Cardiovascular Topics

Correlation of cardiac risk factors with carotid and radial intima–media thickness measurements

Fritz G van Schalkwyk, Stephen C Brown, Francis Smit, Lezelle Botes

Abstract

Aim: Early identification of patients at risk for future cardiovascular events is essential. The aim of this study was to evaluate the relationship between cardiovascular risk factors and carotid intima–media thickness (CIMT) and radial intima–media thickness (RIMT).

Methods: A prospective, descriptive, analytical study design was used. Two hundred and fifty patients with one or more modifiable risk factors underwent an ultrasound measurement of left and right CIMT and RIMT, according to standard guidelines.

Results: Eighty-one per cent of patients had two or more risk factors. Hypertension was the most common modifiable risk factor (89%), followed by obesity (66%). Male gender demonstrated a significant increase in mean CIMT ($p < 0.05$). Hypertension, diabetes mellitus, hypercholesterolaemia and smoking contributed to a thickened mean CIMT with odds ratios of 3.99, 2.82, 2.47 and 2.09, respectively ($p < 0.05$). Combinations associated with a thicker mean CIMT included hypertension and diabetes, and hypertension and smoking, with odds ratios of 6.92 and 3.67, respectively ($p < 0.05$). Only hypercholesterolaemia was significantly associated with a thicker mean RIMT ($p < 0.05$).

Conclusion: Male gender, increased age, hypertension, diabetes, hypercholesterolaemia and smoking significantly contributed to a thickened CIMT, whereas only hypercholesterolaemia was associated with a thickened RIMT. Hypertension had the most significant impact on the mean CIMT thickness. Combinations of risk factors appeared to add summative risks for thickened CIMT and RIMT.

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Early identification of patients at risk for future cardiovascular events is essential since addressing these early stages is more effective than treating advanced atherosclerotic vascular disease.[1] Smoking, hyperlipidaemia, the metabolic syndrome, hypertension and diabetes mellitus (DM) are major cardiac risk factors contributing to intracranial atherosclerosis.[2] The presence of multiple risk factors increases the development of atherosclerosis significantly, which leads to stroke as a result of ruptured plaques.[3]

Raised levels of low-density lipoprotein cholesterol (LDL-C) are a dominant cause of atherosclerosis. However, atherosclerosis can also develop due to or in combination with other risk factors, such as hypertension, DM, smoking, male gender and family history. Plaque rupture is multi-layered, involving foam cell formation, smooth muscle cell proliferation, angiogenesis, inflammation, arterial remodelling, thrombosis, fibrous cap rupture and more. Since plaque formation is heterogeneous, it leads to erratic progression rates and variable outcomes. Although most plaques remain subclinical, some may become obstructive and others may cause thrombosis, leading to a stroke or acute coronary syndrome.[4]

Stroke is the second most common cause of mortality and the third most common cause of disability.[5] Eighty per cent of strokes are ischaemic, while haemorrhagic types are less common, contributing 25 to 50%.[6] Sacco *et al.* emphasised that the most important modifiable risk factor for ischaemic stroke is hypertension; hypertension is a relative risk for stroke when the systolic blood pressure is $\geq$ 160 mmHg and/or diastolic blood pressure is $\geq$ 95 mmHg.[7]

Patients with DM have a two-fold increase in stroke risk. Strokes account for approximately 20% of deaths in diabetic patients.[8] The risk of ischaemic stroke increases in patients with elevated LDL-C levels. Patients with low high-density lipoprotein cholesterol have a greater stroke risk than healthy individuals.[9] Cigarette smoking is a significant risk factor contributing to almost 15% of all annual stroke deaths.[8] The single most important non-modifiable risk factor for stroke is age, and for each successive 10 years after age 55 years in both men and women, the stroke rate doubles. More women die of stroke each year because they tend to live longer than men; however, in men, the stroke incidence rates are 1.25 times higher than in women.[7]

