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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

The relationship of socioeconomic status with coronary artery calcification and pericardial fat

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Abstract

Background: Little data currently exist supporting the correlation of socioeconomic status (SES) to markers of subclinical coronary atherosclerosis.

Aim: The main aim was to investigate the relationship of SES measured by economic status and educational level with coronary artery calcification (CAC) and pericardial fat volume (PFV) assessed by multi-detector computed tomography (MDCT).

Methods: A total of 220 consecutive patients with suspected coronary artery disease, who underwent 64-slice MDCT angiography for assessment of coronary atherosclerosis, were recruited between January 2014 and March 2015. Of these, 186 patients were enrolled in this cross sectional study.

Results: Low economic status patients showed higher PFV values; median (inter-quartile range [IQR] was 94 [50–140] cm^3, $p = 0.00001$ and $r = 0.37$, compared to patients with high economic status, and this association persisted even after multiple logistic regression to conventional cardiac risk factors ($p = 0.004$, CI 7.3–30.4), while patients with low economic status reported a higher calcium score (but statistically non significant) ($p = 0.12$) compared to high economic status patients. Patients with no formal education showed higher PFV (median [IQR] was 93 [48–140] cm^3, $p = 0.01$) compared to patients with bachelor's degree (median [IQR] was 56 [28–92] cm^3), but this association was attenuated after further adjustment for conventional cardiac risk factors ($p = 0.1$, CI –9.52–10.88), while CAC showed no significant correlation with educational level ($p = 0.2$, $r = 0.117$).

Conclusions: Socioeconomic status, particularly economic status measure, reported a significant inverse relationship with PFV independent of conventional cardiac risk factors.

Key words: atherosclerosis, coronary artery, calcification, multi-detector computed tomography, pericardial fat, socioeconomic status

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INTRODUCTION

There is a considerable bulk of evidence that suggests that socioeconomic status (SES) measured by different parameters of socioeconomic level may affect the risk and extent of cardiovascular disease (CVD) in geographically diverse populations [1, 2].

A consistent relationship was observed between carotid intimal thickness and plaque formation as markers of arterial atherosclerosis and socioeconomic class [3].

However, little data currently exists on the correlation of SES to markers of subclinical coronary atherosclerosis.

Various indicators of SES were used to define the social position in society and linked with CVD including household income, family size and educational attainment.

Coronary artery calcification (CAC) as a marker of subclinical coronary atherosclerosis assessed by multi-detector computed tomography (MDCT) has incremental prognostic value beyond that of traditional cardiac risk factors and scores for CVD morbidity and mortality reported in several large follow-up studies, and it may improve risk stratification of patients with suspected coronary atherosclerosis [4, 5].

Pericardial fat volume (PFV) is an emerging imaging biomarker with prognostic significance in assessing the extent and early coronary endothelial dysfunction that may precede the development of mature atherosclerotic changes of coronary artery disease (CAD) [6, 7].

The main aim of our study was to investigate the relationship of SES measured by family income and size and educa-

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tional level indicators with coronary atherosclerosis markers (CAC and PFV) in patients with suspected CAD assessed by MDCT after adjustment to possible confounders including conventional cardiac risk factors.

METHODS

This cross-sectional study was carried out at our Cardiology Centre between January 2014 and March 2015. Informed consent was obtained from all individual participants included in the study. The study was approved by our institution.

A total of 220 consecutive Iraqi patients with suspected CAD based on their age, sex, and cardiac symptoms, who underwent 64-slice MDCT angiography for assessment of CAD, were recruited. Of these, 186 patients were found to be eligible and were enrolled in the study.

Thirty-four patients were excluded because of a poor examination technique or motion artefact (n = 12), had a prior history of an implanted stent in the coronary artery or coronary revascularisation (n = 3), difficulty in accurate PFV calculation or segmentation of fat (n = 7), or data were missing or incomplete (n = 12).

Using standard physician-based questionnaires, a history of conventional cardiac risk factors for CAD was obtained from each patient at the time of coronary MDCT angiography examination including a positive family history of premature CAD (occurring before the age of 55 years in men and before 65 years in women), current smoking history (more than 10 cigarettes per day in the last year), a history of hypertension or use of anti-hypertension medications, a history of diabetes mellitus or use of insulin or diabetes lowering drugs, and measurement of body weight and height to calculate body mass index (BMI) and define obesity (BMI ≥ 30).

