Atherosclerosis 238 (2015) 427–429

Contents lists available at ScienceDirect

Atherosclerosis

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

Invited commentary

Coronary evaluation in patients with stroke: Recognizing the risk

Johann Auer

Department of Cardiology and Intensive Care, General Hospital Braunau, Austria

ARTICLE INFO

Article history:
Received 10 November 2014
Received in revised form
16 November 2014
Accepted 16 November 2014
Available online 18 November 2014

Keywords:
Coronary artery disease
Ischemic stroke
Coronary-artery calcium scores
Coronary computed tomographic angiography

1. Stroke – a heterogenous group of vascular diseases

Patients with acute ischemic stroke are heterogenous with respect to etiology, which makes targeted treatment challenging. Most trials investigating strategies for stroke prevention have targeted patients with stroke of presumed atherothrombotic (small-artery occlusion and large-artery atherosclerosis), or cardioembolic origin. Additionally, some rare causes of stroke are well defined such as single-gene and mitochondrial disorders. The five major categories of the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification are large-artery atherosclerosis, including large-artery thrombosis and artery-to-artery embolism; cardioembolism; small-artery occlusion; stroke of other determined cause; and stroke of undetermined cause [1]. Thus, cerebrovascular atherosclerosis only accounts for a subgroup of ischemic strokes. However, overt atherosclerotic vascular disease beyond cerebrovascular lesions including coronary artery disease (CAD) predicts deaths and future major cardiac events [2–4].

2. The scope of the problem

The prevalence of coronary artery disease in stroke patients is substantial. Amarenco and colleagues found a high prevalence of coronary atherosclerosis based on coronary angiography data in a large series of consecutive patients with a nonfatal cerebral infarction and no previously known coronary heart disease. Coronary plaques on angiography were present in 61.9% of patients and diameter stenosis more than 50% was found in 25.7% of stroke patients [5]. This study included patients largely irrespective of the cause of stroke.

A French study based on systematic 64-section computed tomography coronary angiography shows that almost 20% of patients between 45 and 75 years of age with non-disabling, non-cardioembolic ischemic stroke or transitory ischemic accident (TIA) have asymptomatic coronary artery disease (CAD) defined as coronary diameter stenosis of 50% or more [6]. The results of the present study by Hur and colleagues [7] with a prevalence of obstructive CAD (coronary diameter stenosis of 50% or more) based on coronary computed tomography angiography assessment of 48% corroberate and extend previous findings.

3. Prognostic value of coronary artery calcium scores (CACS) and coronary computed tomography angiography (CCTA)

Computed tomographic measurements of coronary-artery calcium scores (CACS) predict coronary heart disease independently of traditional coronary risk factors [8–11]. A doubling of the calcium score increased the estimated probability of both major coronary events including myocardial infarction and coronary death, and any coronary event by approximately 25% during 4 years follow-up [12].

Beyond CACS, coronary computed tomographic angiography (CCTA)-defined extent and severity of coronary artery disease has been shown to be associated with all-cause mortality [13,14].

4. What is the prognostic value of coronary artery calcium scores (CACS) and coronary computed tomography angiography (CCTA) in individuals with stroke

Previous studies investigating stroke patients for coronary artery disease used either non-invasive testing, coronary computed tomography (CCT), or invasive coronary angiography [5,6]. CCTA is a non-invasive test characterized by high accuracy when compared to invasive coronary angiography [15]. However, no previous trial has investigated the prognostic value of CCTA in stroke patients. In this issue of *Atherosclerosis*, the study by Hur et al. [7] provides for the first time, data on the prognostic utility of CCT in patients with

DOI of original article: http://dx.doi.org/10.1016/j.atherosclerosis.2014.10.102.

http://dx.doi.org/10.1016/j.atherosclerosis.2014.11.010

ischemic stroke. 317 patients without chest pain but with at least one clinical risk factor for coronary artery disease were prospectively included and followed for about 13 months. CCT scans were assessed for CAC, presence and extent of CAD. The primary combined endpoint included cardiac death, nonfatal myocardial infarction, unstable angina requiring hospitalization, or revascularization beyond 90 days following the index CCTA.

Any amount of coronary artery calcium on CCT was present in 73.1% of all patients. Despite the low number of endpoints (only a total of 26 major adverse cardiac events) the authors could demonstrate that the presence and extent (1-vessel disease (VD), 2-VD, and 3-VD) of obstructive CAD (definded as 50% diameter stenosis or more), independently predicted the risk of future events [7].

