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Consensus statement

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Coronary CT angiography evaluation with artificial intelligence for individualized medical treatment of atherosclerosis: a Consensus Statement from the QCI Study Group

Kenrick Schulze ⬤[1,28], Anne-Marieke Stantien[1,28], Michelle C. Williams ⬤[2,28], Vassilios S. Vassiliou[3], Andreas A. Giannopoulos[4], Koen Nieman[5], Pál Maurovich-Horvat[6], Jason M. Tarkin ⬤[7], Rozemarijn Vliegenthart[8], Jonathan Weir-McCall ⬤[9], Mahmoud Mohamed ⬤[1], Bernhard Föllmer ⬤[1], Federico Biavati ⬤[1], Ann-Christine Stahl ⬤[1], Jakob Knape[1], Hanna Balogh[1,6], Nicola Galea[10], Ivana Išgum ⬤[11,12,13], Armin Arbab-Zadeh[14], Hatem Alkadhi ⬤[15], Robert Manka[15,16], David A. Wood[17,18], Edward D. Nicol[19,20], Nick S. Nurmohamed ⬤[21], Fabrice M. A. C. Martens ⬤[21], Damini Dey ⬤[22,23,29], David E. Newby[2,29] & Marc Dewey ⬤[1,24,25,26,27,29] ✉

Abstract

Coronary CT angiography is widely implemented, with an estimated 2.2 million procedures in patients with stable chest pain every year in Europe alone. In parallel, artificial intelligence and machine learning are poised to transform coronary atherosclerotic plaque evaluation by improving reliability and speed. However, little is known about how to use coronary atherosclerosis imaging biomarkers to individualize recommendations for medical treatment. This Consensus Statement from the Quantitative Cardiovascular Imaging (QCI) Study Group outlines key recommendations derived from a three-step Delphi process that took place after the third international QCI Study Group meeting in September 2024. Experts from various fields of cardiovascular imaging agreed on the use of age-adjusted and gender-adjusted percentile curves, based on coronary plaque data from the DISCHARGE and SCOT-HEART trials. Two key issues were addressed: the need to harness the reliability and precision of artificial intelligence and machine learning tools and to tailor treatment on the basis of individualized plaque analysis. The QCI Study Group recommends that the presence of any atherosclerotic plaque should lead to a recommendation of pharmacological treatment, whereas the 70th percentile of total plaque volume warrants high-intensity treatment. The aim of these recommendations is to lay the groundwork for future trials and to unlock the potential of coronary CT angiography to improve patient outcomes globally.

Sections

A full list of affiliations appears at the end of the paper. ✉e-mail: marc.dewey@charite.de

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Introduction

Coronary CT angiography (CCTA) has emerged as a first-line imaging modality for patients with suspected coronary artery disease (CAD), with up to 2.2 million CCTA procedures conducted annually in Europe alone[1–4]. Performing CCTA as the first line of investigation in patients with an intermediate probability of stable CAD[5,6] is supported by pivotal randomized, controlled cardiovascular outcome trials, such as the SCOT-HEART[3] and DISCHARGE[7,8] trials. These studies demonstrated the superiority of CCTA over standard care and invasive coronary angiography in reducing major adverse cardiovascular events (MACEs) and the non-inferiority of CCTA versus invasive coronary angiography in reducing major procedure-related complications. In the SCOT-HEART trial[7], the addition of CCTA to standard care reduced the incidence of the primary outcome measure (MACE; coronary heart disease-related death and non-fatal myocardial infarction) over the initial 5-year study period as well as the extended follow-up period of up to 10 years[9]. These findings were primarily attributed to improved diagnostic precision and optimized preventative therapies[10] and are consistent with evidence from the surgical literature linking the prognostic effect of invasive treatment with accurate risk prediction[11,12]. Similarly, the DISCHARGE trial[8,13] showed that CCTA, as an initial diagnostic strategy in patients with stable chest pain and an intermediate pre-test probability of CAD, led to an incidence of MACE (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke; the primary outcome) that was similar to that with invasive coronary angiography (HR 0.70, 95% CI 0.46–1.07). In terms of secondary outcomes, the use of CCTA was associated with a lower incidence of major procedure-related complications (HR 0.26, 95% CI 0.13–0.55), especially in women (HR 0.14, 95% CI 0.04–0.46)[14] and in patients aged <65 years (OR 0.10, 95% CI 0.02–0.36)[15].

This evidence from clinical trials has led to the global adoption of CCTA and subsequently evolving reimbursement policies. Beyond the detection of obstructive CAD, CCTA enables the quantification of coronary atherosclerosis[6,16] offering crucial insights into atherosclerotic plaque burden. However, the reliability of this quantification remains variable[17] and is the 'Achilles' heel' of successful clinical implementation of CCTA, despite the increasing clinical use of the procedure[18]. Advances in artificial intelligence (AI) and machine learning (ML) now enable detailed quantification and characterization of atherosclerotic plaque with increased speed and reliability[19]. However, challenges to the translation of these technological advances into clinical practice remain. Clear, evidence-based guidance specifying clinical treatment recommendations for each CCTA finding is needed, particularly for patients with stable chest pain and an intermediate probability of CAD, in whom the clinical value of CCTA has been proven. This expert Consensus Statement, formulated through a Delphi process, addresses these challenges and provides evidence-based recommendations for incorporating CCTA and AI tools into cardiovascular care. By linking innovations in imaging technologies with tailored therapeutic strategies, we aim to optimize outcomes and reduce the global burden of atherosclerotic CAD.

The potential of AI-supported tools

AI-supported tools, which often incorporate machine learning techniques, are poised to transform medical image analysis, offering opportunities to improve patient care and accelerate scientific discovery[20–22]. AI-supported tools to evaluate atherosclerotic plaque are reliable and fast, enabling clinicians and researchers to improve efficiency and precision[23]. Most automated tools and services for atherosclerotic plaque analysis first identify and label the coronary branches on CCTA[24], segment the coronary lumen and outer vessel border and, finally, subclassify atherosclerotic plaque, typically based on measured attenuation values[25] or advanced deep learning-supported methods for atherosclerotic plaque characterization[26]. Despite the technical challenges of imaging small, moving structures using CCTA, high accuracy and agreement between AI-supported tools for atherosclerotic plaque quantification and intravascular ultrasonography (IVUS) have been demonstrated[27,28]. To date, however, no large-scale, head-to-head comparisons between atherosclerotic plaque analysis tools and services have been performed.

In principle, AI-supported analysis of coronary atherosclerosis on CCTA allows age-adjusted and gender-adjusted percentile curves to be generated for atherosclerosis imaging biomarkers, such as coronary total plaque volume (TPV)[29]. This approach offers potential for individualized risk stratification and imaging-based treatment. One particular application is to refine thresholds for the initiation of lipid-lowering and anti-atherosclerotic agents in patients with stable chest pain and suspected CAD but no class I indications for statin therapy. Human analysis of CCTA supported by AI ('bionic radiologist') could lead to greater reliability and more cost-effective imaging of atherosclerosis than can be achieved by radiologist evaluation alone[30]. In addition, identification of adverse characteristics of the atherosclerotic plaque enables individualized management strategies[31]. Interestingly, response to therapy can be measured by monitoring changes in the atherosclerotic plaque during follow-up (Fig. 1). This approach is being used in various large-scale, ongoing research projects, but it is not yet included in clinical practice guidelines. Advances in AI-supported tools have further implications for research. The ability to analyse large data sets of images in a fairly short timeframe facilitates pathophysiological, pharmacological and technical discoveries and could improve our understanding of treatment effects[32]. Non-invasive measurement of changes in coronary atherosclerosis also has the potential to expand the role of CCTA in clinical research owing to high agreement between AI-supported tools for atherosclerotic plaque quantification and IVUS[33,34]. The applications, limitations and reliability of AI-supported tools for atherosclerosis imaging are discussed in detail later in this Consensus Statement.

Paradigm shift

Prevention and treatment of coronary atherosclerosis encompass several strategies, including 'treat to target' (LDL cholesterol (LDL-C) reduction) as a stand-alone method or, preferably, as part of a comprehensive risk-factor-based strategy[35,36]. A 'fire-and-forget' model, consisting of intervention and minimal follow-up, also remains prevalent in clinical practice worldwide. Although these conventional approaches to prevention and treatment have contributed to the global reduction in age-standardized mortality from CAD, their limitations are highlighted by the rising prevalence of coronary atherosclerosis and persistent regional disparities[37,38].

