Imaging

Imaging of atherosclerosis: carotid intima–media thickness

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Carotid ultrasound provides quantitative measurements of carotid intima–media thickness (CIMT) that can be used to assess cardiovascular disease (CVD) risk in individuals and monitor ongoing disease progression and regression in clinical trials. It is non-invasive, rapid, reproducible, and carries no risk. Numerous epidemiological studies have established that CIMT is a marker of subclinical atherosclerosis and is associated with established CVD risk factors and with both prevalent and incident CVD. The use of CIMT in outcome trials as a surrogate or predictor of CVD outcomes is widespread. Carotid ultrasound is being employed to test the efficacy of CVD treatment in order to identify potential useful drugs earlier and to possibly speed regulatory approval. Successive trials have generated lessons learned and applied, with slow but steady improvement in CIMT measurement reproducibility.

In 1986 Italian investigators reported the results of an in vitro study of 18 human aorta and common carotid arteries, which compared direct measurements of arterial wall thickness by gross and microscopic examination with B mode real-time imaging of those same specimens.1 They described a characteristic B mode image of the arterial wall composed of two parallel echogenic lines separated by a hypoechoic space. The distance between the two lines did not differ significantly from the intima–media thickness (IMT) measured on pathologic examination, leading the investigators to suggest that B mode imaging could present a useful approach to the measurement of IMT in vivo. Today, less than a quarter century later, calculation of carotid IMT (CIMT) is arguably the most widely used non-invasive measure of atherosclerosis currently employed by clinicians and clinical investigators, both to quantify the extent of subclinical disease and to monitor change over time (Figure 1).

Because cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide, the potential value of a non-invasive imaging method that allowed direct visualization of the arterial wall and provided quantification of all stages of the atherosclerotic process was great. Previously, while ultrasound was widely employed as a screening tool for carotid disease, the B-mode image of the vessel was used as an adjunct to obtaining accurate Doppler flow measurements from the site of maximum lumen narrowing. The vessel wall was largely ignored, since the focus was on identifying patients with high-grade stenosis who might be candidates for carotid endarterectomy. Now there existed the possibility that a technology that was already widely available, non-invasive, and familiar to clinicians, could provide further benefit by quantifying atherosclerosis much earlier in its development in individual subjects and patients. The carotid artery lends itself to study by high-resolution ultrasound devices because it is superficial in location, is relatively stationary, and runs parallel to the surface of the neck, at least to the level of the carotid bifurcation. Employing B-mode ultrasound, the ‘double echo’ pattern shown in that original publication to represent the combined width of the carotid artery intima and media, can be readily and reproducibly visualized in nearly all subjects. Typically, the carotid artery is classified into three segments when undergoing ultrasound study, each approximately 1 cm in length. The most proximal segment, the 1-cm straight segment of the extracranial carotid artery immediately prior to the bifurcation, is the common carotid (CCA). Its distal boundary is identified by a divergence of the near and far walls as the artery begins to...
divide into its internal and external branches. This focal widening of the bifurcation extends over approximately 1 cm and is labelled the carotid bulb (CB). Its distal margin is defined by the tip of the flow divider separating the diverging internal carotid artery (ICA) and external carotid artery. The final segment that is commonly examined is the proximal 1 cm of the ICA. Of the three anatomic segments, the easiest to examine by ultrasound is the CCA, making it an attractive target of study. However, the carotid artery has proven to be an extremely complex vessel, with differing associations for each segment to risk factors and outcomes, complicating the search for a standard imaging protocol that best meets every clinical and investigational requirement.

Because the carotid artery is an elastic artery, CIMT in healthy young subjects consists almost entirely of media. Technically, it is impossible to distinguish between intima and media by ultrasound. The normal carotid arterial wall appears unaffected by age or gender until approximately 18 years of age; thereafter there is diffuse progressive intimal thickening. Carotid IMT varies throughout the cardiac cycle by as much as 0.03 mm, being thickest at end diastole and thinnest at peak systole. It is rare to find carotid atherosclerotic plaque, defined either as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or a thickness \( >1.5 \) mm as measured from the media–adventia interface to the intima–lumen interface, in men under 40 years or in women prior to the onset of menopause. When present, focal atherosclerotic plaques are almost always located in the CB and ICA and rarely in the CCA except in very advanced disease. This is thought to be related in significant part to the varying hemodynamics of the carotid artery, with plaques forming in areas of low, rather than high, shear stress, particularly in regions of marked oscillations in the direction of wall shear stress. Such conditions are present in the CB and ICA but not in the distal CCA, where wall shear stress is high and the shear stress vector is aligned in the forward axial direction throughout the pulse cycle.

