Cardiac Biomarkers in Acute Stroke

Fiori Patrizia1,2, Capaldo Guglielmo1, Corbo Antonio1, Corbo Giulia1, Di Gregorio Maria1, Iorillo Luigi1, Pelosi Chiara2, Savino Patrizia1, Botticella Filomena1, Dragonetti Carmela1, Manganiello Gianvito1, Morella Alessandro1, Pellecchia Vincenzo1, Gennaro Bellizzi1, Alberico Marielisa1, Benigni Giovanni1, De Caro Monica1, Guerriero Barbara1, Pace Erminio1, Raffa Marianna1, Ferrara Maurizio2, Mazza Emerico3, Tammaro C.A.4, Giannetti L.M.5 and Monaco Antonio1

1Neurological Unit, S. Ottone Frangipane Hospital, Ariano Irpino (AV), ASL AV, University of Naples, Italy
2Internal Medicine, S. Ottone Frangipane Hospital, Ariano Irpino (AV), ASL AV, University of Naples, Italy
3Cardiological Unit, S. Ottone Frangipane Hospital, Ariano Irpino (AV), ASL AV, University of Naples, Italy
4Intensive Care, S. Ottone Frangipane Hospital, Ariano Irpino (AV), ASL AV, University of Naples, Italy
5Radiology, S. Ottone Frangipane Hospital, Ariano Irpino (AV), ASL AV, University of Naples, Italy

*Corresponding author: Dr. Fiori Patrizia, Neurological Unit, S. Ottone Frangipane Hospital, Ariano Irpino (AV), ASL AV, University of Naples, Italy Tel: 39-825-877602, Fax: 39-825-828409


Abstract

Background: Serum cardiac biomarkers are increased in cerebrovascular diseases. The aim of our study was to assess their levels according to the severity of cardiac and neurological conditions.

Methods and results: We recruited 552 acute ischaemic stroke (AS), 290 chronic cerebrovascular (CCVD) and 111 other neuropsychiatric diseases (OND) patients. Blood withdrawals were performed within 12-24 hours. Serial assessments were repeated at day 3 and 7.

At admission, high sensitive T Troponin (hs T Tro) and N-Terminal Pro-Brain Natriuretic Peptide II (NT-pro- BNP) levels were increased in AS and CCVD compared to OND (inter-group variability), especially in patients in class II/IV, C/D New York Heart Association and American Cardiology Association scales. Signs of acute myocardial infarction were observed in a minority of patients. No significant fluctuations were found within each group of patients at repeated measurement in one-week time (intra-group unvariability) at ANOVA repeated measures. However, delta criterion allowed identifying malignant cerebrovascular profile. ASPECTS scores were tendentially lower in patients in class III/IV New York Heart Association, C/D American Cardiology Association scales with stable or increased levels of NT-pro-BNP compared to those with 100% relative percentage decrease of such biomarker at day VII. Better clinical course and prognosis were observed in AS patients with at least 50% relative percentage decrease of NT-pro-BNP at day 7.

Conclusions: Although serum cardiac biomarkers may reflect more the chronicity rather than the acuity of ischaemic sufferance, delta criterion helps in differential diagnosis between acute versus chronic condition. NT-pro-BNP may be an early warning marker of either an adaptive or maladaptive response, with volume and pressure overload preceding hs T Tro rise and irreversible systemic, ischaemic damage. Moreover, it is reliable for assessing the severity of clinical conditions and the prognosis 279.

Keywords: Cardiac markers, Cerebrovascular diseases

Introduction

In clinical practice, it is pivotal to identify useful parameters for prompt diagnosis, continuous monitoring, correct treatment, definite prognosis, safe discharge, scheduled follow up. Two cardiac biomarkers, high sensitive T Troponin (hs T Tro) and Brain Natriuretic Peptide (BNP), are commonly assessed in emergency department and for monitoring clinical conditions during hospitalization.

T Tro is a structural myocardial molecule. In myocardial necrosis, the entity of its release is a marker of the severity of acute coronary syndrome [1]. Its level predicts all-cause mortality [2-4], correlates with stroke severity, disability, increased brief and long-term mortality [5-11]. However, the dynamic relative and absolute changes are prognostically more significant than stable elevation in chronic conditions. National Academy of Clinical Biochemistry suggests using the delta criterion (changes greater than 20%) in sensitive assay when the value is above 99th percentile [12,13].

