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ORIGINAL ARTICLE

Accuracy of D-Dimers to diagnose Aortic dissection and its different types keeping CT angiogram as gold standard.

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ABSTRACT… Objective: To determine diagnostic accuracy of D-dimers levels to diagnose aortic dissection and its different types keeping computed tomographic angiogram as gold standard. **Study Design:** Cross-sectional Validation study. **Setting:** Department of Vascular Surgery, Combined Military Hospital, Rawalpindi. **Period:** 1st December 2023 to 31st May 2024. **Methods:** Patients presenting with acute onset "tearing" chest pain with suspicion of aortic dissection were included in the study. Their D-dimer levels and CT angiography were performed in all patients. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of D-dimers to diagnose aortic dissection were calculated. Data was analyzed using SPSS 22. **Results:** A total number of 74 patients were included in this study. In this study, sensitivity of D-dimer levels to diagnose aortic dissection was 90.00% while specificity was 71.43%. For aortic dissection diagnosis positive predictive value, negative predictive value and accuracy of D-dimers levels were 93.10%, 62.50% and 86.49%, respectively. Based on CT Angiogram, there were 47 (63.51%) Stanford type A – Aortic dissection patients while 27 (36.49%) patients were of Stanford type B – Aortic dissection. In Stanford type A – Aortic dissection patients' sensitivity and specificity were 95% and 41% while in Stanford type B – aortic dissection patients' sensitivity and specificity were 80% and 22.22%. Accuracy of D-dimers levels to diagnose Type A – Aortic dissection and Type B – Aortic dissection was 70.27% & 37.84% respectively. **Conclusion:** D-dimers levels can serve as an effective tool to diagnose aortic dissection, in particular for Stanford Type A – Aortic dissection.

Key words: Accuracy, Aortic Dissection, Angiography, Computed Tomography, Diagnosis, D-dimers Levels.

INTRODUCTION

In spite of availability of significant information, a significant number of cases of "aortic dissection" continue to be overlooked in urgent care facilities. Acute "aortic dissection" is a rare disorder that may result in catastrophic outcomes. Historically, those who suffer from this condition typically have an abrupt and intense pain in their chest that is known to be "tearing".[1] The presence of an aortic dissection can be detected when a pseudo-lumen forms in aortic wall due separation of layers of aortic wall. This pseudo-lumen can compress the actual lumen of the aorta.[2] As per Stanford Classification aortic dissection is divided into Type A which incorporates dissections involving the ascending aorta and Type B which includes dissections limited to the descending aorta.[3] Amongst these, type A has been reported to be reported to be more common as compared to type B "aortic dissections.[4]

Aortic dissection is a disorder that, if left untreated, has an estimated fatality rate of as high as 47%; however, this percentage has been reported to fall over time and has decreased to 14%.[5] Owing to such strong association with poor outcome and high rates of mortality associated with aortic dissection, prompt and correct diagnosis is paramount to save precious lives as the symptomatology of this potentially fatal condition is quite similar to various other diseases.[6] For this purpose, most important and accurate test that can ensure the presence of tear within the wall of aorta by passive visualization of the condition of vessel is Computed tomographic angiography (CTA) of the aorta. CT angiography of aorta is gold standard investigation for aortic dissection patients.[7]

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CT angiography is a specialized modality of diagnosis and since Pakistan is a resource depleted nation, particularly in the field of healthcare, that is mostly not available at many tertiary care institutes of the country which necessitates exploring alternative diagnostic modalities. One such modality is D-dimers levels that has been hypothesized to play a pivotal role in making a diagnosis of aortic dissection. In this instance, a study reported that D-dimers levels that are greater than 500 ng/ml have the ability to make a correct diagnosis of aortic dissection.[8]

This exhibits that D-dimers levels may have the ability to make correct and prompt diagnosis of aortic dissection (AD) but at the same time since it is an acute phase reactant, further analysis regarding its diagnostic ability is essential. For this purpose, this study was conducted with aim of determining the diagnostic accuracy of D-dimers levels to diagnose aortic dissection and its different types keeping CT angiogram as gold standard.

