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*Corresponding author

*Dr Abdul-Majeed Salmasi, Department of Cardiovascular Medicine, Central Middlesex hospital, Acton Lane London NW10 7NS, United Kingdom.
Email: a.salmasi@imperial.ac.uk

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Case Report

Systemic Hypertension is Not a Significant Predictor of Positive Stress Echocardiogram

Ademide Olowosale[1], Dr Abdul-Majeed Salmasi[1,2*]

[1]Department of Cardiovascular Medicine, Central Middlesex hospital, Imperial College London, United Kingdom.

[2]Department of Cardiovascular Medicine, Central Middlesex hospital, Acton Lane London NW10 7NS, United Kingdom.

Abstract

Background: Systemic hypertension is the greatest modifiable risk factor for cardiovascular death and contributes significantly to the pathology of chronic coronary syndrome (CCS). Stress echocardiography (SE) is widely used to diagnose myocardial ischaemia. To optimise referral criteria for SE, we aimed to identify the strongest predictors of CAD on SE.

Methods: A retrospective study reviewing the electronic health records of 547 consecutive patients who underwent SE between October and December 2022 at London Northwest University Healthcare NHS Trust hospitals. Risk factors were recorded, including male sex, hypertension, diabetes mellitus, dyslipidaemia, previous CAD, smoking and family history.12-month incidence of revascularisation, major adverse cardiovascular events (MACE) and cardiac mortality were also recorded, and the diagnostic performance of SE was evaluated.

Results: Overall, 42 (7.68%) patients had positive SE, of which 31 (73.8%) were male. While hypertension was the most common risk factor in the cohort, affecting 344 (62.9%) patients, univariate analysis demonstrated that hypertension was not associated with SE result (P= 0.845), which was confirmed on multiple logistic regression analysis (OR = 0.529, P = 0.099). Meanwhile, male sex was identified as the strongest independent predictor for a positive SE (OR = 2.599, P <0.05), followed by diabetes mellitus (OR = 2.239, P <0.05) and previous CAD (OR = 2.215, P <0.05). Positive SE was significantly associated with revascularisation (P <0.001), but the incidence of MACE and cardiac mortality were similar across positive and negative SE cohorts. Sensitivity, specificity and accuracy of SE were 80.8%, 45.5% and 70.3% respectively.

Conclusion: Despite being the most common risk factor, hypertension was not a significant predictor of myocardial ischaemia on SE while male gender, diabetes mellitus and previous CAD were significant predictors. Our findings suggest that current referral criteria for SE may not be optima,l these novel insights warrant further studies to substantiate the prioritisation of these risk factors in optimised referral criteria for SE in patients with suspected CCS.

Background

Ischaemic heart disease (IHD) occurs when myocardial oxygen supply is insufficient (1). Despite significant advancements in our understanding of cardiovascular health, IHD has remained the leading cause of death worldwide over the past two decades, with an alarming increase in annual fatalities, reaching 9.4 million in 2021(2,3).

Whilst there is a comprehensive understanding of how traditional cardiovascular risk factors affect the prognosis of IHD, knowledge of the effect of these risk factors on identifying IHD across various diagnostic modalities still needs to be completed.

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The most common manifestation of IHD is chronic coronary syndrome (CCS), describing patients with a diagnosis of coronary artery disease (CAD) without a recent acute coronary event (4). CAD encompasses the spectrum of pathological disorders of the coronary circulation, from ischaemia with no obstructive coronary arteries to obstructive epicardial CAD (5).

The pathological mechanisms of CAD are amplified by risk factors, including sex, hypertension, diabetes mellitus, dyslipidaemia, smoking history, and positive family history of cardiovascular disease (CVD) (5–7).

By determining the most effective diagnostic modality for CAD based on patients' individual risk profiles, we can optimise the investigation of suspected CCS and reduce its healthcare burden. In symptomatic patients with suspected CCS, both the European Society of Cardiology (ESC) and the National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) advocate for non-invasive testing as first-line when CAD cannot be excluded by clinical assessment alone (4,8).