Globally, ultrasound has been the most common method of evaluating carotid atherosclerosis due to reasonably low-cost ultrasound analyses, easy access to the carotid artery, and readily available equipment.[9] Carotid intima–media thickness (CIMT) is an independent predictor of stroke, although there are limited data on whether an increased IMT predicts stroke. Shimoda *et al.* showed that CIMT was positively associated with the risks of stroke, cardiovascular disease and coronary artery disease (CAD) in the Japanese population.[10] Tsivgoulis *et al*. concluded that a higher risk of long-term recurrence of stroke was associated with increased CIMT values – the probability of experiencing recurrent strokes increased by 18.0% for each increase of 0.1 mm in CIMT.[11]

Carotid ultrasound is one of the few non-invasive imaging techniques that allow the evaluation of vascular function and anatomy.[12] This technique can measure various parameters, including vessel diameter, IMT, presence and diameter of stenosis and carotid plaques. Increased thickness of the carotid intima and the presence of large plaques can predict future cardiovascular events.[9] CIMT is a modest but independent predictor of CAD.

Radial intima–media thickness (RIMT) is related to several cardiovascular risk factors and can be imaged with excellent precision.[12] Increased occurrence of significant coronary artery narrowing is associated with an increased RIMT. Patients have a nearly three-fold increased risk for major adverse cardiovascular events with RIMT values above the median of 0.3 mm.[13] Therefore, RIMT is a significant predictor of major adverse cardiovascular events, along with type 2 diabetes and body mass index (BMI).[14] Myredal *et al*. reported a 19% elevation in RIMT in patients with coronary heart disease compared to healthy subjects.[14]

This study therefore aimed to evaluate which risk factors contribute to increased CIMT and RIMT and whether a correlation exists between risk factors and CIMT and RIMT measurements in patients from central South Africa.

Methods

The study design was a prospective, descriptive, analytical, single-centre study and was conducted at a private physician practice in Bloemfontein. Patients were referred from the Free State, Northern Cape and Lesotho. The study sample included 250 first-time visiting patients presenting with one or more modifiable cardiac risk factors from 1 September 2020 to 30 September 2021.

Ethical clearance was obtained from the Health Sciences Research and Ethics Committee (HSREC) of the University of the Free State (UFS-HSD2020/2018/2601). Standard informed consent was obtained in all subjects.

Demographic (age, gender, ethnicity and geographic location), anthropometric [height (cm), weight (kg) and BMI (kg/m^2)], clinical (modifiable and non-modifiable risk factors, family history and other) and ultrasound data (CIMT, RIMT) were recorded for each patient who consented to participate in the study. The modifiable risk factors recorded included obesity, DM, smoking, hypertension and hypercholesterolaemia. Non-modifiable risk factors included age, gender, ethnicity and family history of CAD. Clinical data recorded from the patient's medical file included HIV status and rheumatoid arthritis.

Patients were classified as overweight if they had a BMI of $\geq$ 25 kg/m^2 and obese if $\geq$ 30 kg/m^2.[15]

Type 1 and 2 diabetes was determined as specified in the patient's medical file. Smoking referred to the use of any tobacco product. Both current and previous smokers were regarded as smokers.

Hypertension was defined as a systolic blood pressure $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg.[16] Hypercholesterolaemia was defined as a total cholesterol level $\geq$ 6.5 mmol/l.[15]

All vascular ultrasound investigations of carotid arteries to determine IMT were carried out by a single qualified and experienced ultrasonographer. The radial and carotid ultrasound examination was performed according to international guidelines.[15] Both the right and left CIMT were measured, and the mean was calculated and analysed. All images were obtained in a supine position using a Philips CX50 diagnostic ultrasound system equipped with a 7.5-MHz multi-frequency linear probe. The carotid bulbus was located, and the CIMT was measured 10 mm proximal to the bulbus. CIMT measurements were classified as normal ($<$ 0.9 mm) and abnormal ($\geq$ 0.9 mm).[15]

The right and left RIMT was measured about 1–2 cm proximal to the skinfold separating the palma manus from the regio antebrachia anterior.[14] The mean RIMT was calculated and analysed. A RIMT $>$ 0.3 mm was considered abnormal.[15]

Statistical analysis

All recorded data were captured in a datasheet using Microsoft® Excel® 2019. Data were quality controlled by an independent investigator for accuracy and transcription errors. The statistical analyses were performed using the R program. Continuous data are summarised using descriptive statistics, including but not limited to mean, standard deviation (SD), median, minimum, maximum and interquartile range (IQR). Descriptive analyses were carried out per subgroup depending on the number of patients.