BNP is synthesized and released by cardiomyocytes in response to cardiac haemodynamic stress with increased transmural wall tension (heart volume and pressure overload). Its level tends to be higher in female gender and increases by aging [14,15]. It is considered a marker of cardiac impairment, as in left ventricular dysfunction and cardiac heart failure [16-19]. N-Terminal Pro-Brain Natriuretic Peptide II (NT-pro-BNP) results from cleavage of the precursor molecule, namely pro-BNP. It is considered the best diagnostic and prognostic parameter in cardiac heart failure [20]. It is a strong predictor for coronary artery disease severity and correlates with left ventricular ejection fraction [21]. Low in-hospital reduction and high discharge level are independent markers for death or readmission after decompensated chronic heart failure [22,23]. Intensive care survivors had significantly lower NT-pro-BNP values than non-survivors [24]. This parameter predicts risk of stroke [25-29], its clinical and radi-
ological severity, recurrence and poor prognosis [30-37], cardioem-
boic genesis [38].

Both cardiovascular biomarkers are associated with increased risk of all-cause mortality [39-41].

The aim of our study was to evaluate hs T Tro and NT-pro-
BNP levels in patients affected with acute stroke and/or chronic cerebrovascular conditions 313.

**Materials and Methods**

Nine-hundred-fifty-three patients, 552 (57.9%) of which affect-
ed with acute ischaemic stroke (AS) (age 78.6 sd 11.5), 290 (30.4%) with chronic cerebrovascular (CCVD) (age 77.3 sd 8.7) and 111 (11.6%) with other neuropsychiatric diseases (OND), as psychoses, epilpesies, minor traumas, (age 49.2 sd 15.4), were recruited in our Neurological Unit/Spoke Unit (Table 1). Blood withdrawals were performed within 12-24 hours after admission. Serial assessments were repeated at day 3 and 7. Results were analyzed in subgroups of patients according to the severity of heart and neurological dysfunc-
tion, evaluated by the CHAD2D5VAs, HAS BLED, New York Heart Association (NYHA), American Cardiology Association (ACA) scales, Simplified Pulmonary Embolism Severity Index (SPESI), Pulmo-

nary Embolism Severity Index (PESI), Apache score, Glasgow Coma (GCS)/Outcome (GOS) scales, Hachinski and Modified Rankin Scale (MRS) scales. ECG, transthoracic and/or transesophageal echocar-
diography were performed within one-week time. We focalized our attention on the following echocardiographic parameters: ejection fraction (EF, normal range 60-80%), pulmonary arterial pressure

