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CORONARY ANGIOGRAPHY

Potential intrinsic error of noninvasive coronary angiography

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Purpose. With current noninvasive techniques compromises have to be accepted for coronary imaging, e.g., partial coverage of the coronary artery tree. The aim of the study was to estimate the potential intrinsic error of partial coverage from a database of invasive angiograms. *Methods and Results.* The localization and severity of coronary artery stenoses and, if percutaneous coronary intervention (PCI) was performed, the balloon and stent size were extracted from a large database of 21,335 selective coronary angiograms. Of stenoses with $\geq$ 50% diameter reduction, 31.4% were located in distal segments and minor side branches, constituting 28.8% of interventional treatment. In 5% of patients undergoing their first invasive angiogram, the most proximal relevant stenosis was found in a distal segment or minor side branch. Most interventions (83.5%) were performed in main coronary artery segments. *Conclusion.* Coronary artery stenoses were found and interventional treatment performed in all coronary segments. Therefore, noninvasive coronary imaging of only proximal and medial segments and major side branches is an inadequate strategy for complete diagnosis or as a guide to therapeutic decisions. However, the currently available noninvasive techniques allow the detection of relevant stenoses in 95% of patients with suspected coronary artery disease (CAD) to prepare for further invasive diagnostic and therapeutic planning.

Key Words: Magnetic resonance imaging; Computed tomography; Coronary disease; Angiography

1. Introduction

The current standard of reference in the diagnosis of CAD is invasive coronary angiography, which is, by definition, invasive, requires the administration of contrast agents, and is burdened with radiation.

Despite the availability of noninvasive tests to identify patients with coronary artery disease, a large number of patients referred to coronary angiography are found not to have significant coronary artery stenoses (1–3).

Magnetic resonance coronary angiography (MRCA) (4–7), electron-beam computed tomography (EBCT) (8, 9), and multislice computed tomography (MSCT) (10–12) have been suggested as noninvasive imaging tools for early diagnosis and monitoring of coronary artery disease.

However, since these techniques have a lower spatial and temporal resolution in comparison to invasive angiography and may only partially cover the coronary artery tree, precise knowledge of localization and severity of coronary artery stenoses could be helpful to optimize interpretation of noninvasive angiograms.

The aim of the current report is to extract information from a sufficiently large database of invasive coronary angiograms to quantify loss of coronary artery stenoses by noninvasive coronary angiography.

2. Methods

2.1. *Patients*

The localization and severity of coronary artery stenoses and, if PCI was performed, the balloon and stent size were extracted from a large database of 21,335 selective coronary angiograms from 14,473 consecutive patients. Of these, 4,138 (28.6%) women and 10,335 (71.4%) men (63.7 ± 9.7 years; range 15 to 98 years), who underwent cardiac catheterization at the German Heart Institute Berlin (= group A) from November 1997 through October 2003 were retrospectively reviewed.

Indications to perform coronary catheterizations were in accordance with the relevant guidelines (13).

PCI with or without stent implantation was performed in 12,280 patients, 3,757 women (30.6%), and 8,523 (69.4%) men.

The total group was analyzed for: sex, coronary artery stenosis localization and diameter reduction in percent, localization of PCI, and luminal size of the balloon or stent used for PCI in millimeters. Stenoses in coronary artery bypasses were excluded. When the dimension of the balloon or stent differed at the same localization or several balloons with different sizes were used, the largest size was entered into the database.

For a more detailed analysis, a subgroup of 352 patients with coronary artery stenoses who underwent their first invasive angiography due to suspected CAD, cardiomyopathy,

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or preoperative assessment of valvular disease was analyzed. This group, 110 (31.2%) women and 242 (68.8%) men, was consecutively extracted from the past 2 years, since more specific information on these patients was available from the electronic database.

No risk factors or primary medical history were analyzed.

2.2. *Coronary angiography*

Coronary angiography was performed using the standard Judkins technique (14).

