Use of Common Carotid Intima-Media Thickness Measured by Ultrasound Echo-Tracking in Cardiovascular Risk Stratification Before Noncardiac Surgery in Low-Risk Category: A Research Idea

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Preoperative cardiac risk stratification algorithms typically use a Bayesian approach to identify a low-risk category group for which the outcome is unlikely to be improved by further testing. This report suggests evaluating common carotid intima-media thickness (CCIMT) as measured by ultrasound to determine whether it strengthens and optimizes perioperative Bayesian risk indices. The idea proposes to use CCIMT *Z* score and vascular age to quantify atherosclerotic burden. CCIMT may be useful as part of shared decision-making for perioperative care. A website (www.suhitam.com/vascularage) designed by one of the authors (S.M.) is a useful resource.)

GLOSSARY

ACC/AHA = American College of Cardiology/American Heart Association; **BMI =** body mass index; **CCA =** common carotid artery; **CCIMT =** common carotid intima-media thickness; **ECG =** electrocardiogram; **POCUS =** point-of-care ultrasound; **RF =** radiofrequency; **ROI =** region of interest; **SD =** standard deviation; **TC-HDL =** total cholesterol to high-density lipoprotein; **WHR =** waist-to-height ratio, total cholesterol HDL ratio (TC-HDL ratio); ***Z* score =** statistical *Z* score

Preoperative cardiac risk stratification algorithms aim to reduce postoperative morbidity and mortality. Typically, a Bayesian approach is used to identify a low-risk category group for which the outcome is unlikely to be improved by further testing. Separation of low risk (<1%) from elevated risk (≥1%) is the key decision point in the 2014 ACC/AHA guidelines for preoperative evaluation for noncardiac surgery. A recent study found that 3 popular prediction models disagreed 29% of the time in allocation of patients to the low-risk (<1%) category.[1] Hence, a technique to afford more unanimity by strengthening and optimizing the Bayesian risk indices would be desirable.[2] One such potential strengthening technique could be common carotid intima-media thickness (CCIMT) measured by ultrasound. It is a validated surrogate marker for atherosclerosis and quantifies atherosclerotic burden in the entire vascular tree.[3]

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CCIMT is usually measured in micrometers. In both men and women, the CCIMT increases progressively with age, for example, 5.2 µm/y in men and 5.0 µm/y in women and can be estimated as follows[4]:

In men,

$$\text{mean CCIMT } (\mu\text{m}) = 323.5 + (5.201 \times \text{age})$$

$$\text{standard deviation (SD) CCIMT } (\mu\text{m}) = 57.24 + (0.9027 \times \text{age})$$

In women,

$$\text{mean CCIMT } (\mu\text{m}) = 321.7 + (4.971 \times \text{age})$$

$$\text{SD CCIMT } (\mu\text{m}) = 54.50 + (0.8256 \times \text{age})$$

Because absolute values of CCIMT are difficult to interpret in a given individual, 2 derived variables, that is, CCIMT *Z* score[4] and vascular age,[5] are used to quantify atherosclerotic burden and hence potential perioperative cardiac risk.

Z score is estimated by the following formula:

$$Z \text{ score} = (\text{observed CCIMT} - \text{mean CCIMT}) / \text{SD CCIMT}$$

Mean and standard deviation (SD) refer to mean and SD of CCIMT for that age and gender.

Vascular age is obtained by comparing the individual's CCIMT against the mean (50th percentile) in the standard age CCIMT table (Supplemental Digital Content, Appendix I, http://links.lww.com/AACR/A297). From a clinical series in an outpatient cardiology clinic, information obtained from CCIMT was explored for feasibility in risk stratification.

DESCRIPTION

As a part of clinical or wellness care, CCIMT was measured by B-mode ultrasonography using 3–13 MHz linear probe. To circumvent the problems related to variability of measurement of CCIMT, a new method called "echo-tracking" is used. The method relies on automated edge detection by radiofrequency signal processing of ultrasound and is therefore more accurate than previous methods.

