Anomalous coronary artery from the opposite sinus of Valsalva Referral to MuSCAT centre Diagnostic evaluation: · Clinical letter, including following information: Medical history Reason for admission/consultation History and physical examination Performed examinations (including original images) Conclusion and treatment · CT angiography, 0.5- to 1-mm slices 1st outpatient clinic visit · Study information and informed consent History with special attention to anginal complaints (none, non-anginal, atypical or typical) and standard physical examination SF-36 QoL questionnaire Work-up • CT angiography 0.5- to 1-mm slices Coronary angiography with IVUS, FFR, iFR and CFR * Transthoracic echocardiogram 1 method of ischaemia detection: · Myoview with exercise stress testing (LUMC, UMCU, AUMC, RUMC, MST) MRI with adenosine (EMC, RUMC) * if the course of the anomalous coronary artery is interarterial or septal Probably benign Potentially malignant **RCA RCA** · Interarterial course, no Retro-aortic (posterior) course Pre-pulmonic (anterior) course · Interarterial course · Interarterial course, regardless of ischaemia in supply area • Retro-aortic (posterior) course Intramural course intramural part · Septal course with compression · Septal course without Proven ischaemia in supply Pre-pulmonic (anterior) course compression area Cardiosurgical meeting to discuss options **Treatment** Surgical intervention Conservative Until surgery: · No exercise restrictions Exercise restrictions No medical therapy Medication (usually beta blockers) if indicated Follow up 6 months 6 months Outpatient clinic visit Outpatient clinic visit SF-36 QoL questionnaire SF-36 QoL questionnaire CT angiography, 0.5- to 1-mm slices Repeat the initial ischaemia detection 12 months 12 months Outpatient clinic visit Outpatient clinic visit SF-36 QoL questionnaire SF-36 QoL questionnaire **Annually** Annually Outpatient clinic visit · Outpatient clinic visit · Additional examinations only if indicated · Additional examinations only if indicated

Fig. 2 Flowchart of study protocol. *IVUS* intravascular ultrasound, *FFR* fractional flow reserve, *iFR* instantaneous wavefree ratio, *CFR* coronary flow reserve, *LUMC* Leiden University Medical Centre, *UMCU* University Medical Centre Utrecht,

AUMC Amsterdam University Medical Centre, EMC Erasmus University Medical Centre, RUMC Radboud University Medical Centre, MST Medisch Spectrum Twente, RCA right coronary artery, LCA left coronary artery, QoL quality of life