Coronary angiograms were visually evaluated by three independent experienced observers according to the clinical review process. Localization and percent luminal diameter reduction were documented for any coronary artery with a stenosis. Significant coronary artery stenosis was defined as luminal diameter reduction of $\geq$ 50%.

Fifteen coronary artery segments were defined in a modified form according to the recommendations of the American Heart Association (AHA) (15) (Fig. 1).

In addition to the modified AHA guidelines, the segments were categorized into five groups:

- proximal main segments: 1; 5; 6; 11
- medial main segments: 2; 7; 13
- distal main segments: 3; 8; 15
- major side branches: 9; 12
- minor side branches: 4; 10; 14

In order to determine whether small or distal segments are involved in the early CAD process, the subgroup was additionally analyzed for the most proximal relevant coronary artery stenosis ($\geq$ 50% diameter reduction) using the five-group scale, beginning at the origin of the coronary artery. For this analysis it was not relevant whether we found another significant stenosis distal to the most proximal artery stenosis. The progression from proximal to distal was defined as: proximal segments, followed by major side branches, medial segments, distal segments, and minor side branches.

2.3. *Statistical analysis*

The chi-square test was used for comparison of variables as appropriate, Student's t-test for analysis of variance.

A difference was considered statistically significant if the two-side probability of the observed result, under the null hypothesis, was $p \leq 0.05$.

Statistical analysis was performed using the software package SPSS (version 9.0).