SE is a non-invasive functional test that indirectly determines the presence of myocardial ischaemia by assessing echocardiograms at rest and following stress (6). Under current guidelines, the referral process for SE investigation of CAD in suspected CCS is based on a clinical assessment of the typicality of chest pain and cardiovascular risk factors (4,8). Identifying the risk factors that are the strongest predictors of CAD on SE could optimise these referral criteria by suggesting the stratification of patients to specific diagnostic modalities based on their individual risk profiles.

Given that hypertension is the leading modifiable risk factor for cardiovascular death and that a previous study at our centre identified hypertension as the strongest predictor of CAD on CCTA, we hypothesise that hypertension may also be the strongest predictor of myocardial ischaemia on SE (2,9). This study aims to investigate the risk factors associated with positive SE in patients with suspected CCS being investigated for CAD to identify the strongest predictors of myocardial ischaemia on SE, which will make up the primary criteria for proposed optimised SE referrals. This would result in more efficient diagnosis of patients with CCS, leading to more timely management and improved patient outcomes.

Methods

Study population and data sources

This single-centre retrospective, observational case-control study was conducted at London NorthWest University Healthcare NHS Trust. The electronic healthcare records of 697 consecutive patients scheduled to undergo either exercise or dobutamine stress echocardiography for assessment of ischaemia between 1st October and 31st December 2022 were reviewed. The final study population consisted of 547 patients. SE data were collected from the Change Healthcare Cardiology™ database, and patient information was collected from Cerner™ and Epro™. Ethical approval was not required as this was an audit, and there is no identifiable patient data in our raw data or results.

Inclusion and exclusion criteria

Consecutive patients who underwent SE to assess inducible ischaemia between 1st October and 31st December 2022 were included. SE done for patients who satisfied any of the following criteria were excluded from the cohort: [1] patients under 18 years old, [2] patients who underwent SE for alternate reasons, [3] patients where an SE was not carried out, [4] patients with sub-optimal SE, and [5] patients with incomplete electronic health records. Hence 150 patients were excluded.

Feature extraction

The following data were collected from patient electronic health records (Cerner™ and Epro™) to determine baseline characteristics: age, gender, ethnicity, BMI (body mass index), cardiovascular risk factors, clinical presentation, and current medications. Ethnicity data was available for 463 patients, and BMI data was available for 203 patients. The cardiovascular risk factors investigated were hypertension, diabetes mellitus, dyslipidaemia, previous history of CAD (and prior therapy), smoking history, family history of CVD and family history of hypertension.

Assessment of CAD

SE and ICA were conducted and reported in accordance with the standard protocols at London North West University Healthcare NHS Trust. At the service provider's discretion, patients underwent exercise or dobutamine SE.

SE characteristics were collected from the imaging database (Change Healthcare Cardiology™). Data collected includes the result for inducible ischaemia (positive or negative), procedure type (exercise or dobutamine) and wall motion score index (WMSI) at rest and following stress. WMSIs were available for only 299 patients. Exercise stress echocardiography was carried out in accordance with the modified Bruce protocol (10). Invasive coronary angiography was performed at the discretion of the referring clinician, often following a positive SE result. Images were acquired at standard views, and interpretations were confirmed by senior cardiologists.

Outcomes : 12-month follow-up included a review of patient electronic health records. The incidence of revascularisation

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[percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG)], changes to medical therapy, stroke or transient ischaemic attack (TIA), major adverse cardiovascular events (MACE) and cardiac mortality were recorded.