METHODS

This cross-sectional validation study (ERB Reg No: 517) was carried out at vascular surgery department of "Combined Military Hospital, Rawalpindi" starting from 1st December 2023 to 31st May 2024. Through the use of the WHO sample size calculator, appropriate sample size required was calculated. Formula used for determining the sample size was[9]:

This was done by assuming a confidence level of 95%, absolute precision 6.5% and anticipated sensitivity of D-dimers levels to diagnose aortic dissection of 91.1%.[10] Upon calculation, sample size was 74.

$$n = \frac{z^2_{1-\alpha/k} P(1-P)}{d^2}$$

Patients who had age more than eighteen years, either male or female and had presented in emergency department with suspected aortic dissection due to presenting complaint of "tearing" chest pain (VAS ≥ 8) were included in the study. Patients who had history of coagulation disorders, history of deep vein thrombosis (DVT), ongoing fever, ECG changes typical of pulmonary embolism, chronic renal failure, those presenting with circulatory collapse, pregnant women and those with contraindication to contrast media administration were excluded from the study. Sampling was done by non-probability consecutive sampling technique. Baseline characteristics of patients were documented including their age, gender, pain VAS, duration of pain (in minutes) and history of hypertension [defined as persistent blood pressure readings of ≥ 130/80[11] and/or intake of anti-hypertensive medications]. After this D-dimers levels were checked in all these patients by sending a 5ml venous blood sample taken under aseptic conditions to the in-hospital laboratory. A D-dimer value of ≥ 500ng/ml was considered as indicative of presence of aortic dissection.[8] After this, all these patients underwent CT angiography of aorta to make diagnosis of aortic dissection and its type as per "Stanford classification.[12]" This radiological diagnosis was made by a consultant radiologist with an experience of minimum of three years. Based on these, operative definitions were formulated. For cases of aortic dissection, True positives were defined as patients having D-dimers levels ≥ 500ng/ml and aortic dissection on CTA. False positives were defined as patients having D-dimers levels ≥ 500ng/ml but no aortic dissection on CTA. False negatives were defined as patients having D-dimers levels < 500ng/ml but had aortic dissection on CTA. True negatives were defined as patients having D-dimers levels < 500ng/ml and no aortic dissection on CTA. Based on these sensitivity, specificity, positive predictive value, negative predictive value and accuracy of D-dimers levels to diagnose aortic dissection were calculated for all patients and separately for both type A and type B aortic dissection patients.

Data was analyzed by using Statistical Package for Social Sciences (SPSS) 22.00. Quantitative data was represented using mean ± standard deviation. Qualitative data was represented by using percentage and frequency. 2x2 tables were drawn to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of D-dimers levels to

diagnose aortic dissection. A p-value of ≤ 0.05 was taken as statistically significant.

RESULTS

A total of 74 patients were included in this study. Mean age of patients was 40.94 ± 6.52 years. There were 63 (85.14%) male patients and 11 (14.86%) female patients. Mean pain VAS score of patients at time of presentation was 9.04 ± 0.53. 9 (12.16%) patients had pain VAS score of 8 at presentation, 53 (71.62%) had pain VAS score 9 at presentation and 12 (16.22%) had pain VAS score of 10 at presentation. Mean duration for which patient had pain was 85.77 ± 40.26 minutes. 57 (77.03%) patients had history of hypertension. Patients in this study who had D-dimers levels ≥ 500ng/ml and had aortic dissection on CT Angiography (true positives) were 54 (72.97%). Patients who had D-dimers levels ≥ 500ng/ml but no aortic dissection on CT Angiography (false positive) were 4 (5.41%). Patients who had D-dimers levels < 500ng/ml but had aortic dissection on CT Angiography (false negatives) were 6 (8.11%). Patients who had D-dimers levels < 500ng/ml and no aortic dissection on CT Angiography (true negatives) were 10 (13.51%) (Table-I).

	Aortic Dissection on CTA	No Aortic Dissection on CTA
D-dimers ≥ 500ng/ml	54 (72.97%) [TP]	4 (5.41%) [FP]
D-dimers < 500ng/ml	6 (8.11%) [FN]	10 (13.51%) [TN]

Table-I. Frequencies of true positives, false positives, false negatives and true negatives patients (n = 74)

Based on this, sensitivity, specificity, positive predictive value, negative predictive value and accuracy of D-dimers levels to diagnose aortic dissection were calculated (Table II):

According to CT Angiography of aorta, 40 (54.05%) were found to have Stanford type A – aortic dissection and 20 (27.02%) were found to have Stanford type B – aortic dissection. For each type of aortic dissection True Positive, False Positive, False Negative and True Negative frequencies were calculated (Table III and IV).