Socioeconomic status was measured by two indicators: economic status and educational attainment. Additional questionnaires on educational level and economic status were obtained by trained medical staff.

Patients were categorised into four groups according to their educational attainment: group 1 patients not receiving formal education (32 patients, 17%), group 2 patients who had elementary school education (78 patients, 42%), group 3 patients who had a bachelor's degree (60 patients, 32%), and group 4 patients who achieved a higher educational degree (MSc or PhD) (16 patients, 9%).

With regard to the economic status, the government provides a food ration card to families with a total monthly income below 1500000 Iraqi Dinar (equal to $1200) according to the Iraqi ministry of trade database.

As the family size (number of children less than 18 years old in the family) may affect the economic status and total income, family size was included in the classification of economic status.

According to the food ration card presence and the number of children in the family, the patients were classified into four groups: group 1 with a monthly income above $1200 and number of children < 4 (high economic status) (18 patients, 10%), group 2 patients with a monthly income above $1200 and number of children ≥ 4 (52 patients, 28%) (high-intermediate economic status), group 3 patients with a monthly income below $1200 and number of children < 4 (26 patients, 14%) (low-intermediate economic status), and group 4 patients with a monthly income below $1200 and number of children ≥ 4 (low economic status) (90 patients, 48%).

CT scan protocol

Computed tomography (CT) coronary angiography was performed with a 64-slice scanner (Aquilon 64, v. 4.51 ER 010; Toshiba Medical Systems, Tochigi, Japan). Before multi-slice CT angiography was performed, a non-contrast CT was acquired to measure the calcium score according to the Agatston method total heart calcium (summed across all lesions identified within coronary arteries) using a sequence scan with a slice thickness of 3 mm. Coronary calcification area was defined as at least three contiguous voxels with a CT density > 130 Hounsfield units (HU). When the patient's heart rate was more than 65 bpm, a beta-blocker (metoprolol; 20–60 mg orally) was administered before the scan. A bolus of 80 mL contrast medium (Omnipaque; 350 mg/mL iodine) was injected intravenously at a rate of 5 mL/s, followed by 30 mL of normal saline. The scan was obtained from the aortic arch to the level of the diaphragm during a single breath hold. Using retrospective electrocardiography (ECG)-gating and ECG-dependent tube current modulation, the following parameters were obtained: collimation, width 32.5 × 32.5 cm; slice thickness, 0.5 mm; rotation time, 0.35 s; tube voltage, 120 kV; maximum effective tube current, 890 mA; and table feed, 0.3 mm/rotation at 75% of R-R cardiac cycle. Examination time took ~10 s.

Computed tomography images were reconstructed using a smooth kernel (B25f) with a slice thickness of 0.5 mm (increment of 0.3 mm). CT data sets were transferred to a dedicated workstation (Vitrea 2 Workstation; Vital Image, Plymouth, MN, USA) for image analysis.

Pericardial fat volume was defined as any fat tissue located within the pericardial sac and measured three-dimensionally with the contrast-enhanced phase. The layer of the pericardium was manually traced, and a three-dimensional image of the heart was constructed. Then the pericardial fat volume was quantified by calculating the total volume of the tissue whose CT density ranged from –250 to –20 HU within the pericardium by using three-dimensional workstation statistical analysis (Fig. 1A, B). All MDCT images were assessed blindly by two radiologists with more than five years' experience in coronary MDCT angiography interpretation. To assess the inter-observer and intra-observer variability of PFV measurement, 50 patients were randomly selected for the assessment. The intra-observer and inter-observer correlation coefficients were 0.97 and 0.95, indicating good reproducibility and reli-