| Table 1: Patients classification bases on their conditions. |
|-----------------|--------|--------|
| Number of patients | OND  | CCVD  | AS   |
| Age              | 111   | 290    | 552  |
| Males            | 63 (56.8%) | 165 (56.9%) | 265 (48%) |
| Females          | 48 (43.2%) | 125 (43.1%) | 287 (52%) |
| Male age         | 51.1 sd 15.5 | 77.3 sd 8.7 | 75.4 sd 12.7 |
| Female age       | 46.3 sd 16.1 | 75.8 sd 9.1 | 81 sd 9.7 |
| Past smokers     | 31 (27.9%) | 90 (31%) | 204 (37%) |
| Current smokers  | 27 (24.3%) | 23 (7.9%) | 45 (8.2%) |
| Potus            | 21 (18.9%) | 70 (24.1%) | 102 (19%) |
| Arterial Hypertension | 46 (41.4%) | 244 (84.1%) | 469 (85%) |
| II type Diabetes | 6 (5.4%) | 64 (22%) | 149 (27%) |
| Hypercholesterolemia (LDL > 100 mg/dl) | 1 (0.9%) | 122 (42.1%) | 221 (40%) |
| CHAD2VASC2       | 1.2 sd 1 | 4.4 sd 1.5 | 5.9 sd 1.7 |
| HAS BLED         | 0.9 sd 1 | 3.1 sd 1.1 | 3.9 sd 1.2 |
| Hachinski scale  | 1.9 sd 2 | 7.3 sd 2.5 | 9.2 sd 2.6 |
| GCS at admission | 14.9 sd 0.3 | 14.1 sd 1.7 | 12.8 sd 2.7 |
| GCS at day 7     | 14.9 sd 1.2 | 14.5 sd 0.9 | 13.5 sd 2.5 |
| GOS at day 7     | 5 sd 0.1 | 4.5 sd 0.7 | 3.9 sd 0.9 |
| pre-stroke MRS   | 0 sd 0.2 | 0.9 sd 1.3 | 1 sd 1.4 |
| MRS at day 7     | 0 sd 0.2 | 1 sd 1.5 | 2.2 sd 1.8 |
| Previous ischaemic strokes | 0 | 38 (13.1%) | 83 (15%) |
| Lacunes          | 0 | 290 (100%) | 61 (11.1%) |
| Significant stenosis or occlusion of major brain arteries (> 50%) | 3 (2.7%) | 96 (33.1%) | 199 (36.1%) |
| Significant kinking of major brain arteries (< 60°) | 0% | 20 (6.9%) | 33 (6%) |
| Significant stenosis or occlusion of major brain arteries (> 50%), potentially related to AS | 0% | 0% | 61 (11.1%) |
| Significant kinking of major brain arteries (< 60°), potentially related to AS | 0% | 0% | 0% |
| Class I/II NYHA, A/B ACA | 109 (98.2%) | 184 (63.4%) | 199 (36%) |
| Class III/IV NYHA, C/D ACA | 2 (1.8%) | 106 (36.6%) | 353 (63.9%) |
| Supraventricular extrasystolia | 30 (27%) | 61 (21%) | 94 (17%) |
| Ventricular extrasystolia | 20 (18%) | 61 (21%) | 94 (17%) |
| Blocks of branches | 12 (10.8%) | 61 (21%) | 110 (19.9%) |
| Atrioventricular blocks | 2 (1.8%) | 14 (4.8%) | 22 (4%) |
| Atrial fibrillation | 0% | 38 (13.1%) | 166 (30%) |
| Myocardial necrosis at ECG | 3 (2.7%) | 3 (1%) | 20 (3.6%) |
| Myocardial necrosis at echocardiography | 5 (4.5%) | 14 (4.8%) | 40 (7.2%) |
Cardiac biomarkers were detected according to standard methods. Serum hs T Tro and NT-pro-BNP II levels were measured by electrochemiluminescence immunoassay with biotinylated monoclonal anti-mouse-T Tro and anti-mouse-NT-pro-BNP-specific antibodies labeled with ruthenium, which formed a sandwich complex. After addition of streptavidin-coated microparticles, it bound to solid phase. The microparticles were aspirated and magnetically captured by an electrode, while unbound particles were removed. Voltage induced chemiluminescence was revealed by Cobas analyzer (Elecsys and Cobas, Roche). The cut off value to rule out myocardial infarction was < 15 pg/ml for hs T Tro. Normal range value of NT-pro-BNP were 0-125 pg/ml.

Statistical analysis was performed by unpaired T test, ANOVA repeated measures, for standard description of baseline characteristics and differences among the studied groups, by Pearson correlation test and regression analysis, for identification of association among examined parameters. Moreover, delta criterion was applied, considering differences of at least 20% for hs T Tro and 50% for NT-pro-BNP 345.

Results

Increased hs T Tro and NT-pro-BNP were detected in AS (hs T Tro: 59.6 sd 356.3 pg/ml, p 0.02; NT-pro-BNP: 3103.6 sd 5772.6 pg/ml, p 0.01) and CCVD (hs T Tro: 28.1 sd 33.6 pg/ml, p 0.03; NT-pro-BNP: 1031.6 sd 2462.2 pg/ml, p 0.03) compared to OND (hs T Tro: 6.8 sd 4.5 pg/ml; NT-pro-BNP: 124.7 sd 245.5 pg/ml) at T test (intergroup variability) (Figure 1). Levels above normal values of hs T Tro were present in 373 (67.5%) AS, 169 (58.2%) CCVD, 7 (6.3%) OND, of NT-pro-BNP in 477 (86.4%) AS, 220 (75.8%) CCVD, 32 (28.8%) OND.