The treat-to-target model, although effective in achieving guideline-recommended LDL-C levels, often fails to address residual cardiovascular risk[39]. A key limitation of this approach is that atherosclerotic plaque burden and morphology are not considered[40], both of which are crucial for accurately personalizing cardiovascular risk assessment[41]. Atheroma burden, identified using advanced techniques for imaging the coronary artery, is not consistently correlated with LDL-C concentration and can remain undetected in the current framework of management strategies[32]. Similarly, risk-factor-based strategies often oversimplify the heterogeneity and vulnerability of both patients and atherosclerotic plaques, overlooking the interaction
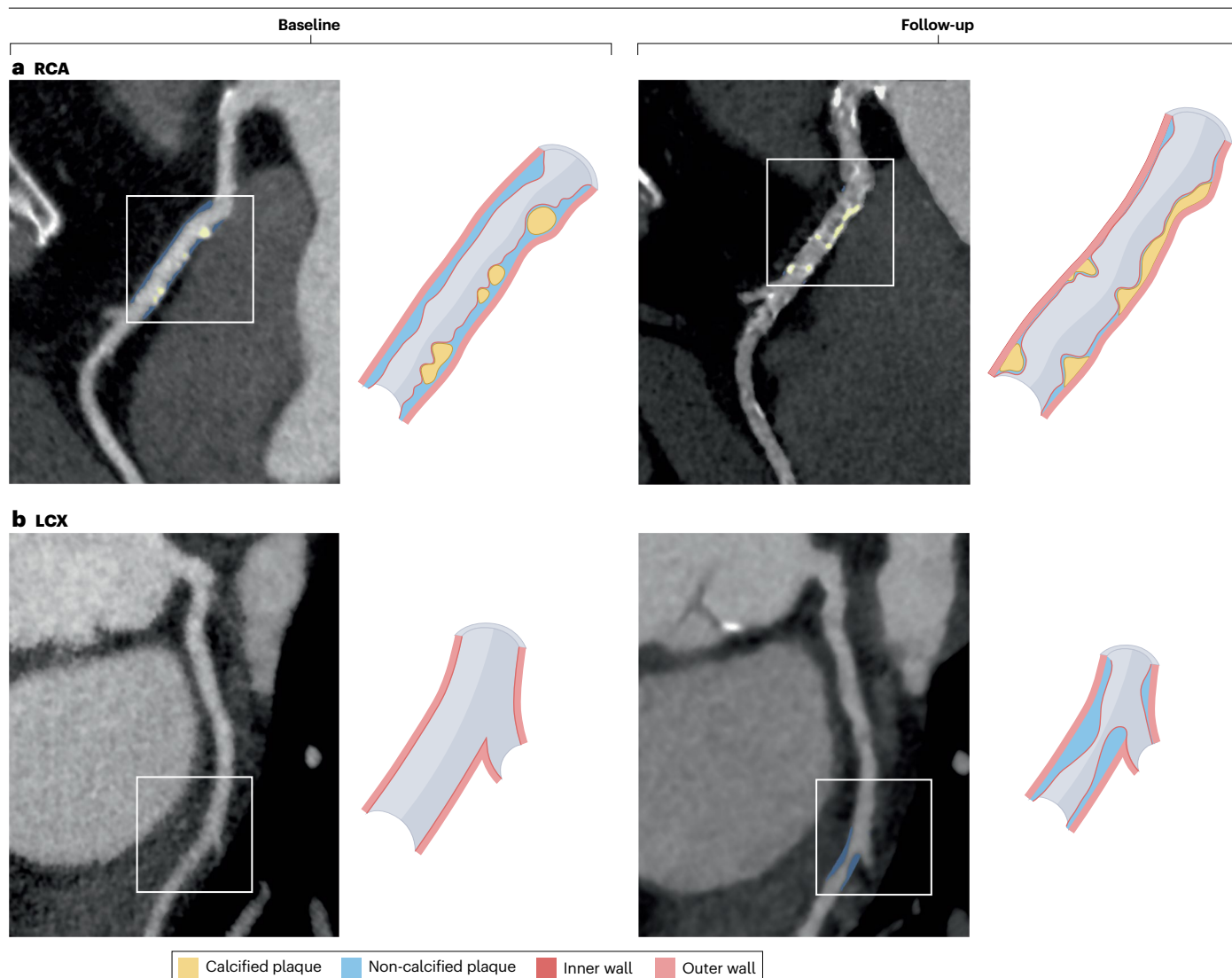
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Fig. 1 | Effects of lipid-lowering medication over 10 years of follow-up. Adherence to recommended statin therapy results in stabilization of atherosclerotic plaque, characterized by an increase in calcified plaque volume and a decrease in non-calcified plaque volume, thereby reducing the risk of atherosclerotic cardiovascular disease events. **a**, Coronary CT angiography of a man aged 71 years, with atypical angina at baseline (left). Guideline-recommended lipid-lowering therapies resulted in stabilization of the atherosclerotic plaque in the right coronary artery (RCA) at 6-year follow-up (right). **b**, Coronary CT angiography of a man aged 59 years, with de novo angina at baseline (left). Dismissing recommendations for lipid-lowering treatment, despite a diagnosis of atherosclerosis, led to the progression of primarily, non-calcified atherosclerotic plaques in the left circumflex artery (LCX) at 12-year follow-up (right), consequently increasing the risk of atherosclerotic cardiovascular disease events.
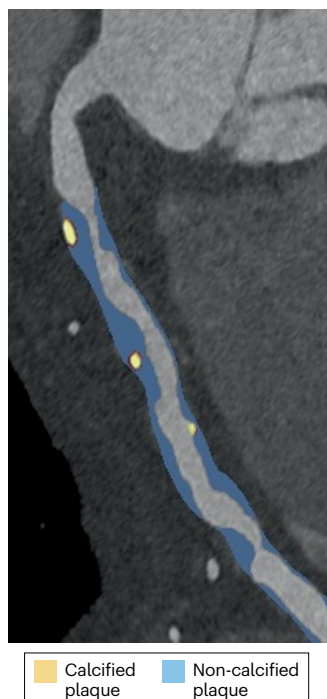
of coexisting pathophysiological mechanisms. Although theoretically comprehensive, these approaches might not identify high-risk individuals, who have minimal traditional risk factors but have coronary atherosclerosis, while overtreating others who have risk factors but no coronary atherosclerosis on CCTA[42,43]. Clinical risk factor estimates are known to be poor predictors of atherosclerotic burden, whereas CCTA-based quantification of atherosclerotic plaque has been shown to have superior predictive value for long-term outcomes[44].

The fire-and-forget approach, which was historically proposed as a population-based management strategy and is mostly used in primary prevention, can also lead to 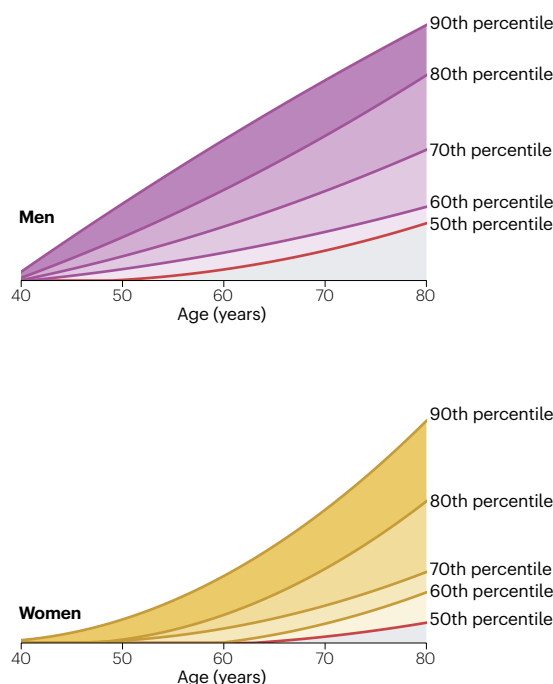overtreatment or undertreatment, potentially increasing adverse effects or leaving atherosclerotic plaque unaddressed[45]. Additionally, approaches involving fixed-dose therapy, without subsequent patient monitoring or inadequate treatment of comorbidities, fail to adapt to changing patient profiles or the dynamic natural history of atherosclerosis. To overcome these limitations, we propose a paradigm shift, emphasizing the integration of individualized treatment recommendations informed by CCTA-derived, AI-supported evaluation of atherosclerotic plaque (Fig. 2). This approach uses percentile-based risk stratification and patient-tailored treatment, combining the strengths of current strategies while mitigating their weaknesses.

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AI-supported plaque evaluation

Calcified plaque | Non-calcified plaque

Age-adjusted and gender-adjusted TPV percentiles

Men

90th percentile
80th percentile
70th percentile
60th percentile
50th percentile

Age (years)

Women

90th percentile
80th percentile
70th percentile
60th percentile
50th percentile

Age (years)

Medical treatment recommendations

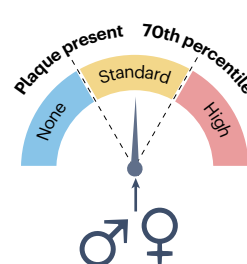Plaque present | 70th percentile
None | Standard | High

Fig. 2 | Paradigm shift towards individualized treatment recommendations based on artificial intelligence-supported evaluation of atherosclerotic plaque. Conventional treatment strategies for coronary artery disease include treat to target (adjusting therapy to achieve specific goals), risk-factor-based treatment (focusing on managing overall cardiovascular risk by addressing multiple risk factors) and fire-and-forget (prescribing fixed doses of drugs without monitoring specific targets). These strategies often overlook the complexity of pathology, ignoring the benefits of individualized therapy. Artificial intelligence (AI)-supported evaluation of atherosclerotic plaque could improve patient management by revealing the extent and nature of disease-regulating coronary atherosclerosis in each patient and by informing individualized treatment recommendations based on age-adjusted and gender-adjusted coronary total plaque volume (TPV) percentiles. The percentile curves depicted are for illustrative purposes only and do not represent real data. On the basis of the Delphi consensus process conducted after the third meeting of the Quantitative Cardiovascular Imaging Study Group, the initiation of lipid-lowering medication is recommended if the presence of any coronary atherosclerotic plaque is detected, and treatment escalation to high-intensity regimens (Table 1) is advised when the 70th percentile TPV threshold is reached on coronary CT angiography.

