ORIGINAL ARTICLE

Multi-detector angio-CT and the use of D-dimer for the diagnosis of acute mesenteric ischemia in geriatric patients

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ABSTRACT

BACKGROUND: There is no specific laboratory method for the diagnosis of acute mesenteric ischemia (AMI). In this study, we aimed to determine the efficacy of the D-dimer test in selected cases prior to multi-detector angio-CT, which is expensive and has side effects.

METHODS: Patients, over 65, with abdominal pain were included in this study. The D-dimer test was applied to 230 (34%) of 676 abdominal pain patients admitted to our emergency service. The D-dimer levels of the patients diagnosed with AMI by angio-CT were compared.

RESULTS: In AMI patients sensitivity of the D-dimer test was 84.6% and the specificity was 47.9%. Elevated D-dimer levels and AF were observed in 90.9% of the patients diagnosed with AMI by CT.

CONCLUSION: D-dimer levels were elevated in the AMI patients. Patients suspected of having AMI with unclear clinical results and patients with D-dimer levels above 1000 ng/ml and AF should undergo further evaluation.

Key words: Acute mesenteric ischemia; D-dimer; multi-detector angio-CT.

INTRODUCTION

Abdominal pain in elderly patients has a broad spectrum of pathologic etiologies of which certain emergency conditions such as acute mesenteric ischemia (AMI) must be ruled out early on. When all causes of abdominal pain in the elderly are considered, mortality in AMI increases should the time for diagnosis lengthen.[1] This disease accounts for 10-14% mortality.[1,2] The incidence of AMI is 1-2% worldwide but can reach 18% in patients over the age of 65.[3] Delays in diagnosis cause the mortality rate to increase up to 50-70%.[4-6]

The prognosis for AMI is positively affected by reperfusion within the first 6 hours, particularly in cases of embolic ischemia. In recent years, the diagnostic tools for this disease have improved, but the mortality rates have not changed. Unclear physical examination findings and symptoms, patients' inability to provide correct complaints, the inability to acquire sufficient patient histories, and anatomical differences complicate the diagnosis of AMI in elderly patients.[4-6] There is no specific laboratory test for early-stage AMI. Although amylase, aspartate transaminase (AST), lactate dehydrogenase (LDH), and creatine kinase (CK) levels have been shown to be elevated in these patients, none of these parameters provide diagnostic sensitivity or specificity.[3] Markers such as D-dimer, alpha-glutathione, S-transferase, D-lactate, intestinal fatty acid binding protein (IFABP), alkaline phosphatase (ALP), procalcitonin and diamine oxidase (DAO) have been researched in this context; however, definitive results have not been reported.[3,7,8] Thus, research into the early diagnosis of AMI continues. Angiography can provide a certain diagnosis of AMI, having recent studies report that multi-detector angio-CT is as effective as angiography in the diagnosis of AMI.

When other causes of acute abdomen are considered, CT

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may come into prominence in AMI suspected patients for differencial diagnosis.[9,10] The diagnostic tools for this disease have improved; however, the mortality rates remain unchanged. Unproportional pain on physical examination is still noted to be a characteristic finding in AMI (generally of the venous thrombus type), raising clinical suspicion and pretest probability. Given the other potential causes of acute abdominal pain, CT may become prominent in the differential diagnoses of patients suspected of having AMI.[9,10]

Kurt et al.[11] have reported that an elevated D-dimer level is 88.8% sensitive in detecting superior mesenteric artery (SMA)-bound rats. Altinyollar et al.[12] have determined that D-dimer levels rise 30 min after the binding of the SMA, and Akyıldız[13] have reported high D-dimer levels in AMI patients (sensitivity: 94.7% and specificity: 78.6%). These findings indicate that D-dimer level may be useful as an early marker of AMI. Thus, we sought to investigate the use of D-dimer and multi-detector angio-CT in selected geriatric patients suspected of having AMI instead of using CT for AMI-suspected patients who cannot be diagnosed with Doppler ultrasound (USG).

MATERIALS AND METHODS

After receiving approval from the ethics committee for this cross-sectional study, we examined 676 suspected AMI patients with abdominal pain over the age of 65, who were admitted to our emergency service between January and June 2012. Patient risk factors for AMI, physical examination findings, the presence of atrial fibrillation (AF) on electrocardiogram (ECG), laboratory results (D-dimer, white blood cell (WBC) and creatine kinase (CK) tests), radiological findings (USG, Doppler USG, and multi-detector angio-CT), and patient outcomes were noted. D-dimer levels were measured with the Trinity Biotech latex-based immune measuring method. The normal range of the results of this test is 0-470 ng/ml. Values over 470 ng/ml were accepted elevated. WBC levels were measured with a Mindray BC 6800 device. The normal range of the outcome of this test in our hospital is 4.300-10.300/mm^3. Values over 10.300/mm^3 were accepted high. CK levels were measured with a Trinity Biotech device. The normal range for the outcome of this test is 39-308 U/L. Values over 308 U/L were accepted elevated.