However, this intriguing finding should be considered hypothesis generating and has to be confirmed in further studies. Important shortcomings regarding design and conduction of the study definitely preclude final conclusions and clinical recommendations at this stage. Some of these shortcomings are mentioned in the paper and include the small number of outcome events with no cardiac deaths and only two non-fatal myocardial infarctions [7]. The outcome was entirely driven by "weak" endpoints (unstable angina requiring hospitalization, and revascularizations). Some of these events (in particular revascularisation procedures) may have been triggered by CCTA results.

5. Predictive value of coronary computed tomography angiography beyond traditional risk factors and coronary artery calcium scoring

Current evidence do not support a predictive value of CCTA over and beyond the CACS and the Framingham risk score (FRS), among unselected asymptomatic individuals without stroke [16]. However, the prognostic value of CCTA may differ for asymptomatic patients, when stratified by CACS severity. Recently, a large multicentre observational registry could demonstrate that CCTA may provide incremental prognostic utility for prediction of mortality and non-fatal myocardial infarction only for asymptomatic individuals with moderately high CACS, but not for lower or higher CACS [17].

No previous trial has investigated the prognostic value of CCTA over CACS and FRS among patients with ischemic stroke. Hur and colleagues found that the presence of obstructive CAD and the number of involved vessels assessed by CCTA improved risk stratification beyond clinical risk factors and CACS [7]. Based on the limitations regarding design and conduction of this study mentioned above, this finding has to be considered hypothesis generating and has to be confirmed in further trials or registries.

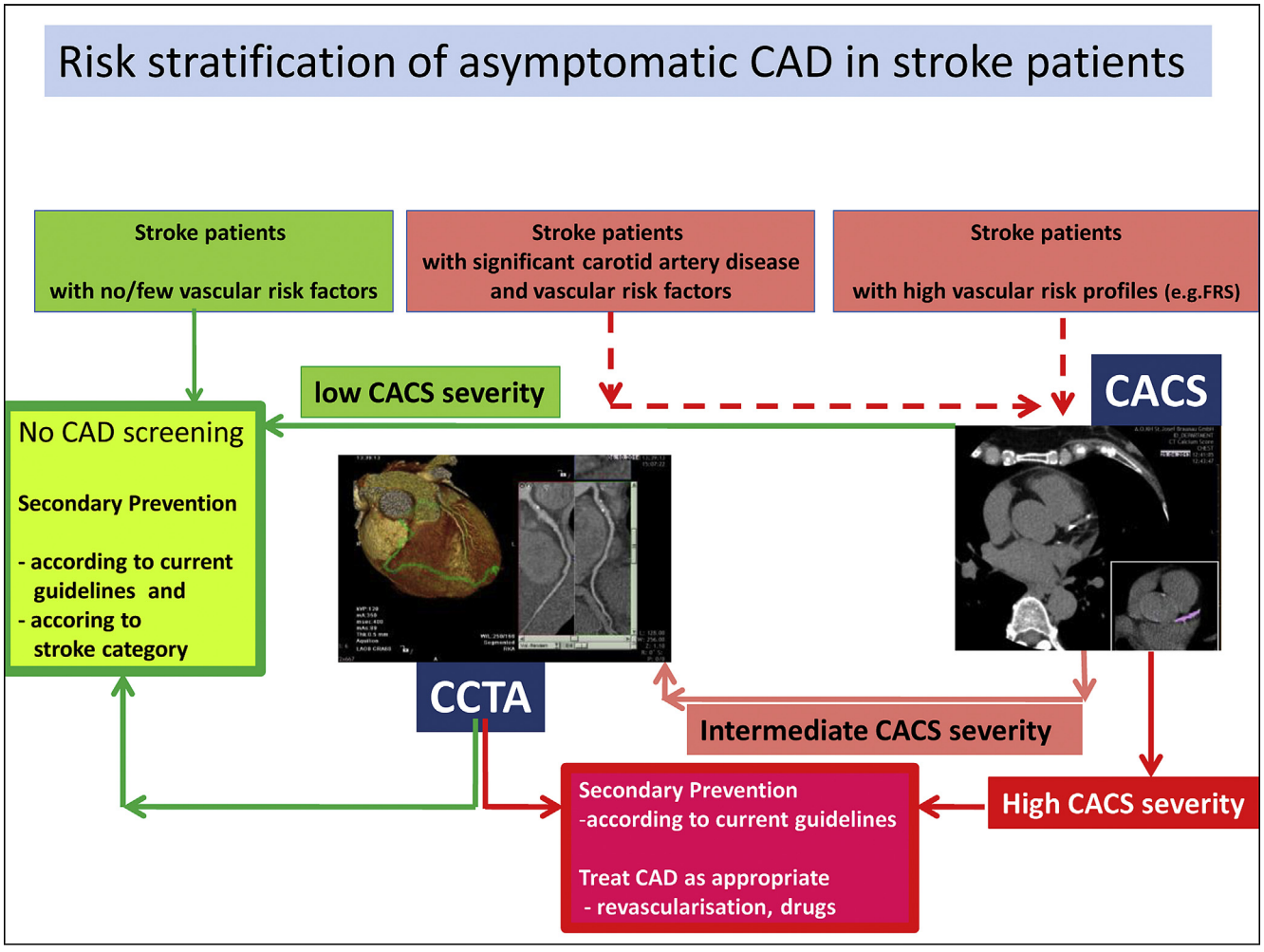

Fig. 1. Coronary artery disease (CAD) detection by CACS and CCTA for risk stratification in patients with ischemic stroke.

