International Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Coronary artery stenoses more often overestimated in older patients Angiographic stenosis overestimation in elderly

Nanette M Borren, Jan Paul Ottervanger *, Martijn A Reinders, Elvin Kedhi

Department of Cardiology, Isala, Zwolle, The Netherlands

ARTICLE INFO

Article history:
Received 20 January 2017
Accepted 27 February 2017
Available online xxxx

Keywords:
Coronary angiography
Fractional flow reserve
Angiographic overestimation
Age

ABSTRACT

Background: Angiographic overestimation of coronary artery stenosis severity may result in unnecessary revascularization and is possibly more prevalent with increasing age.
Aim: To identify whether age is an independent clinical predictor for angiographic overestimation of a coronary artery stenosis.
Methods: Fractional flow reserve (FFR) of 335 coronary lesions was performed in 260 consecutive patients with stable coronary artery disease (CAD). Overestimation was defined as an angiographically significant stenosis, with normal FFR (>0.80). Age was analysed as both continuous variable and quartiles. The highest age quartile was compared to the remaining quartiles. Multivariable analyses were performed to adjust for differences in baseline variables.
Results: Mean age of the total population was 65 ± 10 years, overestimation was observed in 11%. Mean age of patients with overestimation was 69 ± 11 years, compared to 65 ± 10 years in those without overestimation ($p = 0.01$). Overestimation was observed significantly more often in the highest age quartile (22%) in comparison with the younger patients (8.0%) ($p < 0.001$). The adjusted odds ratio for overestimation in the highest quartile group was 3.15 (95% confidence interval: 1.48–6.69).
Conclusion: Increasing age is a strong and independent predictor for angiographic overestimation of the severity of a coronary stenosis. Functional measurement of coronary artery stenoses should be considered more often, particularly in elderly to avoid unnecessary revascularization.

1. Introduction

Prevalence of coronary artery disease (CAD) increases with age [1]. In daily practice invasive coronary angiography is used in the decision-making regarding revascularization in patients with CAD. However, coronary angiography has limited accuracy in demonstrating the functional importance of a coronary stenosis [2,3]. An accurate diagnosis is of great importance for appropriate treatment and estimating prognosis in all patients with ischemic heart disease. Particularly in elderly accurate diagnosis is imperative, because of a higher risk of peri-procedural complications associated with coronary revascularization [4,5]. Despite recommendations in current guidelines to assess the functional severity of a coronary artery stenosis, visual assessment still dominates the treatment decisions in intermediate coronary artery stenoses [6]. Previous studies demonstrated clinical and lesion-specific factors associated with angiographic overestimation of lesion severity [7–9]. Few studies suggested that angiographic overestimation increases with older age [7,10,11]. However the definition of an angiographic significant stenosis was not according to current guidelines [2,7]. The other study included a selected patient population and the third study only investigated overestimation in the left anterior descending artery (LAD) [10,11]. We investigated a more common patient population and aimed to identify whether age is an independent clinical predictor for angiographic overestimation of the severity of coronary stenoses.

2. Methods and materials

2.1. Study population

260 consecutive patients with stable angina pectoris who underwent fractional flow reserve (FFR) measurements after diagnostic invasive coronary angiography in Isala hospital, Zwolle, the Netherlands were included in this study [12]. All 260 patients underwent non-invasive ischemic tests before coronary angiography. Both patients with positive non-invasive tests and patients with equivocal or negative tests but with persisting symptoms were referred for coronary angiography. Experienced interventional cardiologists visually estimated the severity of the coronary artery stenosis. FFR measurements of numerous stenoses in the same patient could be performed. A total of 335 coronary lesions were evaluated by both visual estimation and FFR measurement. The retrospective study was approved by the accredited Committee on Research Ethics of our hospital.

* Corresponding author at: Department of Cardiology, Isala, Dr. Van Heesweg 2, 8025 AB Zwolle, The Netherlands.
E-mail address: j.p.ottervanger@isala.nl (J.P. Ottervanger).

http://dx.doi.org/10.1016/j.ijcard.2017.02.134
0167-5273/

2.2. Clinical information

Information regarding patient age, gender, weight and height were collected retrospectively from medical records. Furthermore demographic information, prior medical history and cardiac risk factors were collected likewise. Current smoking was defined as at least one cigarette, cigar or pipe a day. Diabetes was defined as hyperglycaemia with HbA1C of 6.5% or more, or current use of oral anti-diabetic medication or insulin. Hypertension was described as a blood pressure measured higher than 140/90 mmHg during at least three times, or the use of antihypertensive drugs for the indication of hypertension. Hypercholesterolemia was stated as fasting total cholesterol of 5.0 mmol/L or more, or the use of lipid-lowering drugs. Moreover a positive family history was defined as a first-degree family member <60 year with CAD. Information was stored in IBM SPSS Statistics 20.0 database.

2.3. Coronary angiography

The invasive coronary angiography procedures were performed by a femoral or radial approach, using a 6 Fr diagnostic or guiding catheter. The angiogram was repeated in the projection allowing the best possible visualization of the stenosis. Two independent interventional cardiologists scored the lesions visually. In case of a discrepancy, a third interventional cardiologist was asked. Diameter stenosis < 30% was interpreted as normal in the right coronary artery (RCA), the circumflex artery (Cx) and the LAD. A stenosis of ≥30% but <70% was defined functionally non-significant. Diameter stenoses estimated ≥70% were considered significant. A left main artery (LM) stenosis was interpreted significant when the diameter stenosis was ≥50% [2].