Statistical analysis

Normality was assessed using Kolmogorov-Smirnoff testing. Non-parametric data are presented as median [interquartile range (IQR)]. Descriptive statistics are presented as frequency [percentage (%)]. Univariate analysis was performed of baseline characteristics and clinical outcomes between patients with positive SE and negative SE results, using the Mann-

Whitney U test for non-parametric continuous variables and the chi-squared ($\chi 2$) test for categorical variables. Multivariate analysis to assess the independent association of risk factors with CAD on SE was performed using a binary logistic regression model. A ROC (receiver operating characteristic) curve was generated for this model, and an AUROC (area under receiver operating characteristic curve) was calculated. The Exp(B) value was taken to be the adjusted odds ratio (aOR) of each risk factor for a positive SE outcome. A cohort of 37 patients who underwent SE also underwent ICA. SE results were classified in relation to ICA results as either true positive, true negative, false positive, or false negative. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated using a 2x2 outcome table. Accuracy was then determined by calculating the proportion of true positives and true negatives. Measures of performance were calculated for the overall sub-cohort and also stratified by risk factors present in at least 18 patients.

Statistical analysis was done using IBM SPSS (version 29.0).

Results

Baseline characteristics

Our study yielded 42 (7.68%) positive SE and 505 (92.3%) negative SE. Table 1 shows the characteristics of the study cohort at the time of SE (n=547), including demographics, risk factors, presentation, and medication use.

The median age at time of SE was 65.0 (IQR 47.0-83.0), with a median BMI of 26.8 (IQR 19.634). 288 participants (52.7%) were male, and the most prevalent ethnicity was Indo-Asian (59.0%).

To guide the analysis of results, baseline characteristics were compared between patients with positive SE results and those with negative SE outcomes. On univariate analysis, male sex, BMI, diabetes and previous CAD were the only factors significantly associated with an increased likelihood of a positive SE (P = 0.004, P = 0.017, P= 0.005 and P = 0.002, respectively). Despite being the most prevalent risk factor within the cohort (62.9%), hypertension was not associated with SE outcome.

Stress echocardiography characteristics.

Exercise SE was done in 406 (74.2%) of patients, and the remaining 141 (25.8%) underwent dobutamine SE. The prevalence of positive SE between the two methods was similar (P = 0.067).

Risk Factors as Predictors for Positive Stress Echocardiography

Multivariate analysis was carried out on risk factors making up the NICE referral criteria (8) using a binary logistic regression model (Table 2). BMI was excluded from the binary logistic regression model as it was only recorded for 203/547 patients. All other 3 variables identified to be significantly associated with positive SE using univariate analysis – male sex, diabetes mellitus and previous CAD – remained significant using multivariate analysis. Figure 2 shows a forest plot comparing the adjusted odds ratio (aOR) and 95% confidence intervals for each risk factor as an independent predictor of CAD on SE. Male sex was the strongest predictor of CAD on SE (aOR = 2.599, P =0.014, 95% CI: 1.125-5.559), followed by diabetes mellitus (aOR = 2.239, P = 0.023, 95% CI: 1.117-4.492) and previous CAD (aOR = 2.215, P = 0.029, 95% CI: 1.087-4.511). Surprisingly, hypertension showed a trend towards a protective effect, though this did not reach significance (aOR = 0.529, P = 0.099, 95% CI: 0.248-1.128). There were 18 diabetic hypertensive patients who had positive SE but when compared to hypertensive non-diabetic subjects (n=) using chi square test, the test was not significant. Eight of the 25 (32%) diabetic patients were females.