Linear regression was used to test for the effect of the covariates on the response variables, and logistic regression was used to determine the relative risk. Categorical data were summarised utilising frequency tables. The cell counts were compared using a Chi^2 test or Fisher's exact test. The latter was used if one or more of the cell counts were less than five. A p-value of $<$ 0.05 was considered statistically significant. Correlations were obtained using the Pearson correlation coefficient test.

Results

Two hundred and fifty patients met the inclusion criteria. As expected, most patients came from the Free State (97.2%) and only 2.8% from other provinces. Most of these patients resided in the Mangaung metropolitan district (85.6%). The mean age of patients was 60.2 $\pm$ 16.5 years, with a female predominance (63.6 vs 36.4%), and most patients were Caucasian (76%).

In the total study group, 42% (n = 104) of patients presented with three or more modifiable risk factors, 39% (n = 98) with two risk factors, and 19% (n = 48) with only one modifiable risk factor. Hypertension was the most common modifiable risk factor (89%), followed by obesity (66%). DM was present in 30%

Table 1. Demographic, anthropometric and modifiable risk factors of patients with an abnormal CIMT

Variables	*Hypertension*	*Diabetes*	*Hypercholesterolaemia*	*Obesity*	*Smoking*
Normal CIMT ($n = 143$)	121	26	37	89	29
Age, years (mean ± SD)	60. 4 ± 16.3	60.8 ± 16	60.3 ± 16.3	60.3 ± 16.3	60.1 ± 16.5
Gender:					
Male	35 (28.9)	7 (27)	8 (21.6)	28 (31.5)	12 (41.3)
Female	86 (71.1)	19 (73)	29 (78.4)	61 (68.5)	17 (58.7)
Ethnicity, n (%):					
Caucasian	85 (70)	15 (57.7)	25 (67.6)	62 (70)	27 (93.1)
Mixed race	4 (3)	0	1 (2.7)	2 (2.2)	1 (3.4)
Black African	32 (27)	10 (38.5)	11 (29.7)	24 (27)	1 (3.4)
Asian	0	1 (3.8)	0	1 (2.2)	0
Indian	0	0	0	0	0
BMI, kg/m^2 (mean ± SD):	29.0 ± 6.9	29 ± 6.9	29 ± 7.0	29 ± 7.0	28.9 ± 6.9
Normal	44 (36.4)	6 (23)	8 (21.6)		13 (44.8)
Overweight	77 (63.6)	20 (77)	29 (78.4)		16 (55.2)
Abnormal CIMT ($n = 107$)	102	48	55	71	30
Age, years (mean± SD)	60.4 ± 16.4	61 ± 6.0	60.4 ± 16.4	60.4 ± 16.4	61.9 ± 16.4
Gender, *n* (%):					
Male	46 (45)	27 (56.2)	29 (52.7)	34 (47.9)	20 (66.7)
Female	56 (55)	21 (43.8)	26 (47.3)	37 (52.1)	10 (33.3)
Ethnicity, *n* (%):					
Caucasian	82 (80.1)	36 (75)	47 (85.5)	57 (80.3)	25 (83.3)
Mixed race	4 (3.9)	2 (4.2)	3 (5.5)	4 (5.6)	1 (3.3)
Black African	15 (14.7)	10 (20.8)	4 (7.3)	10 (14.1)	3 (10)
Asian	1 (0.9)	0	0	0	0
Indian	0	0	1 (1.8)	0	1(3.3)
BMI, kg/m^2 (mean ± SD):	28.9 ± 6.9	29 ± 6.7	28.9 ± 6.9	28.9 ± 6.9	29.0 ± 6.9
Normal, *n* (%)	33 (32.4)	16 (33.3)	23 (41.8)		12(40)
Overweight, *n* (%)	69 (67.6)	32 (66.7)	32 (58.2)		18(60)