The sensitivity and specificity of multi-detector angio-CT in the diagnosis of AMI is 90-100%.[14] In this study, all patients suspected of having AMI underwent CT scanning (64-section LightSpeed Volume CT; GE Healthcare, Milwaukee, Wisconsin).

All patients were over the age of 65, had abdominal pain and were suspected of having AMI. Patients who were under the age of 65, with abdominal pain but without AMI suspicion, and were not stable enough for CT or had contrast allergies were excluded.

Statistical Analyses

Descriptive results are reported as the means ± the SD or as medians and ranges as appropriate. The evaluations of the associations of categorical variables with the diagnoses of AMI were performed with Pearson χ^2 tests (or Fisher's exact tests when appropriate), and Mann-Whitney U-tests were used for continuous data. The groups were compared with Mann-Whitney U tests for numerical data and Pearson χ^2 tests for categorical data. Receiver operating characteristic (ROC) curves were applied to determine the most suitable diagnostic D-dimer level. All statistical analyses were performed with SPSS version 13.0 (Chicago, Ill). P values below 0.05 were considered significant. Confidence interval was 95%.

RESULTS

Of 676 patients, 34% (n=230) were suspected of AMI and the D-dimer levels of these patients were measured. The other 66% (n=446) of the patients underwent necessary tests for diagnosing other conditions based on their complaints.

The cause of abdominal pain in 30.6% (n=207) of the 676 patients could not be determined and these patients were diagnosed with nonspecific abdominal pain. Medical treatment was administered to 53.6% (n=111) of these patients. All patients diagnosed with nonspecific abdominal pain were discharged from the emergency service and referred to gastroenterology and general surgery clinics. 1.9% (n=13) of the 676 patients were diagnosed with AMI. The D-dimer levels of 53.9% (124) of the AMI suspected patients who underwent D-dimer assessment were high and 22% (n=28) of the patients with elevated D-dimer levels were diagnosed with nonspecific abdominal pain. AMI was diagnosed in the remaining 8.9% (n=11) of the patients.

Abdominal USG was indicated for 45.7% (n=309) of the 676 patients due to rebound, defensiveness and tenderness during physical examination. Cholelithiasis was detected in 12.6% (n=39) of the patients. AMI was determined in 4.2% (n=13) of the patients who underwent USG. The desired USG ratio in the patients who underwent D-dimer testing was 59.1% (n=136) and 9.6% (n=13) of these patients were diagnosed with AMI.

Of our 676 patients, 31.9% (n=216) underwent CT for differential diagnosis due to insufficient USG findings. CT was indicated for 49.1% (n=106) of these patients owing to the suspected presence of AMI and for 50.9% (n=110) of patients for differential diagnoses.

Although 15.1% (n=29) of all the patients who underwent CT scanning had positive abdominal findings on physical examination, we could not find any pathological findings in the laboratory results or radiological evaluations of these patients who could explain their clinical situations. The

patients with unexplained abdominal pain received consultations with a general surgeon and were hospitalized. Of the patients who underwent CT scans, 12.3% (n=13) were diagnosed with AMI. Of the 230 patients, whose D-dimer levels were elevated, 4.8% (n=11) were diagnosed with AMI. Among the patients with AMI diagnoses, 84.6% (n=11) exhibited elevated D-dimer levels, 92.3% (n=12) exhibited elevated WBC levels and 23% (n=3) exhibited elevated CK levels.

D-dimer ($p<0.05$), WBC ($p<0.05$) and CK ($p<0.05$) values were significantly correlated with mesenteric ischemia. When the patients were grouped according to the presence of AMI, we found significant differences in D-dimer ($p<0.05$), WBC ($p<0.05$) and CK ($p<0.05$) levels between groups. The mean D-dimer, WBC and CK levels of the groups are provided in Table 1.

Eleven of the 13 AMI diagnosed patients had AF, 9 had HT, 8 had DM, 5 had CAD and 3 had CHF (Table 2). Three of the CT-scanned and AMI diagnosed patients had AF, DM and HT. Four AF patients had rapid ventricle response AF.