2.4. Pressure measurement

All patients underwent FFR measurement. By invasive coronary angiography, a 0.014-in. pressure monitoring wire (RADI Pressure™ wire, RADI Medical Systems AB, Uppsala, Sweden or Primewire PRESTIGE® Pressure guide wire, Volcano Inc., Rancho Cordova, California, USA) was advanced through a guiding catheter and positioned distal tot the coronary artery stenosis under investigation. Maximal coronary blood flow was obtained by continuously infusion of adenosine (140 μg/kg/min) through a 5 Fr sheath in the femoral vein, to achieve minimal distal coronary pressure. After steady-state hyperaemia was achieved, FFR was calculated as the mean distal coronary pressure measured by the pressure wire divided through the mean aortic pressure at the tip of guiding catheter. FFR values of ≤0.80 were considered functionally significant [13,14].

2.5. Statistical analysis

Statistical analysis was performed with IBM SPSS statistics 20.0. Quantitative variables were reported as mean ± standard deviation, categorical variables as frequencies and percentage. Age was analysed as continuous variable, as well as divided into quartiles. Continuous variables were compared using unpaired *t*-test or nonparametric Mann–Whitney *U* test. Normal distribution was tested with the test of normality. Categorical variables were compared using Pearson's Chi-square test or Fisher's exact test, as appropriate. Visually assessed diameter stenosis was compared to FFR value of these coronary lesions. Angiographic overestimation of a lesion was defined as a coronary stenosis visually estimated significant, which was functionally not significant, demonstrated by FFR. Subsequently, predictors for angiographic overestimation of coronary artery stenosis severity were analysed. The prevalence of overestimation in the highest age group was compared to the prevalence of overestimation in the other age groups. Logistic regression analysis was performed to identify independent determinants for angiographic overestimation. The adjusted odds ratio and 95% confidence intervals for angiographic overestimation of coronary artery stenosis severity in elderly were calculated. A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical characteristics

In Table 1, the clinical characteristics of the patients are presented. Mean age of the 260 patients was 65 ± 10 years, 65% of the study population was male. Almost 70% of the patients had hypertension. 6% of the patients had undergone previous percutaneous intervention and >50% of the patients already used cardiovascular medication. Data from 335 coronary artery stenoses were analysed. FFR values ranged from 0.22 to 1.00, with a mean resting pressure distal divided trough aortic pressure (Pd/Pa) before administration of adenosine of 0.93 ± 0.07 and a mean FFR of 0.82 ± 0.09. Overall 133 coronary lesions (40%) had a FFR ≤ 0.80.

Table 1
Clinical characteristics in 260 patients.

Clinical characteristics	$n = 260$
Age (years)	64.9 ± 9.8
Male gender	168 (65%)
Body mass index (kg/m^2)	28.1 ± 4.4
Risk factors	
Current smoker	43 (17%)
Diabetes	55 (21%)
Hypercholesterolemia	152 (59%)
Hypertension	175 (67%)
Positive family history	145 (56%)
Comorbidity	
Prior myocardial infarction	9 (3.5%)
Prior PCI	16 (6.2%)
Prior CABG	2 (0.8%)
Prior CVA	21 (8.1%)
PAD	17 (6.5%)
Medication	
Aspirin	142 (55%)
Beta blockade	159 (61%)
ACE/A-II inhibitor	126 (49%)
Ca-channel blocker	55 (21%)
Statin	143 (55%)

Values are n (%) or mean ± SD. *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass grafting, *CVA* cerebro-vascular accident, *PAD* peripheral artery disease, *ACE* angiotensin-converting enzyme.

3.2. Age quartiles

The study population was, as stated above, divided into quartiles based on the age of the patients, ≤58 years, 59–64 years, 65–72 years, and >72 years. Differences in clinical characteristics between patients in the highest age quartile and the remaining patients are summarized in Table 2. Older patients were more often female, all other characteristics were comparable between younger and older patients. A trend was seen in the history of hypertension, which was more often present in older patients ($p = 0.07$). Also, a trend was demonstrated in the frequency of current smokers and hypercholesterolemia. Both were more often present in the younger patients. FFR ≤ 0.80 was less frequent in older patients ($p = 0.003$).

3.3. Overestimation

Angiographic overestimation of coronary artery stenosis severity was demonstrated in 11% of all 335 coronary artery lesions ($n = 37$). Clinical characteristics of the lesions that were overestimated were compared to lesions that were not overestimated (Table 3). Overestimation was less frequently seen in lesions located in the LAD

Table 2
Differences in clinical characteristics between the highest age quartile (≥73 years) and the remaining patients in 335 segments.

Characteristics	<73, $n = 253$	≥73, $n = 82$	p^*
Male gender	188 (74%)	36 (44%)	<0.001*
Body mass index (kg/m^2)	28.1 (±4.5)	27.6 (±4.0)	0.33
Current smoker	47 (19%)	9 (11%)	0.11
Diabetes	53 (21%)	13 (16%)	0.31
Hypercholesterolemia	158 (63%)	43 (52%)	0.11
Hypertension	164 (65%)	62 (76%)	0.07
Positive family history	153 (61%)	42 (51%)	0.14
LAD lesion location	147 (58%)	40 (49%)	0.14
Angiography significant	68 (27%)	30 (37%)	0.09
FFR < 0.80	112 (44%)	21 (26%)	0.003*

Values are *n* (%) or mean ± SD. *FFR* fractional flow reserve; *LAD* left anterior descending artery.
[a]Based on a *t*-test for continuous normally distributed variables, for body mass index the Mann–Whitney *U* test was used, and the χ^2-test was used for dichotomous variables.
* *p* value < 0.05.

Please cite this article as: N.M. Borren, et al., Coronary artery stenoses more often overestimated in older patients, Int J Cardiol (2017), http://dx.doi.org/10.1016/j.ijcard.2017.02.134