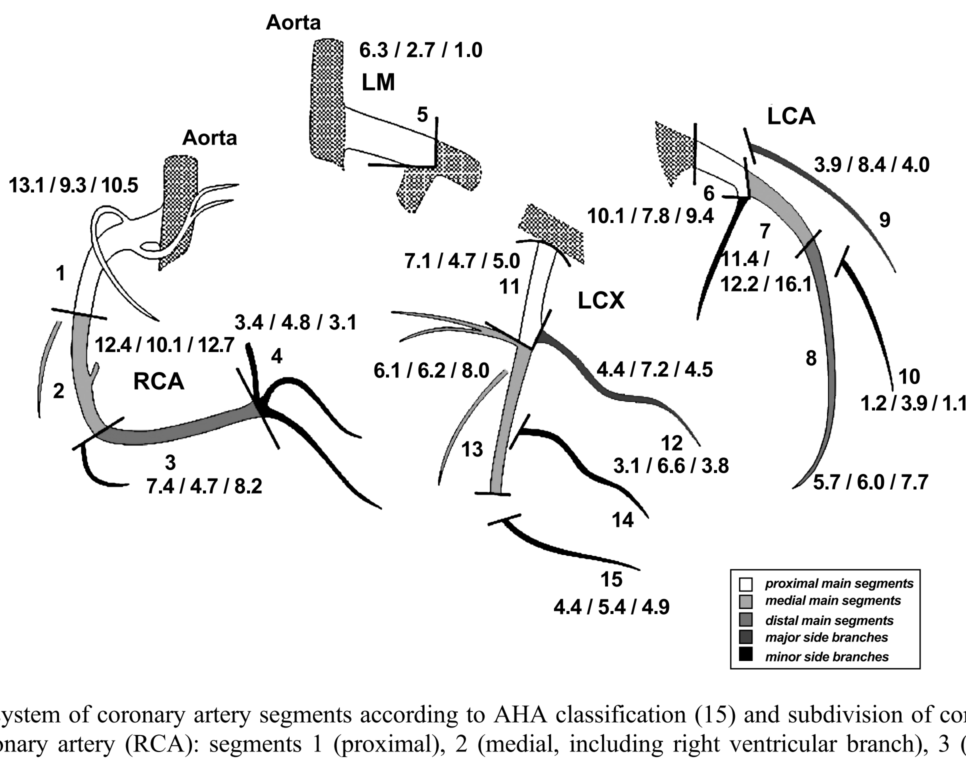

Figure 1. Modified system of coronary artery segments according to AHA classification (15) and subdivision of coronary arteries into 15 segments. Right coronary artery (RCA): segments 1 (proximal), 2 (medial, including right ventricular branch), 3 (distal), 4 [A–V node artery, posterolateral branch (PLV) and posterior descending artery (PDA)]. Left main stem (LM): segment 5. Left anterior descending artery (LAD): segments 6 (proximal), 7 (medial), 8 (distal), 9 [first diagonal branch (D1)], 10 [all septal branches (S1; S2; S3), second (D2), and third (D3) diagonal branch]. Left circumflex artery (LCX): segments 11 (proximal), 13 (medial), 15 (distal), 12 [first marginal obtuse branch (M1) and ramus intermedius], 14 [second (M2) and third (M3) obtuse marginal branch and PLV of LCX]. Grey scale is used to show the classification into five groups. For each coronary segment are shown from left to right: percentage of all stenoses = 25%, stenoses $\geq$ 50%, and PCIs performed.

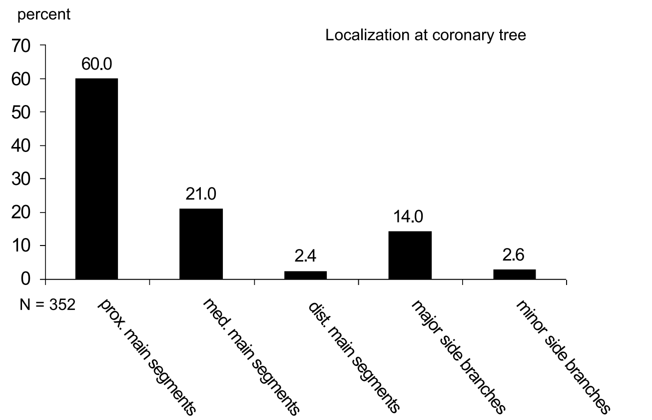

Figure 2. Localization of first coronary artery stenoses ≥ 50% after origin of coronary main segments in patients who underwent first cardiac catheterization (patients with CAD: 352).

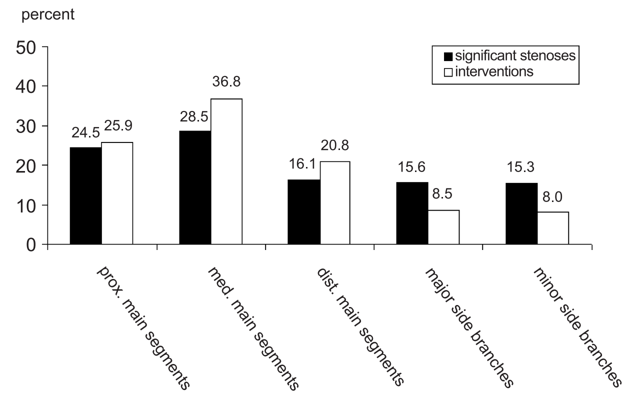

Figure 3. Localization of significant stenoses and interventions.

3. Results

A total of 92,333 coronary artery stenoses were documented and 75.3% (n = 69,564) were considered to show ≥ 50% diameter reduction. These higher grades of stenoses were found more frequently in men (mean: 63.0 ± 27.0) in comparison to women (mean 60.7 ± 26.6); $p < 0.03$.

In patients with suspected or known coronary artery disease, large numbers of nonsignificant and significant stenoses were found in all coronary segments (Fig. 1). Even though a tendency towards proximal and medial segments was found for stenoses ≥ 50%, 30.9% of all stenoses ≥ 50% were located in major or minor side branches. We found no great difference in lesion localization between men and women.

Distal segments contribute an additional 16.1% of stenoses ≥ 50%.

Only 5% of patients who underwent first coronary angiography had stenoses ≥ 50% in distal segments or minor side branches, without a more proximal stenosis in a proximal or medial main segment or a major side branch (Fig. 2).