6. Should we change current recommendations?

Because unrecognized CAD is prevalent in patients with carotid artery disease, current scientific statements recommend evaluation for CAD in selected stroke patients with high cardiovascular risk profiles in the presence of significant carotid artery lesions [18]. Additionally, regardless of stroke subtype, patients with high CAD risk based on Framingham risk calculations should also be considered for such evaluation. In contrast, current recommendations suggest that stroke patients with fewer vascular risk factors and without significant carotid artery disease and patients with stroke subtypes that are not clearly related to atherosclerosis may be at lower risk for presence of coronary artery disease and coronary events and routine testing is not recommended on the basis of available evidence [18].

The present study by Hur and colleagues suggest a high prevalence of CAD in selected stroke patients with CAD risk factors [7]. Surprisingly, Framingham risk score was no indepedent predictor of outcome events in this study. The authors do not provide information about patients with stroke subtypes that are not clearly related to atherosclerosis such as cardioembolism. No information is available about differences in prevalence of CAD and outcome between stroke patients with presumed atherothrombotic or cardioembolic origin [7].

It remains unclear if the incremental risk stratification benefit of CCT findings in ischemic stroke patients without chest pain may translate in improved outcomes. Future large randomized trials with much longer follow up have to be performed to estimate the potential influence of CCT findings on treatment strategies (including pharmacotherapy [19] and revascularisation procedures) to optimize management and outcomes of patients with ischemic stroke.

Additionally, lifetime attributable risk of cancer after a single radiation exposure from 64-slice computed tomographic coronary angiography has to be taken into consideration when patients are exposed to such diagnostic procedures in the absence of any proven outcome benefit [20,21].

In conclusion, based on current evidence, CCT screening for CAD in unselected asymptomatic individuals after ischemic stroke cannot be recommended and current guidelines (as mentioned above) stay valid until results from future large trials on optimization of management and outcomes of stroke patients stratified by CCT are available [18] Fig. 1.

Disclosures

Within the last 36 months. J. Auer has nothing to disclose regarding this paper.

References

[1] H.P. Adams, B.H. Bendixen, L.J. Kappelle, J. Biller, B.B. Love, D.L. Gordon, E.E. Marsh III, Classification of subtype of acute ischemic stroke: definitions for use in a multicenter clinical trial, Stroke 24 (1993) 35–41.

[2] Z.X. He, T.D. Hedrick, C.M. Pratt, et al., Severity of coronary artery calcification by electron beam computed tomography predicts silent myocardial ischemia, Circulation 101 (2000) 244–251.

[3] G.T. Kondos, J.A. Hoff, A. Sevrukov, et al., Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomic low- to intermediate-risk adults, Circulation 107 (2003) 2571–2576.

[4] R. Wayhs, A. Zelinger, P. Raggi, High coronary artery calcium scores pose an extremely elevated risk for hard events, J. Am. Coll. Cardiol. 39 (2002) 225–230.

[5] P. Amarenco, P.C. Lavallée, J. Labreuche, G. Ducrocq, J.M. Juliard, L. Feldman, et al., Prevalence of coronary atherosclerosis in patients with cerebral infarction, Stroke 42 (2011) 22–29.

[6] D. Calvet, E. Touzé, O. Varenne, J.L. Sablayrolles, S. Weber, J.L. Mas, Prevalence of asymptomatic coronary artery disease in ischemic stroke patients: the precoris study, Circulation 121 (2010) 1623–1629.

[7] J. Hur, Kye Ho Lee, Sae Rom Hong, Young Joo Suh, Yoo Jin Hong, Hye-Jeong Lee, Young Jin Kim, Hye Sun Lee, Hyuk-Jae Chang, Byoung Wook Cho, Prognostic value of coronary computed tomography angiography in stroke patients, Atherosclerosis 238 (2014) 271–277.

[8] P. Raggi, T.Q. Callister, L.J. Shaw, Progression of coronary artery calcium and risk of first myocardial infarction in patients receiving cholesterol-lowering therapy, Arterioscler. Thromb. Vasc. Biol. 24 (2004) 1272–1277.

