

## Ems personnel and post-traumatic stress disorder (ptsd): a case report

°Alberto Gabrieli, °Marco Calzoni, \*Costantino Caroselli, °Vittorio Schweiger, °Enrico Polati

°Scuola di Specializzazione in Anestesia, Rianimazione e Terapia Intensiva, Azienda Ospedaliera Universitaria Integrata, Ospedale Policlinico Verona; \*Dipartimento di Emergenza ed Accettazione, Azienda Ospedaliera Universitaria Integrata, Ospedale Civile Maggiore, Verona

### Learning Objective

We discuss a clinical case of serious emotional impact in pre-hospital setting. We use this case to update our knowledge and to understand the underestimated Post-Traumatic Stress Disorder (PTSD) risk among the EMS personnel.

### Case Report

The prehospital medical team was sent for an imminent delivery. An ambulance with ED nurse and 2 EMTs was already on scene. On quick-look the patient was suffering, sweated, screaming and rolling about in pain on bed. She was at end-term pregnancy (38 weeks). The abdomen was an end-term one, with no movement palpable and no trauma signs. Membrane's rupture was recorded at fastcar arrival. The clinical exam showed a cervix dilatation of approximately 2 centimeters. So we decided to evacuate the patient to the nearest hospital for a safe delivery and to prepare ourselves for an emergency delivery in ambulance. During ambulance run the patient started to feel periodic contractions. An on-route evaluation showed an approximately 8 centimeters cervix dilatation with the vertex appearance. During ambulance parking a violent contraction produced the vertex exit with a very abundant hemorrhage. Then the patient screamed and kept pressing hardly her baby vertex. She was promptly immobilized and transferred in the emergency room where an OB/GYN and neonatologist teams was expecting us. Immediately on the ambulance stretcher the team performed a urgent episiotomy with a very abundant blood and meconium discharge. We assisted the delivery of dead baby which at a first look seemed to be dead days before, probably because of a skull malformation. After that the ambulance crew communicated the inoperative status for non specified hygienic reason for all the day-shift. The same crew didn't want to complete the debriefing the subsequent days. The ED-nurse went on sick leave for a while and after one month she was transferred to another ward in another hospital.

### Discussion

Post-Traumatic Stress Disorder (PTSD) is an anxiety disorder that may occur after a psychological trauma exposure. The frequency and the severity of PTSD seem to be related to the proximity to the trauma. Another important factor is the chronic and repeated exposure to stress events, as might happen among rescue and emergency personnel. EMS personnel are constantly exposed to traumatic psychological stress due to the repeated daily high exposure to human suffering and death and working in hazardous

environment. Estimates of prevalence of PTSD in this group have been around 20% [1]. PTSD should be diagnosed if full criteria for PTSD as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-R) are met. Subclinical PTSD can be defined as satisfying re-experiencing category and either avoidance category or hyperarousal one, but not both [2]. Biological studies have demonstrated that patients with PTSD have increased circulating levels of norepinephrine, increased reactivity of alfa2-adrenergic receptors and increased thyroid hormone levels. There are also evidences on neuroanatomical alterations in brain areas involved in fear response. Besides, cognitive problems and some intrusive recollections that characterize PTSD can have a neuroanatomical substrate in hippocampal alterations [3]. The PTSD treatment is based on providing disease knowledge and support. This is the base to build some sort of therapeutic alliance and to emphasize that patients are not alone. Critical Incident Stress Debriefing (CISD) is "a structured intervention designed to promote the emotional processing of traumatic events through the ventilation and normalisation of reactions and preparation for possible future experiences." Medications such as Sertraline and Paroxetine may also benefit traumatized patients [4]. A key imperative for any Emergency Medical Service is to develop strategies for both the prevention and treatment of the significant levels of mental health problems associated with emergency work. In the EMS there is a high underestimated risk of PTSD, but the most important strategy is to create a risk surveillance system about the psychological aspects of this job and to build-up the base of treatment starting with debriefing and defusing.

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## Atorvastatina vs anacetrapib nel controllo del Tromboembolismo Venoso In Pazienti Oncologici

R. Di Filippo<sup>1</sup>, A. Melone<sup>2</sup>, E. Varrato<sup>3</sup>, S. Sofia<sup>4</sup>, C. Balsano\*

<sup>1</sup>U.O. di Medicina Interna, P.O. "S. Salvatore" dell'Aquila;

<sup>2</sup>U.O.C. di Medicina e Chirurgia D'urgenza e Accettazione, P.O. "S.S. Filippo e Nicola" di Avezzano;

<sup>3</sup>U.O. di Medicina Interna, P.O. "G. Mazzini" di Teramo;

<sup>4</sup>U.O. di Medicina Interna, P.O. "Santissima Maria dello Splendore" di Giulianova;

\*Dipartimento di Medicina Interna e Sanità Pubblica, Università degli studi dell'Aquila