CIMT, carotid intima–media thickness; BMI, body mass index.

of patients, of which 55% presented with type 1 DM and 45% with type 2 DM.

The mean CIMT of the total study group was 0.8 ± 0.2 mm, and the maximum CIMT was 1.9 mm in the right carotid artery and 1.7 mm in the left carotid artery. The mean CIMT in men was 0.9 ± 0.2 mm and in women 0.8 ± 0.3 mm. A transient ischaemic attack (TIA) or stroke was recorded in 24% ($n = 61$) of the study population, and 51% ($n = 55$) of patients diagnosed with a stroke or TIA had an abnormal CIMT (≥ 0.9 mm).

An abnormally thickened CIMT (≥ 0.9 mm) was observed in 107 (43%) patients, with a mean CIMT of 1.1 ± 0.15 mm. The demographic, anthropometric and modifiable risk factors of patients with normal and abnormal CIMT are summarised in Table 1.

With regard to non-modifiable risk factors, the mean age of patients with an abnormal CIMT was similar to patients with a normal CIMT (62.4 ± 16.4 vs 60.1 ± 16.5 years, respectively, $p = 0.23$). Significantly more men presented with an abnormal CIMT compared to the normal CIMT group ($p < 0.05$). The number of Caucasians in both groups was similar. A positive family history of cardiovascular disease was recorded in 89% of patients with an abnormal CIMT (Table 1).

Almost two-thirds of patients (63%, $n = 67$) with abnormal CIMT measurements had three or more modifiable risk factors, 31% ($n = 33$) had two risk factors, and only 6% (n=7) presented with one modifiable risk factor.

An abnormal CIMT was recorded in 50% ($n = 112$) of hypertensive patients. Hypertension was the leading modifiable risk factor and was present in almost all patients with an abnormal CIMT (95%). Hypertension was followed by obesity (66%), hypercholesterolaemia (51%), DM (44%), and smoking in 28% of patients. The BMI did not significantly differ between the abnormal and normal CIMT groups (28.9 ± 6.9 vs 27.9 ± 6.8 kg/m^2; $p = 0.99$) (Table 1).

The non-modifiable risk-factor analysis showed that more men with hypertension, DM and hypercholesterolaemia had abnormal CIMT measurements. In contrast, females dominated the normal group (Fig. 1).

The mean CIMT in patients with DM, hypertension, hypercholesterolaemia and smoking was significantly increased compared to those without these risk factors (Table 2). Male gender was associated with a significant increase in mean CIMT ($p < 0.05$). Age had some effect, and analyses projected that each year of ageing added 11% to the risk of having a thickened mean CIMT. This is supported by the fact that only four people under 50 years presented with an abnormal CIMT. The other non-modifiable risk factors did not contribute to a mean increase in CIMT. The odds ratios (OR) of modifiable risk factors associated with an increase in mean CIMT are presented in Table 2.

Several modifiable risk-factor combinations were evaluated to assess whether an association with a thicker mean CIMT was present. The only risk factor combinations that statistically contributed to a thicker mean CIMT were DM and hypertension, DM and hypercholesterolaemia, hypertension and smoking,

Table 2. The effects of individual modifiable risk factors on CIMT and risk associated with increased CIMT

Modifiable risk factor	*Mean CIMT (mm)*	*95% CI*	*OR*	*95% CI*
Hypertension	0.76*	0.05–0.21	3.99	1.50–12.7
Diabetes mellitus	0.74*	0.06–0.17	2.82	1.53–5.24
Hypercholesterolaemia	0.73*	0.05–0.15	2.47	1.39–4.40
Smoker	0.72*	0.03–0.14	2.09	1.07–4.17
Obesity	0.64	–0.04–0.06	1.06	0.60–1.88

*Statistical significance. CI, confidence interval; OR, odds ratio.