Features and technical details of the method are as follows: real-time radiofrequency processing of ultrasound; region of interest is 1.5 cm starting from 1.0 cm of vertical reference line just proximal to carotid bulb (Figure 1A); a table alongside image gives measurements of last 6 cardiac cycles; and each cardiac cycle is automatically detected by the arterial wall movement due to heartbeats (absent an electrocardiogram (ECG); good quality measurement indicators are SD <10 with a thick green overlay within the region of interest; Figure 1B). The methodology ensures accuracy and reliability; the method is a patented technology of Esaote and is now available in all MyLab series of Esaote (Genoa, Italy) ultrasound machines; in the present series, data were obtained using an Esaote MyLab Gamma portable ultrasound machine. The study was approved by the institute ethics committee at Indo-US Hospital in which the first author (S.M.) had additional affiliation.

The American Society of Echocardiography has provided detailed recommendations for the measurement of CCIMT.[3] Briefly, the patient is placed in a supine position

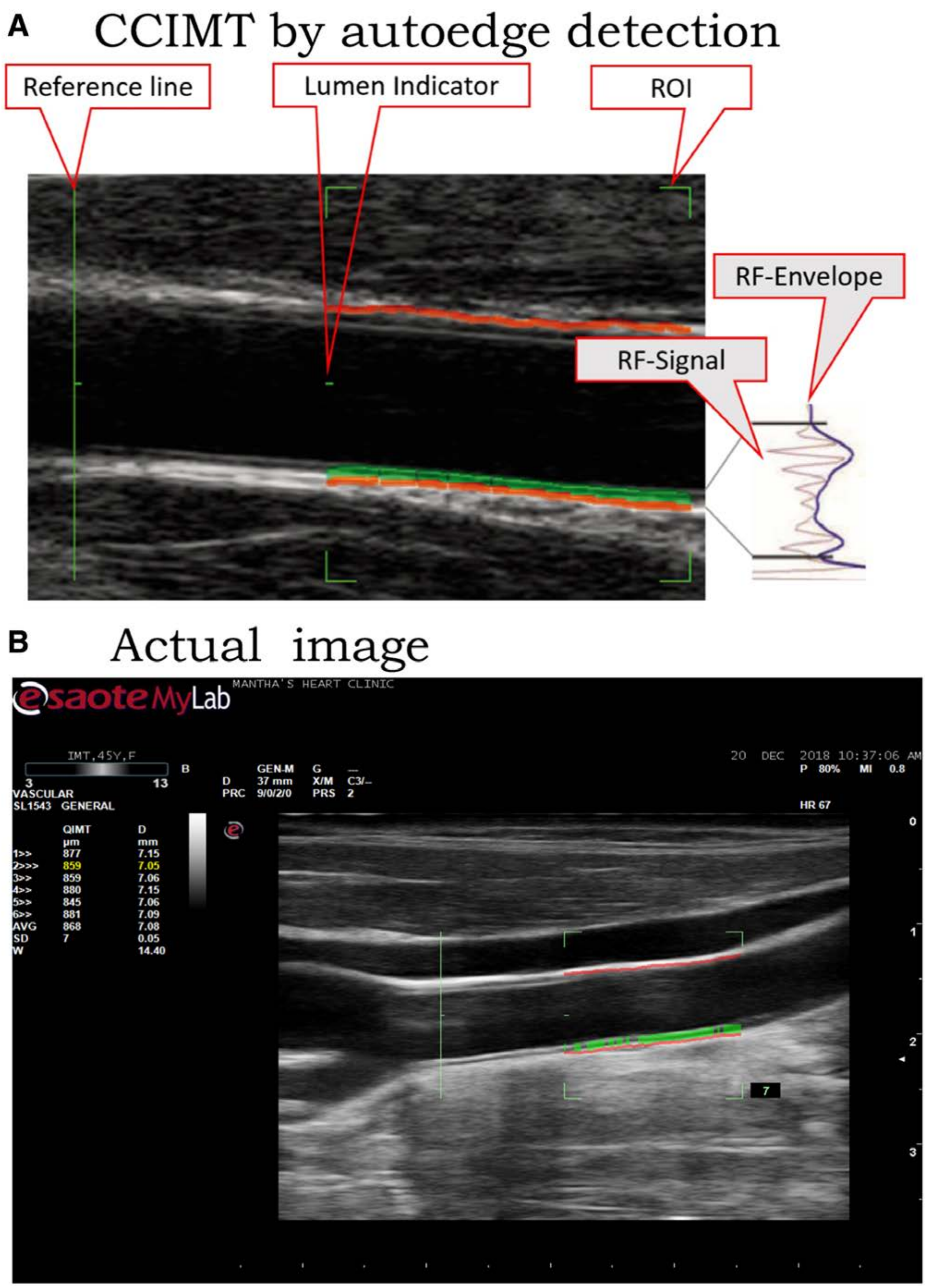

Figure 1. CCIMT measured by echo-tracking: (A) schematic diagram, (B) actual image. CCIMT indicates common carotid intima-media thickness; RF, radiofrequency; ROI, region of interest.

Table. Details of 4 Individuals With a CCIMT *Z* Score ≥1.96

Chronological Age (y)	Gender	Measured CCIMT[a]	CCIMT Reference Standards[b] Mean (SD)	*Z* Score	Percentile	Vascular Age (y)
40	Female	708	521 (88)	2.13	98	78
52	Female	807	580 (97)	2.34	99	98
53	Female	781	585 (98)	2.00	98	92
61	Male	1143	641 (112)	4.48	99	100

Refer to the Supplemental Digital Content, Appendix II (http://links.lww.com/AACR/A297), for further details in raw data section.
Abbreviations: CCIMT, common carotid intima-media thickness; SD, standard deviation.
[a]Unit of measurement in micrometers, higher of 2 sides is taken for computation of *Z* score and vascular age.
[b]With reference to population-based normal values.

