

## Evidence Table

**Clinical Area: Carotid intima-media thickness (IMT)**

**Reference:** Chambless LE, Heiss G, Folsom AR, et al. Association of coronary heart disease incidence with carotid artery wall thickness and major risk factors: The Atherosclerosis Risk in Communities (ARIC) Study, 1987-1993. *Am J Epidemiol.* 1997;146:483-494.

**Study Type:** Prospective cohort study (ARIC Study).

**Study Aim:** To determine the association between the carotid artery intima-media thickness and the incidence of coronary heart disease among middle aged adults.

**Outcomes:**

*Primary:* First coronary heart disease event.

**Design:**

- *Number of subjects:* N=12,841.
- *Description of study population:* The study included participants from four US communities. Their ages ranged from 45 to 64 years, and 43% were men. 26% were smokers, 32% were hypertensive, and 8% had diabetes at enrollment.
- *Setting (Clinical or community):* Community.
- *Inclusion criteria:* Men and women 45-64 years of age with no history of coronary heart disease events.
- *Exclusion criteria:* History of coronary heart disease.
- *Intervention:* All participants underwent a base-line physical examination, laboratory testing, assessment of traditional CHD risk factors, and measurement of carotid artery intima-media thickness (IMT) using B-mode ultrasonography. Analysis was based on mean IMT (measured at the internal, common, right, and left carotids as well as the carotid bifurcation). Only 13% of the participants had data on all 6 carotid sites. Missing data were imputed from specific models.
- *Source of outcome data (e.g. patient self-report, doctor report, lab results):* Annual interviews with participants, hospital records, death records, and interviews with relatives and patients physicians for out of hospital deaths.
- *Length of follow-up:* 4-7 years with a median of 5.2 years (maximum 78 years).
- *Completeness of follow-up:* 99.7% complete.

**Validity:**

- *Is the study type appropriate for the questions being asked?* Yes.
- *Patients followed from a well-defined point in the course of disease?* Yes.
- *Were the treatment/control groups comparable at baseline?* N/A.
- *Likelihood of selection bias?* Probably in the analysis due to exclusion of non-Whites in two of the counties, and those who were neither Black nor White in another county.
- *If human judgment required to determine outcome, was the assessor blinded to prognostic factors?* The authors did not discuss if those who read the ultrasound

images and measured the intima-media thickness were blinded to the participants' clinical information.

- *Results adjusted for confounding factors?* Yes.
- **Conclusions regarding validity of methods:**
- The study had generally valid methodology, but not without limitations. Only 13% of the participants had data on all 6 carotid sites, and missing data were imputed from specific models.

**Results:**

*Incidence of CHD events<sup>†</sup>, and hazard rate ratio  
According to the carotid intima-media thickness (IMT)*

	<i>Women</i>			<i>Men</i>		
	<i>No of events/No at risk (Incidence rate)*</i>		<i>Hazard ratio** (95%CI)</i>	<i>No of events/No at risk (Incidence rate)*</i>		<i>Hazard ratio** (95%CI)</i>
<i>Mean IMT</i>						
<i>&lt;0.6mm</i>	6/2,270	0.6	1.00	10/742	3.0	1.00
<i>0.6-0.7 mm</i>	23/2,497	1.8	2.53 (0.02-6.26)	31/1,528	4.4	1.21 (0.59-2.47)
<i>0.7-0.8 mm</i>	27/1402	3.4	3.56 (1.44-8.76)	47/1,474	6.5	1.56 (0.78-3.15)
<i>0.8-1.0 mm</i>	19/821	3.8	3.35 (1.29-8.68)	70/1,277	10.7	2.44 (1.23-4.84)
<i>≥ 1.0 mm</i>	21/299	11.7	7.40 (2.83-19.38)	36/531	12.9	2.15 (1.02-4.54)

<sup>†</sup> There were 96 incident events among women and 194 among men during follow-up period

\* Incidence rate /1000 person years, adjusted for age, race, and field center.

\*\*Adjusted for age, race, LDL and HDL cholesterol, BMI, sports activity, cigarette smoking-years, hypertension, diabetes, ethanol and fibrinogen.

At IMT <1.0mm the incidence rate of MI was significantly lower for women vs. men. (p<0.05)

At IMT >1mm the difference in MI incidence was insignificant between men and women.

**Authors' Conclusions:**

The authors concluded, "The mean carotid IMT is a noninvasive predictor of future CHD incidence."

**Reviewer's Conclusions:**

This is a large prospective study, conducted in a non-random sample of four US communities. Only 13% of the participants had data on all 6 carotid sites, and missing data were imputed from specific models. The study shows an association between the incidence of CHD events and the carotid intima thickness, however, the authors did not evaluate the predictive ability of carotid IMT, and if it could replace or contribute to the cardiovascular disease risk assessment based on the established factors and Framingham risk stratification.

## Evidence Table

**Clinical Area:** Carotid intima-media thickness (IMT)

**Reference:** O’Leary DH, Polak JF, Kronmal RA, et al, for the Cardiovascular Health Study Collaborative Research Group. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *N Engl J Med.* 1999;340:14-22.

**Study Type:** Prospective cohort study (Cardiovascular Health Study).

**Study Aim:** To determine the association between the carotid artery intima-media thickness and the incidence of new myocardial infarction or stroke among older adults with no clinical cardiovascular disease.

**Outcomes:**

*Primary:* Incidence of myocardial infarction and stroke.

