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BRIEF COMMUNICATION

Association between Carotid Intima-media Thickness and Early-onset Coronary Artery Disease: Does the site of Sonographic Evaluation Matter?

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Background Intima-media thickness (IMT) is frequently used for risk stratification (RS) due to the association with coronary artery disease (CAD). Nonetheless, the best carotid site to scan is uncertain, especially in the young. The aim of this study was to evaluate the diagnostic performance of IMT measurements performed at different carotid sites.

Methods Eighty-nine subjects ≤45 years were studied (55 with known CAD and 34 controls). IMT measurements were performed at the common carotid (CC), bulb and internal branch (IB) of both carotid arteries, (2112 measures). The diagnostic performance of IMT measurements performed at different sites, regarding the presence of CAD, was evaluated with ROC curves.

Results Carotid plaques were found in 20.0% of the patients and 6.0% of the controls. The diagnostic performance of carotid IMT measures obtained at the CC, bulb or IB was not significantly different, with the CC and IB being slightly better (AUC ROC =0.82 and 0.80 respectively).

Conclusions IMT measures obtained at different carotid sites are associated with CAD in young (≤45 years) individuals. The diagnostic performance of IMT measured at the CC and IB is the more accurate measure, and this may be the most adequate for the measurement of IMT in this population.

Keywords Carotid intima-media thickness • Coronary artery disease • Carotid disease • Atherosclerosis • Echocardiography

Introduction

Measurement of intima-media thickness (IMT) is one of the most commonly employed methods for the detection of subclinical atherosclerosis. It is a noninvasive, safe and cheap test which can be repeatedly performed [1] and has a well-known association with coronary artery disease (CAD). Nonetheless, IMT measurement is challenging due to reproducibility and operator-dependence issues, besides uncertainty about the best carotid segment to scan [2]. In young individuals, the important social and economic consequences of CAD are compelling reasons for an adequate determination of IMT during cardiovascular risk stratification (RS). Therefore, the aim of this study was to evaluate

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the diagnostic performance of IMT measurements performed at different carotid sites in individuals ≤45 years old.

Methods

Ninety-four subjects ≤45 years old were recruited, among whom 58 were patients with a history of myocardial infarction, percutaneous coronary angioplasty or coronary artery bypass grafting, and 36 were volunteers without known CAD (control). The study was performed in compliance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the National Institute of Cardiology (n.0182/12.12.07). All subjects gave written, informed consent before participation in the study.

IMT measures were performed by a certified observer, recorded and reviewed by a second certified observer (both unaware of each individuaĺs medical history). Measures were performed manually and semi-automatically according to the American Society of Echocardiography Guidelines [3], in a Vivid-6 equipment with a 7.5 MHz linear transducer (GE Healthcare, Wisconsin, EUA). IMT was measured at the common carotid (CC), bulb and internal branch (IB) of the right and left carotid arteries. Measurements were performed 1 cm away from the distal segment of the CC, 1 cm proximal to the carotid bifurcation, and within 1 cm of the IB. Carotid plaque was defined as focal echo-structures encroaching into the vessel lumen where the IMT was >1.2 mm. Three patients and two control individuals were excluded due to unavailability of all IMT measures. Thus, 2112 measures from 55 patients and 34 controls were analysed.

Continuous variables were expressed as mean ± standard deviation or median and 25th-75th percentiles, and compared with Studentś t test or Wilcoxońs test. Categorical variables were expressed as number and percentage and compared with chi-square or Fisheŕs exact test. For the analysis of agreement between observers, a Bland-Altman analysis was employed. ROC curves were built using the largest mean IMT value (among right or left arteries and the two observers) obtained at different carotid sites, and considering the presence of CAD as the endpoint. Statistical analysis was performed with Stata software (version 12). Statistical significance was defined as a p-value <0.05.

Results

The mean age of the entire population was 43.0 ±4.0 years and 56.0% were male. Patients with CAD were more frequently hypertensive (94.8 vs 3.0%), diabetic (31.0 vs 0%) and hypercholesterolaemic (89.6 vs 8.3%) than controls (p<0.05). In the former, a history of myocardial infarction was found in 82.7%, percutaneous coronary angioplasty in 65.5% and coronary artery bypass surgery in 37.9%.

Carotid plaques were found in 20.0% of the patients and 6.0% of the controls. Table 1 displays medians, 25th and 75th percentiles of IMT evaluated at different carotid segments. There was good concordance between observers (0.73-0.91). CAD patients had increased IMT (mean 0.15 mm higher than controls). Measures taken at the bulb were 0.12 mm higher than those obtained at the CC, while those from the IB were 0.11 mm smaller. Measures

Table 1 IMT measures of patients and controls, obtained at different carotid sites and their accuracy.