Three-hundred-fifty-three (63.9%) AS, 106 (36.6%) CCVD and two (1.8%) OND were classified in class III/IV NYHA, C/D ACA (Table 1). Significant differences were found between patients in class I/II, A/B compared to class III/IV, C/D NYHA and ACA scales in AS (hs T Tro 18.9 sd 27.6 vs. 79.7 sd 380.7 pg/ml, p 0.001; NT-pro-BNP 241.8 sd 238.5 vs. 7202.1 sd 4821.5 pg/ml, p 0.01) (Figure 2).

Moreover, the subgroup of AS with CCVD had higher levels compared to AS without CCVD (hs T Tro: 50.1 sd 117.9 vs.17.6 sd 27.7 pg/ml, p 0.01; NT-pro-BNP 3609.5 sd 6121.7 vs. 1092.1 sd 3449.8 pg/ml, p 0.03) (Figure 3).

Supraventricular extrasystolia was present in 30 (27%) OND, 61 (21%) CCVD, 94 (17%) AS, ventricular extrasystolia in 20 (18%) OND, 61 (21%) CCVD, 94 (17%) AS, blocks of branches in 12 (10.8%) OND, 61 (21%) CCVD, 110 (19.9%) AS, atrioventricular blocks in 2 (1.8%) OND, 14 (4.8%) CCVD, 22 (4%) AS, atrial fibrillation in 38 (13.1%) CCVD, 166 (30%) AS, minor valvular dysfunctions in 28 (25.2%) OND, 159 (54.8%) CCVD, 267 (48.4%) AS, moderate-severe valvular cardi-

opathy in 44 (15.2%) CCVD, 144 (26.1%) AS (Table 1). The reliability of cardiac biomarkers concerning myocardial infarction is shown in Table 2. Significant correlation was observed between levels of NT-pro-BNP and severity of cardiac dysfunction evaluated by NYHA and ACA scales, the severity of which were scored in the range of 1 to 4 (r 0.50).

Serial assessment did not show significant fluctuations within each groups of patients at day 3 and 7 compared to admission (intragroup unvariability) (Figure 4) and at different time lag in bounce backs (preliminary data, not shown) at ANOVA repeated measures.

Overall, according to the delta criterion, significant relative decrease > 20% of hs T Tro was found in CCVD (-31.16%) (Figure 5a). Significant relative percentage decreases > 50% of NT-pro-BNP were observed in OND (-124.2%), in CCVD (-58.04%) and in AS (-91.17%) (Figure 5b). Relative percentage decreases > 20% of hs T Tro were present in 28 (25.2%) OND, 85 (29.3%) CCVD, 186 (33.7%) AS. Relative percentage decreases > 50% of NT-PBNP were detected in 58 (52.3%) OND, 103 (35.5%) CCVD, 235 (42.6%) AS. No significant

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**Figure 3:** Levels of hs T Tro (a) and NT-pro-BNP (b) in AS patients without or with CCVD at admission.

**Figure 4:** Serial assessment of hs T Tro (a) and NT-pro-BNP (b) at day 0-1, 3 and 7 in patients affected with OND (left columns), CCVD (columns at center), AS (right columns).
relative percentage changes were revealed in 65 (58.6%) OND, 157 (54.1%) CCVD, 243 (44%) AS concerning hs T Tro, 44 (39.6%) OND, 156 (53.8%) CCVD, 248 (44.9%) AS concerning NT-pro-BNP.

Significant differences were present between AS with relative decrease of at least 50% in NT-pro-BNP levels compared with AS without significant changing of such marker regarding GCS (12.6 sd 2.7 vs. 11.9 sd 2.9, p 0.02), pre-stroke MRS (1 sd 1.46 vs. 1.34 sd 1.56, p 0.03), Hachinski scale (9.9 sd 2 vs. 10.4 sd 2.1, p 0.01), HAS (4.2 sd 1 vs. 4.4 sd 1, p 0.02) at admission, GCS (13.6 sd 2.1 vs. 12.8 sd 2.6, p 0.0004), GOS (3.8 sd 0.8 vs. 3.5 sd 0.8, p 0.0001), MRS (2.6 sd 1.7 vs. 3.1 sd 1.6, p 0.0006) at day 7 (Table 3). The highest levels of hs T Tro were detected in class III/IV, C/D patients with at least 50% relative increase compared to those with at least 50% relative decrease of NT-Pro-BNP at day VII. These patients had the lowest GCS at admission, as well as the lowest GCS and highest MRS at day VII.

