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INCIDENCE AND RISK FACTORS OF CORONARY CALCIFICATIONS ON STAGING AND FOLLOW-UP CT CHEST IN CANCER PATIENTS IN SAUDI ARABIA

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ABSTRACT

Objectives: Cardiovascular diseases have collectively remained as the leading causes of mortality globally. This research aimed to assess the incidence and risk factors of coronary calcifications (CC) on staging and follow-up CT chest.

Methods: This retrospective study involved 124 patients from Saudi Arabia who have been diagnosed with previous malignancies from October 15, 2023 to June 6, 2024.

Results: We had 75 (60.5%) females and 49 (39.5%) males, ages between 1 and 86 years, with a mean age of 56.71 years (SD = 15.9). Common cardiac risk factors in this study were hypertension (23.4%) and diabetes (21.8%). The most frequent treatment type used for these patients was chemotherapy (63.7%), followed by radiotherapy (18.5%). Out of the 124 patients, 30.6% exhibited coronary calcifications. Significant predictors of coronary calcifications included age ($p < 0.001$), gender ($p < 0.001$), hypertension ($p = 0.019$), diabetes ($p = 0.002$), and dyslipidemia ($p = 0.016$). Regression model revealed that males ($p = 0.006$) and older age groups ($p < 0.05$) have significantly higher odds of having coronary calcifications. Diabetes, with close significance values ($p = 0.064$), could potentially be a significant risk factor in a larger population.

Conclusion: Reporting coronary calcifications on staging and follow-up CT scans could be a useful method for pinpointing patients at high risk for cardiovascular disease events, allowing them to receive beneficial preventive measures.

Keywords: cardiovascular disease, coronary artery disease, coronary calcifications, cancer

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1. INTRODUCTION

Cardiovascular disease (CVD) is a primary cause of health-related death worldwide with coronary artery disease (CAD) being the major contributor [1]. Currently, it is the princi-

pal cause of Saudi Arabia's mortality, approximating 45.7% of all mortality, with an annual mortality rate of 294 per 100,000 people, in addition to the 3,702 per 100,000 individuals suffering from non-fatal CVD. It is estimated that CVD prevalence will rise affecting more than 479,500 individuals in the country by 2035 [2].

As such, the optimization of CVD management was identified as a critical area that can help saving lives over the next ten years based on the 2019 NHS Long Term Plan and the 2021 National Institute of Health and Care Excellence (NICE) Impact Cardiovascular Disease Management Report. The advancements in cardio-oncology field have developed in the recent years, optimizing outcomes in oncology patients who have heart disease. Cardio-oncologists' role is to assess patients' cardiac risks as part of safe and guided cancer therapy, consequently limiting the death linked with cardiotoxic therapies and cardiovascular complications that may progress after the cancer treatment. The prognosis for cancer patients treated with anti-cancer signaling inhibitors, radiation therapy, and chemotherapy has significantly improved due to these developments [1, 3].

Evaluating the occurrence and impact of coronary artery calcifications (CAC) has become a choice for cardiovascular risk stratification as cancer patients are commonly subjected to routine screening chest CT scans on which CAC is readily spotted. CAC is an imaging biomarker of CAD, and its severity can be an overview of the general impacts of underlying CAD and its prognosis [1, 3]. Although CAC score is typically quantitatively assessed using electrocardiogram (ECG) gated non-contrast enhanced cardiac computed tomography (CT) scans [4] utilizing the Agatston scoring system, in recent studies it was noted that using non-gated CT showed excellent diagnostic accuracy. Coronary artery calcifications are often underreported despite its role in determining patients at risk for cardiovascular events who could benefit from early risk stratification and main prevention of coronary events [5, 6].

The presence of incidental CAC was significantly linked with an elevated risk of cardiovascular-associated mortality in the National Lung Screening Trial [7]. A 2021 work by Yu et al. demonstrated that incidental CAC visualized on unenhanced non-gated CT scans is linked with higher major adverse cardiovascular events (MACE) among hospitalized patients [8]. The underreporting of these findings may signify a missed chance to spot subclinical coronary disease among such patients and in improving preventive cardiology care. Hence, international guidelines suggest reporting CAC on all unenhanced chest CTs. A 2020 consensus report by the British Society of Cardiovascular Imaging/British Society of Cardiac Computer Tomography (BSCI/BSCCT) and British Society of Thoracic Imaging (BSTI) stated that CAC must be reported regardless of the indication or acquisition protocol. This initiative represents a significant advancement in patient management. [9].