Nella popolazione generale l'incidenza annuale di eventi tromboembolici (TEV) è di 117 casi ogni 100.000 abitanti. La presenza di una neoplasia aumenta di circa quattro volte tale rischio, mentre nei pazienti che ricevono la chemioterapia il rischio è aumentato di circa sette volte. Le cellule tumorali possono attivare il sistema coagulativo attraverso meccanismi indiretti, determinando l'attivazione di cellule ematiche quali i monociti, le piastrine e le cellule endoteliali ed inducendo, in questo modo, l'espressione di un fenotipo procoagulante. Infatti, piastrine e cellule endoteliali entrano comunemente a far parte dell'avvio della cascata coagulativa e sono inoltre suscettibili di attivazione da parte delle citochine (IL-1; VEGF; TNF-alfaetc.), anch'esse prodotte dalle cellule tumorali. Il trattamento standard del TEV in pazienti con cancro, in assenza di controindicazioni note, non differisce da quello dei pazienti non affetti da neoplasia (somministrazione di eparina a basso peso molecolare, ENF o EBPM, seguita dall'anticoagulazione con anticoagulanti orali).

I pazienti neoplastici con TEV, durante il trattamento anticoagulante orale, sono esposti ad un rischio significativo sia di recidive trombotiche che di complicanze emorragiche, rispetto ai pazienti non neoplastici. Da quanto detto si evince come la condotta terapeutica da far seguire a questi pazienti debba tener conto sia dell'elevato rischio di recidiva, che del rischio emorragico. Infatti, nonostante un'adeguata anticoagulazione circa il 5-7% dei pazienti con cancro sviluppa una recidiva di TEV. Nonostante i dati incoraggianti mostrati dall'uso delle statine nei pazienti oncologici, il loro uso spesso è associato ad un ben noto incremento dose-dipendente delle transaminasi; quindi si tratta di farmaci di difficile utilizzo nei pazienti sottoposti a chemioterapia e sono assolutamente sconsigliati nei pazienti con insufficienza epatica o con epatocarcinoma.

Recentemente, è stata messa in luce l'efficacia degli inibitori della Proteina di Trasferimento degli Esteri del Colesterolo (CETP), in particolare dell'Anacetrapid, nell'aumentare i livelli di colesterolo

HDL. Nei pazienti oncologici sottoposti a regime chemioterapico la somministrazione di inibitori delle CETP potrebbe determinare una migliore prevenzione e/o ridurre l'incidenza di rischio di TEV rispetto ai pazienti sottoposti a regime chemioterapico trattati con statine (Atorvastatina).

Il nostro gruppo vuole, quindi, valutare la possibilità di trattamenti di combinazione con chemioterapici e ipolipemizzanti in modo da ottenere trattamenti più efficaci per la terapia a lungo termine del TEV in pazienti con patologia neoplastica.

Verrà pertanto effettuato uno studio randomizzato su due gruppi omogenei di pazienti sottoposti a regime chemioterapico, a cui verrà associato Atorvastatina o Anacetrapib per osservare gli effetti sull'incidenza di TEV e sul rischio emorragico.

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## Biomarkers And Fever in the Emergency Department: BAFED study

V. Mura\*, B. De Berardinis\*, F. Travaglino\*, E. Salvatori\*, CS. Gori\*, C. Bongiovanni\*, V. Russo\*, O. Piras\*, G. Salerno\*\*, M. Candelli\*\*\*, N. Gentiloni Silveri\*\*\*, P. Cardelli\*\*, S. Di Somma\*.

\*Emergency department Azienda Ospedaliera Sant'Andrea, II School of Medicine "La Sapienza" University, Rome, Italy;

\*\* Clinical and molecular medicine department Azienda Ospedaliera Sant'Andrea, II School of Medicine "La Sapienza" University, Rome, Italy;

\*\*\* Emergency department Policlinico A. Gemelli, Catholic University of the Sacred Heart, Rome - Italy

### Introduzione

La pro-calcitonina (PCT) e la pro-adrenomedullina (Mid-Regional pro-Adrenomedullin - MR pro-ADM) sono tra quei peptidi le cui concentrazioni plasmatiche subiscono incrementi di rilievo nelle infezioni batteriche. Obiettivo del nostro studio è stato quello di valutare all'arrivo del paziente in PS per febbre, con o senza dispnea: i livelli di Procalcitonina e di MR proADM, la correlazione tra APACHE II score e PCT, la correlazione tra APACHE II score e MR proADM, al fine di vedere se i

livelli dei suddetti biomarkers possono essere correlati in modo lineare con uno score complesso e "multiparametrico" come l'APACHE II.

### Materiali e metodi

Studio non profit, osservazionale, multicentrico. Sono stati arruolati, in maniera competitiva, 98 pazienti con febbre, con o senza dispnea, ammessi in Pronto Soccorso nel periodo compreso tra Settembre 2009 e Settembre 2010.