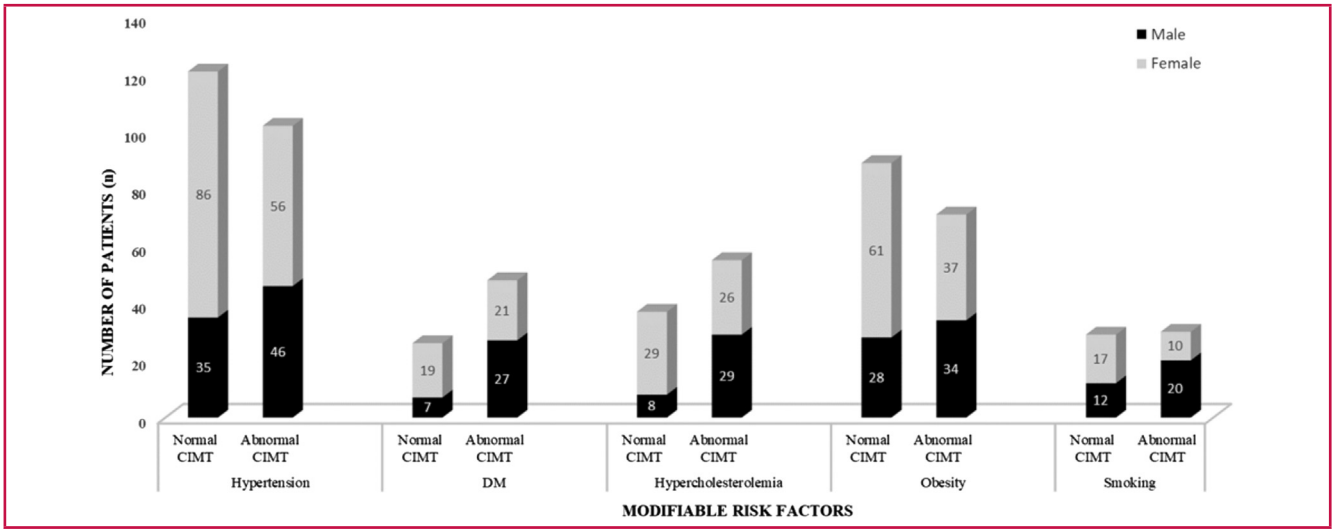

Fig. 1. Gender distribution for normal and abnormal CIMT in patient groups with modifiable risk factors.

and hypercholesterolaemia and obesity (Table 3). Unexpectedly, the combination of hypercholesterolaemia and DM, and hypercholesterolaemia and obesity appeared to reduce the risk of an increased mean CIMT and may have a protective effect. More than 50% of patients diagnosed with hypercholesterolaemia were on anti-hypercholesterol treatment (Table 3).

A minority of the study population (22%, $n = 55/250$) had an abnormally thickened RIMT. As expected, the mean internal radial diameter of the abnormal RIMT group (2.6 ± 0.5 mm) was significantly greater than the normal RIMT group (2.3 ± 0.5 mm, $p < 0.05$). Only 38% of patients with abnormal CIMT also had an abnormal RIMT.

The mean age of the abnormal and normal RIMT patient groups was similar (61 ± 16.1 vs 60 ± 16.5 years, respectively). In contrast to CIMT, more female patients presented with an abnormal RIMT than men (57 vs 43%), and most patients were Caucasian (82%). Most patients in the abnormal RIMT group had a positive family history of ischaemic heart disease (82%).