In healthy middle-age adults, the distance from the CCA lumen–intima interface and the media–adventia interface measures 0.6–0.7 mm (Figure 2). In the CB, CIMT is generally higher, whereas values for the ICA resemble those of the CCA in healthy individuals. Thickness varies with age, gender, and ethnicity. It increases with age and is generally thicker in men than women. While certain risk factors, such as diastolic blood pressure and fasting glucose, relate better to the CCA, others demonstrate a stronger relationship to the CB or ICA. However, normal values for CIMT are difficult to provide because in addition to risk factors, the absolute CIMT value also depends on the location of the measurement (segments, near, or far wall), the ultrasound equipment used, and the offline reading system (automated, manual tracings) employed. These latter aspects are one of the reasons why mean CIMT values may differ considerably between studies.

Automated edge detection programmes have been suggested as a better approach to reduce variability in the measurement of CIMT. Most automated edge detection programmes have been...
designed for the measurement of far wall CCA, whereas the near wall is not considered, nor are measurements of the CB or the ICA. The main potential advantage of automated edge detection programmes is that they may reduce variability in CIMT readings as a result of reduction in differences between readers and by the elimination of change in reading behaviour over time (reader drift). The beneficial effect of automated edge detection in reduction of measurement variability depends on the contribution of sonographers and readers on the total variability in the CIMT measurement. A number of studies have indicated that differences between sonographers have a much larger effect on CIMT measurements than differences between readers. Furthermore, a formal quantification of the extent of reduction in measurement error using either approach has not been done. In general, when ultrasound images show clear interfaces automated edge detection programmes work well, whereas when the interfaces on the ultrasound images are less clear, the automated edge detection programme needs to be manually overridden, thereby eliminating the advantages of the use of automated edge detection.10,11

Relationship with future vascular events

Following publication of the first CIMT paper, with attention now redirected from the arterial lumen to the arterial wall, several large observational studies were initiated to ascertain the relationship of CIMT with established CVD risk factors, with prevalent CVD, atherosclerosis elsewhere, and, most importantly, with incident vascular disease independent of other risk factors. In the Kuopio Ischemic Heart Disease (KIHD) risk factor study, 1288 Finnish men were followed for 2.5 years; an increased CIMT (>1 mm) at baseline was related to a 2.2-fold (95% confidence interval [CI]: 0.7–6.74) increased risk of myocardial infarction (MI).12 In 1997 the Atherosclerosis Risk in Communities Study (ARIC) reported the results of a study of 15 792 healthy subjects aged 45–65 years who had been followed in four US communities for 4–7 years after undergoing baseline carotid ultrasound. ARIC demonstrated that increased CIMT was prospectively associated with increased risk of CHD, with a hazard ratio (HR) of 1.13 for MI per 0.1 mm difference in CCA IMT, adjusted for age and gender.13 Similar findings were reported that same year by the Rotterdam Study for 7983 subjects, the HR being 1.19 for the same measurement.14 Two years later the Cardiovascular Health Study (CHS) reported on a study of 4476 subjects without clinical CVD followed for a median period of 6.2 years, using a combined CCA and ICA CIMT measure.15 For MI, the HR was 1.15. Dividing their population into quintiles based on CIMT, CHS showed that the 7-year rates for MI or stroke was over 25% for participants in the fifth quintile compared with less than 5% for those in the first quintile (Figure 3).

When analysed separately, there was a stronger association between ICA IMT and incident MI than CCA IMT, while the opposite was true for stroke. After adjustment for traditional risk factors, CIMT was the variable most strongly associated with CVD events, and by itself was as powerful a predictor of these as any combination of the traditional risk factors. In 2007 Lorenz et al.16 published a systematic review and meta-analysis of eight relevant general population-based studies that had reported on the ability of CIMT to predict future cardiovascular end points, including the three above, involving a total of 37 197 subjects followed for a mean of 5.5 years. They reported that for an absolute CIMT difference of 0.1 mm, the future risk of MI increases by 10–15%, and the stroke risk increases by 13–18%. Currently, over 20 cohort studies performed among subjects with or without previous vascular disease, and with and without CVD risk factors, showed consistently that increased CIMT relates to increased cardiovascular risk, independently of established vascular risk factors.