Our study aimed to (1) evaluate and measure the incidence of coronary calcifications in patients who are undergoing staging and follow-up CT chest scans and (2) determine the potential impact on cardiovascular risk assessment in this population.

2. METHODS

A retrospective observational study was performed for cancer patients from King Abdulaziz University Hospital (KAU Hospital) from October 15, 2023 to June 6, 2024 who had CAC identified on staging and follow-up CT scans. Chest CT scans were screened individually by one certified radiologist specialized in CardioThoracic Imaging. Each CT scan was reviewed using visual assessment to determine the occurrence and degree of severity of CAC. Patients were not included if their clinical information was incomplete, and the presence of cardiovascular risk factors could not be determined. For the 124 patients chosen, medical records such as demographic characteristics (age and gender), documented cardiac risk factors, and type of cancer treatment undergone, were extracted.

Collected data was organized and visualized using IBM SPSS version 27 (IBM Corp. Inc., Armonk, NY). Descriptive statistics were utilized to summarize the study variables, with categorical variables presented as counts and percentages, while continuous variables were described by means and standard deviations. Relationships between categorical variables were evaluated using chi-square tests, assuming normal distribution. A binary logistic regression model with backward conditional elimination was employed to determine significant predictors of coronary calcifications, with the entry criterion set at $p < 0.05$ and elimination at $p < 0.10$. Results were interpreted with a 95% confidence interval, and significant correlations was considered at $p < 0.05$. Non-significant outcomes may be attributed to the small sample size and should be considered a limitation, as clinically relevant trends were observed even when statistical significance was not achieved.

3. RESULTS

This study reviewed 124 medical records, including 75 females (60.5%) and 49 males (39.5%). The average age was found to be 56.71 years (SD of 15.9), ranging from 1 to 86 years. Common cardiac risk factors included hypertension (23.4%) and diabetes (21.8%), while 64.5% reported no cardiac risk factors. The most frequent treatment type was chemotherapy (63.7%), followed by radiotherapy (18.5%), with a small percentage receiving hormonal, steroid, or biological therapies. The demographic characteristics, known cardiac risk factors, and type of cancer treatment undergone for the included patients from KAU hospital are described in Table 1.

Table 1 Demographic characteristics, known cardiac risk factors, and type of cancer treatment donefor the included patients from KAU hospital.

Demographics	**N**	**Min**	**Max**		
Age	124	1	86	56.71	15.9
		Count		**%**	
Total		124		100.0	
Gender	Male	49		39.5	
	Female	75		60.5	
Age	<=45	28		22.6	
	46-60	35		28.2	
	61-75	51		41.1	
	75>	10		8.1	
C ardiac risk factors					
Total			124		100.0
Hypertension			29		23.4
Diabetes			27		21.8
Dyslipidemia			7		5.6
Cardiac pacemaker			1		0.8
None			80		64.5
Type of Cancer treatment			124		100.0
Chemotherapy			79		63.7
Hormonal therapy			5		4.0
Radiotherapy			23		18.5
Steroid therapy			1		0.8
Biological therapy			1		0.8
Treated surgically or Not treated			37		29.8

Table 2 shows the CT chest types done and the classification of coronary calcifications found in the included patients from KAU hospital. Most patients underwent CT Chest C+ (90.3%), on which only 38 (30.6%) patients were identified with coronary calcifications, while the remaining 69.4% were not. The severity of coronary calcifications was classified into mild, moderate, and severe, distributed across LAD, LCX, LCA, and RCA (Figure 1).

Table 3 , Figures 2, 3 and 4 shows the association of coronary calcifications and the followingdemographic characteristics, known cardiac risk factors and type of cancer treatment done for the included patients from KAU hospital. Significant predictors of coronary calcifications include gender ($p < 0.001$), age ($p < 0.001$), hypertension ($p = 0.019$), diabetes ($p = 0.002$), and dyslipidemia ($p = 0.016$). Males, older age groups, and those with hypertension, diabetes, or dyslipidemia have significantly higher rates of calcifications.

describes the binary logistic regression among the variables and coronary calcifications. The regression model shows that males ($p = 0.006$) and patients aged 46-60 and 61-75 ($p = 0.035$) have significantly higher odds of having coronary calcifications. Diabetes showed

Table 2 CT chest types and classification of severity of coronary calcifications found from the included patients fromKAU hospital.