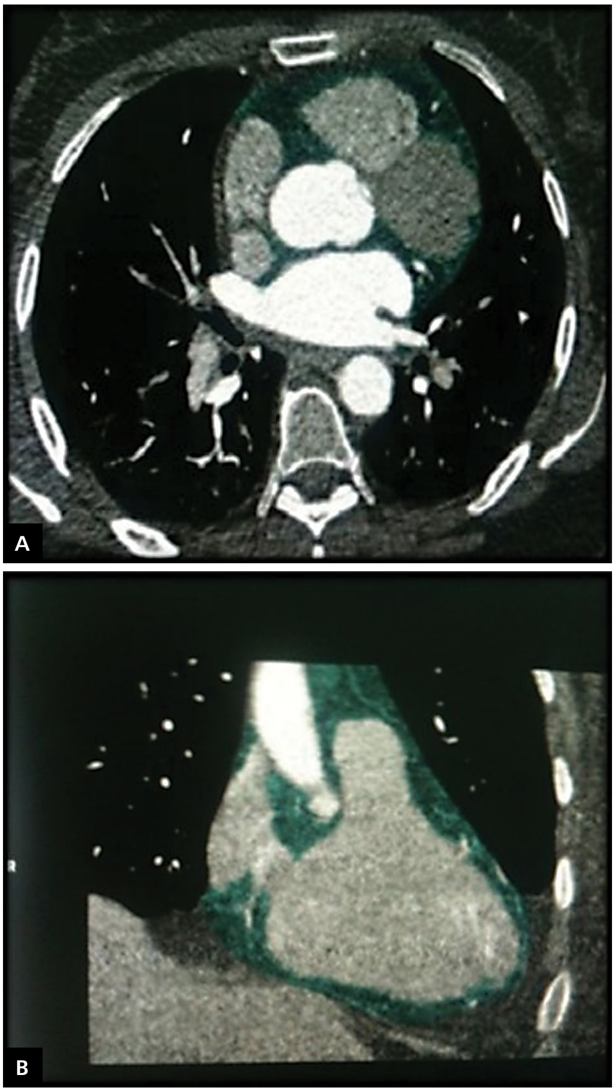

Figure 1. Measurement of pericardial fat volume (green shading) by multi-detector computed tomography in the (**A**) axial and (**B**) coronal sections of the heart

ability. In the case of observer readings differences, the mean of two measurements taken by two radiologists was reported in our study.

Statistical analysis

Data are presented as mean ± standard deviation, numbers with percentages, or as median (inter-quartile range [IQR]), as appropriate. Continuous variables were compared using the analysis of variance or non-parametric test (Mann Whitney U test), as appropriate. Associations between CAC and PFV with cardiac risk factors, educational level, and economic status were examined using Spearman's rank correlation for nonparametric data. Multiple regression analysis was used to analyse the association of educational level and economic status with PFV after adjustment for age, sex, hypertension, smoking, diabetes mellitus, BMI, and family history of premature coronary disease. A p-value of less than 0.05 was considered statistically significant. SPSS ver. 13.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis.

RESULTS

This study comprised 186 patients (108 females [58%] and 78 males [42%] with a mean age of 51.7 ± 12 years and range from 34 to 71 years) with a prior history of chest pain (n = 129), dyspnoea (n = 35), syncope (n = 9), an equivocal exercise tolerance test (n = 8), and others (n = 5) who underwent 64-slice MDCT angiography examinations for assessment of CAD. PFV median (IQR) was 68 (33–112) cm^3 and coronary calcium score median (IQR) was 0 (0–52). Patients' characteristics are summarised in Table 1.

Economic status

Low economic status patients showed higher PFV values (median [IQR] was 94 (50–140] cm^3), p = 0.00001 and r = 0.37, compared to patients with high income (PFV median [IQR] was 30 [19–40] cm^3).

The association between low economic status and high PFV persisted even after multiple logistic regression to conventional cardiac risk factors (p = 0.004, CI 7.3–30.4).

Patients with low economic status showed a higher calcium score (but statistically non significant, p = 0.12) (median [IQR] 0 [0–93]) compared to high economic status patients (CAC median [IQR] was 0 [0–12]).

With regards to the distribution of cardiac risk factors, hypertension and family history of premature coronary disease were more prevalent in low economic status patients compared to high economic status patients (p = 0.002, p = 0.03, respectively) while there were no significant differences in the distribution of other risk factors between the economic status groups (Tables 2, 3)

Educational level

Pericardial fat volume showed a significant inverse correlation with educational level (p = 0.01, r = 0.184) where patients with no formal education reported a higher PFV (median [IQR] was 93 [48–140] cm^3, p= 0.01) compared to patients with a bachelor's degree (median [IQR] was 56 [28–92] cm^3, p = 0.05). However, this association was attenuated after further adjustment for cardiac risk factors, age, and sex (p = 0.1, CI –9.52–10.88).

Coronary artery calcification showed no significant correlation with educational level (p= 0.2, r = 0.117). Hypertension was more prevalent in patients with lower educational levels compared to patients with higher educational levels (p = 0.002) as in Tables 3 and 4.