Incremental value for risk stratification

While it was clear that ultrasonically derived carotid wall measurements provided offered a powerful new tool in assessing CVD risk, it was less certain how much additional value CIMT measurement added to existing risk-assessment methods such as the Framingham risk score or the Systematic Coronary Risk Evaluation (SCORE) system. Framingham divides subjects into three risk categories based principally on age, gender, cholesterol, blood pressure, and smoking: low (<10% risk of an vascular event in 10 years); intermediate(10–20%); and high (>20%).17 Treatment recommendations, which have become progressively more aggressive over the past two decades, are linked to these categories. Several studies indicated that the risk stratification by Framingham leaves room for improvement. Recognizing that treating major CVD risk factors for primary and secondary prevention works and the guidelines support this, and seeking to provide clinicians with better risk indicators, in 2001 the American Heart Association Prevention V Conference suggested that persons over 50 years of age at intermediate risk for CVD might be suitable for screening by non-invasive tests, including carotid ultrasound.18 In 2003 the 34th Bethesda Conference wrote that patients at intermediate risk for total CVD event possibly warrant further risk stratification by non-invasive tests such as CIMT and coronary artery calcium (CAC) scoring to assess atherosclerotic burden.19 Initially in

![Figure 3 Unadjusted cumulative event-free rates for the combined end point of MI or stroke, according to quintile of CIMT.](image-url)
2003, and again in 2007, the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension and of the European Society of Cardiology recommended carotid ultrasound in hypertensive patients both to provide better stratification and to assess end-organ damage.20 Because of their concern that ultrasound scanning limited to the CCA was likely to measure vascular hypertrophy only, they suggested that scanning the CB and/or the ICA provided a better measure of atherosclerosis.

One of the first reports on the incremental value of CIMT measurement in risk stratification among 55-year-old subjects came from the Rotterdam Study in 2001. At that time, evaluation of the incremental value was generally based on the change in area under the receiver operating characteristic curve (ROC), the c statistic, although recently Cook21 has challenged the use of this approach as the best choice for evaluating the utility of novel risk factors. In the Rotterdam Study analyses, when CCA CIMT was added to a basic risk factor model, the ROC area increased from 0.72 (95% CI: 0.69–0.75) to 0.75 (95% CI: 0.72–0.78). The authors concluded that adding CIMT to a risk function for CVD did not result in a substantial increase in predictive value when used as a screening tool.22 In addition, a recent systematic review of the role of CIMT measurements in CVD screening programmes concluded that at present it seems that the published evidence to quantitatively support the use of a CIMT measurement to help in risk stratification on top of such standard risk functions such as Framingham or SCORE is limited.23

While there remains a paucity of information on the effectiveness of screening using carotid ultrasound, existing data does support some conclusions. The prevalence of severe carotid stenosis (≥70%) in the general population is low and does not provide a rationale for widespread screening of asymptomatic patients.24 And while there has been extensive focus on the concept of using bioimaging to detect the "vulnerable plaque", plaque characterization by ultrasound has not shown to be of any value in therapeutic decision-making and should not be used as a justification for screening. Finally, for reasons discussed below, serial CIMT studies to assess the efficacy of treatment in individuals is not recommended.

### Change over time in CIMT and trials

Because external ultrasound is non-invasive and has no known risk, early consideration was given to obtaining longitudinal CIMT measures to assess the impact of treatment on individuals. Annual CIMT progression rates average 0.005–0.01 mm/year. In a pooled analysis of lipid lowering trials the estimate for rate of change in CIMT was 0.0147 mm/year (95% CI: 0.0122–0.0173) for mean CCA IMT and 0.0176 mm/year (95% CI: 0.0149–0.0203) for combined mean maximum CCA, bulb, and ICA IMT.9 As these estimates reflect group averages, it means that some participants progress more rapidly than others, and that some may not change at all. The axial resolution of an ultrasound unit is between 0.1 and 0.3 mm. Measurement error is consistently reported to be at least 5–10% of baseline CIMT. Thus for individuals, the error involved in CIMT measurement precludes identification of real change over any reasonable time period. However, while serial CIMT studies cannot track change in single subjects, they have become widely used in clinical trials involving hundreds of subjects in each trial arm. The above data determines the appropriate design for progression studies. The longer the duration of the trial, the larger the study population, the more rigorous the imaging protocol, and the more significant the expected impact of the therapeutic intervention, the more likely divergent rates of CIMT change will be identified. Such studies began in the mid-1990s, largely focusing on the impact of statins vs. placebo and demonstrated that aggressive statin therapy reduced CIMT progression relative to placebo or lower dose statin therapy. By way of example, in one of the earliest such trials published, the ACAPS study reported on 919 patients treated for with lovastatin or placebo along with warfarin or its placebo. They were able to demonstrate that after 3 years CIMT progression between lovastatin and its placebo was statistically significant (P = 0.001).25

