measurements per patient. Details of the assessment criteria used are reported below.

Domain 1: patient selection

Question 1: Was a consecutive or random sample of patients enrolled?

- 'yes' → low risk of bias
- 'unclear' → unclear risk of bias
- 'no' → high risk of bias

Question 2: Was a case–control design avoided?

- 'yes' → low risk of bias
- 'unclear' → unclear risk of bias
- 'no' → high risk of bias

Question 3: Did the study avoid inappropriate exclusions?

- 'no' for < 10% of patients or 'yes' → low risk of bias
- 'unclear' → unclear risk of bias
- 'no' for ≥ 10% of patients → high risk of bias

Domain 2: index test

Question 1: Were the index test results interpreted without knowledge of the results of the reference standard?

Question 2: Did the study prespecify the threshold for a positive result?

Question 3: Did the study avoid using multiple data sets per patient (reporting of per-segment data only)?

The same criteria applied to each of the three signalling questions:

- 'yes' → low risk of bias
- 'unclear' → unclear risk of bias
- 'no' → high risk of bias

Domain 3: reference standard

Question 1: Is the reference standard likely to correctly classify the target condition?

The use of a reference standard, likely to correctly classify the target condition (i.e. coronary angiography), was an inclusion criterion, hence the answer to this question was always 'yes'.

- 'yes' → low risk of bias

Question 2: Were the reference standard results interpreted without knowledge of the results of the index test?

- 'yes' → low risk of bias
- 'unclear' → unclear risk of bias
- 'no' → high risk of bias

Domain 4: flow and timing

Question 1: Was there an appropriate interval between index test and reference standard?

The time interval between index and reference standard had to be ≤ 3 months in order to be judged as 'adequate'.

- 'no' but only for < 10% of patients or 'yes' → low risk of bias
- the answer was judged to be 'unclear' if the time interval was not reported or if it was unclear what proportion of patients had an inadequate time interval between index test and reference standard → unclear risk of bias
- 'no' for ≥ 10% of patients → high risk of bias

Question 2: Did all patients receive a reference standard?

- 'no' but only for < 10% of patients or 'yes' → low risk of bias
- 'unclear' → unclear risk of bias
- 'no' for ≥ 10% of patients → high risk of bias

Question 3: Did patients receive the same reference standard?
As ICA was the only reference standard allowed in the inclusion criteria this item was always answered with 'yes' → low risk of bias.

Question 4: Were all patients included in the analysis?

- 'no' but only for < 10% of patients or 'yes' → low risk of bias
- 'yes', or < 10% of patients excluded, but unclear how exclusion of non-diagnostic segments may have affected per-patient results → unclear risk of bias
- 'unclear' → unclear risk of bias
- 'no' for ≥ 10% of patients → high risk of bias

The following criteria were used to reach a per-domain judgement of risk of bias:

- If at least one of the signalling questions of a domain had an answer associated with a high risk of bias the domain was judged to have a high risk of bias.
- If the answer to any of the signalling questions was 'unclear' and the answers to the remaining questions were 'yes', the risk of bias was judged to be unclear.
- The answer to all the signalling questions had to be 'yes' in order for the domain to be judged as having a low risk of bias.