	Observer 1		Observer 2	
	CAD	Control	CAD	Control
Anterior right CC	1.0(0.9-1.1)	0.8(0.8-1.0)	1.0(0.9-1.1)	0.9(0.8-1.0)
Lateral right CC	1.0(0.9-1.1)	0.9(0.8-1.0)	1.0(0.9-1.1)	0.9(0.8-1.0)
Posterior right CC	1.1(0.9-1.2)	0.9(0.8-1.0)	1.0(1.0-1.1)	0.8(0.8-0.9)
Right bulb	1.2(1.1-1.3)	1.1(1.0-1.2)	1.2(1.1-1.3)	1.1(1.0-1.2)
Right internal branch	1.0(0.8-1.1)	0.8(0.7-0.9)	1.0(0.9-1.1)	0.8(0.8-0.9)
Anterior Left CC	1.0(0.9-1.1)	0.8(0.8-1.0)	1.0(0.9-1.1)	0.8(0.8-0.9)
Lateral Left CC	1.1(0.9-1.2)	0.9(0.8-1.0)	1.1(0.9-1.2)	0.9(0.8-0.9)
Posterior Left CC	1.1(1.0-1.2)	0.9(0.8-1.0)	1.1(0.95-1.15)	0.8(0.8-0.9)
Left bulb	1.3(1.1-1.30)	1.1(1.0-1.2)	1.2(1.1-1.3)	1.1(1.0-1.2)
Left internal branch	1.0(0.85-1.1)	1.0(0.85-1.1)	0.8(0.7-0.9)	0.8(0.8-0.9)

	Sensitivity (%) IC 95%	Specificity (%) IC 95%	AUC (IC 95%)	LR (+)	LR (-)
CC	78(0.66-0.87)	82(0.67-0,92)	0.82 (0.74-0,91)	4.4	0.3
Bulb	93(0.83-0.97)	19(0.19-0,49)	0.77 (0.67-0,86)	1.4	0.2
Internal branch	56(0.43-0.69)	85(0.70-0,94)	0.80 (0.70-0,89)	3.8	0.5

CAD, coronary artery disease; CC, common carotid; LR, likelihood ratio; AUC, area under ROC curve

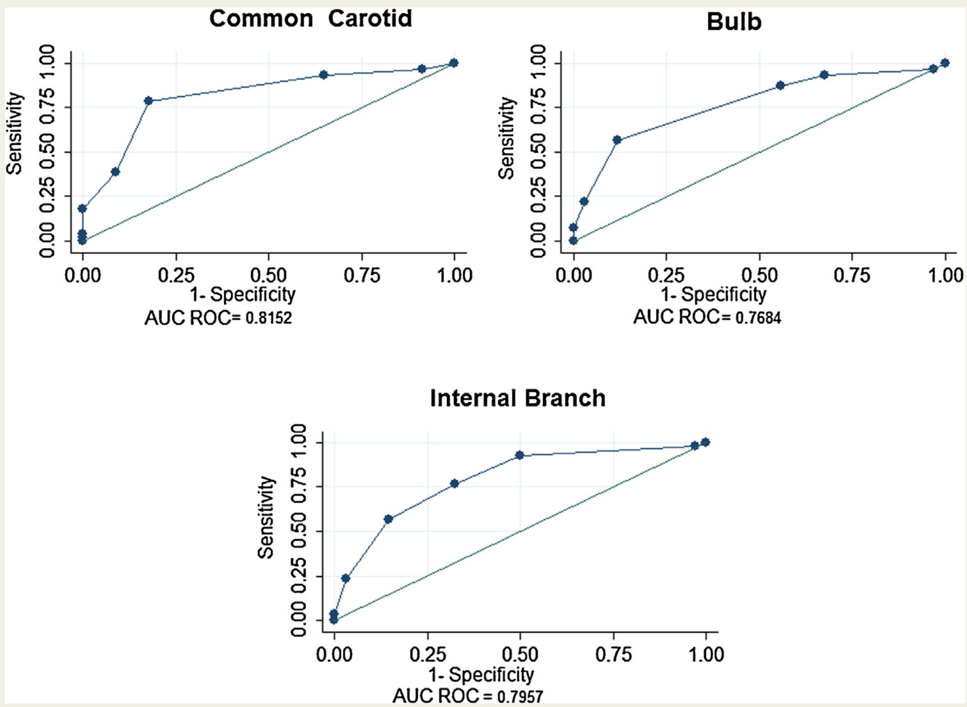

Figure 1 ROC curves for IMT measurements obtained at the common carotid, bulb or internal branch.

performed at all sites were associated with CAD; however, the diagnostic performances of the CC and of the IB were slightly better (Figure 1).