Diagnostic performance of SE : 37 (6.76%) patients

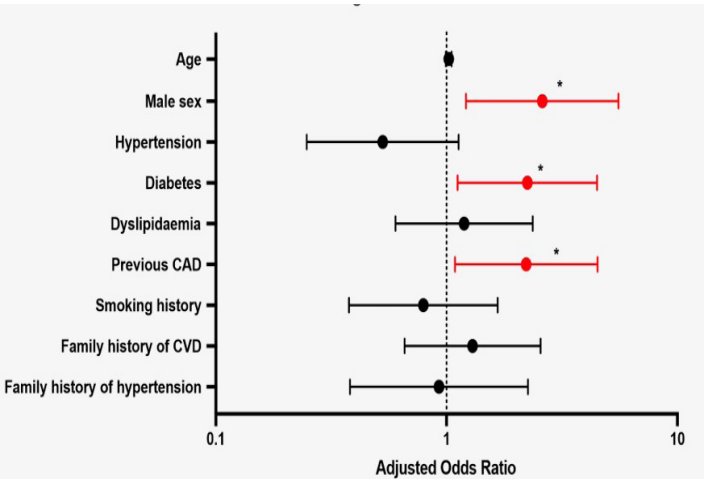

Figure 1: *Forest plot: Adjusted Odds Raqtio of risk factor associated with positive stress echocardiography result.*

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Table 1: *Baseline characteristics*

VARIABLE	TOTAL (n=547)	POSITIVE SE (n=42)	NEGATIVE SE (n=505)	P VALUE (PvN SE)
AGE (YEARS)	65 (47-83)	67.5 (50.5-84.5)	65 (46-84)	0.057
BMI (KG/M^2)	26.8 (19.6-34)	26.0 (23.1-29.0)	27.5 (20.0-35.0)	0.017*
MALE (%)	288 (52.7)	31 (73.8)	257 (50.9)	0.004*
ETHNICITY				0.630
White	112 (20.5)	7 (16.7)	105 (20.8)	
Indo-Asian	323 (59.0)	29 (69.0)	294 (58.2)	
East Asian	2 (0.4)	0 (0.0)	2 (0.4)	
Black	21 (3.8)	0 (0.0)	21 (4.1)	
Mixed	5 (0.9)	0 (0.0)	5 (1.0)	
RISK FACTORS				
Hypertension (%)	344 (62.9)	27 (64.3)	317 (62.8)	0.845
Diabetes mellitus (%)	214 (39.1)	25 (59.5)	189 (37.4)	0.005*
Dyslipidaemia (%)	289 (52.8)	26 (61.9)	263 (52.1)	0.220
Smoking history				
Never smoker (%)	389 (71.1)	30 (71.4)	359 (71.1)	0.963
Ex-smoker (%)	99 (18.1)	9 (21.4)	90 (17.8)	0.560
Current smoker (%)	59 (10.8)	3 (7.1)	56 (11.1)	0.428
Previous CAD (%)	178 (32.5)	24 (57.1)	154 (30.5)	0.002*
PCI (%)	117 (21.4)	13 (31.0)	104 (20.6)	0.116
CABG(%)	31 (5.7)	8 (19.0)	23 (4.6)	<0.001*
Medical therapy (%)	24 (4.4)	2 (4.8)	22 (4.4)	0.902
Family history of CVD (%)	292 (53.4)	24 (57.1)	268 (53.1)	0.611
Family history of hypertension (%)	91 (16.6)	7 (16.7)	84 (16.6)	0.996
PRESENTATION				
Chest pain (%)	446 (81.5)	32 (76.2)	414 (82.0)	0.353
Dyspnoea (%)	285 (52.1)	20 (47.6)	265 (52.5)	0.545
MEDICATION				
Beta blockers (%)	180 (32.9)	24 (57.1)	156 (20.9)	<0.001*
Calcium channel blockers (%)	144 (26.3)	13 (31.0)	131 (25.9)	0.750
ACEi or ARBs (%)	257 (47.0)	24 (57.1)	233 (46.1)	0.170
Nitrates (%)	115 (21.0)	12 (28.6)	103 (20.4)	0.212
Ranolazine (%)	33 (6.0)	3 (7.1)	30 (5.9)	0.914
Statins (%)	328 (60.0)	35 (83.3)	293 (58.0)	0.001*
Diuretics (%)	77 (14.1)	9 (21.4)	68 (13.5)	0.154
Antiplatelets (%)	231 (42.2)	29 (69.0)	202 (40.0)	<0.001*