Method for generating consensus recommendations

Developing explicit treatment recommendations based on population percentiles of AI-supported distribution of atherosclerotic plaque volume requires experts from numerous fields. Therefore, we assembled the Quantitative Cardiovascular Imaging (QCI) Study Group of 35 experts, comprising 12 cardiologists, 11 radiologists, 5 computer scientists, 3 biomedical engineers and scientists, 2 general practitioners, 1 radiographer and 1 epidemiologist. The expert talks were held during the third QCI Study Group consensus meeting at Charité – Universitätsmedizin Berlin, Germany, on 6 September 2024. Similar to our previous consensus processes[6,20,46], we used the Delphi method to generate and ask participants a set of 12 questions (Supplementary Material 1) in a total of three rounds.

The questionnaire was designed to derive expert opinion on the feasibility and best way of translating atherosclerotic plaque imaging on CCTA to medical treatment recommendations. We assessed four key points: the reliability of atherosclerotic plaque measures, the meaningfulness of atherosclerotic plaque phenotypes for treatment initiation and escalation, the translation of atherosclerotic plaque analysis to explicit medical treatment recommendations and risk modulators for the escalation of treatment recommendations. We included various types of question, including binary questions, ranking questions and quantitative questions (Supplementary Material 2). A 5-point Likert scale was primarily used for the quantitative questions, but when comparisons across more than five categories were required, a 9-point scale was used to capture finer distinctions in expert opinions.

The first Delphi round took place online 2 weeks after the third QCI Study Group consensus meeting. Participants received a personalized and anonymous link to the questionnaire via the 'Welphi' web application. The second and third Delphi rounds each started 1 week after the previous round. The process was designed to facilitate the exchange and convergence of expert opinions to gain a collective understanding of the subject discussed and, ideally, to reach a consensus in a streamlined and consistent manner. To achieve this goal, in the second and third rounds of questions, participants were shown their answers from the previous round in the online tool and could revise them when deemed appropriate. In addition, in the second and third rounds, anonymized interim responses given by all experts in the previous round of questions were shown as boxplots and bar plots. Related information was provided for multiple questions in the questionnaires, including current literature and both published and unpublished evidence derived

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from analyses of data from the SCOT-HEART and DISCHARGE trials[29] (Supplementary Material 3). The consensus recommendations of the QCI Study Group are summarized in Box 1.

In many of the trials discussed in this article, participants self-reported as 'male', 'female' or 'other' based on a questionnaire, without further clarification on biological sex. Given that this information was collected as self-reported identity rather than a biological classification, we have chosen to use the term 'gender' rather than 'sex', for consistency with the original data.

Biomarkers and clinical parameters for individualized treatment recommendations
Coronary atherosclerotic plaque
In clinical practice, CCTA is commonly used to differentiate between calcified and non-calcified plaque (NCP) components. Each atherosclerotic plaque phenotype has different clinical indications, making them uniquely suited for defining treatment recommendations (Box 2). Available evidence suggests that atherosclerosis begins with endothelial dysfunction, leading to increased permeability of the endothelium to LDL. The subsequent inflammatory response attracts macrophages that infiltrate the intima and phagocytize oxidized LDL to form foam cells, which amplify inflammation and stimulate the proliferation of smooth muscle cells. Atherosclerotic plaque progression continues with the development of a lipid-rich necrotic core and fibrous cap. Some atherosclerotic plaques calcify, with large calcium deposits contributing to stability, whereas others remain vulnerable owing to a thin fibrous cap and ongoing inflammation[47,48].

Calcified plaque. Coronary artery calcium (CAC) scoring is widely used for risk stratification, particularly for primary prevention in patients who are asymptomatic. CAC has also been shown to have prognostic relevance beyond risk-factor-based assessment in patients who are symptomatic[49]. The prognostic utility of CAC scoring and calcified plaque volume (CPV), assessed by CCTA, have been demonstrated in many observational studies[49–57]. In addition, the EISNER study[58] demonstrated that shared decision-making using CAC scoring positively influenced adherence to lifestyle changes and medical treatment recommendations in a cohort of 2,137 patients who are asymptomatic with a low pre-test probability. Notably, the high negative predictive value of CAC scoring can rule out extensive atherosclerotic CAD, leveraged with easily performed, low-risk and low-cost imaging.

Despite its prognostic relevance, the use of CAC score or CPV to make treatment recommendations is limited by several factors. First, although several studies have demonstrated a strong association between CAC score and MACE, a direct causal relationship has not been demonstrated. Vulnerable atherosclerotic plaques prone to rupture primarily consist of inflammatory NCP[32], whereas the proportion of densely calcified atherosclerotic plaque on a per-patient and per-lesion basis is inversely related to the risk of atherosclerotic CAD events[59]. Second, CAC score and CPV are strongly correlated with age, and the use of these measures for prognostication of atherosclerotic CAD events can overestimate risk, especially in elderly individuals. Conversely, focusing on CPV (or CAC score) as a predictor can lead to an underestimation of risk in those with low CPV and high NCP volume (NCPV), especially in younger individuals (Fig. 3) with MACE (25% of whom had a CAC score of 0 on imaging before the event in the Multi-Ethnic Study of Atherosclerosis)[60,61]. Third, after atherosclerotic plaque stabilization with lipid-lowering therapies, CAC score and CPV increase, whereas the risk of MACE decreases[62]. As a consequence of the widespread prescription of lipid-lowering medication, the correlation between CAC score or CPV and MACE is vague[63]. Therefore, CAC score or CPV is not the preferred marker for the longitudinal evaluation of treatment efficacy. Collectively, the data suggest that, although proven to be prognostic at the general population level, CAC score and CPV have limited suitability for determining individual treatment recommendations. Nevertheless, the number of studies with a head-to-head comparison between the use of CPV and NCPV or total plaque burden for prognostication is limited, and further randomized studies are needed.

Non-calcified plaque. NCP is an important component of coronary atherosclerotic plaque, which cannot be visualized on non-contrast CT. On CCTA, NCP can be identified and quantified as the NCPV or normalized to vessel or segment volume or area. NCP incorporates a range of attenuation values comprising various subtypes, including fibrous, fibrofatty and low-attenuation NCP. Atherosclerotic plaques in the early stages of development are usually non-calcified; they could represent metabolically active CAD, particularly in the presence of low-attenuation plaque, or could signify older, 'burnt-out' fibrotic disease. Owing to this pathophysiology, younger patients tend to have a greater volume of NCP than calcified atherosclerotic plaque. Over time, NCP can progress and calcify, thereby indicating response to treatment through an increase in CPV and a decrease in NCPV or remain stable. NCPV is a valuable prognostic marker, associated with an increased risk of MACEs on both visual and quantitative assessments[32,64]. In a retrospective analysis of the SCOT-HEART trial[32] of 1,769 patients with stable chest pain, low-attenuation NCP burden was the strongest predictor of fatal or non-fatal myocardial infarction after 5 years of follow-up (adjusted HR 1.60, 95% CI 1.10–2.34 per doubling of atherosclerotic plaque burden). In a post hoc assessment of 422 patients in the RAPID-CTCA trial[65], TPV (HR 25.4, 95% CI 3.44–188.0), NCPV (HR 26.4, 95% CI 3.58–196.0) and low-attenuation atherosclerotic plaque (HR 7.80, 95% CI 2.33–26.0) were the strongest predictors of

> ## Box 1 | Quantitative Cardiovascular Imaging Study Group consensus treatment recommendations
>
> - Age-adjusted and gender-adjusted percentiles are the preferred format rather than numerical cut-off values of atherosclerotic plaque volumes for individualized medical treatment recommendations.
> - Pharmaceutical lipid-lowering therapy is recommended after detecting any atherosclerotic plaque, with escalation to high-intensity treatment recommended when the total plaque volume is ≥70th percentile adjusted for age and gender.
> - Non-calcified plaque is most suited for monitoring of treatment and might be beneficial for the adjustment of treatment recommendations. Future trials must determine the definitive role of non-calcified plaque in individualized treatment recommendations.
> - The strongest risk-factor-based indication for escalating treatment to high intensity is the presence of a positive family history of atherosclerotic cardiovascular disease, smoking or the presence of low-attenuation plaque and positive remodelling.