In class 0/I OND, a significant reduction of NT-pro-BNP levels was already detected at day 3 (38.7 sd 34.6 vs. 77.2 sd 71.3, p 0.0001), especially in females, compared to males (females 45.7 sd 30.4 vs. 103.3 sd 74.2, p 0.0002; males 33.1 sd 37.1 vs. 55.2 sd 61.6, p 0.06). This finding was confirmed at day 7 (40.3 sd 54.3 vs. 77.2 sd 71.3, p 0.01; females 43.3 sd 28.3 vs. 103,3 sd 74.2, p 0.007; males 37.2 sd 73 vs. 55.2 sd 61.6, p 0.08) (Figure 6). Any stressful event, diagnostic procedures included, were responsible of fluctuations of such marker.

**Table 2:** The reliability of cardiac biomarkers concerning myocardial infarction.

<table>
<thead>
<tr>
<th></th>
<th>hs T Tro</th>
<th>NT-pro-BNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensibility</td>
<td>82.40%</td>
<td>92%</td>
</tr>
<tr>
<td>Specificity</td>
<td>97.60%</td>
<td>75%</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>91.30%</td>
<td>61.80%</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>90.20%</td>
<td>84.60%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>90.60%</td>
<td>78.90%</td>
</tr>
</tbody>
</table>

**Table 3:** Significant differences were present between AS with relative decrease of at least 50% in NT-pro-BNP levels compared with AS without significant changes.

<table>
<thead>
<tr>
<th>No NT-pro-BNP Changes</th>
<th>At Least 50% Decrease of NT-pro-BNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>I GCS</td>
<td>11.9 sd 2.9</td>
</tr>
<tr>
<td>VII GCS</td>
<td>12.8 sd 2.6</td>
</tr>
<tr>
<td>GOS</td>
<td>3.5 sd 0.8</td>
</tr>
<tr>
<td>Pre-stroke MRS</td>
<td>1.34 sd 1.56</td>
</tr>
<tr>
<td>VII MRS</td>
<td>3.1 sd 1.6</td>
</tr>
<tr>
<td>Hachinski scale</td>
<td>10.4 sd 2.1</td>
</tr>
<tr>
<td>HASBLED</td>
<td>4.4 sd 1</td>
</tr>
</tbody>
</table>