**Design:**

- *Number of subjects:* N=4,476.
- *Description of study population:* The study participants were enrolled from multiple centers in the US from June 1989 to May 1990, and June 1992 to June 1993. Their ages ranged from 65 to 84 years with a mean of 42.5 years, 38.8% were men and 85% were White. 13% had diabetes, 39.9% were hypertensive, and 12% were smokers at enrollment.
- *Setting (Clinical or community):* Patients were enrolled from random samples of Medicare eligibility lists.
- *Inclusion criteria:* Men and women 65 years of age or older, with no a history of cardiovascular disease at enrollment.
- *Exclusion criteria:* History of cardiac or cerebrovascular disease.
- *Intervention:* All participants underwent a base-line physical examination, laboratory testing, assessment of cardiovascular disease status, and evaluation of the carotid arteries with high-resolution B-mode ultrasonography. One longitudinal image of the common carotid artery, and three longitudinal images of the internal carotid artery were taken. The maximal intima-media thickness was used rather than the mean thickness.
- *Source of outcome data (e.g. patient self-report, doctor report, lab results):* Annual visits with interim telephone interviews every six months, reporting of events by participants, medical records, and Medicare hospital records.
- *Length of follow-up:* Median of 6.2 years (maximum 78 years).
- *Completeness of follow-up:* 99.7% complete.

**Validity:**

- *Is the study type appropriate for the questions being asked?* Yes.
- *Patients followed from a well-defined point in the course of disease?* Yes.
- *Were the treatment/control groups comparable at baseline?* N/A.
- *Likelihood of selection bias?* No.
- *If human judgment required to determine outcome, was the assessor blinded to prognostic factors?* Reading of the carotid artery images, and measurements of the

intima-media thickness was performed by readers blinded to the participants' clinical information.

- *Results adjusted for confounding factors?* Yes.

- **Conclusions regarding validity of methods:**

The study had valid methodology, however it was conducted among older adults, which limits generalization of the results to a similar age group.

**Results:**

(Only the results on the incidence of MI will be presented in this evidence table)

*Incidence of myocardial infarction  
According to the maximal carotid IMT*

	<i>No of events/No at risk</i>		<i>Relative risk (95% CI): adjusted for</i>	
	<i>risk</i>	<i>%</i>	<i>Age and sex</i>	<i>Age, sex and other risk factors<sup>‡</sup></i>
<i>Maximal CCA IMT*</i>				
<0.87 mm	22/897	2.45	1.00	1.00
0.87-0.96 mm	47/906	5.19	1.92 (1.16-3.19)	1.79 (1.08-2.98)
0.97-1.05 mm	41/891	4.60	1.58 (0.94-2.62)	1.40 (0.83-2.38)
1.06-1.17 mm	66/888	7.43	2.39 (1.47-3.91)	2.07 (1.27-3.39)
≥ 1.18 mm	91/894	10.18	3.17 (1.96-5.12)	2.46 (1.51-4.01)
Per 1 SD (0.2mm) increase			1.33 (1.21-1.48)	1.24 (1.12-1.38)
P value by test for trend			<0.001	<0.001
<i>Maximal ICA IMT**</i>				
<0.90 mm	19/894	2.13	1.00	1.00
0.91-1.10 mm	34/896	3.79	1.54 (0.88-2.70)	1.55 (0.89-2.73)
1.11-1.39 mm	58/895	6.48	2.45 (1.46-4.13)	2.30 (1.36-3.88)
1.40-1.80 mm	70/895	7.82	2.95 (1.77-4.93)	2.68 (1.60-4.48)
≥ 1.81 mm	85/895	9.50	3.52 (2.12-5.84)	3.00 (1.80-5.01)
Per 1 SD (0.55mm) increase			1.43 (1.28-1.59)	1.34 (1.20-1.50)
P value by test for trend			<0.001	<0.001

\*Common carotid artery intima-media thickness.

\*\* Internal carotid artery intima-media thickness

<sup>‡</sup> Systolic and diastolic blood pressure, presence or absence of atrial fibrillation, pack years of smoking, and history of diabetes.

*Incidence of myocardial infarction/stroke according to quintiles of carotid artery  
Intima media thickness (maximal average of CCA and ICA IMT)*

	<i>No of events/No at risk</i>		<i>Relative risk (95% CI): adjusted for</i>	
		<i>%</i>	<i>Age and sex</i>	<i>Age, sex, and other risk factors‡</i>
<i>Maximal CCA and ICA IMT (average, standardized)</i>				
1 <sup>st</sup> quintile	18/895	2.01	1.00	1.00
2 <sup>nd</sup> quintile	33/895	3.69	1.62 (0.91-2.88)	1.58 (0.89-2.81)
3 <sup>rd</sup> quintile	52/896	5.80	2.46 (1.43-4.22)	2.20 (1.28-3.78)
4 <sup>th</sup> quintile	62/895	6.93	2.78 (1.63-4.73)	2.45 (1.44-4.19)
5 <sup>th</sup> quintile	102/895	12.18	4.51 (2.69-7.55)	3.61 (2.13-6.11)
Per 1SD (0.55mm) increase			1.46 (1.32-1.61)	1.36 (1.23-1.52)
P value by test for trend			<0.001	<0.001

**Authors' Conclusions:**

The authors concluded that there is a direct association between the increase in carotid intima-media thickness as measured by ultrasonography, and the incidence of myocardial infarction and stroke in older adults with no history of cardiovascular disease.

**Reviewer's Conclusions:**

The study had valid methodology. It showed that the risk of myocardial infarction tends to increase with the increase in carotid intima-media thickness among subjects 65 to 84 years of age. The relative risk among those in the fifth quintile of the average of CCA and ICA IMT was more than three times of those in the lowest quintile after adjusting for traditional risk factors. The authors did not show if measuring carotid ITM would improve the prediction CHD risk beyond Framingham Risk score