*Comparison of patient characteristics at the time of stress echocardiogram between patients who had positive SE results and those who had negative SE results. Continuous data are reported as median (interquartile range) and categorical data as frequency (percentage). Statistical analysis was done using the Mann-Whitney U test for continuous test for continuous variables and the chi-square test for categorical variables. * P ≤ 0.05.*

Abbreviations: SE, Stress Echocardiography; BMI, Body Mass Index; PCI, Percutaneous Coronary Intervention; CABG, Coronary Artery Bypass Grafting; ACEi, Angiotensin-Converting Enzyme Inhibitors; ARB, Angiotensin Receptor Blocker; PvN; Positive SE vs Negative SE

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Table 2: *Multivariate Analysis of Risk Factors for Positive Stress Echocardiography Result*

VARIABLES	B ± STANDARD ERROR	P-VALUE	EXP(B) / ODDS RATIO	95% CI FOR EXP(B)	
				LOWER	UPPER
AGE	0.022 ± 0.025	0.138	1.022	0.993	1.052
SEX	0.955 ± 0.388	0.014*	2.599	1.215	5.559
HYPERTENSION	-0.636 ± 0.386	0.099	0.529	0.248	1.128
DIABETES MELLITUS	0.806 ± 0.355	0.023*	2.239	1.117	4.492
DYSLIPIDAEMIA	0.175 ± 0.349	0.616	1.191	0.601	2.362
PREVIOUS CAD	0.795 ± 0.363	0.029*	2.215	1.087	4.511
SMOKING HISTORY	-0.232 ± 0.378	0.540	0.793	0.378	1.665
FAMILY HISTORY OF CVD	0.260 ± 0.346	0.453	1.296	0.658	2.554
FAMILY HISTORY OF HYPERTENSION	-0.075 ± 0.452	0.869	0.928	0.382	2.253

Binary logistic regression analysis was conducted to investigate the relationship between risk factors and the probability of a positive stress echocardiogram result. The coefficients, P-values, odds ratios, and 95% confidence interval are reported for each risk factor.

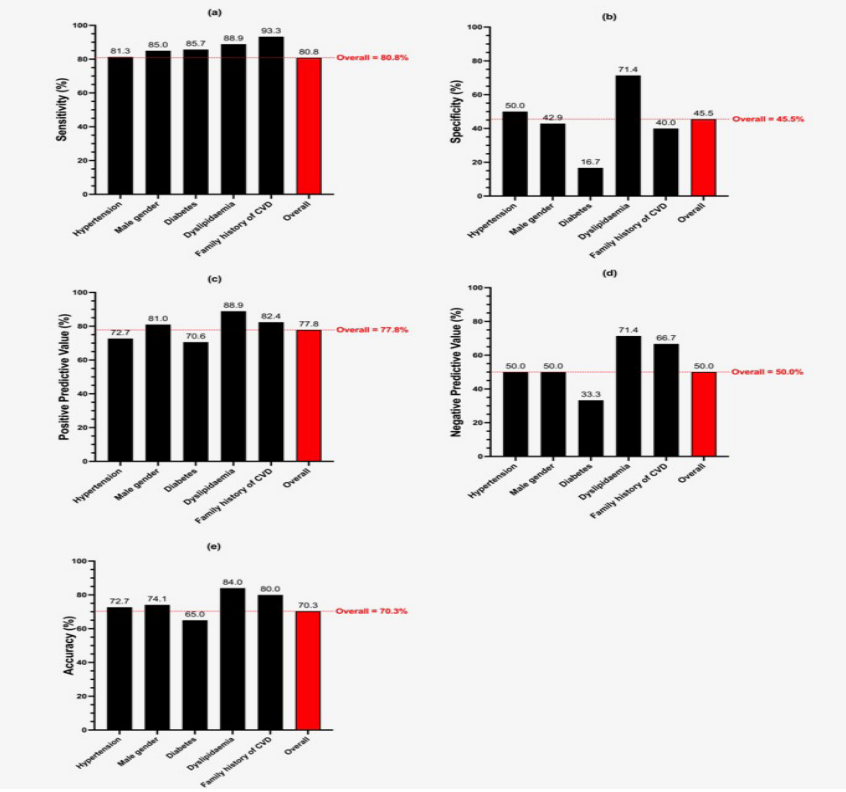
Abbreviations: *SE, Stress Echocardiography; CAD, Coronary artery disease; CVD, Cardiovascular disease*