CAC and PFV

Coronary artery calcification was significantly correlated with male sex (p = 0.000, r = 0.3), increasing age (p = 0.00004, r = 0.27), and hypertension (p = 0.007, r = 0.19).

Table 1. Patients' characteristics

Parameter	Male N = 78 (42%)	Female N = 108 (58%)	p
Age [years], mean ± SD	56 ± 10	49 ± 11	0.0001
Coronary calcium score, median (IQR)	18 (0–112)	0 (0–7)	0.003
PFV [cm^3], median (IQR)	65 (35–101)	70 (30–128)	0.3
Risk factors:			
Hypertension	44 (56%)	52 (48%)	0.5
Smoking	4 (5%)	3 (2.5%)	0.7
Diabetes mellitus	18 (23%)	32 (29%)	0.4
Obesity	26 (33%)	52 (48%)	0.1
Family history	26 (33%)	20 (19%)	0.07
Educational status:			
Lower education (no formal education	8 (10%)	24 (22%)	0.07
Higher education (MSc or PhD)	8 (10%)	8 (7%)	0.5
Economic status:			
Low	38 (49%)	52 (48%)	0.9
High	4 (5%)	14 (13%)	0.1

IQR — interquartile range; SD — standard deviation; PVF — pericardial fat volume

Table 2. Distribution of pericardial fat volume (PFV), coronary artery calcification, and cardiac risk factors between economic status groups

Parameter	Group 4 (low economic status; n = 90)	Group 3 (low-intermediate economic status; n = 26)	Group 2 (high-intermediate economic status; n = 52)	Group 1 (high economic status; n = 18)	p
Calcium score, median (IQR)	0 (0–93)	0 (0–0)	0 (0–35)	0 (0–12)	0.12
PFV [cm^3], median (IQR)	94 (50–140)	70 (31–81)	50 (25–93)	30 (19–40)	0.00001
Hypertension	60	7	17	12	0.002
Diabetes mellitus	23	7	14	6	0.3
Smoking	2	1	2	2	0.7
Family history	23	8	10	5	0.03
Obesity	38	13	15	12	0.3
Male	40	10	20	8	0.6
Female	50	16	32	10	0.6

IQR — interquartile range

Pericardial fat volume was significantly correlated with obesity ($p = 0.00003$, $r = 0.4$), hypertension ($p = 0.00001$, $r = 0.36$), and increasing age ($p = 0.00005$, $r = 0.29$).

Coronary artery calcification showed no significant statistical correlation with PFV in our study ($p = 0.8$, $r = 0.01$), as in Figure 2.

DISCUSSION

In the present study, a high PFV was significantly associated with lower SES, particularly economic status measure, while CAC showed no significant association with SES despite the high calcium score observed in lower SES.

Several prospective and cross-sectional studies in different countries have reported the inverse association of social class with cardiovascular morbidity and mortality independent of conventional risk factors or access to health care, and this association was also found in countries with universal healthcare systems, as in our country [8–11].

However, the pathways and mechanisms through which SES is linked to CVD are not fully determined and remain unclear.

Table 3. Multiple regression analysis of pericardial fat volume (PFV) with conventional cardiac risk factors, educational status, and economic status

Variables	PFV		
	β	CI	P
Low economic status	0.181	7.3–30.4	0.004
High educational status	0.011	–9.52–10.88	0.1
Age	0.135	–0.13–1.55	0.09
Hypertension	0.242	11.2–50.3	0.002
Diabetes mellitus	0.072	–8.1–29.4	0.2
Smoking	0.084	–131–28.5	0.3
Family history	0.131	–0.25–38.7	0.05
Body mass index	0.342	2.9–6.8	0.0001
Male gender	0.047	12.3–24.5	0.5