Discussion

Atherosclerotic cardiovascular disease is the main cause of death worldwide [4]. Estimating cardiovascular risk of asymptomatic individuals, such that adequate therapy can be initiated and clinical manifestations of the disease potentially prevented, is a huge challenge [5]. This is even more relevant for young individuals at risk for early CAD [6]. IMT has been suggested to be the best screening test for young people with low risk in traditional risk models [7]; in one study of young and middle-aged asymptomatic individuals with low Framingham score, 47% of those with zero calcium score had evidence of carotid atherosclerosis, while only 15% of those with normal IMT had coronary calcification [8].

One difficulty in IMT evaluation is the determination of the best site for measurement – that is, the one providing the highest accuracy for the diagnosis of carotid atherosclerosis (which, in its turn, will define the increased cardiovascular risk, mostly accounted for the association with CAD). A meta-analysis showed that sensitivity, specificity and odds ratio for the diagnosis of CAD were 68%, 61.5% e 3.2, respectively, when measures were performed in the CC, and 79%, 74.4% e 7.9 when measures were obtained in the IB [9].

Despite the relatively young age, CAD patients had increased IMT, similarly to what has been described in other studies of older patients [3]. The diagnostic performance of carotid IMT measures obtained at the CC, bulb or IB was not significantly different, with the CC and IB being slightly better according to the ROC curve. A previous study reported that IMT measured at the CC has higher reproducibility due to less susceptibility to vessel tortuosity and anatomic variations, suggesting that this would be the best site [10]. Taken together, these data may underscore the larger suitability of the CC and IB for IMT measurement [11,12].

This study is limited due to sample size, and we cannot make a definitive point for best measurement sites; larger studies are needed to address this issue. Nonetheless, it may provide additional information for a better understanding of the relationship between IMT and CAD and the ideal way to detect it.

Conclusions

IMT measures obtained at different carotid sites (common carotid, bulb and internal branch) were associated with CAD in young (≤45 year-old) individuals. The diagnostic performance of IMT measured at the common carotid and internal branch was the highest among all studied sites, suggesting those may be the most adequate for the measurement of IMT in this population.

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References

[1] Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al., European Association for Cardiovascular Prevention & Rehabilitation (EACPR); ESC Committee for Practice Guidelines (CPG). European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J 2012;33(Jul (13)):1635–701.

[2] Inci MF, Ozkan F, Ark B, Vurdem UE, Ege MR, Sincer I, et al. Sonographic evaluation for predicting the presence and severity of coronary artery disease. Ultrasound Q 2013;29(Jun (2)):125–30.

[3] Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness TaskForce. Endorsed by the Society for Vascular Medicine. J Am Soc Echocardiogr 2008;21:93–111.

[4] American Heart Association. Heart Disease and Stroke Statistics, Update, Dallas, Tex, USA, 2014. Circulation 2014;129:e28–e292.

[5] Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2010;56:50–103.

[6] Ferket BS, Genders TS, Colkesen EB, Visser JJ, Spronk S, Steyerberg EW, et al. Systematic review of guidelines on imaging of asymptomatic coronary artery disease. J Am Coll Cardiol 2011;57:1591–600.

[7] Peters SAE, den Ruijter HM, Bots ML, Moons KGM. Improvements in risk stratification for the occurrence of cardiovascular disease by imaging subclinical atherosclerosis: a systematic review. Heart 2012;98:177–84.

[8] Lester SJ, Eleid MF, Khandheria BK, Hurst RT. Carotid intima-media thickness and coronary artery calcium score as indications of subclinical atherosclerosis. Mayo Clin Proc 2009;84:229–33.

[9] Inaba Yoichi, Chenb Jennifer A, Bergmann Steven R. Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: A meta-analysis. Atherosclerosis 2012;220:128–33.

[10] Vijay N, Lloyd C, Max H, Aaron RF, Tom M, Eric B, et al. Common carotid artery intima–media thickness is as good as carotid intima–media thickness of all carotid artery segments in improving prediction of coronary heart disease risk in the Atherosclerosis Risk in Communities (ARIC) study. European Heart Journal 2012;33:183–90.

[11] van den Oord SC, Sijbrands EJ, ten Kate GL, van Klaveren D, van Domburg RT, van der Steen AF, et al. Carotid intima-media thickness for cardiovascular risk assessment: systematic review and meta-analysis. Atherosclerosis 2013;228(May (1)):1–11.

[12] Darabian S, Hormuz M, Latif MA, Pahlevan S, Budoff MJ. The Role of Carotid Intimal Thickness Testing and Risk Prediction for the Development of Coronary Atherosclerosis. Current Atherosclerosis Reports 2013;15:306–12.