[9] P. Raggi, B. Cooil, T.Q. Callister, Use of electron beam tomography data to develop models for prediction of hard coronary events, Am. Heart J. 141 (2001) 375–382.

[10] L.J. Shaw, P. Raggi, E. Schisterman, D.S. Berman, T.Q. Callister, Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality, Radiology 228 (2005) 826–833.

[11] A.J. Taylor, J. Bindeman, I. Feuerstein, F. Cao, M. Brazaitis, P.G. O'Malley, Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the prospective army coronary calcium (PACC) project, J. Am. Coll. Cardiol. 46 (2005) 807–814.

[12] R. Detrano, A.D. Guerci, J.J. Carr, D.E. Bild, G. Burke, A.R. Folsom, K. Liu, S. Shea, M. Szklo, D.A. Bluemke, D.H. O'Leary, R. Tracy, K. Watson, N.D. Wong, R.A. Kronmal, Coronary calcium as a predictor of coronary events in four racial or ethnic groups, N. Engl. J. Med. 358 (2008) 1336–1345.

[13] J.K. Min, L.J. Shaw, R.B. Devereux, P.M. Okin, J.W. Weinsaft, D.J. Russo, et al., Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality, J. Am. Coll. Cardiol. 50 (2007) 1161–1170.

[14] T.P. Carrigan, D. Nair, P. Schoenhagen, R.J. Curtin, Z.B. Popovic, S. Halliburton, S. Kuzmiak, R.D. White, S.D. Flamm, M.Y. Desai, Prognostic utility of 64-slice computed tomography in patients with suspected but no documented coronary artery disease, Eur. Heart J. 30 (2009) 362–371.

[15] M. Hamon, G.G. Biondi-Zoccai, P. Malagutti, P. Agostoni, R. Morello, M. Valgimigli, et al., Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography: a metaanalysis, J. Am. Coll. Cardiol. 48 (2006) 1896–1910.

[16] I. Cho, H.J. Chang, J.M. Sung, M.J. Pencina, F.Y. Lin, A.M. Dunning, S. Achenbach, M. Al-Mallah, D.S. Berman, M.J. Budoff, T.Q. Callister, B.J. Chow, A. Delago, M. Hadamitzky, J. Hausleiter, E. Maffei, F. Cademartiri, P. Kaufmann, L.J. Shaw, G.L. Raff, K.M. Chinnaiyan, T.C. Villines, V. Cheng, K. Nasir, M. Gomez, J.K. Min, C. Investigators, Coronary computed tomographic angiography and risk of all-cause mortality and nonfatal myocardial infarction in subjects without chest pain syndrome from the CONFIRMRegistry (coronaryCT angiography evaluation for clinical outcomes: an international multicenter registry), Circulation 126 (2012) 304–313.

[17] I. Cho, H.J. Chang, B. O Hartaigh, S. Shin, J.M. Sung, F.Y. Lin, S. Achenbach, R. Heo, D.S. Berman, M.J. Budoff, T.Q. Callister, M.H. Al-Mallah, F. Cademartiri, K. Chinnaiyan, B.J. Chow, A.M. Dunning, A. DeLago, T.C. Villines, M. Hadamitzky, J. Hausleiter, J. Leipsic, L.J. Shaw, P.A. Kaufmann, R.C. Cury, G. Feuchtner, Y.J. Kim, E. Maffei, G. Raff, G. Pontone, D. Andreini, J.K. Min, Incremental prognostic utility of coronary CT angiography for asymptomatic patients based upon extent and severity of coronary artery calcium: results from the coronary CT angiography evaluation for clinical outcomes international multicenter (confirm) study, Eur. Heart J. (2014 Sep 8) (published ahead of print).

[18] R.J. Adams, M.I. Chimowitz, J.S. Alpert, I.A. Awad, M.D. Cerqueria, P. Fayad, et al., Stroke Council and the Council on Clinical Cardiology of the American Heart Association, American Stroke Association, Coronary risk evaluation in patients with transient ischemic attack and ischemic stroke: a scientific statement for healthcare professionals from the stroke council and the council on clinical cardiology of the American heart association/American stroke association, Circulation 108 (2003) 1278–1290.

[19] J. Auer, R. Berent, B. Eber, Statins and cerebrovascular events, Herz 27 (2002) 765–771.

[20] F.F. Faletra, I. D'Angeli, C. Klersy, et al., Estimates of lifetime attributable risk of cancer after a single radiation exposure from 64-slice computed tomographic coronary angiography, Heart 96 (2010) 927–932.

[21] J. Auer, R. Berent, Computed tomographic colonoscopy for colorectal cancer diagnosis, Lancet 382 (2013) 124–125.