Similar to patients with abnormal CIMTs, hypertension was the most common modifiable risk factor in the abnormal RIMT group (91%), followed by obesity (73%) and hypercholesterolaemia (56%). DM was present in 36% of patients with an abnormal RIMT. Hypercholesterolaemia was the only individual risk factor that significantly contributed to a thicker mean RIMT ($p < 0.05$). The only risk factor combinations that significantly contributed to a thicker mean RIMT were hypertension and obesity, DM and obesity, and hypertension and hypercholesterolaemia (Table 4).

A strong correlation was observed between left and right CIMT and left and right RIMT. However, there was a poor correlation between CIMT and RIMT (Table 5). The latter is not unexpected, as only 38% of patients with abnormal CIMT had an abnormal RIMT.

Interestingly, 40 patients in the study presented with rheumatoid arthritis. In this subgroup, 70% of patients had an abnormal CIMT. The numbers were too small to analyse further, and the study was not designed to assess co-morbidity risks.

Table 3. The effects of modifiable-factor combinations on mean CIMT

	Linear regression		*Logistic regression*	
Modifiable risk-factor combinations	p-*value*	*95% CI*	*OR*	*95% CI*
Diabetes mellitus + hypertension	0.018	0.07 to 0.75	6.92	2.32–20.7
Hypertension + smoker	0.033	0.02 to 0.52	3.67	1.43–9.41
Diabetes mellitus + hypercholesterolaemia	0.019	–0.24 to –0.02	0.15	0.03–0.70
Hypercholesterolaemia + obesity	0.003	–0.27 to –0.06	0.12	0.03–0.51

Only results of statistical significance are reported. CI, confidence interval; OR, odds ratio.

Table 4. The effects of modifiable risk factors and combinations on mean RIMT

	Linear regression		*Logistic regression*	
Modifiable risk-factor combinations	p-*value*	*95% CI*	*OR*	*95% CI*
Hypertension	0.5	0.00–0.09		
Hypercholesterolaemia	< 0.001	0.02–0.08		
Hypertension + obesity		0.05–0.15	0.13	0.03–0.61
Hypertension + hypercholesterolaemia	0.004	0.03–0.14	2.87	1.41–5.84
Diabetes mellitus + obesity	0.009	–0.04–0.06	3.64	0.69–19.2

Only the results of statistical significance are reported. CI, confidence interval; OR, odds ratio.

Table 5. Correlation coefficients (*r*) between left and right CIMT and RIMT

	Left CIMT	*Right RIMT*	*Left RIMT*
Right CIMT	0.93	0.47	0.48
Left CIMT	-	0.42	0.43
Right RIMT	-	-	0.98

Discussion

The prognostic and predictive value of CIMT measurements and cardiovascular disease is a topic that is hotly debated in the current literature.[17] It is, however, clear that an increase in IMT is an independent predictor for the risk of stroke, apart from the traditional well-described risk factors.[15] Only patients with individual risk factors for future cardiovascular system events, such as stroke and CAD, were included in this study. This is the first study describing ultrasound measurements of CIMT and RIMT in patients with modifiable risk factors in central South Africa.

The study group primarily consisted of older, affluent patients presenting at a general physician private practice, which explains the demographic composition. The CIMT diameters of the total study group, men and women, were similar to the findings of a study conducted by Mostaza *et al.*[16] Despite the presence of several risk factors, 80% of patients had two or more risk factors. Only 40% of patients with risk factors had pathological thickening of the carotid intima. However, most patients with a CIMT of $\geq$ 0.9 mm had two or more risk factors.

It is perturbing that hypertension was present in more than 90% of patients, and hypertension was the single most common risk factor observed in the study population. Two-thirds were obese, followed by the presence of hypercholesterolaemia, diabetes and smoking.

Male gender was the only non-modifiable risk factor associated with abnormal CIMT measurements. As a matter of fact, where females tended to be dominant in the normal CIMT group, an almost 50/50 distribution of gender was observed for those with an abnormal CIMT.