				Count	%
Total				124	100.0
	CT CHEST C-			6	4.8
	CT CHEST C+			112	90.3
	CT HIGH RESOLUTION CHEST HRCT			6	4.8
Coronary	Yes			38	30.6
	No			86	69.4
Coronary calcifications = Yes n=38	**LAD**	**LCX**	**LCA**		**RCA**
Mild	15(41.7)	4(30.8)	1(33.3)		3(50.0)
Moderate	9(25.0)	4(30.8)	1(33.3)		2(33.3)
Severe	12(33.3)	5(38.4)	1(33.3)		1(16.7)

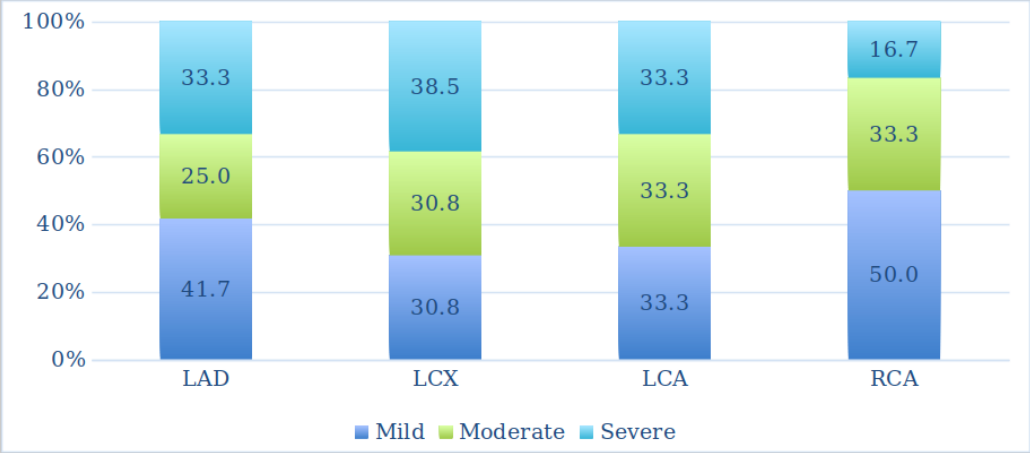

Figure 1 The severity of coronary calcifications.