with head slightly tilted to the opposite side of the measurement. The carotid artery is imaged in longitudinal view at a depth of approximately 4 cm deep but can be increased in individuals with thick necks and deep-seated vessels. The extracranial carotid arteries are scanned in such a way that distal common carotid artery (CCA), carotid bulb, and its bifurcation are all visualized simultaneously (the "tuning fork view": Figure 1B). In case of difficulty in obtaining the tuning fork view, at least distal CCA and carotid bulb are visualized. In addition, "double-line" sign representing intima and media in the far wall of CCA should also be visualized. Specific to the echo-tracking method of Esaote machines adopted in the present series, the operator gets real-time feedback of measurement quality, which in turn helps to optimize ultrasound probe position.

From a series of 44 cases, 22 were segregated who would otherwise qualify for a low-risk category should they present for preoperative evaluation for noncardiac surgery. A low risk implies <1% risk as evaluated by all 3 risk prediction tools used by Glance et al.[1] Refer to Appendix II in the Supplemental Digital Content (http://links.lww.com/AACR/A297) in raw data section for details related to risk assessment. CCIMT *Z* scores and percentiles for vascular age were computed based on population-based normal values at different ages in either gender. According to the American Society of Echocardiography, a CCIMT *Z* score of ≥1.96 equivalent to ≥97.5 percentile is defined as "abnormal" that requires immediate attention and further evaluation.

Mean (SD) for age was 48 years (12), with equal men and women. There were 4 cases in this low-risk group who had a *Z* score ≥1.96 (Table).

DISCUSSION

Potential application of CCIMT in cardiac risk stratification would require further study, including outcome data. A suitable model to predict the CCIMT *Z* score using readily available clinical and laboratory variables could be developed in the research setting. In addition, the scope of substituting vascular age for chronological age and/or categorizing individuals with *Z* score ≥1.96 as having severe systemic disease in existing risk stratification algorithms may be explored. We believe that the suggested approach would provide better insights for future research in the area.