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Box 2 | Atherosclerotic plaque subtypes and their suitability for treatment recommendations

Calcified plaque

The applicability of calcified plaque for individual treatment recommendations is limited in patients who are symptomatic. Although a strong association between coronary artery calcium score and cardiovascular events has been shown in multiple studies, a direct causal relationship between calcified plaque and myocardial infarction has not been demonstrated. The atherosclerotic plaques that are most likely to rupture and trigger events are primarily inflammatory and non-calcified.

Non-calcified plaque

The assessment of non-calcified plaque offers valuable clinical insights that can complement patient management. However, not all patients with atherosclerotic plaque have non-calcified components,

limiting its standalone utility. Non-calcified plaque is the plaque subtype best suited for monitoring of treatment.

Total plaque

Owing to its superior sensitivity, total plaque is the most generalizable standalone biomarker for individualized, age-adjusted and gender-adjusted medical treatment recommendations.

High-risk plaque features

The high variance and limited prevalence of high-risk plaque features limit their value for guiding medical treatment. However, the strong predictive power of high-risk plaque features makes them ideal risk modulators.

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future non-fatal myocardial infarction and all-cause death. In addition, NCPV can be used in the assessment of new medical therapies as a surrogate imaging end point that occurs years before MACEs[66]. For example, the primary outcome analysis of the EVAPORATE trial[37] showed a reduction in low-attenuation NCPV after 18 months of treatment with icosapent ethyl in 68 patients with elevated triglyceride levels, and a retrospective substudy of the REPRIEVE trial[33,67] showed that pitavastatin therapy led to a reduction in NCPV in 611 patients with HIV and no known cardiovascular disease (CVD).

Despite the advantages of measuring NCPV in coronary imaging, not all patients have NCP. In the Miami Heart study cohort (*n* = 2,459), almost 50% of participants with atherosclerotic plaques were observed to have exclusively calcified plaques, underscoring the heterogeneity of plaque composition in populations[68]. The role of NCPV is, therefore, unclear. The QCI Study Group reached consensus on the use of NCPV per se; however, no consensus was achieved on its specific role in treatment recommendations, whether as a risk modulator (57% of votes), as a complementary factor alongside TPV (40% of votes) or to use TPV only (3% of votes) (Supplementary Material 1). If proven to be an actionable imaging biomarker, NCPV could help to guide patient management in the future and might be the marker best suited to monitoring response to treatment.

Total plaque. CCTA effectively identifies and stratifies the future risk of myocardial infarction by providing detailed evidence of CAD. The absence of atherosclerotic disease is associated with extremely low rates of MACEs (less than one myocardial infarction per 1,000 patient-years)[69]. Historically, risk stratification for CAD has been focused on the presence of obstructive disease, with both the number and severity of stenoses carrying prognostic value. However, most myocardial infarctions are caused by non-obstructive disease, partly due to the higher prevalence of non-obstructive disease in the general population. Several CT-based clinical trials have demonstrated the dominance of non-obstructive disease in the occurrence of subsequent myocardial infarctions, as well as the fact that most people who have a myocardial infarction will have no evidence of ischaemia on functional stress testing[70,71]. These findings have led to the hypothesis that TPV is the most important metric for risk stratification. Indeed, the extent of stenotic disease is more important than simply the presence of

disease and is a very powerful predictor of risk[69]. TPV combines CPV and NCPV and, using AI-supported analysis, is the most reliable imaging biomarker for clinical practice[25,72,73]. The QCI Study Group deemed TPV to be the most meaningful parameter for recommendations to initiate or escalate medical treatment (Fig. 4). Moreover, TPV can be reliably assessed using AI tools and has prognostic value for MACEs in clinical trial populations[74]. However, similar to CPV, TPV is not suitable for monitoring drug response, because this measure does not differentiate between changes in NCPV and CPV, which is necessary for risk assessment.

High-risk plaque features. Among the various semiquantitative characteristics of atherosclerotic plaque that have been studied, four have demonstrated prognostic relevance and are collectively referred to as 'high-risk plaque features'[6,25,75]: low-attenuation plaque, napkin-ring sign, positive remodelling and spotty calcification[18,76]. In the SCOT-HEART trial[32], low-attenuation plaque burden was the strongest predictor of the future risk of myocardial infarction. Furthermore, a meta-analysis in patients with stable CAD identified the napkin-ring sign as the strongest high-risk plaque feature for predicting MACEs (HR 5.06, 95% CI 3.23–7.94)[76]. Several studies have shown that patients with acute coronary syndrome have a higher remodelling index than patients with stable CAD[77–79]. Although atherosclerotic plaques with extensive calcification typically remain clinically silent, spotty calcifications are associated with accelerated disease progression and culprit lesions in acute coronary syndrome[80,81]. Of the high-risk plaque features defined on CCTA, low-attenuation plaque and positive remodelling have emerged as the most important features for the assessment of cardiovascular risk[82].

CT attenuation measurements in atherosclerotic plaques are influenced by factors such as intraluminal contrast concentration, tube voltage, slice thickness and reconstruction filters[83–86]. Moreover, high-risk plaque features are largely reported as visual measures in daily practice[87,88]. Differences in image quality, reader experience and software can affect the consistency of atherosclerotic plaque characterization[89]. This situation results in moderate interobserver agreement for the identification of high-risk plaque features, with κ values ranging from 0.56 to 0.69 in research settings[90,91]. In addition, different virtual monoenergetic images from photon-counting

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CT alter attenuation values and, therefore, corresponding atherosclerotic plaque characteristics, further contributing to reduced reproducibility[92].

Although high-risk plaque features show strong overall predictive performance, they are not well suited to determining treatment recommendations, for three reasons. First, their positive predictive value is low and most patients with such features will not have events. Second, high-risk plaque features are not present in all patients with atherosclerotic plaque and, therefore, patients without such features who might benefit from treatment would be missed. Third, the reliability of assessing high-risk plaque features is limited. However, high-risk plaque features could inform the adjustment of existing treatment, such as escalating dose intensity. Further investigation and improvements are needed to improve reproducibility and interobserver agreement in assessing high-risk plaque features[93].

Additional risk modulators

Cardiovascular risk factors, such as smoking, obesity and a family history of CVD, have been well defined for many years and can be directly linked to an increase in the rate of CVD progression. Shifting the focus of treatment from LDL-C to plaque-based recommendations does not diminish the importance of risk factors. Their integration as factors that modulate treatment intensity is crucial to the individualization of patient management.

Non-modifiable and modifiable risk factors. Assessment of cardiovascular risk using validated scoring systems, such as the Systematic Coronary Risk Evaluation (SCORE), SCORE2 and atherosclerotic CVD (ASCVD) 2013 Risk Calculator, is a fundamental component of the clinical decision trees recommended by major international guidelines to inform the use of preventative therapies[94,95]. In general, the higher the risk, the greater the benefit from risk factor modification, including pharmacological interventions. Although some cardiovascular risk factors, such as age and genetic predisposition, are non-modifiable, modifying dyslipidaemia, hypertension, diabetes mellitus and smoking can drastically improve long-term prognosis. In the primary analysis of the prospective SPRINT trial[91] involving 9,361 patients with hypertension but no diabetes, intensive blood pressure lowering to <120 mmHg was associated with a reduced risk of MACEs (primary myocardial infarction, other acute coronary syndrome, stroke, heart failure or death from cardiovascular causes) compared with standard therapy (HR 0.73, 95% CI 0.60–0.90). Similarly, the primary analysis of the ADVANCE trial[96] showed that intensive glycaemic control reduced MACEs (cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke) compared with standard control (HR 0.86, 95% CI 0.77–0.97) in 11,140 patients with type 2 diabetes.