Table 3: *Clinical Outcomes by Stress Echocardiography Result*

Clinical Outcome	TOTAL (n=547)	POSITIVE SE (n=42	NEGATIVE SE (n=505)	P VALUE (POSITIVE VS NEGATIVE SE)
REVASCULARISATION				
PCI (%)	11 (2.0)	9 (21.4)	2 (0.4)	<0.001*
CABG (%)	5 (0.9)	5 (11.9)	0 (0.0)	<0.001*
CHANGE IN MEDICAL MANAGEMENT	50 (9.1)	35 (83.3)	15 (3.0)	<0.001*
CARDIAC MORTALITY	2 (0.4)	0 (0.0)	2 (0.4)	0.683
STROKE OR TIA	4 (0.7)	0 (0.0)	4 (0.8)	0.563
MACE	1 (0.2)	0 (0.0)	1 (0.2)	0.773

Comparison of clinical outcomes at 12-month follow-up between patients who had positive SE results and those who had negative SE results. Data is reported as frequency (percentage). Statistical analysis was done using the chi-square test for categorical variables. ** P ≤ 0.05*

Abbreviations*: SE, Stress Echocardiography; PCI, Percutaneous Coronary Intervention; CABG, Coronary Artery Bypass Grafting; TIA, Transient Ischaemic Attack; MACE, Major Adverse Cardiovascular Event*



underwent ICA in addition to SE, making up the cohort used to assess the diagnostic performance of SE. The mean number of days between SE and ICA was 71.4 ± 71.3 days. Figure 3 shows the overall diagnostic performance of SE in our study, as well as the diagnostic performance stratified by risk factor. The diagnostic performance of hypertension as a risk factor was at or above the cohort overall average for all measures other than positive predictive value (hypertension = 72.7%, overall = 77.8%).

Clinical outcomes by Stress Echocardiography result

Table 3 shows the frequency of clinical outcomes in negative and positive SE patient cohorts at 12-month follow-up. Positive SE was significantly associated with revascularisation both through PCI ($P < 0.001$) and CABG ($P < 0.001$), as well as a change in medical management ($P < 0.001$). The occurrence of cardiac mortality, stroke/TIA, and MACE was similar between patients with positive and negative SE results. Notably, none of the patients with a positive SE experienced cardiac mortality, stroke/TIA, or MACE within the 12-month follow-up period.

Discussion

Hypertension was identified as not a significant predictor of myocardial ischaemia on SE. In contrast, male gender was the strongest predictor of myocardial ischaemia on SE, followed by diabetes mellitus and previous CAD. This novel finding offers valuable insights for developing future optimised referral guidelines for the use of SE in the diagnosis of myocardial ischemia.

Evaluation of current SE referrals

The percentage of positive SE in our study was much lower than in the Real-world performance and accuracy of stress echocardiography: the EVAREST observational multi-centre study (EVAREST), which comprised data from 31 hospital trusts across the United Kingdom (UK) (7.68% vs 19.3%) (11). This lower rate of positive SE in our study may reflect more inappropriate SE referrals being made at our centre compared to the national average. This, coupled with the heterogeneity of results reported in EVAREST, highlights the need for improved referral criteria to reduce inappropriate SE referrals consistently nationwide (11).