CCIMT has the potential to be incorporated into shared decision-making for perioperative care.[6] The concept of vascular age is easily understandable. CCIMT results identify patients who warrant preoperative statin therapy and close monitoring with troponin to reduce immediate perioperative risk.[7] For example, if individuals in our series were to undergo surgery, then 4 individuals with a *Z* score ≥1.96 could be suitable for such perioperative intervention. CCIMT measurement can be performed by the anesthesiologist during preoperative evaluation as part of expanding our role as perioperative physicians. It could as well be incorporated in point-of-care ultrasound (POCUS).[8] The anesthesiologist could directly visualize the intima and implement strategies to reduce cardiovascular events.

A website designed by the first author (S.M.), www.suhitam.com/vascularage, takes 4 input variables, that is, age, gender, and CCIMT in micrometers of the right and left sides, and yields a clinically useful report. The algorithm uses a maximum CCIMT of 2 sides. Report of a male individual aged 40 years with CCIMT values of 700 and 730 µm, respectively, on the right and left sides, is as depicted in Figure 2. Visitors of the website can login using "visitor" for both user ID and password to view representative cases with different risk grades along with the CCIMT images.

While we focused on one imaging device, other techniques of auto-edge detection are available in other machines. The series used the Engelen et al[4] data to compute the *Z* score and vascular age because of similarity of method of CCIMT measurement. Other population data that include racial information[9] or at other geographical areas (eg, India)[10] with CCIMT measurement done by conventional means are also available.

Further study is planned to identify determinants of CCIMT in healthy individuals. Protocol summary may be viewed from a clinical trial registry using "ccimt" in the key word search http://ctri.nic.in/Clinicaltrials/advancesearchmain.php. The planned study proposes to perform multivariate linear regression analysis with CCIMT *Z* score as the dependent variable and the following as independent variables: cigarette smoking status, body mass index (BMI), waist-to-height ratio (WHR), total cholesterol HDL ratio (TC-HDL ratio), and serum vitamin D3 levels. The rationale for including vitamin D3 levels as an independent variable in our planned prospective study may be noted. A retrospective study that involved 3509 patients found that decreased vitamin D concentrations in blood were associated with a composite of increased in-hospital death, serious infections, and serious cardiovascular events after noncardiac surgery.[11] An editorial by Roizen and Roizen[12] that accompanied this study has called for data from prospective studies.

In conclusion, the present study proposes a research idea to use CCIMT *Z* score and vascular age to quantify atherosclerotic burden as a part of preoperative cardiac risk

IMT-Measured	IMT-Standard	Z-score	Percentile	Vascular Age	Risk Grade
730	532	2.12	98	78	4

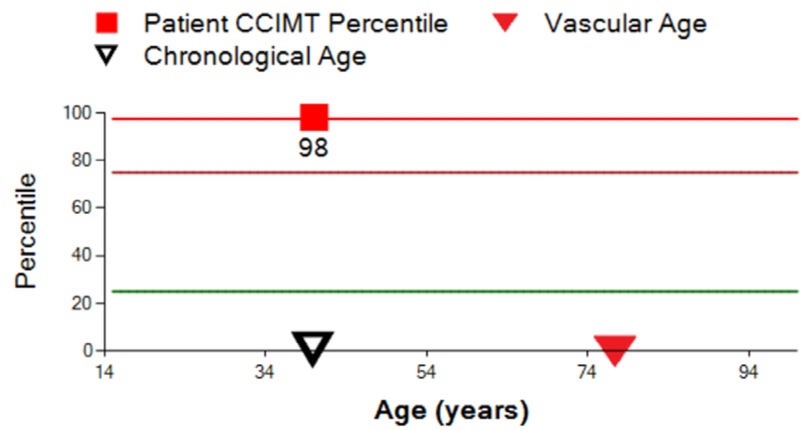

Figure 2. Report from the website of a male individual aged 40 years with CCIMT values of 700 and 730 µm, respectively, on right and left sides. The algorithm uses maximum CCIMT of 2 sides and standard values from Engelen et al.[4] CCIMT indicates common carotid intima-media thickness.

stratification for noncardiac surgery. Atherosclerosis typically progresses from fatty streaks (microscopic definition) to the advanced stage as manifested by atheromatous plaques (intima-media thickness of 1500 µm or more) identified by ultrasound. Between these extremes, the scheme proposed in this study attempts to identify accelerated atherosclerosis by CCIMT by comparing with population standards. While epidemiological studies use a threshold value ≥75th percentile for defining abnormality to identify long-term risk,[13] the present study proposes a more conservative threshold value ≥97.5 percentile for further workup and/or perioperative risk-reducing strategies. Some epidemiological studies showed that internal carotid artery intima-media thickness is a more powerful variable than CCIMT.[13] Feasibility, additional value of such evaluation, and related outcome studies in the context of perioperative care may be areas for future research, hopefully stimulated by this report.