However, some clinical risk factors are not well captured by conventional risk algorithms, including obesity, physical inactivity, metabolic syndrome, chronic kidney disease, immune-mediated inflammatory diseases, psychosocial stress, psychiatric disorders, social deprivation and frailty[97–99]. Moreover, a high proportion of asymptomatic individuals undergoing CCTA in population-based screening studies, such as the MIAMI Heart Study[64] and SCAPIS[96] cohorts, had subclinical atherosclerosis, despite seemingly low 10-year event risk calculations. In addition, the optimal treatment of patients with a borderline indication for statins is often unclear, and most individuals who present with acute myocardial infarction do not have a history of angina or other symptoms that could herald their underlying condition. Therefore, a need exists for more refined risk stratification than can be achieved through the assessment of clinical risk factors alone. In the SCOT-HEART trial[100], the use of CCTA led to greater diagnostic certainty and risk stratification, with increased use of procedural and pharmacological interventions, compared with standard care despite similar 10-year cardiovascular risk scores between groups.
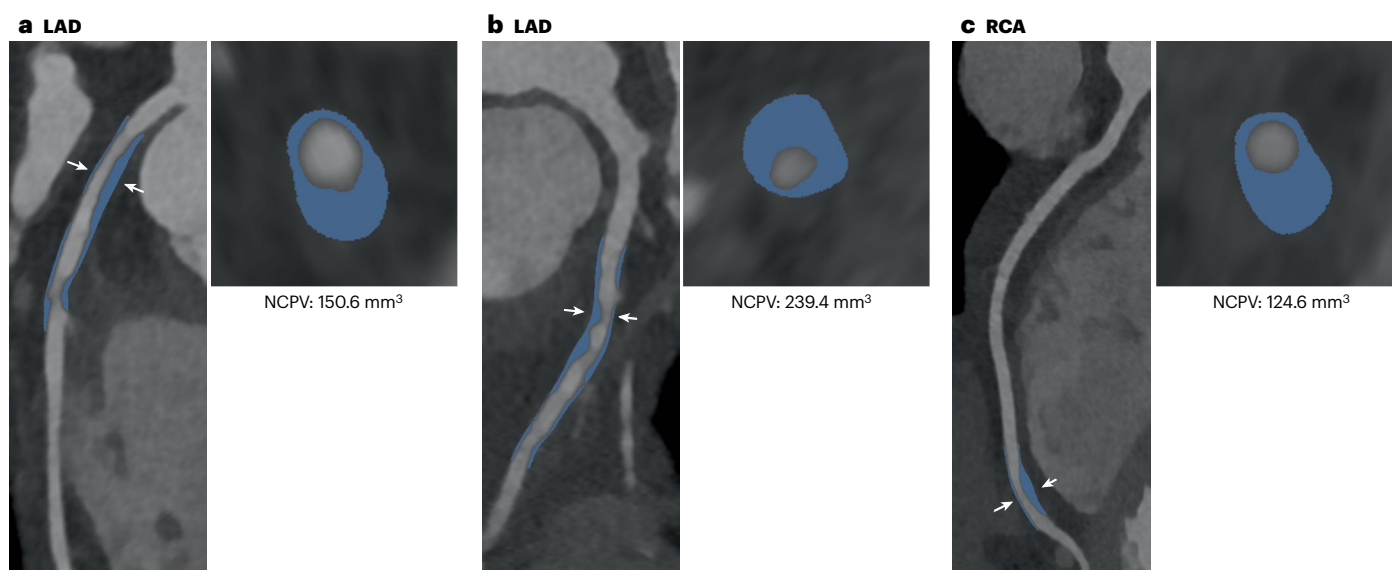

a LAD

NCPV: 150.6 mm³

b LAD

NCPV: 239.4 mm³

c RCA

NCPV: 124.6 mm³

Fig. 3 | Absence of calcified plaque in middle-aged patients with coronary atherosclerosis. Coronary arteries with non-calcified plaque (NCP; blue) emphasize the presence of clinically relevant atherosclerotic plaques that are undetected by coronary artery calcium (CAC) scoring alone. **a**, Left anterior descending artery (LAD) of a man aged 39 years, with typical angina and a CAC score of 0. **b**, LAD of a man aged 48 years, with atypical angina and a CAC score of 0. **c**, Right coronary artery (RCA) of an asymptomatic woman aged 52 years, with a CAC score of 0. The absence of calcified plaques underscores the importance of incorporating measurement of NCP volume (NCPV) into treatment recommendations, complementing traditional calcium-based assessments, to ensure comprehensive management. The NCPV is quantified for the segment shown, whereas CAC scoring is quantified over the entire cardiovascular tree.

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a

Is there a need for more individualized medicine?

Yes (100%)

Are AI-supported coronary plaque quantification data suitable to define appropriate thresholds for medical treatment?

Yes (85%)	No (15%)

Preferred format for the assessment of plaque to provide individualized, age-adjusted and gender-adjusted treatment recommendations
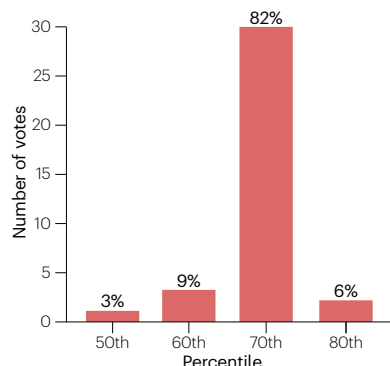
Percentiles (74%)	Cut-off[a] (26%)

Should we treat any plaque detected on CT?

Yes (54%)	No (46%)

b

c

	TPV	NCPV	CPV
Reliability			
Accuracy of AI-supported evaluation compared with IVUS	4	4	4
Intraobserver agreement of the AI-supported evaluation	4	4	4
Interobserver agreement of the AI-supported evaluation	4	3	4
Inter-tool agreement of the AI-supported evaluation	3	3	4
Meaningfulness for...			
The initiation of lipid-lowering treatment recommendation in patients with CAD?	5	4	3
Deciding the intensity (standard or high intensity) of medical treatment recommendation?	5	4	3

d

Risk factors		High-risk plaque features	
Arterial hypertension	6	Positive remodelling	7
Obesity (BMI >30 kg/m²)	5	Low-attenuation plaques	7
Smoking	7	Napkin-ring sign	6
Positive family history	7	Spotty calcifications	5
Chronic kidney disease	6		

■ Appropriate   ■ Uncertain

Fig. 4 | Results from the Delphi consensus for individualized treatment recommendations. Key recommendations from the 35 experts (the Quantitative Cardiovascular Imaging Study Group) completing the three-round Delphi process are shown with regard to individualized medical treatment based on artificial intelligence (AI)-supported quantification of atherosclerotic plaque. **a**, Questions on the suitability and preferred measures of coronary atherosclerotic plaque for guiding treatment recommendations. **b**, Results of the vote on the appropriate age-adjusted and gender-adjusted percentile threshold of total plaque volume (TPV) for initiating high-intensity lipid-lowering treatment. The expert group reached consensus (82%) on escalating to high-intensity regimens when TPV is above the 70th percentile. **c**, Reliability and meaningfulness of AI-supported quantification of TPV, non-calcified plaque volume (NCPV) and calcified plaque volume (CPV) for medical treatment recommendations on a 5-point Likert scale (1–2 = inappropriate, 3 = uncertain, 4–5 = appropriate). **d**, Appropriateness of medical treatment escalation in the presence of risk factors or high-risk plaque features on a 9-point Likert scale (1–3 = inappropriate, 4–6 = uncertain, 7–9 = appropriate). No atherosclerotic plaque measure or risk modulator was deemed inappropriate. The values in panels **c** and **d** are medians. [a]Numerical cut-off values of atherosclerotic plaque volumes. BMI, body mass index; CAD, coronary artery disease; IVUS, intravascular ultrasonography.

Crucially, this finding was independent of the presentation of symptoms, with the greatest benefit seen in patients without angina owing to coronary heart disease[100]. These data suggest that CCTA could be a powerful clinical adjunct for assessing total cardiovascular risk in asymptomatic individuals with risk factors. This hypothesis is the subject of the ongoing, randomized SCOT-HEART 2 study[101], in which the investigators will assess whether CCTA-guided care leads to improvements in management and outcomes in patients with stable angina and suspected CAD after a 10-year follow-up period.

Surrounding adipose tissue. CCTA-derived metrics of fat surrounding the coronary arteries and heart represent promising markers of inflammation, a key mechanism in atherosclerosis[102]. On non-contrast CT scans, standardized at 120 kVp for calcium scoring, increased volume of epicardial adipose tissue is linked to an increased risk of cardiovascular

events, offering predictive value beyond the CAC score[103]. Although previously constrained by lengthy segmentation processes, advances in AI-supported software now enable automated evaluation of epicardial adipose tissue[104]. Moreover, on CCTA, pericoronary adipose tissue (PCAT) attenuation can be quantified[105]. PCAT is currently incorporated into proprietary measurements and risk scores, which may add prognostic value[106]. In the ORFAN study[106] cohort of 40,091 patients with a clinical indication for CCTA, the PCAT attenuation score was independently associated with cardiovascular mortality (HR 29.8, 95% CI 13.9–63.9) and MACEs (myocardial infarction, new heart failure and cardiac death; HR 12.6, 95% CI 8.5–18.6) irrespective of CAD severity, although this PCAT score contributed only marginally to the area under the curve. Moreover, the difference in PCAT attenuation values between healthy and stenosed arteries is subtle[105], and PCAT attenuation measurements are affected by tube voltage, image reconstruction

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kernel and iterative reconstruction techniques, which can result in attenuation differences far greater than those between healthy and diseased vessels[107,108]. Further validation of epicardial adipose tissue and PCAT for clinical decision-making in a prospective, randomized, controlled, cardiovascular outcomes trial is required to determine the clinical value for individualized management[102].

AI in atherosclerosis imaging
Applications and limitations
AI and ML are transforming the landscape of atherosclerotic cardiovascular risk assessment: first, through the direct application of deep learning algorithms to image data for automated quantification of imaging biomarkers, such as atherosclerotic plaque[24], and second, by combining clinical and AI-supported imaging metrics for individualized outcome prediction[31]. Applications for deep learning models in cardiac CT are diverse and include CAC quantification on non-contrast CT[109–111], quantification of CAD Reporting and Data System score, identification of atherosclerotic plaque type and atherosclerotic plaque quantification on CCTA (Fig. 5). Fully automated, deep learning methods for atherosclerotic plaque and vessel lumen segmentation promise to provide accelerated quantification, saving the reader time[19].