A total number of 13,661 coronary interventions (PCI or stent implantation) were documented. Interventions were

Table 1. Balloon/stent size (mm) compared to modified classification of coronary artery segments, according to AHA classification

Balloon/stent size in mm		5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.5	Treated in %	Coronary artery	
Coronary artery segment	According to Fig. 1[b]											
Proximal RCA	1	[a]	0.1	1.0	3.5	4.3	1.4	0.2	[a]	10.5	34.5	RCA
Medial RCA, RVB	2	[a]	0.1	0.9	3.6	5.6	2.2	0.2	[a]	12.7[a]		
Distal RCA	3	*	*	0.2	1.3	3.7	2.8	0.3	*	8.2*		
PLV/PDA	4	*	*	*	0.1	0.5	1.9	0.6	*	3.1		
LM	5	*	*	0.1	0.3	0.4	0.1	*	*	1.0*	1.0	LM
Proximal LAD	6	*	*	0.3	2.0	4.9	1.9	0.2	*	9.4*	38.3	LAD
Medial LAD	7	*	*	0.2	1.9	8.4	5.2	0.4	*	16.1		
Distal LAD	8	*	*	*	0.2	1.9	4.7	0.9	*	7.7		
D1	9	*	*	*	*	0.5	2.4	1.0	*	4.0*		
S1-3, D2-3	10	*	*	*	*	*	0.6	0.4	*	1.1*		
Proximal LCX	11	*	*	*	0.8	2.2	1.7	0.3	*	5.0*	26.2	LCX
M1	12	*	*	*	0.1	1.0	2.6	0.7	*	4.5*		
Medial LCX	13	*	*	0.1	0.7	3.0	3.5	0.6	*	8.0*		
M2-3, PLV	14	*	*	*	0.1	0.8	2.1	0.7	*	3.8*		
Distal LCX	15	*	*	*	0.3	1.1	2.8	0.7	*	4.9		
Total in %		0.1*	0.2	2.8	14.9	38.4*	35.9	7.2	0.5*	100	100	
Cumulative in %		0.1	0.3	3.1	18.0	56.4	92.3	99.5	100			

[a]In some cases original data were not in relevant quantity in every box of table (empty boxes); they were summarized and rounded.
[From Ref. (15).]
[b]Figure 1 demonstrates modified system of coronary arteries according to AHA classification.

done in 12,280 patients [3,757 women (30.6%) and 8,523 men (69.4%)]. Gender distribution of interventions was similar to the distribution of included women and men of all patients. Interventional treatment was performed in all coronary segments (Fig. 1).

The size in millimeters of the balloon or stent used for PCI for all coronary artery segments is shown in Table 1. The great majority of interventions (92.3%) are performed with balloons or stents of $\geq$ 2.5 mm and 83.5% of PCIs are performed in main coronary artery segments.

Figure 3 shows the localization of significant stenoses and interventions for the five groups of coronary artery segments.

4. Discussion

From a large dataset of invasive coronary angiograms and PCIs, we were able to draw the following observations, which are relevant for users of noninvasive imaging techniques to optimize their imaging strategies:

1. Significant numbers of coronary artery stenoses can be found in all coronary segments with a tendency towards location in the proximal and medial segments. Major and minor side branches contribute more than 30% of significant stenoses.
2. Only 5% of patients who undergo first catheterization have relevant coronary artery stenoses only in distal segments or minor side branches.
3. 83.5% of PCIs are performed in main coronary artery segments.
4. More than 90% of interventions are performed in coronary arteries with vessel size of 2.5 mm or more.

Our observations have significant influence on noninvasive imaging strategies since noninvasive imaging may be used for several reasons, requiring different degrees of accuracy.

The imaging technique is used to decide on the therapy regimen. This requires accurate information on the **existence**, **location**, **distribution**, and **quantification** of disease.