Over the past 15 years, change in CIMT over time has been used as an alternative for CVD events as the primary outcome in a variety of intervention studies such as evaluating lipid modifying therapy, glucose lowering therapy and antioxidant therapy, and hormonal replacement therapy.26–29 In addition, a recent review reported on the effects of blood pressure lowering on rate of change in CIMT using data from randomized controlled trials. Of 22 trials identified through a PubMed search, 8 included 3329 patients with diabetes or coronary heart disease. In these studies, blood pressure lowering treatment with an angiotensin-converting enzyme (ACE) inhibitor, a beta-blocker, or a calcium-channel blocker, reduce the rate of change in CIMT 0.007 mm/year as compared with placebo or no treatment (P = 0.01). In 9 trials including 4564 hypertensive patients, CCBs, ACE inhibitors, an angiotensin II receptor blocker, or an α-blocker, compared with diuretics or beta-blockers, in the presence of similar blood pressure reductions, significantly decreased the rate of change in CIMT 0.003 mm/year (P = 0.03).30

The design of CIMT trials has varied. Some studied only the CCA, while others included all three segments; some imaged only the far wall, others both the near and far wall. Some focused on studying the vessel from a single predetermined angle, while others obtained and averaged measurements from multiple angles. Some controlled for cardiac cycle, others did not; some used hand-drawn methods to define interfaces, while others employed various automated edge-detection techniques. Even today, no single ‘best practice’ CIMT protocol has emerged. Two recent studies illustrate this. In 2008 METEOR reported on 984 subjects with a low Framingham risk score and a maximum CIMT ≥1.2 to <3.5 mm who were treated with rosuvastatin 40 mg vs. placebo. The protocol employed utilized measurements of the near and far wall of all carotid artery segments using a single fixed angle at each level, and the primary endpoint was the rate of change of maximum CIMT at 12 carotid sites. Two scans were performed at baseline, one every 6 months thereafter; then two at end of study. All seven scans were read randomly by a single reader at the end of study, using a manual method to draw the interfaces, with control for the cardiac cycle. Rosuvastatin 40 mg show a rate of maximum CIMT progression of −0.0014 mm/year vs. 0.0131 mm/year for placebo (P < 0.0001) (Figure 4).31
CIMT change and reduction in events

Unfortunately, no study to date has been powered to demonstrate whether a reduction in CIMT progression led to a corresponding reduction in CVD events. For the large epidemiology studies, no comparison of progression rates linked to outcomes is available since no systematic intervention occurs. For the prospective trials, none has been large enough or of sufficient duration to convincingly confirm or refute the hypothesis that novel therapies that slow or reverse CIMT progression have a corresponding impact on hard clinical outcomes. One early study has provided information on the relation of change in CIMT and the risk of future events. In a population of 146 men with coronary disease, aged 40–59 years with a follow-up of 8.8 years, Hodis et al.\(^ {37}\) showed that a 0.03 mm/year increase in CCA IMT was related to a 2.2-fold increased risk of coronary events. In addition, Espeland et al.\(^ {38}\) recently performed a meta-analysis showing that across the trials, statin therapy was associated with an average decrease of CIMT progression of 0.012 mm/year (95% CI: −0.016 to −0.007). Using the same studies, a meta-analysis yielded a risk reduction of 52% for CVD events. In this approach, the authors linked the CIMT benefit to the reduction of events. In contrast with these findings was the report from the European Lacidipine Study on Atherosclerosis (ELSA), a randomized trial in which 2334 hypertensive patients from 7 European countries were followed under effective antihypertensive treatment for 3.75 years. The authors concluded that while baseline CIMT strongly predicted CVD events during the follow-up period, differences in CIMT measured yearly compared with baseline did not.\(^ {39}\)

