

DETERMINANTS OF COMMON CAROTID INTIMA-MEDIA THICKNESS Z SCORE: IMPLICATIONS IN RESEARCH RELATED TO MYOCARDIAL INJURY AFTER NONCARDIAC SURGERY

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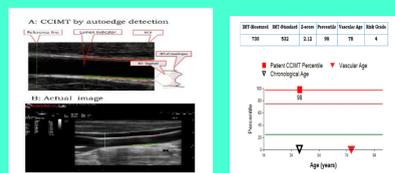
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INTRODUCTION

Introduction:

- Common Carotid Intima-media Thickness (CCIMT) measured by ultrasound is a validated surrogate quantitative marker for atherosclerotic burden
- A recent study proposed a 'Research Idea' to explore potential use of CCIMT in cardiac risk stratification and in the management of MINS[1]
- The study used an advanced method called “echo-tracking” that relies on automated edge detection by radiofrequency signal processing of ultrasound to measure the thickness [1]
- To account for increasing thickness with age, a derived variable i.e. 'CCIMT Z-score', is more useful
- CCIMT value ≥ 1.96 (≥ 97.5 percentile) was proposed for further management.

- Z score is computed by a web-based algorithm designed by the first author for the purpose¹ w.suhitam.com/vascularage.
- The principle of echo-tracking and auto-edge detection, the CCIMT image and output of the algorithm are shown.



- The method is “accurate” and “reliable” compared to other methods of CCIMT measurement
- Underlying coronary atherosclerosis is implicated in the pathogenesis of perioperative myocardial injuries associated with noncardiac surgery
 - “myocardial infarction” – traditional criteria
 - “myocardial injury after noncardiac surgery (MINS)”- identified only biomarker elevation [2]
- A recent study found that preoperative N-terminal pro-B-type natriuretic peptide (NT-proBNP) improves cardiac risk stratification of MINS as identified by monitoring with serial high-sensitivity cardiac troponin-T. [3]
- Aim of the current study Primary: To identify the determinants of CCIMT Z score with the thickness measured auto-edge detection by echo-tracking

METHODS

- Study Design: Cross-sectional, Prospective collected data**
- A multivariate linear regression analysis was planned with CCIMT z score as dependent variable and following independent variables: age, gender, body mass index (BMI), waist-to-height ratio (WHR), diabetes mellitus(DM) & current smoking status, total cholesterol-to-HDL ratio (TC-HDL) ratio and serum vitamin D3 levels (ng/ml)
- These indicators were selected *a priori* and defined in the protocol
- Setting: Outpatient vascular wellness clinic
- Inclusion Criteria
 - 20 to 60 years
 - Healthy or mild systemic disease (diabetes mellitus, hypertension etc.) controlled with oral medications
- Exclusion criteria
 - Known cardiovascular disease or cerebrovascular disease
 - Treatment for dyslipidemia
 - History of treatment for vitamin D deficiency.
- Sample size estimation: . The sample size required was adequate as calculated for eight variables to be evaluated, Cohen's medium 'effect size' of 0.15 and other standard criteria.
- IRB approval and Trial Registration
 - Study protocol was approved by the Institute Ethics Committee at Indo-US Hospital, Ameerpet, Hyderabad, India
 - Registered prospectively in a clinical trial registry in India (<http://ctri.nic.in>)
 - Protocol summary may be viewed from a registry using 'ccimt' in the key word search <http://ctri.nic.in/Clinicaltrials/advancesearchmain.php>
- Methodology of CCIMT measurement
 - CCIMT measurement was made by B-mode ultrasonography using 3-13 MHz linear probe
 - 'double line' sign representing intima and media in the far wall of CCA is visualized.
 - A new method called 'echo-tracking' that relies on automated edge detection by real-time radiofrequency signal processing of ultrasound was used.[1]
- Analysis:**
 - Final linear model was developed from the variables significantly associated with CCIMT z score

RESULTS

- A CCIMT z score of ≥ 1.96 (≥ 97.5 percentile) is defined as highly abnormal that requires immediate attention and further evaluation.[1]
- There were 26 (22.22%) individuals in this category and 14 (23.33%) in those < 40 y.
- Of the variables tested, current smoking, TC-HDL ratio and vitamin D3 were significantly associated with high CCIMT z score.
- Analysis of variance revealed model P value of 0.0003
- variance inflation factor analysis did not reveal existence of multicollinearity issue among the tested variables
- Analysis using the three significant variables yielded the following linear model to estimate the score:
- CCIMT Z score = $0.80 + (0.841 \times \text{current smoking}=1) + (0.156 \times \text{TC-HDL ratio}) - (0.0263 \times \text{vitamin D3 blood level in ng/mL})$.
- R square was 0.21
- Evaluation of standardized coefficients revealed weightage for smoking, TC-HDL ratio and vitamin D3 in that decreasing rank order (Figure)

Figure: Relative Contribution (Weightage) of Determinants of CCIMT Z score

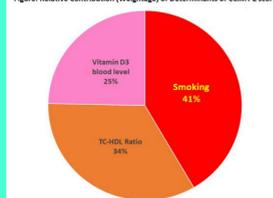


Table: Application of the Model with Hypothetical Data

Serial #	Smoking	TC-HDL ratio	Vitamin D3 (ng/mL)	CCIMT Z score	? Abnormal*
1	0 (No)	4.5	15	1.1075	No
2	1 (Yes)	4.5	15	1.9485	No
3	1 (Yes)	4.5	14	1.9748	Yes
4	0 (No)	8	15	1.6535	No
5	1 (Yes)	4.5	9	2.1063	Yes
6	1 (Yes)	6	25	1.9195	No
7	0 (No)	8.5	6	1.9682	Yes

*Abnormal implies Common Carotid Intima Media Thickness (CCIMT) Z score ≥ 1.96
Vitamin D3 levels: 1 ng/mL=2.496 nmol/L (SI units)

Model Characteristics	Point estimate (95% CIs)	
Sensitivity	0.23 (0.069 to 0.39)	Positive test = model Z score ≥ 1.96
Specificity	0.93 (0.83 to 0.98)	Negative test = model Z score < 1.96
Likelihood ratio for positive test	3.5 (1.23 to 9.94)	
Likelihood ratio for negative test	0.83 (0.66 to 1.02)	

DISCUSSION & REFERENCES

- The method is “accurate” and “reliable” compared to other methods of CCIMT measurement.
- Decreased vitamin D3 concentrations in blood were associated with serious cardiovascular events after noncardiac surgery [4].
- Smoking and high TC-HDL ratio (normal < 4.5) are known risk factors for atherosclerosis.
- Current study showed low serum vitamin D3 is also associated with high CCIMT Z score
- Vitamin D3 deficiency is associated with incident cardiovascular disease and there is graded increase in risk across categories of deficiency for levels 10 to < 15 ng/ml and for levels < 10 [5].
- Deriving CCIMT Z score either by direct measurement by ultrasound or by estimating from the linear model e.g. as shown in the Table may identify a sub-set (i.e. with score ≥ 1.96) among 'low risk' individuals in whom stratification and/or monitoring with biomarkers may be beneficial. CCIMT seems to be an independent variable for predicting MINS

References

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