**Figure 5:** Relative percentage decreases hs T Tro (a) and NT-pro-BNP (b) in OND, CCVD and AS patients at day 7.

**Figure 6:** Serial assessment of NT-pro-BNP at day 0-1, 3 and 7 in male (left) and female (right) patients affected with OND and respective relative percentage decreases at day 7.
Significant differences were observed in AD between OND, CCVD and AS (OND 3.5 sd 0.6 cm vs. CCVD 4.2 sd 0.6 cm, p 0.03; OND 3.5 sd 0.6 cm vs. AS 4.8 sd 4.3 cm, p 0.01) (Figure 7). The most significant correlations were present between hs T Tro and EF (r 0.22), AD (r 0.28), PAP (r 0.23), between NT-pro-BNP and EF (r -0.24), AD (r 0.25), PAP (r 0.48) in CCVD, between NT-pro-BNP and EF (r -0.34), PAP (r 0.47) in AS. Lacunes were present in all CCVD and in 61 (11.1%) AS. Signs of previous ischaemic strokes were evident in 38 (13.1%) CCVD and 83 (15%) AS. Acute infarcts were in the territory of anterior circulation in 320 (58%) AS, in vertebro-basilar areas in 110 (19.9%) AS. Haemorrhagic infarction occurred in 22 (4%) AS. Other 122 (22.1%) AS were considered lacunar. No significant differences of cardiac biomarkers were related to the region of the cerebral infarction (Internal Carotid Artery, Middle Cerebral Artery, Anterior Cerebral Artery AS: hs T Tro 73.4 sd 430.2 pg/ml, NT-pro-BNP 3898.6 sd 6648.4 pg/ml; Vertebro-Basilar AS: hs T Tro 60 sd 153.5 pg/ml; NT-pro-BNP: 3607.9 sd 6143.7 pg/ml, p ns). This was confirmed in subgroups’ analysis among cardiac biomarkers in fronto-parietal (hs T Tro 24.93 sd 19.37 pg/ml; NT-pro-BNP 1717.1 sd 1996.4 pg/ml), temporo-insular (hs T Tro 23.9 sd 15.1 pg/ml; NT-pro-BNP 2581 sd 4166.1 pg/ml), capsulo-nuclear (hs T Tro 27.73 sd 27.27 pg/ml; NT-pro-BNP 2022.4 sd 2435.5 pg/ml), occipital (hs T Tro 41.68 sd 42.57 pg/ml; NT-pro-BNP 2398.8 sd 2198.4 pg/ml), cerebellar-brainstem (hs T Tro 30.6 sd 26.4 pg/ml; NT-pro-BNP 2080.8 sd 2771.9 pg/ml) AS (Figure 8). Their levels as the extension of cerebral ischaemia were related to the overall severity of neurocardiological dysfunction, responsible of diffuse hypoxic encephalopathy in severe cases. In patients with early neuroradiological signs of cerebral ischaemia at admission, ASPECTS scores were tendentially lower in patients with stable or increased levels of NT-pro-BNP compared to those with at least 100% relative decrease of NT-pro-BNP at day VII (class I/II NYHA, A/B ACA patients 5.33 sd 1.56 vs. 5.83 sd 1.6, p ns; class III/IV NYHA, C/D ACA 4.25 sd 1.71 vs. 5.03 sd 1.66, p 0.07) (Figure 9). In the latter, significant correlations were found between ASPECTS, GCS (r 0.47) at admission, GCS (r 0.30), MRS (r -0.20), hs T Tro (-0.58) at day VII 1192.

Discussion

Cardiac markers are increased in cerebrovascular conditions, particularly in AS in class III/IV, C/D NYHA and ACA scales and in the contest of chronic cerebrovascular disease (CCVD), compared to other neurological diseases (OND) (inter-group variability). No significant fluctuations were found within each group of patients at repeated measurements in one-week time (intra-group unvariability) and at different time lag in bounce backs (preliminary data). However, significant absolute and relative changes of such parameters are pivotal for early detection of sudden acuity or worsening of chronicity. Moreover, their decreases are associated with better outcomes while their increases point out a malignant prognosis.

NYHA scale allows a quick assessment of the severity of cardiologic conditions. Together with cardiac biomarkers speed up diagnostic iter for appropriate emergency treatments. According to cardiologic criteria, since cardiac biomarkers reveal myocardial injury, independently on the etiopathogenetic cause, their elevation is not sufficient for a definite diagnosis of acute coronary syndrome. At least one of the following clinical criteria has to be present: symptoms of ischemia, electrocardiogram changes (new ST-T changes or patterns).

Left Bundle Branch Block, new Q waves), imaging evidence, such as
ing and guided therapy may prevent heart failure, reducing cardio
of evidence for diagnosis and prognosis. Natriuretic peptide screen
consider natriuretic peptides in class I of recommendation, level A
ellation in emergency. Clinical practice guidelines on Heart Failure
latter is strongly associated with myocardial infarction, microsize
-ment of BNP is pivotal for urgent decision making, although contin
(heart failure), and can be quantified accurately and eco
vent of NT-pro-BNP seems to be even higher than that of T Tro

Among cardiac biomarkers, NT-pro-BNP has the features of an ideal

However, in real-world practice, comorbidities are frequent, re-
duce penumbra and collaterals, account for increased levels of both
ecardium on the echocardiogram or intracoronary thrombus at cor-
nocardiography [42]. We found significant ECG/echocardiograph-
ic acute ischaemic signs in a minority of our patients. Therefore, we
the value of cardiac biomarkers for risk evaluation and for
monitoring clinical conditions. Moreover, their levels predict the se-
verity at ACA scale.

