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S-CK and S-CK B in Suspected Acute Myocardial Infarction

Routine methodology and diagnostic strategy evaluated by the Scandinavian Committee on Enzymes

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Methodology

Creatine kinase (EC. 2.7.3.2. CK) B-subunit activity in serum may be routinely measured by the Scandinavian Committee on Enzymes (SCE) recommended CK method after complete immunoinhibition of all A-subunit activity by anti-M. Separate determination and substraction of sample residual adenylate kinase (EC 2.7.4.3, S-rAK) prevents false positive S-CK B results, e.g. NOT-AMI patients with heart failure and hypoxic liver damage (3,6).

The complete methodology with quality criteria for anti-M and day-to-day imprecision has been described in detail in (5). We advise use of liquid human control material in 50% glycerol or 30% ethylene glycol. Day-to-day imprecision with such controls are given in (4). We have recently designed a liquid quality control material consisting of high human CK MM activity and low CK MM activity in the same solution. This combination simultaneously verifies complete immunoinhibition of about 33 µkat/l (2 000 U/l) CK M-subunit activity and day-to-day imprecision at a relatively low CK B level.

Day-to-day imprecision, 54 working days:

$\bar{x}$ = 37 ± 2 U/l (0.62 ± 0.03 µkat/l) CV 5.4%

Supplemantary CK MB control, 54 working days:

$\bar{x}$ = 178 ± 6.0 U/l (2.97 ± 0.1 µkat/l)CV 3.4%.

The described methodology is analytically specific for CK B activity. Results should not be multiplied by two in order to simulate S-CK MB activity. Interference by S-CK BB, extracardial S CK MB, and S-macro CK BB has been discussed in (3).

Diagnostic strategy in suspected AMI

The SCE has field tested and evaluated a diagnostic strategy in suspected acute myocardial infarction (AMI) comprising the sequential application of:

1. Clinical suspicion of an AMI; establishing of time of onset of acute symptoms.
2. S-CK determined two bloodsamples drawn 10-20 hours after onset.
3. S-CK-B determination on all samples with increased S-CK activity.

1. The prevalence of AMI in the Coronary Care Unit (CCU) may vary between 0.40 and 0.55 depending on the admitting clinician's decision criteria. In the SCE Evaluation I (6) the prevalence was 0.43. An AMI enzyme form (fig.1) has been designed in cooperation with our cardiologists. It is part of the patient's journal records. It admonishes the admitting clinician to establish time of onset of the patient's acute symptoms as accurately as possible and prerequest 10 hour and 16 hour S-CK if possible.

ADMITTING M.D.: ESTABLISH TIME OF ONSET OF ACUTE SYMPTOMS AS ACCURATELY AS POSSIBLE

ADMISSION: <10 HOURS: REQUEST S-CK: 10 AND 16 HOURS
>10 <20 : ADM. & <20 H.
>20 : ADM. & LD-ISO.

POORLY DEFINED SYMPTOMS: USE MOST PROBABLE TIME OF ONSET

ACUTE SYMPTOMS: 1981 | mo | day | h
welldefined ☐ protracted ☐

SAMPLES:			
date			EGG:
hour			
hours after symptoms			date:
S-CK, U/l ♀ 150 ♂ 200			date:
S-CK B, 12 U/l			date:
S-LD 1, 24h AFTER ONSET 200 U/l			
S-LD 24h AFTER ONSET 450 U/l			

DIAGNOSIS :

2. The discriminator values for S-CK have been selected so low that the diagnostic sensitivity for the highest of the two 10-20 hours samples is 0.99 (6). The sex-related discriminators are 150 U/l (2.5 µkat/l) for women, 200 U/l (3.3 µkat/l for men) (6). Two negative 10-20 hour S-CK results excluded 70% of all NOT-AMI cases within 24 hours at PP_{neg} (Predictive probability) of 0.99 (6). 30% false positive S-CK were verified by subsequent S-CK B. As a consequence, our cardiologists discontinued all intramuscular injections to AMI-suspected patients during 1981. This increased the diagnostic specificity of 10-20 hours S-CK in 1981 so that about 80% of all NOT-AMI cases in 1981 were identified by two negative S-CK at a $PP_{neg} > 0.99$ (2).

3. S-CK B is determined on all S-CK positive samples (2,3,6) On basis of previous materials of patients from the CCU our S-CK B discriminator is defined as: S-CK B $\geq$ 12 U/l in the absence of positive recognition criteria for macro CK. These recognition criteria are: a relatively high and constant S-CK B activity in both samples, exceeding 10% of total S-CK activity (3,6). In CCU materials this S-CK B discriminator has a diagnostic sensitivity of 0.99 (6) and a diagnostic specificity higher than 0.95 (2,6).

S-CK B discriminator in the CCU

Heart muscle contains about 20% CK B. Skeletal muscle contains 1% - 1.5% CK B activity as measured by the SCE analytically specific methodology with AP_5A (Diadenosinepentaphosphate) and correction for residual adenylate kinase. We have confirmed 1-1.5% B in patients and "Vasalopp" skiers (2). Older German results from 1976-1978 indicated 3% - 4% CK B (6%-8% MB) in skeletal muscle. These data were obtained by a glutathion-activated "CK MB" immunoinhibition kit in the absence of AP_5A (survey in 1) and must be considered too high.

The SCE discriminator of 12 U/l (0.2 μkat/l)S-CK B was designed to discriminate between AMI and NOT-AMI patients in the CCU (6). In contrast, the German discriminator of 3% CK B was designed to discriminate between AMI and patients with extensive skeletal muscle damage (1). We have compared the two in the clinical setting of the CCU. The diagnostic sensitivity of "12 U/l" S-CK B is higher than 3% B. In (2,6) all AMI have above 12 U/l, (see also fig 4 in ref. 6 and ref. 7).

In the case of a falsely positive S-CK in a NOT-AMI patient only a 10-20 hours S-CK B activity below 12 U/l can exclude an AMI (6). In cases of both extensive skeletal muscle damage and an AMI neither discriminator can verify the AMI. In the CCU, this occurs after defibrillations and/or resuscitation by precordial thumping, external heartmassage (2).

Two examples are given below:

Condition	Time	S-CK	S-CK B	%B
♂41, L.Å.	adm	114	---	---
ECG: Aut, AMI	10 h	5700	132	2.3
Multiple defibrill.	16 h	10020	208	2.1
♂51, K-H				
Autopsy massive: AMI	10 h	6420	95	1.5
Multiple defibrill.	16 h	9780	136	1.4

The damage to thoracal skeletal muscle releases very high CK with 1% extracardial CK B (2% CK B) into the blood. In such cases neither immunoinhibition, electrophoresis, chromatography nor RIA can identify an additional, cardial CK MB activity.Only an extremely large AMI (80% CK MM, 20% CK MB in myocardium!) can increase the S-CK B to exceed 3% activity.

The diagnostic specificity of the 3% CK B limit may be higher than that of the 12 U/l discriminator, depending on the frequency of patients with extensive skeletal muscle damage in the CCU.

The Final verification of AMI versus NOT-AMI may be done by determination of S-LD isoenzyme activity, either by electrophoresis or as S-LD 1 activity measured after isolation by ISOMUNE (8). With the latter technique diagnostic sensitivity and specificity are about 0.95 in samples drawn 24 hours after onset of acute symptoms (2). Correlations between 16 h S-CK B and 24 h S-LD 1 has been found to 0.94 (2).

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