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Age-Linked Variations of troponin-I Values in Patients with Acute Coronary Syndrome

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Abstract
Background: The cardio-peptide troponin-I (CTn-I) can regulate actin-myosin cross-bridging, specifically to cardiomyocytes**.** Age alterations in the levels of CTn-I levels have become a new debatable emphasis. As well, it is frequently hard to interpreting how to manage aging people when a high CTn-I level is noticed. Acute coronary syndrome (ACS) is the principal cause of mortality worldwide mainly in elderly people. In the present work, we aimed to determine whether an increased CTn-I level varies with age in patients with ACS. **Methodology:** This observational study, involved 150-patients diagnosed as ACS during the period from January to March 2021 from patients attending the ED of Alimam-Alsadiq hospital. Hematological investigations had started at the time of presentation included creatinine, urea, and serum CTn-I. **Results:** mean applicants' age was 59.7years (> $3/4^{th}$ were men), and the mean BMI was 27.0±5.0kg/m^2. The current smokers represented 43.3% of the total. Likewise, the incidence of DM and hypertension were significantly high (42% and 49.8%) respectively. Blood chemical analysis revealed mean creatinine, urea, and CTn-I values were 85.2±9.0mmol/l, 14.1±3.6mmol/l, and 8.9±0.4ng/ml consequently. The sex revealed no much influence on most of the included variables apart from CTn-I that was lesser in females (p-0.005). Risk factors were significantly (*p*-0.001) more among males, which not the case for the incidence of DM. There were no significant deviations of concentrations of CTn-I with increasing ages of ACS patients (*P*>0.05). **Conclusion:** This study highlights that in patients with ACS presented to ED, the routine of CTn-I for the diagnosis of ACS should be interpreted based on the patient's age/sex to adjust diagnostic precision of CTn-I for both sexes.

Keywords: acute myocardial infarction, troponin, chest pain, age.

Introduction
The cardio-peptide troponin-I (CTn-I) can regulate muscles' actin-myosin cross-bridging, specifically to cardiomyocytes since no other biological isoforms of this fraction have even been detected in other muscular tissues. Henceforth, the recent guiding principle for the recognition of ACS and myocardial injury has recommended CTn-I values as a gold-standard indicator of cardiac damage [1, 2].
Acute coronary syndrome (ACS) is the chief source of lethality worldwide [3-7].
Over the past couple of decades, analyses of CTn-I have undergone vast perfections, permitting fast finding of troponin at lower levels with improved precision [8]. These enhanced (high-sensitive) assays have led to a considerable rise in the number of patients with positive CTn-I results of undefined worth. Age and gender variances in the extent of

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CTn-I levels have become a new debatable emphasis [7, 9, 10]. As well, it is often hard to interpret how to manage aging people when a high CTn-I level is noticed.
In the present work, we aimed to determine whether an increased CTn-I level varies with age in patients with ACS.

Methodology and subjects

This observational study, involved 150-patients with a final diagnosis of ACS during the period from January to March 2021 from patients attending the ED of Alimam-Alsadiq hospital. The clinical diagnosis of ACS was confirmed by the cardiologists at the hospital. The hematological investigations had started at the time of presentation included creatinine and urea and had completed based on local available conventional methods. CTn-I had assessed by CALBIOTECH® ELISA assay kit. The chemical analyses had confirmed as quantified by the manufacturing conventions.

A conversant consent at first had gotten from all patients (or attendants), and the entire work had been arranged and authorized by the hospital committee for research ethics.

Statistical analysis
The comparisons of continuous data (expressed as mean±SD) had completed by independent students' *t*-tests for independent variables. A *p*-value < 0.05 agrees statistical significance. The statistical estimations had finished by SPSS, version-17 for Windows. Patients with ACS had classified based on their ages into two classes above and below 40 years.

Results

The mean age of participants was 59.7years, more than 3/4th of them were men, while the mean BMI was 27.0±5.0kg/m^2. The incidence of diabetes mellitus (DM) and hypertension were significantly high (42% and 49.8%) respectively. The current smokers represented 43.3% of the total. Biochemical analysis revealed mean creatinine, urea, and CTn-I values were 85.2±9.0mmol/l, 14.1±3.6mmol/l, and 8.9±0.4ng/ml separately (table-1).