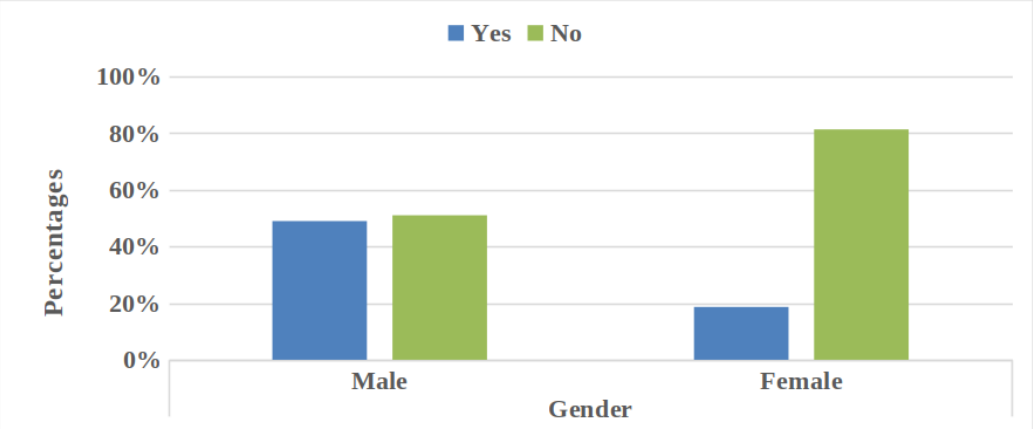

Figure 2 Gender as predictor of coronary calcifications

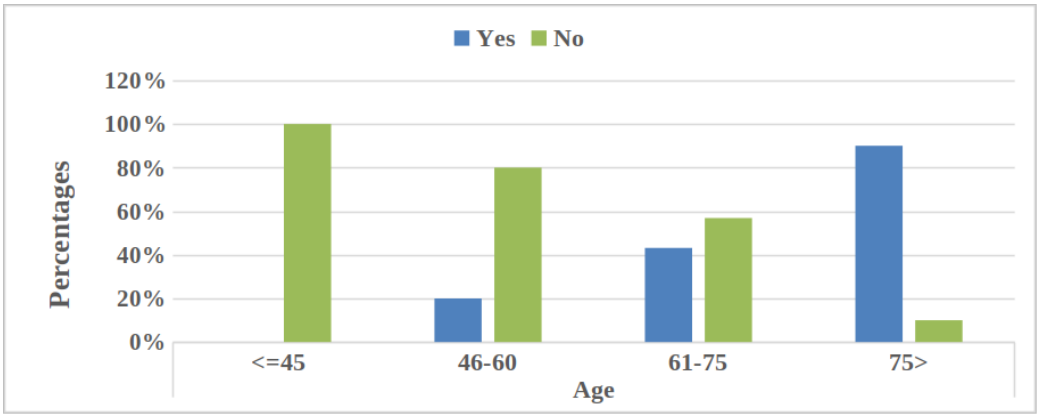

Figure 3 Age as predictor of coronary calcifications.

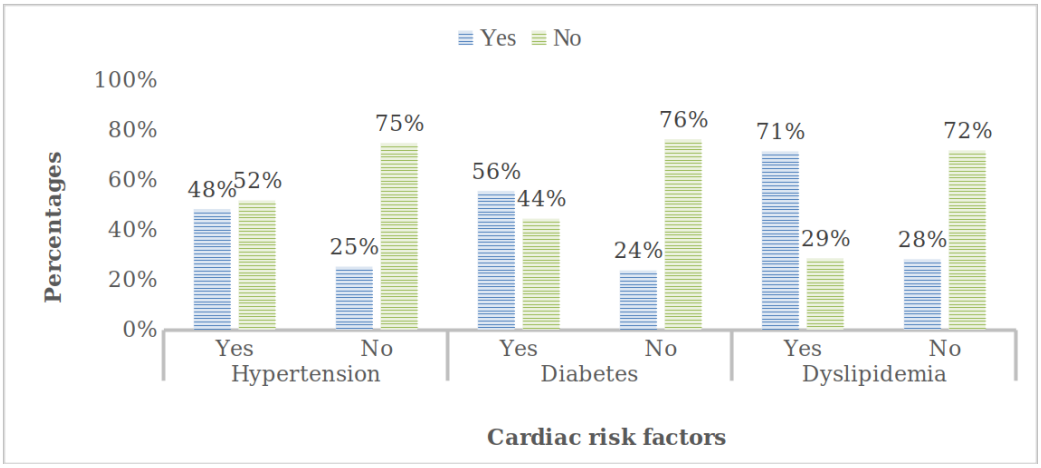

Figure 4 Cardiac risk factors as predictor of coronary calcifications.

a value close to significance (p = 0.064), as part of cardiac risk factor.

4. DISCUSSION

This retrospective study is an analysis of the incidence of coronary calcifications on staging and follow-up CT chest of cancer patients in Saudi Arabia and how cardiovascular risk assessment affects the clinical outcomes for this population.

The study suggested a female predominance of 60.5% compared to 39.5% of males, with ages between 1 and 86 years, and a mean age of 56.71 years (SD = 15.9). Common cardiac risk factors in the study were hypertension (23.4%) and diabetes (21.8%). Supporting this, is a 10-year cohort study from Iran, where age was the main risk factor indicative of CAD events, with a hazard ratio (HR) and confidence interval (CI) of 5.56 (3.87–7.97, p

Table 3 Relationship Between Coronary Calcifications and Variables.

Variables		Total	Coronary calcifications		p-value
			Yes	No	
Total		124	38(30.6%)	86(69.4%)	-
Gender	Male	49	24(49.0%)	25(51.0%)	<0.001[a]
	Female	75	14(18.7%)	61(81.3%)	
Age	<=45	28	0(0.0%)	28(100.0%)	<0.001[a]
	46-60	35	7(20.0%)	28(80.0%)	
	61-75	51	22(43.1%)	29(56.9%)	
	75>	10	9(90.0%)	1(10.0%)	
Exam Type	CT CHEST C-	6	2(33.3%)	4(66.7%)	0.978
	CT CHEST C+	112	34(30.4%)	78(69.6%)	
	CT HIGH RESOLUTION CHEST HRCT	6	2(33.3%)	4(66.7%)	
Type of cancer treatment:					
Chemotherapy	Yes	79	22(27.8%)	57(72.2%)	0.371
	No	45	16(35.6%)	29(64.4%)	
Hormonal	Yes	5	2(40.0%)	3(60.0%)	0.643
	No	119	36(30.3%)	83(69.7%)	
Radiotherapy	Yes	23	4(17.4%)	19(82.6%)	0.127
	No	101	34(33.7%)	67(66.3%)	
Treated surgically or Not treated	Yes	37	13(35.1%)	24(64.9%)	0.479
	No	87	25(28.7%)	62(71.3%)	
Cardiac risk factors					
Hypertension	Yes	29	14(48.3%)	15(51.7%)	0.019[a]
	No	95	24(25.3%)	71(74.7%)	
Diabetes	Yes	27	15(55.6%)	12(44.4%)	0.002[a]
	No	97	23(23.7%)	74(76.3%)	
Dyslipidemia	Yes	7	5(71.4%)	2(28.6%)	0.016[a]
	No	117	33(28.2%)	84(71.8%)	