More than 50% of patients diagnosed with stroke or TIA had an abnormal CIMT. This finding concurs with Roquer *et al.*, who demonstrated that an increase in IMT thickness was an independent marker of major cardiovascular events. For each increment of 0.1 mm in IMT, the probability of experiencing a recurrent stroke was increased by 18%.[17]

Our results show that individual risk factors played a role in a thickened CIMT. However, the high prevalence of hypertension in central South Africa is cause for concern. Hypertension was markedly higher in this study (90%) than that reported by Ren *et al.* and Dias *et al.* (67 and 72%, respectively).[3,18] Forty-six per cent of the hypertension group presented with an abnormal CIMT. Interestingly, only 20% of the hypertension group in the study of Ren *et al.* presented with carotid atherosclerosis.[3] In our study, hypertension contributed to a thicker mean CIMT with an OR of 3.99. This result corresponds to the findings of Ferreira *et al.*, demonstrating that individuals with a CIMT $\geq$ 0.9 mm had a significant association with a hypertension history, with an OR of 2.11.[19]

Shear forces produced by chronically high blood pressure damage the endothelial layer in the cerebral and coronary arteries, and the aorta.[20] According to Shrestha *et al.*, an increase in systolic blood pressure correlates with atherosclerotic changes in the carotid arteries. An association of low- and high-grade lesions correlates with increased systolic blood pressure.[21]

Patients with cognitive dysfunction who are hypertensive have changes in the vascular morphology, supported by an increased CIMT, enhanced atherosclerotic lipid profile and impaired haemodynamic function. This is manifested by elevated central systolic blood pressure. Increased systolic blood pressure causes morphological changes, characterised by an increased CIMT.[22]

DM was a prominent risk factor and was recorded in 30% of the study population. The prevalence of DM in our study is lower than the findings of Poznyak *et al.*, who investigated 3 001 patients in South Africa and reported a 49.5% prevalence of DM.[22] In 60% of our patients with DM, an abnormal CIMT was recorded. The mean CIMT in the diabetic patients was 0.9 $\pm$ 0.2 mm, concurring with Yafei *et al.*[23] They reported that CIMT was significantly thicker in diabetic patients compared to controls (0.79 $\pm$ 0.16 vs 0.58 $\pm$ 0.08 mm).[24]

In our study, DM significantly contributed to a thicker mean CIMT with an OR of 2.82. This agrees with Ren *et al.*, who showed that DM is one of the significant risk factors associated with carotid atherosclerosis.[3] All types of DM have been shown to be independent risk factors for accelerated development of atherosclerosis.[24] The pathogenesis of DM and atherosclerosis are closely linked, and among the known pathological mechanisms linking atherosclerosis and DM are hyperglycaemia, inflammation, increased oxidative stress and dyslipidaemia.[24]

Hypercholesterolaemia was present in more than half of the patients in the abnormal CIMT group. Interestingly, 86% of patients who presented with hypercholesterolaemia and an abnormal CIMT were Caucasian, and only 7% were black Africans. Hypercholesterolaemia contributed to a thickened CIMT with an OR of 2.47; this finding has also been reported in several other studies.[3,24,25]

Our study showed that risk-factor combinations such as DM and hypertension, and hypertension and smoking significantly increased the risk of having greater CIMT measurements. The OR of the combinations were markedly higher than isolated risk factors, most likely indicating the summative effects when individual risk factors occur in combination. However, it appears that having hypercholesterolaemia and DM or hypercholesterolaemia and obesity reduced the risk of having a thickened CIMT.

We speculate that many of our patients were on statin treatment, which may have provided protection against an increased CIMT. According to Lind, statin treatment is known to reduce cardiovascular events and age-related progression of CIMT in subjects with and without cardiovascular disease.[24]

A real-life observational study showed that statin treatment reduced the increase in IMT seen over 10 years compared to subjects not treated with statins. This is further supported by Kerola *et al.*, who concluded that in hypercholesterolaemic adults with subclinical atherosclerosis, one-year treatment with rosuvastatin significantly reduced the CIMTs bilaterally and improved the lipoprotein and lipid levels.[25]