Predictors of CAD on SE

With the aim of optimising SE referrals, we identified the risk factors significantly associated with positive SE. Male gender was the strongest predictor of a CAD on SE, followed by diabetes mellitus and previous CAD. All 3 risk factors were associated with more than a 2-fold greater risk of a positive SE outcome. EVAREST corroborates the significant association between the aforementioned risk factors and a positive SE outcome; however, EVAREST also identified age and hypertension as factors associated with a positive SE, while our findings did not (11).

By evaluating and comparing the strength of different risk factors as predictors of CAD on different imaging modalities, novel perspectives can be gained about the suitability of each modality for patients with these risk factors.

Tserioti et al. identified hypertension as the strongest predictor of CAD on CCTA (9). The relationship between hypertension and CAD is well-documented, with hypertension forming the criteria of several risk scores used to calculate CAD likelihood in patients (12–14). However, our findings show that hypertension had the lowest odds ratio for a positive SE result – though it should be noted that this did not reach significance (aOR: 0.529, P= 0.099). Given that hypertension is an established independent risk factor for CAD, our findings may imply that SE is not the most appropriate imaging modality for CAD assessment in patients with hypertension but to elucidate if there is or there is no myocardial ischaemia. Considering the findings of Tserioti et al., perhaps hypertensive patients should be prioritised to undergo CCTA rather than SE to assess CAD(9). This suggestion is supported by the fact that both studies were conducted at the same centre with comparable patient populations, attributing the discrepancy in findings to the different modalities investigated. Alternatively, as CCTA cannot assess the functional significance of myocardial ischaemia, it is possible that the lesions identified by Tserioti et al.(9) amongst hypertensive patients lacked functional significance, explaining why hypertension was not associated with an increased likelihood of positive SE in our study. Further study may be suggested for hypertensive subjects to undergo both SE and CCTA in order to elucidate the significance of both tests and assess which test modality is appropriate.

Furthermore, Tserioti et al. determined that diabetes was not an independent predictor of CAD on CCTA (9) whilst our study shows diabetes to be the only modifiable risk factor significantly associated with SE outcome. This may suggest that patients with diabetes mellitus may have underlying microvascular disease more than pure hypertensive subjects. It is important to determine the optimal diagnostic modality for diabetic patients as CVD remains the leading cause of death in patients with diabetes (14,15). The following criteria have been proposed for coronary microvascular disease: the presence of symptoms suggestive of myocardial ischemia, objective documentation of myocardial ischemia, assessed by currently available techniques, absence of obstructive coronary artery disease defined as < 50% coronary diameter reduction and/or fractional flow reserve of > 0.80, and confirmation of a reduced coronary blood flow reserve and/or inducible

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microvascular spasm.(16)

The lack of association between diabetes and CAD on CCTA as opposed to its significance as a predictor of CAD on SE is particularly intriguing, given that diabetic patients have a 2-fold higher risk of vascular complications, including IHD (17). These findings could be due to the temporal relationship between the vascular complications of diabetes, as microvascular complications often manifest prior to macrovascular complications. Therefore, SE may have been able to assess the haemodynamic effect of coronary microvascular dysfunction (CMD) in diabetic patients with ischaemia with no obstructive coronary arteries before the development of epicardial obstructive CAD detectable by CCTA.

Diabetes has been shown to have a unique bi-directional relationship with CMD; chronic hyperglycaemia, hyperinsulinemia, and insulin resistance lead to impaired microvascular vasodilation via increased oxidative stress and inflammation, contributing to the development of CMD, whilst CMD increases the progression of diabetes mellitus by reducing insulin and glucose delivery to skeletal muscles (18). Furthermore, coronary microvascular function has been demonstrated to be impaired in diabetes, even in the absence of hypertension or dyslipidaemia (19). This may explain why, in this study, diabetes mellitus emerged as a significant predictor of myocardial ischaemia on SE and not on CCTA (9), while hypertension and dyslipidaemia did not.

