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The Diagnostic and Prognostic Value of Serum-myoglobin Determinations in Acute Myocardial Infarction

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Myoglobin is a small-molecular weight protein contained within skeletal and cardiac muscles. Upon damage to the muscle cell myoglobin escapes to the environment and can be found in plasma by means of sensitive radioimmunoassays. Previous reports have suggested that myoglobin might serve as a very early indicator of damage to the myocardium since increments in serum-myoglobin could be detected as early as one to two hours after chest-pain in infarct patients. One obstacle in the use of myoglobin as an early indicator of heart infarction, however, has been the long assay time for most radioimmunoassays. This obstacle has recently been overcome by the development of an assay which allows the assay of serum-myoglobin with sufficient sensitivity within one hour or even less (2).

Although several reports have suggested the clinical utility of myoglobin measurements early in the diagnosis of myocardial infarction few have actually established the utility in comparison with other diagnostic means such as serum-enzyme measurements (CK and ASAT). We therefore started a prospective study where serum-samples were collected with regular intervals from all patients admitted to the hospital on suspicion of acute myocardial infarction (AMI) during a three months period. The total number of patients included in the material became 305 individuals of which 80 were found to have acute myocardial infarction based on the WHO-criteria. This communication will briefly review the results of the study (1) and demonstrate that serum-myoglobin measurement in comparison with CK and ASAT is a superior diagnostic means early in the course of acute myocardial infarction. It will also be shown that myoglobin is closer related to the prognosis of the patients than CK and ASAT.

The kinetics of appearance in serum of myoglobin, ASAT and CK after AMI

In table I the serum-levels of myoglobin, ASAT and CK are shown in the 80 patients with AMI on admission and 4 hours after admission. On admission myoglobin was increased almost eight fold in comparison with a 2-3 fold increase of ASAT and CK. Four hours after admission myoglobin showed on average a 12-fold increase with a 3-4 fold increase for ASAT and CK. When

Table I

The mean levels in serum of myoglobin, CK and ASAT on admission and within 4 hours after admission in 80 patients with AMI.

	On admission	Within 4 hours after admission	Normal levels
	mean±SEM	mean±SEM	mean±2SD
Myoglobin	412±50 µg/l	692±58µg/l	55±42 µg/l
CK	7.2±1.3 µkat/l	10.6±1.5 µkat/l	2.9±2.7 µkat/l
ASAT	0.98±0.11 µkat/l	1.30±0.14 µkat/l	0.37±0.20 µkat/l

comparing the number of positive and negative observations at the same time-points myoglobin was positive i.e. above mean+2SD, in 71 % percent of the cases with 54 % for ASAT and 41 % for CK on admission and 96 % for myoglobin and 71 % and 68 % for respectively ASAT and CK four hours after admission. These figures confirm and establish the earlier appearance of myoglobin in serum after AMI when compared with ASAT and CK. When individual patients were followed every hour after infarction serum-myoglobin was elevated on average 5 hours before either of ASAT and CK (Fig).

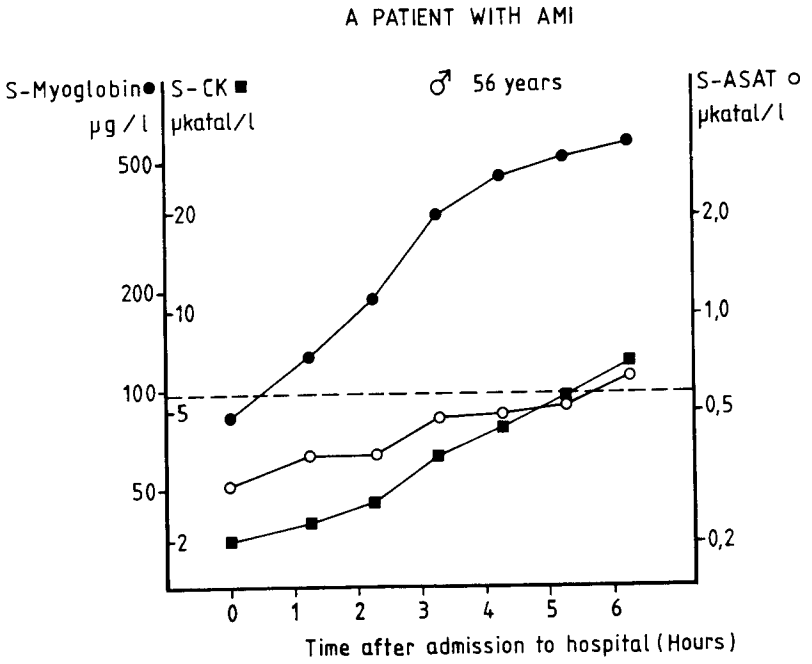

Fig. 1. The variations of S-Myoglobin, S-CK and S-ASAT in a patient with AMI. The horizontal line indicates the + 2SD limit for all three variables. The patient arrived to the hospital one hour after onset of chest pain.