Age and male gender were the only non-modifiable risk factors contributing to the risk of an increase in mean CIMT; each year of age added 11% to the risk of having a thickened CIMT. This finding concurs with Ren *et al.* In their study, the authors demonstrated that middle-aged and older individuals with cardiac risk factors displayed an increased CIMT and higher severity grade than the younger age groups.[3] Interestingly, Zyriax *et al.* found that each year of life translated to an additional 0.004-mm increase in CIMT. Apart from demonstrating a risk for thicker CIMTs, significantly more men had an abnormal CIMT compared to the normal CIMT group, indicating male gender

is a noteworthy risk factor.[1] Similar findings were reported by Mostaza *et al*., where male gender was associated with a thickened CIMT.[16]

According to Wahood *et al*., patients with hypertension and congestive heart failure usually had an increased radial artery diameter.[26] Furthermore, Loh *et al*. concluded that hypertension, hyperlipidaemia and male gender increased the radial artery diameter, whereas age, DM, race and smoking did not significantly influence the size of the radial artery. Vessel dilation is promoted by the release of endothelium-derived nitric oxide and defective synthesis.[27]

Interestingly, more female patients presented with an abnormal RIMT than men (57 vs 43%). Similar to that in the CIMT group, hypertension was the most common modifiable risk factor, followed by obesity and hypercholesterolaemia. Hypercholesterolaemia was the only individual risk factor significantly contributing to a thicker RIMT with an OR of 3.00. In contrast to CIMT, hypertension and obesity was the only combination contributing to a thicker RIMT.

Eklund *et al*. concluded that RIMT assessed by ultrasound conferred prognostic information in patients with suspected CAD. Similar findings were reported by Eklund *et al*., where RIMT may constitute a feasible imaging biomarker for systemic atherosclerotic burden.[13] Our results demonstrated a poor correlation between RIMT and CIMT. We speculate that RIMT may be more valuable as a potential marker of coronary atherosclerotic disease, while CIMT appears to be more valuable for neurovascular disease. This provides some explanation for the difference in association with risk factors found in the study.

It is thought provoking that in this study, 40 patients with risk factors also had rheumatoid arthritis as a co-morbidity, and 70% had an abnormal thickened CIMT. According to Hannawi *et al*., CIMT in rheumatoid arthritis patients was increased compared to healthy individuals matched for age, gender and cardiovascular risk.[28]

This statement is supported by Komici *et al.*, who showed that CIMT was previously found to be increased in patients with longstanding rheumatoid arthritis.[29] Patients over 20 years of age with longstanding rheumatoid arthritis had a higher CIMT compared to patients of similar age but shorter disease duration (< seven years).

An important factor related to cardiovascular risk in rheumatoid arthritis patients is an impairment of endothelial function, which is a key element in the development of the atherosclerotic process. Endothelial impairment is related to rheumatoid arthritis being a chronic inflammatory process. Altered endothelial reactivity has been documented in rheumatoid arthritis patients prior to atherosclerotic plaque detection, even without cardiovascular risk factors.[28]

Study limitations

This study was conducted during the Covid-19 pandemic, resulting in relatively small numbers. Patients were recruited from private practice, therefore consisting mainly of an affluent population. The lack of long-term follow up of patients with abnormal CIMT was also regarded as a limitation. Based on the results obtained in this study, further studies are indicated.

Conclusion

Most patients had two or more risk factors, and hypertension was present in almost 90% of patients. Results showed that male gender, increasing age, hypertension, DM, hypercholesterolaemia and smoking significantly contributed to a thickened CIMT. In contrast, only hypercholesterolaemia was associated with a thickened RIMT. Hypertension had the biggest impact on increased mean CIMT compared to the other modifiable risk factors. Certain risk-factor combinations were also associated with a thickened CIMT and RIMT, and combinations of risk factors appeared to add summative risk. A good correlation was observed between left and right CIMT and between left and right RIMT measurements. However, CIMT and RIMT did not correlate with each other.

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