	Age	Males No (%)	Creatinine (mmol/l)	Urea (mmol/l)	BMI (Kg/m^2)	TN-I (ng/ml)	Diabetes No (%)	Hypertension No (%)	Smoking No (%)
Mean	59.7	114 (76)	85.2	14.1	27.0	8.9	63 (42)	74 (49.8)	65 (43.3)
Std. Deviation	12.9		9.0	3.6	5.0	0.4			

The impact of sex variation on the studied variables was shown in tables 2 and 3. There was no influence of sex on most of the included variables (table-2) other than CTn-I that was lesser in females (p-0.005).

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Table-2: Differences of the study variables distributed according to the sex			
Characteristics	**Sex**	**Mean± SD**	***P*-value**
Age (years)	*M*	56.1±0.8	0.28
	F	62.1±1.5	
	F	9.1±0.7	
Creatinine	*M*	85.1±1.9	0.31
	F	75.1±2.9	
Urea	*M*	13.1±1.1	0.35
	F	11.9±1.2	
	F	9.1±1.1	
Cardiac Troponin-I	*M*	9.9±0.1	0.005
	F	5.4±0.3	

The risk factors in this study were significantly (*p*-0.001) more among males, which not the case for the incidence of DM. The males in this study were heavier significantly than females (*p*-0.001) (table-3).

Table-3: Differences in the incidence of risk factors distributed according to the sex			
Risk factors	**Men**	**Women**	***P*-value**
Diabetic	48 (76.2)	15 (23.8)	0.47
Hypertensive	47(63.5)	27 (36.5)	0.001
Smokers	57 (38)	8 (12.3)	0.001
BMI (N %)	29.3 ± (7.8)	21.8 ± 2.6	0.001

Figure-1 revealed that there were no significant deviations of concentrations of CTn-I with increasing ages of ACS patients.

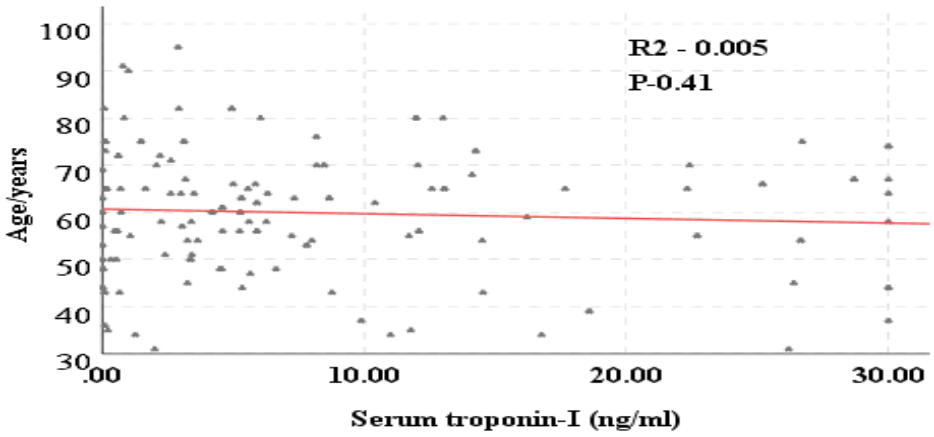

Figure-1: Regression fit of the serum levels of troponin-I with ages of patients

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Figure-2 displayed a nonsignificant statistical difference in the mean serum levels of CTn-I in ACS patients when classified according to their ages (0.34).

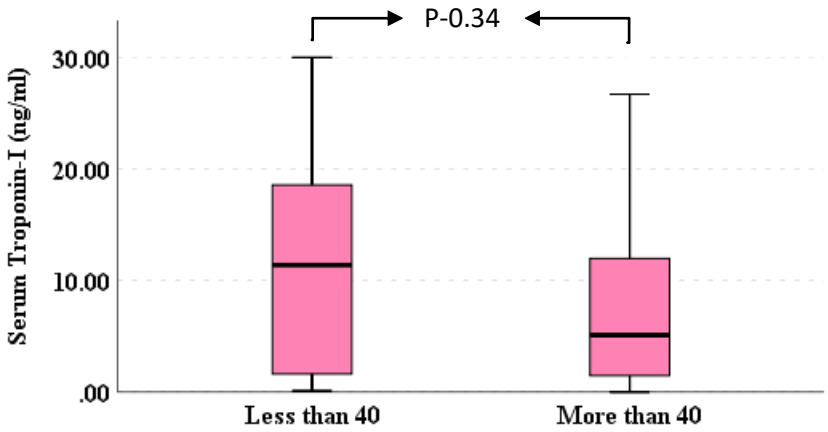

Figure-2: Mean serum levels of troponin-I (ng/ml) according to the age classes

Discussion:

The key finding from the current study is that the serum CTn-I levels relatively unaffected by the increasing ages of patients diagnosed with ACS. The ideologies for the universal definition of ACS estimates are focused on CTn-I measures [1, 11]. Given that the absolute concentration of CTn-I is persuasive in guiding therapeutic protocol, the authors hypothesized that CTn-I levels in the serum varied with the increasing age of the ACS patients. It was recognized, that an increased CTn-I value is well-defined as a measure above the 99th-centile value for the specific assay in ordinary reference people. Nevertheless, there is no agreement about the criteria for picking reference people, and the classification of "normal" is debatable [12]. Similar to our outcomes, the predictive value of CTn-I in ACS attenuates with increased patient' age also reported by another study [13]. The authors had explained this phenomenon partway by frailty and other indefinite confounders. The more lethality in the elders with ACS might cause by insufficient physiological reserve, frailty and increased comorbidities thought similarly driven by less receipt of evidence-based management besides the fact they tend to be treated with an extra conservative approach compared with youngers [14].

Unlike our outcomes, numerous relevant experimental and clinical studies had been published (focusing on ACS), demonstrated obvious rising values of plasma CTn-I among elder patients [15, 16]. In contrast, only limited researchers had observed that the percentile CTn-I values were reliably decreased with increasing age in both sexes [17].

The results of the prior studies conflicting with our results that exposed a circulating CTn-I unaffected by increments of patients' ages. These contradictions have several potential explanations. One of the probable causes is the inequality in inclusion/exclusion criteria of the patients (among the surveys) concerning associated risk factors including DM, systemic hypertension, obesity, and tobacco smoke, which were rather high in this work.

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As well, the application of analytic algorithms that comprise various cutoff values for dissimilar time points (after the time of acute chest pain), in aging subjects and women, presents a level of intricacy that can be unreasonable in a busy ED milieu [18] like that in our situation. Still, a minor CTn-I increase associated with ST-T segment deviations might also arise in stable peoples [19].

Another important issue could be insistent high CTn-I is often detected among patients with end-stage renal disease (ESRD). The prevalence of raised CTn-I among asymptomatic ESRD patients may be as high as 53% [20], which might result from trivial sites of silent clinical cardiomyocyte-necrosis [15].

One more possible explanation is CTn-I assays had executed in aliquoted samples kept at –70°C for an inconstant time, and some "CTn-I loss" is expected with prolonged freezing, which might have led to an underestimation in some samples [12]

It is worth mentioning, the fact that well 70-years elders with values exceeding the 99^{th} centile <60 years elders, but under the 99^{th} centile for the whole reference people, experienced a meaningly higher mortality rate through a 10-years follow-up period than those having values under the 99^{th} centile for the younger people, that is the "true" 99^{th} percentile URL [21].

In agreement with the study outcomes, the overwhelming volume of data generated by researchers revealed sex-related changes in plasma CTn-I levels due to inferior 99^{th} upper reference limit (URL) concentrations in women than men [22]. It is anticipated that these alterations owing to dissimilar cardiac mass [23], and inconsistency of cardiomyocyte regeneration [24].

In light of these studies, it seems that the serial measures of patients with suspected ACS should be practiced to distinguish significant variations in the CTn-I levels. We should also obey strictly the complimentary standards of defining ACS [19]. Nevertheless, the lack of reliable data made no precise numeric endorsement. Consequently, the statistical power of any future study necessitates the use of more explicit over and above sex/age-specific 99^{th} percentile cutoffs for the CTn-I evaluates would be anticipated to reduce false negative and positive ACS diagnosis with the CTn-I analysis. A problem with foremost clinical and communal health implications. Watchful valuations are desirable in elderly subjects because *"one size fits all"* is not applicable in measuring CTn-I.

The utmost updated consensus definition of AMI recommended that sex/age-based cutoff standards may be approved in the upcoming era for cardiac troponin analyzes.

Conclusion:

This study highlights that in patients with ACS, the routine of CTn-I for the diagnosis of ACS should be interpreted based on the patient's age/sex to adjust the diagnostic precision of CTn-I for both sexes and different ages.

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