In a retrospective analysis of 1,611 patients from the SCOT-HEART trial, a deep learning-supported method for atherosclerotic plaque quantification on CCTA was shown to be concordant with IVUS and also predictive of myocardial infraction[19]. The deep learning-based TPV threshold was associated with an increased risk of myocardial infarction (HR 5.36, 95% CI 1.70–16.86) after adjustment for the presence of deep learning-based obstructive stenosis (HR 2.49, 95% CI 1.07–5.50) and the ASSIGN clinical risk score (HR 1.01, 95% CI 0.99–1.04)[15]. In the ISCHEMIA trial[72], CCTA data were available from 3,711 participants with myocardial ischaemia. AI-based TPV was associated with cardiovascular death or myocardial infarction (HR 1.56, 95% CI 1.25–1.97 per interquartile range increase (559 mm³)), with atherosclerotic plaque volume and composition metrics modestly improving event prediction compared with ASCVD risk score alone[72]. Owing to the inclusion of patients who had previously undergone percutaneous coronary intervention and the limited image quality in this study, further randomized controlled trials are needed to support these findings.

The main challenge associated with AI tools is the limited availability of the large, well-curated and diverse data sets required for training and generalizability[112]. A wide range of scanners and scan protocols should be included in training data to improve performance. As with other diagnostic approaches, deep learning-supported methods must be evaluated before integration with the corresponding invasive reference standards, such as IVUS for atherosclerotic plaque quantification, and also externally with fully independent data[25]. High image quality (and the absence of artefacts) is central to quantitative assessment of atherosclerotic plaque and, together with vessel size, determines whether quantitative analysis of atherosclerotic plaque should be performed for that vessel segment[25].

Reliability
AI-supported CCTA quantification of atherosclerotic plaque has been compared with assessment by human readers and using IVUS. The reliability of AI tools between scans performed at short intervals was also evaluated. Agreement between AI tools and expert human readers is excellent (intraclass correlation coefficient (ICC) 0.96)[19]. However, wide limits of agreement between humans and AI (−114 mm³ to 126 mm³) have been reported, although this range is narrower than

between two human readers (−157 mm³ to 203 mm³)[19]. Agreement with experts is best for TPV (ICC 0.96) and worst for low-density NCP (ICC 0.81). AI-supported quantification of atherosclerotic plaque also shows excellent agreement with IVUS for TPV ($r = 0.91$), NCPV ($r = 0.87$) and CPV ($r = 0.91$), but poor agreement for low-density NCP ($r = 0.28$)[27]. Interscan reliability is also good and, again, better for TPV, NCPV and CPV ($r = 0.93$–0.98) than for low-density NCP ($r = 0.74$)[65,113].

The reliability of AI tools is not without limitations. Although population-level agreement is good, limits of agreement between scan and rescan are wide (±50% for TPV, NCPV and CPV and ±100% for low-density NCP[55,96]). These findings mean that, for individual patient follow-up, it is not possible to determine whether shifts in atherosclerotic plaque volume of up to 50% represent response to therapy, disease progression or simply interscan variability. This effect is further compounded by intersoftware variability. An evaluation of various software packages on a single vessel demonstrated that the TPV (normalized to vessel volume) ranged from 58% to 88% across software vendors, NCPV ranged from 75% to 99% and the proportion of low-density NCP varied from 0.3% to 35% of the TPV[25]. This variability has important clinical implications for patients whose scores fall near the thresholds of risk categories and who could be reclassified solely on the basis of the software used for their scans on different days.
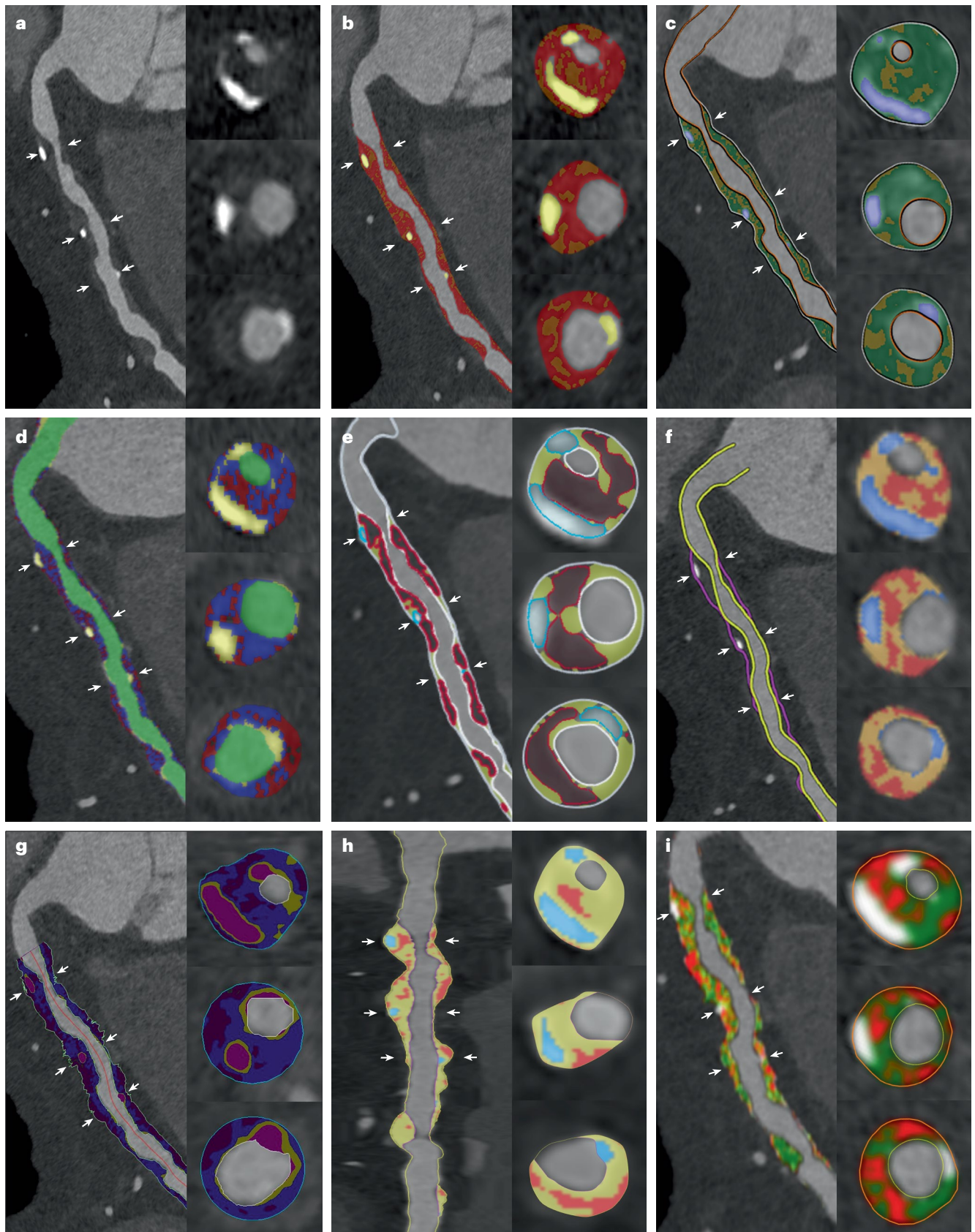
Individualized recommendations for medical treatment
Metrics
Population-based CCTA studies, such as the Multi-Ethnic Study of Atherosclerosis[66] and the subsequent Miami Heart Study[68,114], have greatly advanced our knowledge of atherosclerotic plaque prevalence and its association with cardiovascular events. The 2018 multisociety clinical guideline on the management of blood cholesterol recommends using CAC scores to guide decisions on statin therapy for adults aged 40–75 years without diabetes, LDL-C concentration of 70–189 mg/dl (1.81–4.89 mmol/l) and a 10-year ASCVD risk of 7.5–20% when the need for statins is unclear[36]. If the CAC score is 0, statin therapy can generally be delayed, except for patients who smoke or those with diabetes or a strong family history of premature heart disease[36].

CCTA is a first-line test in patients with chest pain and can visualize both the coronary artery lumen and atherosclerotic plaque (calcified and non-calcified), including the high-risk, low-attenuation component of NCP. In the SCOT-HEART trial[7], women presenting with stable chest pain had lower atherosclerotic plaque volumes of all subtypes than men, although quantitative low-attenuation plaque burden was as strong a predictor of subsequent myocardial infarction in both women and men[115]. As a consequence, fixed cut-off values for atherosclerotic plaque volumes have been proposed for risk stratification[73,116–118]. However, atherosclerotic plaque distribution is known to vary according to age and gender and, therefore, requires a wide range of cut-off values. Age-specific and gender-specific percentile thresholds have been proposed in two separate studies with different AI software applications for atherosclerotic plaque analysis[29,119]. In a 2024 study[29], per-patient age-specific and gender-specific atherosclerotic plaque distributions were shown to be strongly predictive of myocardial infarction, with the highest risk seen in patients with coronary plaque volumes above the 75th percentile (HR 2.65, 95% CI 1.47–4.78). Therefore, percentiles adjusted for age and gender could provide context to better interpret risk assessment from atherosclerotic plaque imaging and allow practical, individualized clinical treatment recommendations. In contrast to large deviations in proposed cut-off values[73,116,117], two multicentre

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studies on different patient cohorts showed similarities between the age-adjusted and gender-adjusted percentile curves[29,119] (Fig. 6).