Such an approach requires detection and quantification of stenoses within the full coronary artery tree, since more than 30% of significant stenoses can be found in major or minor side branches. In addition, since interventions are also performed in distal main segments (20.8%) and major and minor side branches (16.5%), visualization and quantitative assessment of these lesions would be necessary.

However, since interventions are mainly performed with balloon/stent sizes of $\geq$ 2.5 mm and only 7.7% of PCIs are performed with smaller devices, one might argue that the spatial resolution used in invasive angiography (approximately 0.3 $\times$ 0.3 mm) might currently not be fully required for noninvasive imaging.

Indeed, other observers found that the absolute number of new lesions was high in distal coronary segments but low in segments with diameters < 2 mm. Their conclusion was that angiographic follow-up studies should analyze coronary segments at all locations but may neglect segments with diameters smaller than 2 mm (16, 17).

The imaging technique is used to decide whether or not to proceed to invasive angiography.

This requires accurate information on the *existence or absence* of significant disease only. Again, full coverage of the whole coronary artery tree is the only imaging strategy that would allow complete exclusion of disease. However, only 5% of patients present with stenoses only in their distal main segments or minor side branches and 95% of all other patients have at least one significant stenosis in a proximal or medial main segment or major side branch. The decision whether or not to proceed to invasive angiography could be based on the visualization of proximal and medial main segments and major side branches only. This strategy would result in an intrinsic error of approximately 5%.

4.1. *Limitations of current imaging techniques*

Several noninvasive methods have been suggested for visualization of the coronary arteries. MRCA, EBCT, and MSCT are rapidly evolving techniques and have been examined in larger trials and reported to be useful for the detection or exclusion of significant coronary artery disease. Each of those modalities has its specific advantages and disadvantages.

4.2. *Magnetic resonance coronary angiography*

While magnetic resonance (MR) clearly has the advantage, in comparison to computed tomography (CT) techniques, of relying on magnetization and thus not requiring radiation or contrast agents, the disadvantage is the relatively low signal-to-noise ratio. Whereas this can be compensated for by longer examination times, such prolongation of imaging time requires not only cardiac gating (similarly to CT), but also suppression of breathing motion, which is performed with either breath holding or navigator algorithms, which determine and correct for the position of the diaphragm immediately before data acquisition (18–20). Especially the navigator approach has the advantage of achieving a very high spatial resolution and reducing the acquisition time per heart beat to below 100 ms, which may be required to fully suppress coronary artery motion even if imaging is restricted to mid-diastole (20, 21). In the literature diagnostic accuracy rates ranging from 38% to 90% are reported for single center studies (4, 5, 22) and 72% for a recent multi-center trial (5). However, in all these studies the investigators restricted themselves to the more proximal portions of the coronary artery tree. Spatial resolution ranged from 1.6 $\times$ 0.8 $\times$ 5.0 mm to 0.7 $\times$ 0.7 $\times$ 1.5 mm in most studies (5, 6, 23). Thus, according to the specifications set forth in the current study, the paper by Kim et al. (5) concludes that a specific group of patients (those with triple vessel disease) can be reliable detected—since at least one of the stenoses in these patients can be found with the local coverage described.

Cardiac magnetic resonance (CMR) has the advantage of simultaneous functional assessment. The general question is, if the visualization of the coronary arteries alone is clinically important or even solely, the evaluation of functional consequences of ischemia would be sufficient. Currently, the major therapeutic decisions (PCI, implantation of stent, aortocoronary bypass) are based on coronary angiograms and the presence of treatable coronary stenoses. We believe that the detection of ischemia rather than the current possible noninvasive visualization of the coronary arteries and quantification of stenoses can help to make a treatment decision.

Future studies need to cover larger proportions of the coronary artery tree, especially major side branches. This will be achieved by using sequences with higher signal-to-noise ratio, better motion compensation, higher field strength (e.g., 3 Tesla), and intravascular contrast agents.