Table 1. Mean D-Dimer, WBC and CK Values According to the Presence of AMI

	Myocardial infarction				p
	Yes		No		
	n	Mean.±SD	n	Mean.±SD	
D-Dimer	13	1177.77±710.4	217	744.89±1752.4	0.003
White blood cells	13	20.38±7.18	629	10.28±5.32	0.001
Creatine kinase	13	347.92±380.64	630	124.44±164.05	0.010

*Mann-Whitney U analysis.

Table 2. Comorbid disease distribution according to the presence of acute mesenteric ischemia

		Acute mesenteric ischemia				Total		p
		Yes		No				
		n	%	n	%	n	%	
Hypertension	Yes	9	69.2	408	61.5	417	61.7	0.775
	No	4	30.8	255	38.5	259	38.3	
Diabetes mellitus	Yes	8	61.5	217	32.7	225	33.3	0.038
	No	5	38.5	446	67.3	451	66.7	
Coronery artery disease	Yes	5	38.5	114	17.2	119	17.6	0.061
	No	8	61.5	549	82.8	557	82.4	
Congestive heart failure	Yes	3	23.1	132	19.9	135	20.0	0.730
	No	10	76.9	531	80.1	541	80.0	
COPD	Yes	1	7.7	120	18.1	121	17.9	0.482
	No	12	92.3	543	81.9	555	82.1	
SVD	Yes	1	7.7	49	7.4	50	7.4	1.000
	No	12	92.3	614	92.6	626	92.6	
Cancer	Yes	2	15.4	90	13.6	92	13.6	0.694
	No	11	84.6	573	86.4	584	86.4	
Atrial fibrillation	Yes	11	84.6	110	16.6	121	17.9	0.001
	No	2	15.4	553	83.4	555	82.1	
Total		13	1.9	663	98.1	676	100.0	

COPD: Chronic obstructive pulmonary disease.

Table 3. D-dimer level distribution in patients underwent CT according to the presence of atrial fibrillation

	D-Dimer				Total		p
	High		Normal				
Atrial fibrillation	n	%	n	%	n	%	
(+)	10	90.9	1	50.0	11	84.6	0.295
(–)	1	9.1	1	50.0	2	15.4	
Total	11	84.6	2	15.4	13	100.0	

Table 4. D-Dimer level distribution of myocardial Infarction patients according to survival

	D-Dimer				Total		p
	High		Normal				
Survival	n	%	n	%	n	%	
Not exitus	6	54.5	1	50	7	53.8	1.000
Exitus	5	45.5	1	50	6	46.2	
Total	11	84.6	2	15.4	13	100.0	

The D-dimer levels of the CT scanned patients according to the presence of AF were not significantly different (p>0.05) (Table 3).

Eleven of the 13 AMI diagnosed patients underwent emergency surgery. Two patients were deemed inoperable due to total ischemia and were hospitalized in the intensive care unit. One of these 2 patients died within 24 hours and the other patient died 2 days later. The operation of one patient was terminated due to total necrosis and he also died within 24 hours. A right hemicolectomy was performed in one patient and intestinal resection was performed in the other 9 patients. Three of the intestinal resection patients died after the operations (Table 4). D-dimer levels were not related to the survival of the AMI patients (p>0.05).

DISCUSSION

Abdominal pain accounts for 5-10% of all emergency service admissions. The distributions of the causes of abdominal pain based on age, gender, comorbid diseases, symptoms and physical examination findings help to determine the causes of abdominal pain in specific patients. Moreover, early and specific diagnostic tools are needed for accurate and early diagnoses.[15]

One study found that 6% of geriatric emergency service patients are admitted with abdominal pain.[16] In this study, it was 6.39% (n=676).

AMI is a geriatric disease. In most AMI studies, the mean age of the study is above 65. Kougias et al.[17] reported that the mean age of their study group was 71, and Huang[18] and Hawkins[19] studied a group with a mean age of 65. These findings indicate that AMI is common after the age of 65 and thus we studied patients over the age of 65.

Nonspecific abdominal pain was diagnosed in 30.6% of our patients. Bugliosi et al.[20] have reported that 23% of geriatric abdominal pain patients are diagnosed with nonspecific abdominal pain in the emergency department. AMI was diagnosed in 1.9% (n=13) of our patients, and this percentage is similar to that found in the literature.[21]

The usage of biomarkers for the early diagnosis of AMI is quite limited, but the use of D-dimer levels for this purpose has been researched in recent years. Acosta et al.[7] have reported that D-dimer levels are elevated in (17.5 mg/l) in SMA occluded patients.