A treatment paradigm based on population distribution percentiles was deemed by the QCI Study Group to be the most suitable approach for medical treatment recommendations, with the 70th percentile being the threshold for recommending high-intensity treatment and the presence of any atherosclerotic plaque for standard-dose medical treatment (Fig. 4). Although the percentile distributions from both studies follow similar trajectories, very divergent patient groups (in terms of ethnicities or risk profiles) could have greater differences in atherosclerotic plaque distributions. Further research is needed on whether treatment recommendations derived from average atherosclerotic plaque distribution can be effectively translated from one end of the spectrum of risk to the other.

Medical therapies and dose intensity

The aim of pharmacological management of chronic coronary syndrome is to prevent MACEs and to alleviate ischaemic symptoms. Central to this management strategy is the optimization of cardiovascular risk factors. Lifestyle interventions, such as diet modification and exercise, serve as basic measures, but are often insufficient to achieve the stringent LDL-C targets recommended for high-risk patients with chronic coronary syndrome. Effective blood pressure control in the general population and precise glucose level management in patients with diabetes are essential to reduce vascular complications and associated risk. The antihypertensive agents olmesartan and amlodipine have been shown to have beneficial effects on atherosclerotic plaque progression[120,121]. Medications indicated for diabetes, such as sodium–glucose cotransporter 2 inhibitors and glucagon-like peptide 1 receptor agonists, are also thought to have beneficial effects on CAD progression and could have a role in future treatment strategies[122].

Statins are the cornerstone of pharmacological lipid-lowering strategies, with a central role in reducing atherogenic burden and the occurrence of MACEs through LDL-C reduction, and secondary benefits such as atherosclerotic plaque stabilization and modulation of inflammation. The 2023 American[123] and 2024 European[124] guidelines emphasize the importance of LDL-C lowering and advocate for precise targets based on individual risk profiles. Both guidelines reinforce the treat-to-target paradigm, specifying both percentage-based LDL-C reductions and absolute thresholds for patients with chronic coronary syndrome. Meta-analyses of data from patients with stable CAD or acute coronary syndrome, in trials comparing statins versus no statin or low-dose versus high-dose statin theapy[125,126], have revealed that standard-intensity statin therapy effectively reduces MACEs (coronary death, myocardial infarction, coronary revascularization and ischaemic stroke), but is inferior to high-intensity statin therapy[125]. The recommendations from the QCI Study Group for standard-intensity and high-intensity statin regimens are summarized in Table 1. These recommendations on statin doses should be supplemented with adequate guideline-adherent lifestyle changes, antihypertensive therapy and antiplatelet therapy, if indicated.

Although statins are the first-line lipid-lowering therapy, other medications, such as cholesterol-absorption inhibitors (ezetimibe) and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, are potential adjunctive treatments for patients who are at very high risk or unable to achieve the required LDL-C goals, despite the maximum-tolerated statin dose. PCSK9 inhibitors, such as alirocumab and evolocumab, markedly lower LDL-C levels by up to 60% when used in combination with statins[127–130]. Other lipid-lowering agents available or currently under investigation, such as bempedoic acid, monoclonal antibodies (canakinumab)[124] and small interfering RNA-based agents (inclisiran), hold promise for the future individualization of CAD management, although data are not yet available from CCTA-based clinical studies evaluating their effects on atherosclerotic plaque.

Percentile-based treatment recommendations

The presence of atherosclerotic plaque, even if non-obstructive, detected by CCTA is associated with increased cardiovascular risk. The majority of the QCI Study Group members voted for a 'treat any plaque' strategy (Fig. 4), involving standard-intensity medical treatment after the detection of any atherosclerotic plaque, irrespective of size or composition. This strategy was found to be beneficial for patients in the prospective, randomized, controlled SCOT-HEART[3] and DISCHARGE[7,8] trials. As recommended in international guidelines, dose escalation might be warranted for stronger lipid-lowering and anti-atherosclerotic effects. However, many individuals with elevated LDL-C levels, but no signs of atherosclerosis, will not have a cardiovascular event[43,131], suggesting that a treatment paradigm based on atherosclerotic plaque quantification rather than surrogate markers could improve patient outcome[122]. The QCI Study Group defined the TPV threshold for treatment escalation to high-intensity treatment as the age-adjusted and gender-adjusted 70th percentile (Fig. 4).

Clinical risk factors and other atherosclerotic plaque features also have a pivotal role in risk modulation. Smoking, a positive family history of CVD, the presence of low-attenuation plaque and positive remodelling were deemed to be the most important factors in the decision to escalate towards high-intensity treatment (Fig. 4). By contrast, very small fibrotic and calcified plaques almost never cause cardiovascular events and, consequently, allow for the de-escalation of medical treatment recommendations.

Limitations and future directions

Although consensus was reached on treatment percentiles, the Delphi process did not produce a unanimous position on the treatment of any atherosclerotic plaque. Standard-intensity medical treatment addresses the underlying pathophysiology of atherosclerosis, reduces
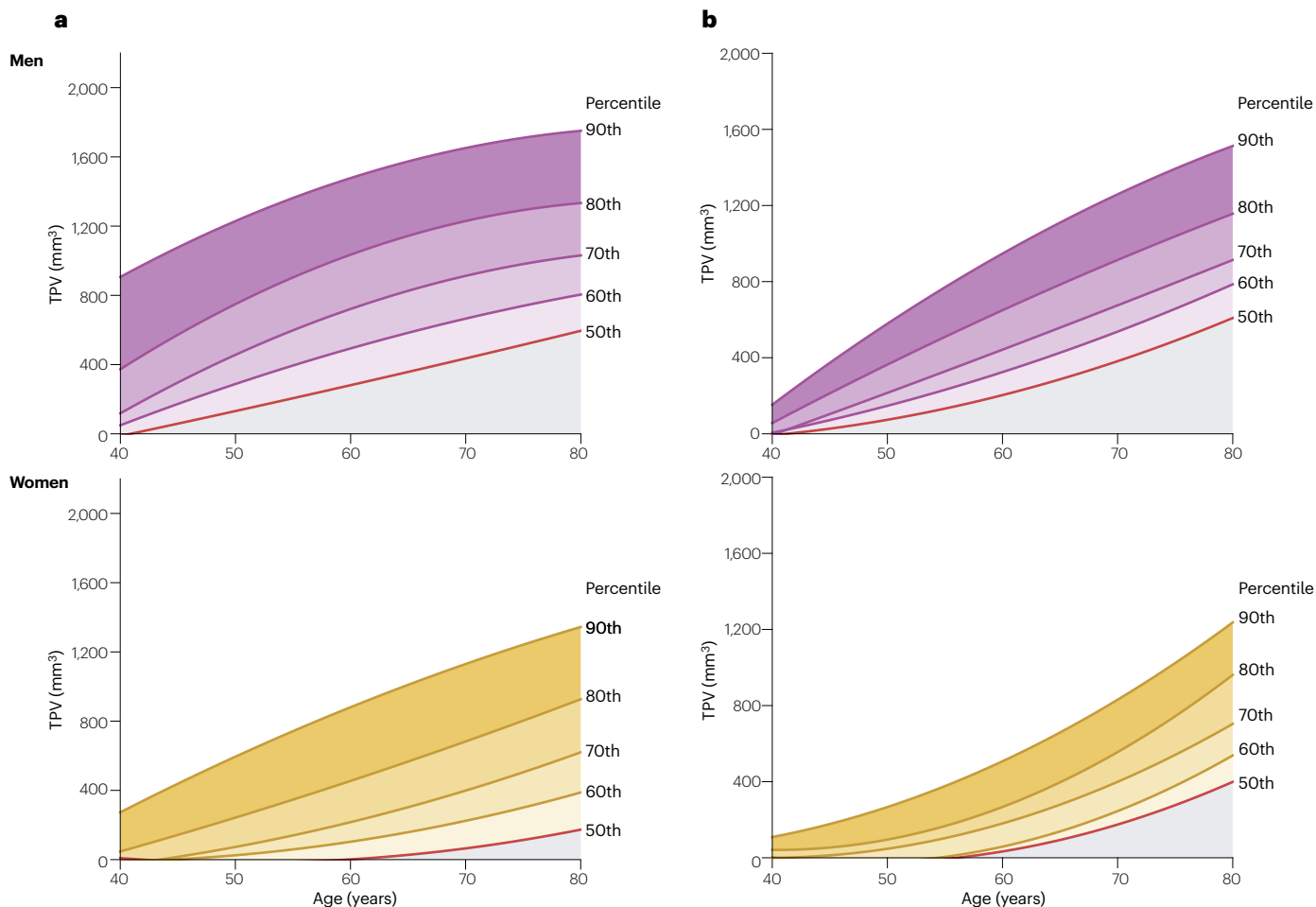
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Fig. 6 | Percentile-based quantification of total plaque volume for individualized management. Age-adjusted and gender-adjusted percentiles of total plaque volume (TPV) are shown for men (purple) and women (yellow). Data obtained from refs. 29,119.

the risk of cardiovascular events and stabilizes existing atherosclerotic plaques. However, with advances in scanner technology and increased scan availability, detecting small atherosclerotic plaques in patients with stable chest pain, or even healthy individuals, with low cardiovascular risk will become more common. Therefore, defining an optimal treatment threshold might be warranted in the future. The integration of NCP also proved to be a divisive topic, and no consensus could be reached. Although agreement was reached that NCP should not be disregarded, its role in individualized treatment recommendations and monitoring of treatment response is yet to be determined on the basis of data from future randomized trials.