4.3. *Electron-beam computed tomography*

EBCT is a method with high spatial resolution (0.7 × 0.7 × 2.0 mm) and signal-to-noise ratio. The main disadvantages are its limited availability and the difficulty of visualizing stenoses in calcified areas of the coronary artery tree. However, small vessel diameters (< 1.5 mm) were found to lead to false-positive findings (9). Diagnostic accuracy has been reported to be 70% (8); however, 20–25% of coronary artery segments could not be evaluated (8, 24). Thus, the technique may be suited to making a decision whether or not to proceed to invasive angiography but not able to prove or exclude significant coronary artery disease. However, since nondiagnostic segments may be found in proximal or medial parts of the coronary artery tree, the intrinsic error is variable and depends on the number of visible segments.

4.4. *Multislice computed tomography*

The enormous advances in hardware for MSCT have encouraged its application for coronary artery imaging. Major limitations are high radiation and a relatively long acquisition duration per heart beat—around 125–250 ms (12), depending on the equipment. Methods to further shorten this time lead to an even higher radiation and may also increase the duration of the breath hold—which is already between 20 and 35 seconds depending on heart rate and imaging volume (10). However, continuous X-ray radiation during systole and diastole with MSCT leads to an exposure of approx. 9 mSv or more (EBCT: 1.5 mSv). A new technique, which reduces the current of the X-ray during systole, can lower the radiation exposure (25). Another limitation is motion artifacts, especially of the rapidly moving right coronary artery (RCA) and coronary calcifications, which make a large number of coronary segments unevaluable (26, 27).

Diagnostic accuracy has been reported to be between 58% and 78% (10–12); again around 30% of coronary artery segments had to be excluded from the analyses (12, 28). Premedication with oral ß-blockade to minimize motion artifacts and improved spatial resolution seem to permit higher accuracy in the detection of coronary artery stenoses (11, 29). Thus, the technique may also be suitable to make a decision whether or not to proceed to invasive angiography but not to prove or exclude significant coronary artery disease. However, the high number of nondiagnostic segments causes an intrinsic error dependent on the location of these segments.

4.5. *Limitations*

A potential limitation of the current study may be the patient population, since all patients had an indication for cardiac catheterization. Thus, the results cannot be transferred to a group with a lower pretest probability.

A further potential limitation is the visual assessment of the coronary angiograms without quantitative determination. The accuracy of such a visual assessment depends on the experience of the observers and is approximately 90% within our quality control program.

The number of stenoses at distal position at coronary artery tree could be interpreted too low, because of high grade stenosis at proximal or medial localization.

Some investigators would conclude segment 4 to be a major side branch; we acquired this segment as a minor side branch.

In this study we did not assess the impact of MRCA spatial resolution and image contrast for evaluation of small and distal vessels. However, from the data obtained, we may conclude that for the utilization of MRCA as a screening method for treatable CAD the detection of stenoses in vessels greater than 2 mm in size is sufficient. For the purpose of stenosis quantification in vessels with a diameter as small as 2 mm, the spatial resolution would have to be around 0.2 mm in all three dimensions (30). Potentially, this can be advised with MRCA; however, current available methods usually result in a spatial resolution of approximately 1.2 × 1.2 mm (31).

No direct determination of vessel size was performed; however, an estimation of vessel size can be devised from the balloon or stent used for PCIs. For interventional treatment, usually a stent with a slightly larger diameter than the vessel itself is chosen (32). In a study with quantitative determination of vessel size, stent size was 10–20% larger than that of the artery (33). Thus, a mild overestimation of vessel size may be assumed with the reported approach.

5. Conclusion

Imaging strategies with noninvasive modalities can be adapted to the size of vessels and distribution of coronary artery lesions. The decision whether or not a patient with suspected CAD should proceed to invasive angiography can be reliably made from a visualization of proximal and medial main segments and major side branches, yielding an intrinsic error of only 5%. This approach, however, cannot be used to detect or exclude disease or make a treatment decision.

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