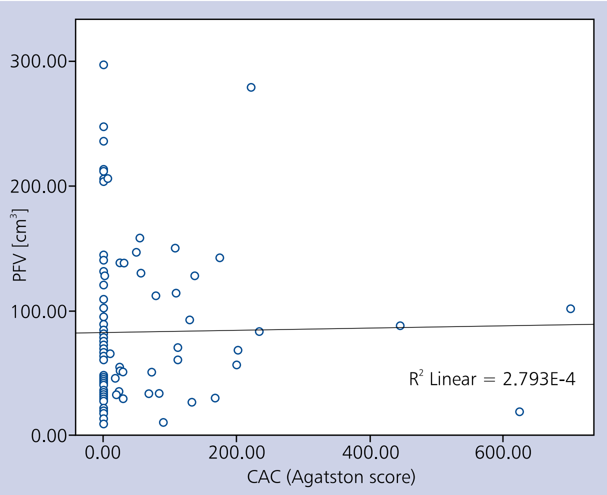

Figure 2. No significant correlation was observed between coronary artery calcification (CAC) and pericardial fat volume (PFV)

There is difficulty in the analysis of our results due to the lack of directly comparable research on the relationship between SES and PFV.

However, PFV was found in recent literature to be related to myocardial ischaemia, acute coronary syndrome and coronary atherosclerosis severity, and prognosis via a local paracrine effect on adjacent coronary artery segments leading to local inflammation [7, 12].

It has been postulated that cardiac adipose tissue, as a source of inflammatory mediators, which modulates a number of physiological and pathophysiological processes, may have a fundamental role in the development and progression of coronary atherosclerosis with potential therapeutical implications of these inflammatory activities in CAD interventions [13, 14].

Interestingly, the inflammatory activity of cardiac fat deposit is reported to be greater than in thoracic and subcutaneous fat deposit and independent of BMI, and may contribute to coronary atherosclerosis burden [14].

Furthermore, a significant correlation was observed between PFV and coronary endothelial dysfunction and carotid intima–media thickness independent of conventional risk factors [15].

Cooper et al. [9] studied the relationship of endothelial dysfunction with SES measured by education, occupation, and income indicators in 72 healthy adults and found that patients with lower SES reported reduced endothelial function, suggesting that impaired arterial endothelial function, which often precedes CAD, could be a possible pathway linking SES with CVD.

Moreover, low educational status was significantly associated with cardiac inflammatory markers, especially C-reactive protein and interleukins [11, 16].

Pericardial fat, owing to the anatomical proximity with coronary arteries and heart, was found to contain higher levels of inflammatory markers that can locally accelerate the atherosclerotic process by endothelial dysfunction [7, 17, 18].

Table 4. Distribution of pericardial fat volume (PFV), coronary artery calcification, and cardiac risk factors between educational status groups

Parameter	No formal education N = 32	Elementary school N = 78	Bachelor's degree N = 60	MSc or PhD N = 16	p
Calcium score, median (IQR)	0 (0–68)	0 (0–30)	0 (0–31)	0 (0–77)	0.23
PFV [cm³], median (IQR)	93 (48–140)	67 (32–114)	56 (28–92)	61 (35–122)	0.01
Hypertension	24	48	18	6	0.002
Diabetes mellitus	12	21	15	2	0.2
Smoking	3	1	2	1	0.6
Family history	10	17	12	7	0.1
Obesity	16	38	22	2	0.08
Male	6	36	28	8	0.02
Female	26	42	32	8	0.02

IQR — interquartile range

There is a considerable uncertainty regarding the mechanisms linking SES to CAD. Several studies suggest that conventional cardiac risk factors, biological markers, and mental stress or depression are important pathways that may explain the association of SES with CAD [11, 19, 20].

The findings of our study highlight the possible role of PFV in linking SES to CAD.

The relationship of SES with CAC showed inconsistent results in previous studies [21–23].

A cross-sectional study conducted by Colhoun et al. [21] investigated the impact of socioeconomic position measured by current occupation and educational status on the prevalence of CAC in 149 young people without a history of CAD. They found a significant association between socioeconomic class and prevalence of CAC [21].

However, this study used different measures of social class definition in relatively young healthy cohorts.

A Dan Risk screening sub-study analysed the SES measured by occupation and educational level in healthy Danish males and females aged over 50 years found that CAC was associated with lower occupational status in females but not males [22].

Furthermore, an analysis of the Multi-Ethnic Study of Atherosclerosis (MESA) demonstrated an inverse association between education and the presence of CAC in white participants but not in other ethnic groups, and the association was no longer significant after adjustment for cardiac risk factors [23].

On the other hand, Steptoe et al. [3] reported that social status did not predict the presence of calcification but was related to the severity of CAC, suggesting that lower social class may be particularly relevant at advanced stages of subclinical CAD when calcification has developed [3].