AI in plaque assessment
Research shows that fully automated AI methods for the analysis of atherosclerotic plaque in conventional, single-energy CT perform at the level of inter-observer agreement with fast inferences[19,26,132]. Further advances in the robustness and resilience of these methods have the potential to bring the analysis to clinical use. Crucially, AI-supported analysis of CT imaging depends on high image quality, and a novel treatment paradigm based on AI-supported quantification of TPV requires

accurate detection of atherosclerotic plaque. Owing to limited spatial resolution of CCTA, atherosclerotic plaque quantification is recommended only in vessels with a diameter >2 mm (refs. 25,93). In addition, the presence of artefacts and noise can impede detailed delineation of plaque contours. For example, blooming of calcified components can affect the accurate characterization of adjacent low-attenuation plaque[16]. Variations in scanner systems and acquisition protocols affect atherosclerotic plaque characterization, presenting challenges for the accurate quantification of atherosclerotic plaques near to intensity-based cut-off points. Efforts to standardize CT acquisition and analysis are crucial to mitigate such differences[25,132].

Advances in CT image reconstruction[133] and photon-counting CT technology are expected to substantially advance the imaging of atherosclerotic plaque in the near future, owing to increased spatial resolution[134] and spectral capabilities[135]. Nevertheless, the application of AI-supported analysis of these novel CT images will be associated with new challenges, mainly concerning optimal image reconstruction and the exploitation of multienergy level imaging[136]. Further development of existing AI methods for use with (spectral) photon-counting CT could involve the handling of large and high-dimensional data. In the

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next few years, advances in AI technologies could unlock the potential for the improved analysis of atherosclerotic plaque anatomy and easier identification of vulnerable plaque, facilitating individualized treatment recommendations.

Clinical implications

The increased use of AI-supported coronary atherosclerosis imaging will generate unprecedented volumes of data. The challenge will be to integrate these data into meaningful information for effective guidance of patient management. We should resist the temptation to generate hypotheses based on the data but instead focus on testing hypotheses that are firmly grounded in our understanding of CAD pathophysiology. By integrating quantitative assessments of coronary plaque burden, composition and progression, advanced algorithms for patient management have the potential to deliver truly individualized treatment, considering crucial factors such as ethnic variability, comorbidities and concurrent therapies.

Given the expanding options for medical therapy, with the growing armamentarium of lipid-lowering and anti-inflammatory therapies, a need clearly exists to individualize treatment intensity. The relationship among disease burden, inflammatory activity and atherosclerotic plaque progression must guide these advances, because they are the key determinants of cardiovascular risk. AI-supported imaging, incorporating age-adjusted and gender-adjusted TPV percentiles, could provide a foundation to refine treatment thresholds. Inflammatory markers and coronary imaging risk modifiers could inform the treatment intensity required to halt disease progression. Finally, atherosclerotic plaque characteristics will add nuanced adjustments to optimize treatment. The effectiveness of these innovative approaches must be rigorously validated through well-designed, prospective, randomized, controlled clinical trials. This requirement presents a major challenge, given the many options for tailored management and the need for individual effectiveness research. The recommendations contained in this Consensus Statement could provide a foundation for these trials.

Conclusions

AI-supported tools to evaluate atherosclerotic plaque offer the potential to refine the precision of risk stratification and improve clinical decision-making by providing reliable and accurate assessments of atherosclerotic plaque burden and morphology. The QCI Study Group deemed the age-adjusted and gender-adjusted percentiles of TPV to be the most meaningful parameter for the individualized initiation and escalation of medical treatment. TPV is a major risk predictor for MACEs and outperforms other atherosclerotic plaque subtype metrics, such as

CPV or NCPV, as well as providing modest independent discrimination in addition to cardiovascular risk factors[72]. Treatment escalation to high-intensity regimens is recommended for patients with TPV above the 70th percentile. Clinical risk factors and high-risk plaque features can also inform decisions on treatment escalation.

The implementation of individualized treatment recommendations, guided by AI-supported assessment of coronary atherosclerotic plaque, represents a substantial paradigm shift in cardiovascular risk management. Although these consensus recommendations provide a practical framework for integrating AI-supported evaluation of atherosclerotic plaque into routine clinical practice, further large-scale, randomized, controlled cardiovascular outcome trials integrating novel anti-atherosclerotic agents are necessary to validate these recommendations. This evolving approach highlights the growing importance of advanced imaging of coronary atherosclerosis biomarkers and AI-driven analysis as companion diagnostics in transforming cardiovascular care, moving from generalized risk scoring to individualized treatment pathways based on coronary atherosclerotic plaque morphology and should be tested in trials of CT versus CT with AI.

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Table 1 | Standard-intensity and high-intensity doses for commonly prescribed statins

Drug	Standard intensity (mg)	High intensity (mg)
Rosuvastatin	5–10	20–40
Atorvastatin	10–20	40–80
Simvastatin	20–40	NA
Pravastatin	40–80	NA
Lovastatin	40–80	NA
Fluvastatin	40–80	NA

Once-daily doses. See also ref. 36. NA, not applicable (these medications are not given at high-intensity doses).

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Author contributions
K.S., A.-M.S., M.C.W., A.-C.S., H.B., D.D., D.E.N. and M.D. researched data for the article. K.S., A.-M.S., M.C.W., P.M.-H., B.F., F.B., D.D., D.E.N. and M.D. discussed the content of the article. K.S., A.-M.S., M.C.W., V.S.V., A.A.G., K.N., P.M.-H., J.M.T., R.V., J.W.-M., M.M., B.F., F.B., N.G., I.I., A.A.-Z., H.A., E.D.N., N.S.N., F.M.A.C.M., D.D., D.E.N. and M.D. wrote the manuscript. All the authors reviewed/edited the manuscript before submission.

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[1]Department of Radiology, Charité Universitätsmedizin Berlin, Berlin, Germany. [2]British Heart Foundation Centre of Research Excellence, University of Edinburgh, Edinburgh, UK. [3]Department of Cardiac Medicine, Norwich Medical School, University of East Anglia, Norwich, England. [4]Department of Nuclear Medicine, Cardiac Imaging, University Hospital Zurich, Zurich, Switzerland. [5]Department of Medicine/Cardiovascular and Radiology, Stanford University, Stanford, CA, USA. [6]Department of Radiology, Medical Imaging Center, Semmelweis University, Budapest, Hungary. [7]Section of Cardiorespiratory Medicine, Victor Phillip Dahdaleh Heart & Lung Research Institute, University of Cambridge, Cambridge, UK. [8]Department of Radiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. [9]Department of Cardiovascular Imaging, Biomedical Engineering and Imaging Sciences, King's College London, London, UK. [10]Department of Radiological, Oncological and Pathological Sciences, Sapienza University of Rome, Rome, Italy. [11]Department of Biomedical Engineering and Physics, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, The Netherlands. [12]Department of Radiology and Nuclear Medicine, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, The Netherlands. [13]Informatics Institute, University of Amsterdam, Amsterdam, The Netherlands. [14]Division of Cardiology, Department of Medicine, Johns Hopkins University, Baltimore, MD, USA. [15]Diagnostic and Interventional Radiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland. [16]Institute for Biomedical Engineering, University and ETH, Zurich, Switzerland. [17]National Heart and Lung Institute, Imperial College London, London, UK. [18]National Institute for Prevention and Cardiovascular Health, University of Galway, Galway, Republic of Ireland. [19]School of Biomedical Engineering & Imaging Sciences, King's College London, London, UK. [20]Department of Cardiology and Radiology, Royal Brompton Hospital, London, UK. [21]Department of Cardiology, Amsterdam University Medical Centers, Amsterdam, The Netherlands. [22]Departments of Biomedical Sciences, Cedars–Sinai Medical Center, Los Angeles, CA, USA. [23]Departments of Medicine, Cedars–Sinai Medical Center, Los Angeles, CA, USA. [24]Berlin Institute of Health at Charité — Universitätsmedizin Berlin, Berlin, Germany. [25]Berlin University Alliance, Berlin, Germany. [26]DZHK (German Centre for Cardiovascular Research), Partner Site Berlin, Berlin, Germany. [27]Deutsches Herzzentrum der Charité (DHZC), Berlin, Germany. [28]These authors contributed equally: Kenrick Schulze, Anne-Marieke Stantien, Michelle C. Williams. [29]These authors jointly supervised this work: Damini Dey, David E. Newby, Marc Dewey.