However, in real-world practice, comorbidities are frequent, re-
duce penumbra and collaterals, account for increased levels of T Tro
and NT-pro-BNP. In Dallas Heart Study, up to 40% of patients have
troponin levels in the range of myocardial infarction [43]. Asso-
ction with age, male gender, trauma, burns, inflammation, hyper-
tension, diabetes, heart failure, cerebrovascular accidents, pul-
monary emboli, renal impairment is reported. More than 90% of
patients with stable coronary artery disease, without heart failure,
have levels of T Tro within the measuring range [44]. Nonetheless,
the utility of delta criterion to distinguish acute from chronic con-
ditions is undeniable. In this regard, we observe that relative per-
centage decreases ought to be considered together with absolute
levels and changes, especially in critical conditions (e.g. the relative
percentage decrease has a different meaning if the absolute value
is in the range of thousand or ten picograms). Prognostic sensibility
of NT-pro-BNP seems to be even higher than that of T Tro [45,46].

Figure 9: ASPECTS scores and relative percentage changes of NT-pro-
BNP at day VII in AS patients.

Our finding of significant fluctuations of NT-pro-BNP in class 0/I
OND patients suggests that the burden may be wider than expected
as well as the reversibility of physiological response versus a shift
toward pathological dysfunctions. Any stressful event may interfere
with physiological circulation, because of a prevalence of sympathetic
activity. NT-pro-BNP may be a warning marker of either an adaptive or maladaptive response. It is reported that the risk of cardiovascular disease in individuals with relatively
low levels of NT-pro-BNP [55-124 pg/ml] was 1.9-fold higher than in
those with the lowest levels (< 55 pg/ml) [55], independently of
conventional risk factors [55,56]. Patients with elevated natriureti-

cidal advice on risk stratification according to baseline clinical

table III/IV, C/D

Figure 9: ASPECTS scores and relative percentage changes of NT-pro-
BNP at day VII in AS patients.

Left Bundle Branch Block, new Q waves), imaging evidence, such as
a new regional wall motion abnormality, new loss of viable myo-
cardium on the echocardiogram or intracoronary thrombus at cor-
nocardiography [42]. We found significant ECG/echocardiograph-
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highlight the value of cardiac biomarkers for risk evaluation and for
monitoring clinical conditions. Moreover, their levels predict the se-
verity at ACA scale.

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cardiac biomarkers in AS in cortical-subcortical encephalic regions, as insula, diencephalon and brainstem, may predict a faster necrotic evolution and account for malignant dysautonomia. Moreover, the higher risk of stroke in patients suffering from sleep apnoea [62] suggests that transient or persistent lacunar, ischaemic sufferance may predispose to more severe ischaemic events, hinder the recovery and worsen the outcomes in vertebral-basilar AS, when respiratory centers in brainstem are early involved. Indeed, an association of sleep apnoea with clinically silent microvascular brain tissue changes in general population and in AS and between sleep disordered breathing and brainstem infarction are reported 1249 [63-65].

Conclusion

NT-pro-BNP and hs T Tro are pivotal for a prompt assessment of circulatory condition for the most appropriate treatment, directed to widen the therapeutic window and limit the costs related to invalidating outcomes. While the former is a sign of functional alteration, the latter represents already a structural damage. Although serum cardiac biomarkers may reflect more the chronicity rather than the acuity of ischaemic sufferance, delta criterion helps in differential diagnosis between acute versus chronic condition. Since apparently physiological conditions may evolve to subtle or overt pathological conditions, parallel haematological and urinary parameters, together with more sophisticated electrophysiological and neuroradiological techniques, may help in defining the burden and lesion load and establish the criteria for rational procedures. Further studies are needed for better defining the therapeutic window in AS patients suffering from heart failure, decision making concerning the strategy of “scoop and run” to mechanical thrombectomy or “stay and play” with plasminogen activators and/or other pharmacological agents 157 TOT 3270.

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Declarations of conflict of interests: None.

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References

25. Folsom AR, Nimi V, Bell EJ, Oluleye OW, Gottesman RF, et al. (2013)


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