It should be noted that the characteristic regional wall motion abnormalities (RMWA) of SE may be absent in CMD, hence the 2021 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend using stress PET MPI or stress CMR before SE for the non-invasive evaluation of INOCA (20). Using CT-MPI and CCTA, Yu et al. demonstrated that the incidence of microvascular INOCA was significantly higher in diabetic patients compared to the control (36.3% vs 10.3%, P<0.001) (21). Coronary angiography-derived index of microcirculatory resistance (caIMR) also demonstrated that the incidence of CMD was greater amongst diabetic patients than non-diabetic controls (57.8% vs 38.3%, P=0.001) (22). Our results demonstrate a similar trend with a significantly higher incidence of positive SE in diabetic patients compared to non-diabetics (11.68% vs 5.11%, P<0.005). However, due to the limitations of SE as a diagnostic modality, we are unable to definitively attribute our findings to CMD and INOCA. Furthermore, the lower incidence of positive CAD results across both diabetic and non-diabetic patients in our study is likely to be due to a greater proportion of inappropriate referrals for SE.

Nevertheless, the accessibility, affordability and mitigated radiation risk of SE, make it an ideal sustainable diagnostic modality.

These insights highlight the utility of different imaging modalities in assessing CAD in diabetic patients and perhaps suggest that diabetic patients should be prioritised for SE over CCTA, especially as CMD is a strong predictor of MACE, even prior to the development of obstructive epicardial CAD detectable on CCTA (23). Meanwhile, hypertensive patients may benefit from prioritisation to receive CCTA over SE.

Limitations

Being retrospective and observational, our study carries the inherent risk of bias. Whilst we have interpreted the differences between our findings and those of Tserioti et al. (9) as due to the different imaging modalities investigated, they could have resulted from clinician selection bias when referring patients. With SE carrying lower risks than CCTA, clinicians may be more inclined to refer patients with a lower probability of CAD for SE rather than CCTA. Conversely, ESC guidelines recommend that in patients with a low clinical likelihood of CAD, CCTA can be preferentially considered over functional testing as it has a high accuracy in low-likelihood populations (4,24). Additional studies where patients with suspected CAD should undergo CCTA and SE could provide a more comprehensive understanding of the association between risk factors and positive outcomes while controlling for potential clinician bias.

Future directions

Expanding on our novel insights into the utility of SE, we suggest conducting further research into the relationship between risk factors and the identification of CAD using other diagnostic modalities, including stress CMR, stress SPECT and stress PET. This would provide a comprehensive understanding of the utilities of each diagnostic test, enabling us to refer patients for the most suitable test based on their individual risk factors. We propose achieving this by establishing an international registry of patients with suspected CCS, including their risk factors, presentations, results of any diagnostic tests they underwent and long-term clinical outcomes. Alternatively, these parameters could be considered for integration into the ESC Chronic Coronary Syndrome Snapshot Study, which is due to commence soon at the time of writing (25).

Whilst the analysis of this data would be retrospective in nature, it could provide valuable insights into the impact of risk factors of a range of diagnostic tests without the increased expense, use of patient time and radiation exposure associated with a prospective study design where each patient receives all the diagnostic tests for comparison of their outcomes.

Conclusion

Contrary to hypertension, diabetes mellitus is an independent predictor of myocardial ischaemia on SE.

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When compared to the findings on CCTA, it appears that microvascular disease rather than overt atherosclerotic CAD may have played a role in the results. Our findings, therefore, suggest that while there may significant degree of atherosclerotic CAD, it may not suggest a significant functional myocardial ischaemia. This situation may be contrary to patients with diabetes mellitus where less significant degree of atherosclerotic CAD may be associated with higher degree of myocardial ischaemia due possibly to associated microvascular coronary disease. The novel results of our study warrant a prospective study with a larger cohort to confirm our findings and justify their application to clinical practice.

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