The diagnostic sensitivity and specificity of serum-myoglobin in AMI

The sensitivity and specificity of a method can be estimated by the calculation of the frequency of false-negative and false-positive results, respectively. In table II the figures are given for the frequency of false positive and false negative myoglobin, ASAT and CK observations in the study. The results were considered false negative when values were below the mean+2SD in the AMI-group of patients and the results were considered false positive when the values exceeded the mean+2SD in the group of patients in whom AMI could be excluded. The latter group comprised 78 of the patients. It is obvious from the table that myoglobin presents with considerably fewer false negative results in particular during the early period after

AMI. However, still after 15 hours the number of false negative results are fewer for myoglobin than for ASAT and CK. In fact the number of false-negative was zero within that period when the two patients who arrived to the hospital more than 48 hours after onset of symptoms were excluded. The exclusion of patients arriving that long after onset of symptoms is justified since it is well documented that myoglobin may be normalized after this time of period due to its fast elimination from the circulation. The frequency of false-positive observation was equal for all three analyses i.e. from 14-18%.

Table II

The relative frequency of false negative and false positive cases in classification based on S-Myoglobin, S-CK and S-ASAT at various times after admission.

	On admission	Within 4 hour after admission	Within 15 hours after admission
False negative			
S-Myoglobin	29 % (28 %)*	4 % (2 %)*	2.5 % (0 %)*
S-CK	73 % (60 %)+	41 % (31 %)+	11 % (5 %)+
S-ASAT	46 %	29 %	5 %
False positive:			
S-Myoglobin	17 %		18 %
S-CK	4 % (14 %)+		8 % (18 %)+
S-ASAT	17 %		18 %

+Results within parentheses indicate frequency of false negative and false positive cases when the discrimination limit of 3.33 µkat/l (200 u/l) has been used as recommended by Gerhardt et al. (7).

*Indicates results when the two patients have been excluded who arrived more than 48 hours after onset of symptoms.

The positive predictive value (PV_{pos}) was for myoglobin at admission and 4 and 15 hours admission 0.81-0.86 and not significantly different from the PV_{pos} of CK and ASAT. The negative predictive value (PV_{neg}), however, was significantly ($p<0.01$-$p<0.001$) higher for myoglobin within the first 4 hours after admission and was 1.00 when calculated on data obtained within 15 hours after admission. This means that myoglobin, CK and ASAT are equally good at confirming the diagnosis AMI whereas myoglobin is a superior means to exclude the diagnosis in particular in the early period of disease.

The relationship of serum-myoglobin levels to prognosis and complications

In table III are given some results from the group of patients with established AMI where the levels of myoglobin, CK and ASAT have been related to some complications of the patients and to the short-term and long-term prognosis of the patients. In general the myoglobin levels are significantly higher in those groups with complications or with bad prognosis quoad vitam and similar to those of CK and ASAT. In the group of patients who died in a second infarction within 6 month after the first one however, myoglobin was significantly higher in contrast to CK and ASAT.

In conclusion

Measurement of serum-myoglobin is a more sensitive means to exclude AMI in the early diagnosis of the disease than S-CK and S-ASAT. The specificity of myoglobin in the establishment of the diagnosis AMI is similar to CK and ASAT. Myoglobin seems to be somewhat closer related to the prognosis of the AMI patients than CK and ASAT.

Table III

The relationship of S-Myoglobin, S-CK and S-ASAT to the complications and prognosis of the AMI-patients.

	n	S-Myoglobin ug/l	p	S-CK ukat/l	p	S-ASAT ukat/l	p
No circulatory complications	58	803± 67*	<0.01	19.2± 2.1	NS	2.16± 0.21	<0.01
Circulatory complications	22	1240± 137		26.6± 4.7		3.71± 0.63	
No arrhythmias	56	829± 75	<0.05	17.5± 1.9	<0.01	2.19± 0.21	<0.01
Arrhythmias	24	1141± 116		29.9± 4.6		3.65± 0.57	
Dead in the present infarction	19	1295± 153	<0.001	29.0± 5.0	<0.05	4.08± 0.68	<0.01
Survived the present infarction	61	807± 64		18.8± 2.1		2.12± 0.20	
Dead within 6 months in a second infarction	7	1223± 172	<0.05	18.4± 3.3	NS	2.66± 0.49	NS
Alive 6 months after the first infarction	54	753± 66		18.9± 2.3		2.05± 0.21	

* The results are means ± SEM of the maximum serum values obtained within 15 hours after admission.

References

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