In our study, coronary calcium scores were non-normally distributed because of large percentages of zero readings where the CAC median was zero for both low and high educational and economic status, and hence may contribute to the non significant relationship with socioeconomic parameters.

In the present study, PFV showed no significant correlation with CAC, and this finding supported the hypothesis that PFV is associated with an active atherosclerosis process that may precede CAC, and CAC could represent a stable and late phase of coronary atherosclerosis [6, 7].

A potential strength of our study is that we used objective markers of subclinical coronary atherosclerosis (CAC and PFV) plus the adjustment of our results for multiple confounders.

Limitations of the study

There were several limitations in this study. First, the study was a single-centre investigation and the population was not randomly selected because it involved only patients with suspected CAD based on physician referral. There is, therefore, the possibility of selection bias. Second, the number of patients was relatively small. Third, a causal relationship between SES measures with CAC and PFV cannot be established because of the cross-sectional nature of our study. Fourth, dyslipidaemia was not included in the statistical analysis due to the absence of lipid profile data or patients were already on lipid lowering drugs.

Further studies using larger population sizes and including follow-up are needed to establish a causal relationship of SES with coronary atherosclerosis markers that will facilitate better risk stratification for CVDs and help physicians to initiate appropriate interventions earlier, which in turn may arrest the progression of coronary atherosclerosis.

CONCLUSIONS

Socioeconomic status, particularly economic status measure, showed a significant inverse relationship with PFV independent of conventional cardiac risk factors. Further studies using larger population sizes are required to highlight the possible role of PFV in linking SES to coronary atherosclerosis.

What is already known: Little data currently exists on the correlation of SES to markers of coronary atherosclerosis.

What this study adds: The findings highlighted the possible role of PFV in linking SES to coronary atherosclerosis.

Conflict of interest: *none declared*

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Zależności między statusem socjoekonomicznym a zwapnieniem tętnic wieńcowych i objętością okołosercowej tkanki tłuszczowej

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Streszczenie

Wstęp: Niewiele danych potwierdza korelacje między statusem socjoekonomicznym (SES) a wskaźnikami subklinicznej miażdżycy tętnic wieńcowych.

Cel: Głównym celem badania była analiza zależności między SES mierzonym na podstawie sytuacji ekonomicznej i poziomu wykształcenia a zwapnieniem tętnic wieńcowych (CAC) oraz objętością okołosercowej tkanki tłuszczowej (PFV) ocenianą metodą multidetektorowej tomografii komputerowej (MDCT).

Metody: W okresie od stycznia 2014 r. do marca 2015 r. do badania włączono 220 kolejnych pacjentów z podejrzeniem choroby wieńcowej, u których wykonano angiografię metodą 64-rzędowej MDCT w celu oceny miażdżycy tętnic wieńcowych. Spośród tej grupy ostatecznie do niniejszego badania przekrojowego włączono 186 chorych

Wyniki: U osób o niskim SES stwierdzono wyższe wartości PFV — mediana (zakres międzykwartylowy [IQR]) wynosiły 94 (50–140) cm^3, p = 0,00001, r = 0,37 — w porównaniu z osobami o wysokim SES. Zależność ta utrzymywała się nawet po wielokrotnej regresji logistycznej w odniesieniu do tradycyjnych czynników ryzyka chorób serca (p = 0,004; CI = 7,3–30,4). Wskaźnik uwapnienia tętnic był wyższy u chorych o niskim SES niż u osób o wyższym SES, ale różnica nie była statystycznie istotna (p = 0,12). U chorych nieposiadających formalnego wykształcenia wartości PFV (mediana [IQR] były wyższe niż u absolwentów wyższych uczelni (odpowiednio 93 [48–140] cm^3, p = 0,01 i 56 [28–92] cm^3), jednak te zależności były słabsze po skorygowaniu względem tradycyjnych czynników ryzyka chorób serca (p = 0,1;CI –9,52–10,88). Nie stwierdzono natomiast istotnych korelacji między CAC a poziomem edukacji (p = 0,2; r = 0,117).

Wnioski: Istnieje istotna odwrotna zależność między SES, zwłaszcza sytuacją ekonomiczną, a PFV, niezależnie od tradycyjnych czynników ryzyka chorób serca.

Słowa kluczowe: miażdżyca, tętnica wieńcowa, zwapnienie, MDCT, okołosercowa tkanka tłuszczowa, stan socjoekonomiczny

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