Sensitivity	90.00%
Specificity	71.43%
Positive predictive value	93.10%
Negative predictive value	62.50%
Accuracy	86.49%

Table-II. Diagnostic parameters of D-dimers levels to diagnose aortic dissection in patients (n = 74)

	Type A – AD on CTA	No type A – AD on CTA
D-dimers ≥ 500ng/ml	38 (51.35%) [TP]	20 (27.03%) [FP]
D-dimers < 500ng/ml	2 (2.70%) [FN]	14 (18.92%) [TN]

Table-III. Frequencies of Stanford type A-aortic dissection patients (True Positives, False positives, False Negatives and True Negatives) in study population (n = 74).

	Type B – AD on CTA	No Type B – AD on CTA
D-dimers ≥ 500ng/ml	16 (21.62%) [TP]	42 (56.75%) [FP]
D-dimers < 500ng/ml	4 (5.41%) [FN]	12 (16.22%) [TN]

Table-IV. Frequencies of Stanford type B-aortic dissection patients (True Positives, False positives, False Negatives and True Negatives) in study population (n = 74).

Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of D-dimers levels to diagnose Stanford type A and type B aortic dissection were calculated which are given below in Table-V:

	Type A – AD on CTA	Type B – AD on CTA
Sensitivity	95.00%	80.00%
Specificity	41.18%	22.22%
Positive predictive value	65.52%	27.59%
Negative predictive value	87.50%	75.00%
Accuracy	70.27%	37.84%

Table-V. Diagnostic parameters of D-dimers levels to diagnose different types of aortic dissection (n = 74)

DISCUSSION

Acute onset aortic dissection is a highly dangerous disorder that carries a substantial risk of illness and death. In fact, even in developed nations, the likelihood of death within twenty-four hours of its onset is roughly 50%, with half of the patients dying before they can reach a specialized medical facility.[13,14] The lack of timely diagnosis and surgical intervention in cases of aortic dissection is strongly correlated with a high death rate. This delay in treatment significantly raises the likelihood of disease advancement and the development of comorbidities, posing a substantial threat to the life and well-being of patients.[15,16] This study, therefore, focused on one of the diagnostic modalities of aortic dissection. Our study is unique because this is the first study in Pakistan that is focusing on this non-invasive, cheaper and quicker diagnostic modality for aortic dissection.

In current study, most patients were young men who were admitted with the suspicion of aortic dissection. This synchronizes with the finding of the study conducted by Rylski et al.[17] who reported that men have twice the likelihood to develop aortic dissection as compared to women. Hypertension was present among more than half of the patients prior to their presentation which is consistent with the fact that hypertension is a major risk factor of developing acute aortic dissection.[18] In addition, majority of the patients who were ultimately diagnosed with aortic dissection on CT Angiography were found to have Type A- aortic dissection which was in line with findings of previous literature in this regard.[19] When it comes to diagnostic accuracy of D-dimers levels to diagnose aortic dissection, current study found its sensitivity and specificity to be 90.00% and 71.43%, respectively. This was comparable to what has been reported in a study conducted by Zitek et al.[10] who found these values to be 91.1% and 71.4%, respectively. However, in current study, sensitivity of D-dimers levels for diagnosing aortic dissection was much lower as compared to what was reported by Rafla et al.[20] who found it to be 100% but specificity of present study was higher that what was reported in Rafla et al.[20] in which it was found to be at only 64%. When it comes to difference of diagnostic accuracy of D-dimers levels to diagnose different types of aortic dissection, it was much higher for Type A-aortic dissection as compared to Type B-aortic dissection. Similar was the case in a study conducted by Wang et al.[21] whose results were comparable to our study.

Present study had multiple limitations like small sample size, selection of patients with a particular clinical picture and study being limited to a single center. Since, this study is a unique one a national level, it is highly recommended that large sample studies should be conducted in future in this regard to ascertain the diagnostic ability of D-dimers levels to diagnose aortic dissection and its different types.

CONCLUSION

D-dimers levels can serve as an effective tool to diagnose aortic dissection, in particular for Stanford Type A – Aortic dissection.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Saqib Qayyum:** Conceived idea, literature search, manuscript writing.
2	**Muhammad Taimur:** Data interpretation, Statistical analysis, manuscript writing.
3	**Nadia Attiq:** Manuscript writing, designed research methodology.
4	**Mahvish Noor:** Data collection and compilation, literature review.
5	**Athar Badshah:** Manuscript writing, literature search.
6	**Muhammad Imran:** Manuscript writing, literature review.