Elevations in D-dimer levels are specific to AMI. Some studies have revealed elevations in D-dimer levels in acute pancreatitis and coeliac diseases. Radenkovic have reported that D-dimer levels are 90% sensitive and 89% specific for the diagnosis of acute pancreatitis.[22] A study conducted by Block found that D-dimer level was 60% sensitive and 82% specific in the diagnosis of AMI.[23] Kurt et al.[11] have found that D-dimer level produces a sensitivity of 88.8%, a positive prediction rate of

88.8%, and a negative prediction rate of 100% in rats. Another study has found a sensitivity of 94.7% and a specificity of 78.6%.[13] Our results showed that the sensitivity of the D-dimer level was 84.6% and that the specificity was 47.9%. The sensitivity of WBC level in our study was 92.3%. Meyer and Akyüz have put forward that the sensitivity and specificity of WBC level in the diagnosis of AMI are 90% and 86.6%, respectively.[24,25] Similar to the findings reported in the literature, we found elevated CK levels in our AMI patients.[26,27]

The sensitivities and specificities of multi-detector CT in the diagnosis of AMI have been reported to be between 90-100% in the literature.[28,29] We found that the sensitivity of this test was 100%.

Comorbid diseases prolong the time until diagnosis and increase the occurrence and severity of complications. AF is the major comorbid situation in AMI patients.[13,30,31] In our study, 84.6% of AMI patients had AF. Furthermore, 62.2% (n=9) of the AMI patients had HT, and 61.5% (n=8) had DM. These proportions are higher than those reported in the literature.[32]

The mortality of the AMI patients in our study was 46.2%. The mortalities reported in the literature range between 40-51%.[33-35]

The extent to which D-dimer levels are incremented in acute abdominal diseases has not been clearly determined in the literature. In our study, the mean D-dimer value of the cases of nonspecific abdominal pain was 425 ng/ml. The results of our study showed that D-dimer values over 1000 ng/ml are significant for patients suspected of having AMI. However, D-dimer levels alone are not sufficient to exclude the diagnosis of AMI.

Limitations

This is a single center cross-sectional study, which is a major limitation. Moreover, patients did not receive the gold standard angiography to determine presence of AMI. CTA is nonspecific for non-occlusive MI and these cases may have been missed and identified as non-specific abdominal pain.

In our hospital, D-dimer levels were measured using latex. The measurement of D-dimer levels with the ELISA method may have produced more significant results.

Conclusion

The sensitivity of D-dimer level in the diagnosis of AMI was found to be 84.6% and that of the specificity was 47.9%. WBC values above 15000/mm^3 were significant for AMI patients. The sensitivity of multi-detector angio-CT was 100%. Abdominal pain patients with suspected AMI over the age of 65 with AF, DM and HT should undergo multi-detector angio-CT to avoid delaying certain diagnosis of this condition.

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All authors declare that they have no conflict of interest.

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KLİNİK ÇALIŞMA - *ÖZET*

Geriatrik hastalarda akut mezenterik iskemi tanısında multidedektör anjiyo BT ve D-dimer kullanımı

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AMAÇ: Akut mezenter iskemi (AMİ) tanısında belirli bir laboratuvar yöntemi yoktur. Çalışmamızda AMİ şüphesinde yüksek maliyet ve yan etkilere sahip bir tanı yöntemi olan multi dedektör anjiyo BT öncesi D-dimer düzeyi bakılarak, seçilmiş olgularda bu incelemenin kullanımının uygunluğunu araştırdık.
GEREÇ VE YÖNTEM: Çalışmamıza 65 yaş üzeri karın ağrılı hastalar alındı. Acil servisimize başvuran toplam 676 hastanın 230'una (%34) D-dimer testi yapıldı. Anjiyo BT ile AMİ tanısı konulan hastaların D-dimer düzeyleri değerlendirildi.
BULGULAR: Çalışmamızda AMİ tanısı olan hastalarda D-dimer %84.6 sensitif %47.9 spesifik bulundu. BT ile AMİ tanısı konan hastaların %90.9'unda D-dimer yüksekliği ile AF birlikteliğini saptadık.
TARTIŞMA: AMİ'den iskemiden şüphelenilen kliniği net olmayan hastalarda D-dimer değeri 1000 ng/ml ve üzerinde AF'si olan hastalarda ise mezenter iskemiden şüphelenilmesi ve ileri incelemeye gidilmesi faydalı olacaktır.
Anahtar sözcükler: Akut mezenter iskemi; D-dimer; multi dedektör anjiyo BT.

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