DISCLOSURES

Name: Srinivas Mantha, MD.
Contribution: This author conceived the research idea and performed the ultrasound examination and measurement of IMT in all the subjects. He has collected the data, performed the analysis, and written the initial draft of the manuscript.
Name: Sudha Lakshmi Tripuraneni, MD, DM.
Contribution: This author helped revise the manuscript.
Name: Lee A. Fleisher, MD.
Contribution: This author helped improve the analysis and present the manuscript.
Name: Michael F. Roizen, MD.
Contribution: This author provided useful inputs to revise the manuscript substantially.
This manuscript was handled by: Kent H. Rehfeldt, MD.

REFERENCES

1. Glance LG, Faden E, Dutton RP, et al. Impact of the choice of risk model for identifying low-risk patients using the 2014 American College of Cardiology/American Heart Association perioperative guidelines. *Anesthesiology.* 2018;129:889–900.
2. Fleisher LA. Preoperative cardiac evaluation before noncardiac surgery: Reverend Bayes's risk indices and optimal variables. *Anesthesiology.* 2018;129:867–868.
3. Stein JH, Korcarz CE, Hurst RT, et al; American Society of Echocardiography Carotid Intima-Media Thickness Task Force. 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 Task Force. Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr.* 2008;21:93–111.
4. Engelen L, Ferreira I, Stehouwer CD, Boutouyrie P, Laurent S; Reference Values for Arterial Measurements Collaboration. Reference intervals for common carotid intima-media thickness measured with echotracking: relation with risk factors. *Eur Heart J.* 2013;34:2368–2380.
5. Stein JH. Carotid intima-media thickness and vascular age: you are only as old as your arteries look. *J Am Soc Echocardiogr.* 2004;17:686–689.
6. Raymond BL, Wanderer JP, Hawkins AT, et al. Use of the American College of Surgeons National Surgical Quality Improvement Program surgical risk calculator during preoperative risk discussion: the patient perspective. *Anesth Analg.* 2019;128:643–650.
7. Mantha S, Foss J, Ellis JE, Roizen MF. Intense cardiac troponin surveillance for long-term benefits is cost-effective in patients undergoing open abdominal aortic surgery: a decision analysis model. *Anesth Analg.* 2007;105:1346–1356.
8. Mahmood F, Matyal R, Skubas N, et al. Perioperative ultrasound training in anesthesiology: a call to action. *Anesth Analg.* 2016;122:1794–1804.
9. Howard G, Sharrett AR, Heiss G, et al. Carotid artery intimal-medial thickness distribution in general populations as evaluated by B-mode ultrasound. ARIC Investigators. *Stroke.* 1993;24:1297–1304.
10. Kasliwal RR, Bansal M, Desai N, et al; SCORE-India collaborators. A Study to derive distribution of carotid intima media thickness and to determine its COrrelation with cardiovascular Risk factors in asymptomatic nationwidE Indian population (SCORE-India). *Indian Heart J.* 2016;68:821–827.
11. Turan A, Hesler BD, You J, et al. The association of serum vitamin D concentration with serious complications after noncardiac surgery. *Anesth Analg.* 2014;119:603–612.
12. Roizen MF, Roizen JD. Vitamin D and your patients: don't accept wimpy. *Anesth Analg.* 2014;119:503–505.
13. Darabian S, Hormuz M, Latif MA, Pahlevan S, Budoff MJ. The role of carotid intimal thickness testing and risk prediction in the development of coronary atherosclerosis. *Curr Atheroscler Rep.* 2013;15:306.