**Figure 4** Change in maximum CIMT for rosvustatin vs. placebo over the 2 year period of the METEOR Trial.

The recently published ARBITER 6-HALTS trial compared the effects of two combination therapies—either niacin or ezetimibe added to long-term statin therapy—on far wall CCA IMT only, employing two scanning angles on the right and left. Scans were obtained at baseline, at 8 months and at 14 months and were read by a single reader employing an automated border-detection algorithm. The primary end point was the between-group difference in mean CIMT after 14 months. Ezetimibe showed a change from baseline to 14 months of −0.0007 ± 0.0035 mm, while niacin showed a change of −0.0142 ± 0.0041 mm, demonstrating that niacin had greater efficacy in mean CCA CIMT (\(P = 0.003\)).\(^ {32}\) Two approaches, but each providing a definitive result.

Recent publications have appeared in which attempts were made to provide data on ‘best’ CIMT measurements strategy for trials based on comparing various strategies on reproducibility, progression, and treatment effect.\(^ {33,34}\) These analyses assumed that the best CIMT protocol would be one that combines high reproducibility, a large and precise estimate of the rate of CIMT progression, and a large and precise estimate of the treatment effect. It has been proposed that employing three-dimensional measurement of carotid plaque would allow mark reductions in the size and duration of ultrasound studies assessing the efficacy of new therapies.\(^ {35}\) In the Troms Study, involving 6226 participants aged 25–84 years with no previous MI, carotid plaque area was a stronger predictor of MI than was CIMT.\(^ {36}\) However, we are not aware of any randomized controlled trial to date that has employed total plaque volume as the outcome measure.

**Concurrence between CIMT and IVUS trials**

There have been at least five parallel clinical trials that have used both CIMT and intravascular coronary artery ultrasound (IVUS) to evaluate the efficacy of different therapeutic approaches on atherosclerosis progression.\(^ {31,40–49}\) IVUS employs a miniaturized ultrasound device attached to the end of a catheter to obtain a series of images of the coronary artery wall from which measurements of wall thickness can be derived. While in no instance to date have the identical subjects been studied by both CIMT and IVUS, in at least four instances the therapeutic interventions—and therefore the expected therapeutic effect on different vascular beds—were similar. In the ASAP trial, 325 patients with familial hypercholesterolemia (FMH) having an average age of 48 years and a baseline CIMT of 0.093 mm were treated with either atorvastatin 80 mg (intensively treated) or simvastatin 40 mg (moderately treated). At 2 years atorvastatin CIMT decreased −0.03 mm (\(P = 0.0017\)) while simvastatin CIMT increased 0.036 mm (\(P = 0.0005\)).\(^ {40}\) In the REVERSAL trial 654 patients undergoing coronary artery catheterization were randomly assigned to either atorvastatin 80 mg (intensive) or pravastatin 40 mg (moderate). The primary IVUS endpoint (percentage change in atheroma volume) showed a significantly lower progression rate in the atorvastatin group (\(P = 0.02\)). Progression of coronary atherosclerosis did occur in the pravastatin group (2.7%) compared with baseline but not in the atorvastatin group (−0.4%).\(^ {41}\) These two studies supported the thesis that greater low-density lipoprotein cholesterol (LDL-C) lowering is beneficial, a hypothesis that was subsequently supported by a
number of clinical outcomes studies.\textsuperscript{50,51} Radiance 1 was a CIMT study of 850 FMH patients who were randomly assigned to either torcetrapib, an inhibitor of cholesteryl ester transfer protein, 60 mg and atorvastatin or atorvastatin alone. After 2 years the use of torcetrapib showed no benefit despite an increase in high-density lipoprotein cholesterol (52%), and a substantial decrease in LDL-C (21%).\textsuperscript{52} In a parallel IVUS study, ILLUMINATE, involving 950 subjects with symptomatic coronary artery disease, the change in percent atheroma volume was nearly identical in both groups (P = 0.72).\textsuperscript{43} The torcetrapib outcomes study ILLUMINATE, involving 15 067 subjects, was terminated coincident with the conclusion of the two imaging studies; at termination the torcetrapib group showed a 25% increased risk over the group that received atorvastatin alone (HR, 1.25; 95% CI: 1.09–1.44; P = 0.001).\textsuperscript{52} The above examples were chosen because they allow comparison of two techniques, CIMT and IVUS, which are used to obtain sequential measurement of atherosclerosis progression in different vascular beds and with results that can be linked to clinical outcomes trials. One of the therapeutic trials had a positive outcome for both imaging modalities, and one had a negative outcome for both. The clinical trials had the same results, one positive and one negative. To date, although the number of studies is small, there has been concordance between trial outcomes as determined by ultrasonic wall measurements in the carotid and coronary arteries, and, in at least two instances, by clinical outcomes.\textsuperscript{53}