[a]-significant using Chi-Square Test at 0.05 level.

< 0.001) among men older than 45 years and females over 55 years in comparison to lower age groups. Nearly 80% of the patients also had dyslipidemia, with an HR of 2.19 (CI: 1.40-3.44, p = 0.01). Among the participants, 28.9% had hypertension, and 17% had diabetes, with an HR of 2.63 (CI: 2 -3.47, p < 0.001) [10]. The most common treatment type was chemotherapy (63.7%), followed by radiotherapy (18.5%). Cancer treatments are known to have long-term cardiovascular effects, which may contribute to the observed calcifications. A 2018 retrospective study revealed significant increase in CAC, having mean rise of $\geq$ 35% in the CAC score. Chemotherapy may negatively impact coronary calcium scoring (CCS), consequently acting as an early indicator of chemotherapy-induced cardiac toxicity in lymphoma patients [11]. Another 2020 study revealed on interval CT scans that a greater

Table 4 Binary logistic regression among the variables and coronary calcifications.

Variables in the Equation		B	S.E.	Exp(B)	95% C.I.for EXP(B)		p-value
Dependent Variable: Coronary calcifications					**Lower**	**Upper**	
First Step[a]	**Gender**						
	Male	-1.264	0.506	0.282	0.105	0.761	0.012[b]
	Age						0.018[b]
	<=45	22.894	7398.048	8.760E+09	0.000		0.998
	46-60	3.587	1.184	36.112	3.544	367.934	0.002[b]
	61-75	2.488	1.120	12.038	1.339	108.219	0.026[b]
	Cardiac risk factors:						
	Hypertensio	-0.337	0.568	0.714	0.234	2.176	0.554
	Diabetes	-0.614	0.604	0.541	0.165	1.768	0.309
	Dyslipidemi	-1.016	0.992	0.362	0.052	2.532	0.306
	Constant	-1.221	1.128	0.295			0.279
Last Step[a]	**Gender**						
	Male	-1.365	0.495	0.255	0.097	0.674	0.006[b]
	Age						0.024[b]
	<=45	22.799	7383.199	7.967E+09	0.000		0.998
	46-60	3.381	1.164	29.390	3.003	287.618	0.004[b]
	61-75	2.349	1.115	10.471	1.178	93.054	0.035[b]
	Cardiac risk factors:						
	Diabetes	-0.984	0.532	0.374	0.132	1.060	0.064
	Constant	-1.105	1.118	0.331			0.323

[a]-Variable(s) entered on step 1: Gender, Age, Cardiac risk factors: Hypertension, Diabetes, Dyslipidemia.[b]-Significant using Binary Logistic Regression Model, with Backward Conditional Elimination with Enter Criteria=0.05, Elimination =0.10.

proportion of patients who received radiation demonstrated new coronary calcifications (P = 0.007) and progression within the LAD (P = 0.003) [12].

Older age ($p < 0.001$), male gender ($p < 0.001$), and specific cardiac risk factors including hypertension ($p = 0.019$), diabetes ($p = 0.002$), and dyslipidemia ($p = 0.016$) contribute significantly to the presence of coronary calcifications. Moreover, in the study, the results from the regression confirm that male gender ($p = 0.006$) and patients ages 46-60 and 61-75 ($p < 0.05$) are strong predictors of coronary calcifications. Diabetes, having close significance ($p = 0.064$), could potentially be an important clinical factor, especially in larger populations.

5. CONCLUSION

Improving cardiovascular outcomes for cancer patients and survivors is a vital global health goal. Coronary artery calcium screening on staging and follow-up CT scans is a proposed modality for identifying patients with high risk for cardiovascular disease, consequently giving them the benefits of preventive interventions.

6. FUNDING

This research was conducted without any specific funding from public, commercial, or not-for-profit organizations.

CONFLICT OF INTEREST

The author declares no conflict of interests.

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