**CIMT and CAC**

As earlier noted, a number of consensus panels have suggested that CIMT and CAC might be useful additions to standard risk assessment scores. While there continues to be honest debate about the value of such screening, two recent studies have addressed the question of which study is more predictive of incident CVD events. Using 559 subjects enrolled in the Pittsburgh Field Center of CHS, Newman et al.\textsuperscript{54} found that CIMT and CAC had similar hazards ratios for total CVD and CHD. CIMT was more strongly related to stroke than CAC. The Multi-Ethnic Study of Atherosclerosis (MESA) studied 6814 adults with both CIMT and CAC. The cohort was followed for incident CVD events for a median of 3.9 years. After adjusting for each other and traditional CVD risk factors, the HR of CVD increased 2.1-fold (95% CI: 1.8–2.5) for each one-standard deviation (SD) increment of log-transformed CAC score, vs. 1.3-fold (95% CI: 1.1–1.4) for each 1-SD increment of CIMT.\textsuperscript{55} A ROC curve analysis also suggested that CIMT was a better predictor of incident CVD than was CAC, with areas under the curve of 0.81 vs. 0.78, respectively. In MESA, CIMT was more predictive of stroke than was CAC.

Similar to CAC, there have been several reports comparing the direction, magnitude, and precision of the relation for CIMT with that found for other atherosclerotic measurements. The latter includes measurement of carotid plaque presence or total plaque area assessed with ultrasound. An in-depth description of these studies is however beyond the scope of the current review.\textsuperscript{56,57}

**Conclusion**

Advances in the field of carotid ultrasound have been incremental, resulting in a steady decrease in measurement variability. Improvements in edge detection algorithms point towards increasing automation of CIMT measurements, though the use of this approach has so far been limited to the CCA. The major advantage of CIMT is that it is completely non-invasive and can be repeated as often as required. It provides a continuous measure, since all subjects have a measurable carotid wall. It is also relatively inexpensive to perform, and the technology is widely available. Increased CIMT has been shown consistently to predict future vascular events. Furthermore, intervention for established CVD risk factors has been shown to affect CIMT progression within 12–18 months in properly designed trials with results congruent with clinical events trials. For all these reasons, and the wealth of experience with this approach, external carotid external ultrasound is likely to remain among the most widely employed imaging technique for the quantification and tracking of subclinical atherosclerosis.

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**References**


A 50-year-old woman with highly symptomatic, drug refractory paroxysmal atrial fibrillation (AF) was referred to our institution for transcatheter pulmonary vein isolation.

The pre-operative magnetic resonance imaging (MRI) scan showed a congenital vascular anomaly: right superior vena cava was absent and both brachiocephalic veins drained in a persistent left superior vena cava (LSVC) that ended up in a huge coronary sinus (Panel A).

Before performing the transseptal puncture, a self-terminating AF episode triggered by focal activity from LSVC was observed. Planned pulmonary vein isolation was then abandoned, and the electrical isolation of the LSVC from distal coronary sinus was attempted.

A three-dimensional reconstruction of the right atrium and the giant coronary sinus together with the proximal persistent LSVC was obtained merging the MRI scan and the Carto 3 map.

Circumferential ablation at the junction between LSVC and distal coronary sinus was performed (Panel B, red dots: ablation sites). Complete isolation was documented by the presence of focal activity in the vein, highlighted by asterisk in Panel C, dissociated from the atrium.

The patient was discharged without antiarrhythmic drugs and experienced no clinical recurrence during 6-month follow-up. Persistent LSVC is the most common congenital thoracic venous anomaly. The association between LSVC and AF has already been documented in small series of cases, in which both pulmonary veins and LSVC isolation were performed. This is the first reported case in which LSVC disconnection alone was effective in the cure of paroxysmal focal AF.