All'arrivo dei pazienti in PS sono stati eseguiti: anamnesi ed esame obiettivo (compreso Glasgow Coma Scale), EGA, prelievo per chimica clinica, emocromo, PCT e MR pro-ADM, APACHE II score. Il dosaggio della PCT e dell'MR pro-ADM sono stati effettuati utilizzando il Kripton (Brahms).

### Risultati

Sono stati arruolati 98 pazienti. I risultati hanno dimostrato valori medi di PCT 4.05 ng/ml e di MR pro-ADM 1.99 nmol/L. La

correlazione tra APACHE II score e PCT è risultata statisticamente significativa ( $p < 0.001$ ), ugualmente significativa è risultata la correlazione tra APACHE II e MR pro-ADM ( $p < 0.001$ ) e tra PCT e MR pro-ADM ( $p < 0.001$ ).

### Conclusioni

Nei pazienti con febbre i valori della PCT e dell'MR pro-ADM assumono un significato prognostico nella valutazione del paziente con febbre in Pronto Soccorso.

## Le variazioni meteorologiche a breve termine come fattore di rischio per colica renale: analisi su 8168 coliche renali rilevate in sette anni di attività del Pronto Soccorso di Parma

Ivan Comelli

Scuola di Specializzazione in Medicina in Emergenza-Urgenza, Università degli Studi di Parma

La patogenesi della formazione dei calcoli renali è un processo complesso, ampiamente variabile in base alla composizione chimica dei calcoli stessi. È inoltre documentata una ampia variabilità geografica, in gran parte attribuibile alla temperatura media annuale (Mean Annual Temperature, MAT) delle diverse aree, ed una variabilità stagionale non altrettanto compiutamente documentata. La prevalenza di nefrolitiasi è stimata intorno all'1-6,6% a livello mondiale; la suddetta variabilità geografica si esplicita sinteticamente come segue: 1-5% in Asia, 20% in Arabia Saudita, 13% in Nord America, 5-9% in Europa; in Italia si aggira intorno al 10%. Alcuni ricercatori hanno riportato un aumento di visite in Pronto Soccorso per colica renale durante l'estate, ma non è chiaro il nesso tra variazione meteorologica e insorgenza della colica, in considerazione del fatto che la formazione del calcolo è un processo lento, che dura diverse settimane (alcuni ricercatori hanno riportato una latenza media di 90 giorni tra il trasferimento in aree caratterizzate da caldo intenso e secco e formazione dei calcoli). In base ai suddetti dati, l'autore si è proposto con questo studio di valutare l'influenza delle variazioni meteorologiche rilevate su base giornaliera sul numero di visite per coliche renali nel Pronto Soccorso dell'Azienda Ospedaliero-Universitaria di Parma (bacino d'utenza provinciale, in area caratterizzata da clima continentale temperato). Sono stati estratti i dati dal database informatico del nostro Pronto Soccorso, utilizzando una doppia chiave di ricerca (codice ICD-9: 7880, e "stringhe" verbali estratte dalla diagnosi descrittiva di dimissione). Con tale metodologia sono stati identificati, nel corso del periodo di 2557 giorni presi in considerazione (1° gennaio 2002 - 31 dicembre 2008), 8168 episo-

di di colica renale. Il numero totale di accessi al PS nello stesso periodo è stato di 557990, risultandone una percentuale pari a 1.46% delle visite per colica renale, dato in linea con altri report di letteratura. Il numero di coliche per giorno, e la temperatura media giornaliera di ogni singola giornata (forniti dall'Agenzia Regionale Per l'Ambiente, ARPA) sono stati sottoposti ad analisi di regressione lineare, dimostrando una correlazione molto significativa ( $R = 0.88$ ;  $p < 0.0001$ ). In sintesi, tra pieno inverno ( $T^\circ$  prossime allo 0) e piena estate ( $T^\circ$  prossime ai 30  $^\circ\text{C}$ ) il numero di accessi medio giornaliero per colica renale aumenta del 47%. Successivamente è stata eseguita una analisi di regressione lineare multipla univariata tra ogni singolo episodio di colica e la temperatura media di ogni singola giornata dei trenta giorni precedenti l'episodio clinico; per tale analisi è stato utilizzato il programma Mathematica 7®. Sono state dimostrate analoghe significative correlazioni, particolarmente forti nei giorni compresi tra il 5° e il 7° precedenti l'episodio clinico ( $R = 0.80$ ;  $p < 0.0001$  per il 6° giorno precedente l'episodio), ma ancora altamente significative per il 14° giorno ( $R = 0.77$ ;  $p < 0.0001$ ) ed il 20° giorno ( $R = 0.70$ ;  $p < 0.0001$ ) precedenti la colica. I nostri dati suggeriscono l'esistenza di un processo "accelerativo" della formazione del calcolo che, nel contesto di un processo già avviato, porti alla rapida crescita del calcolo e quindi all'episodio clinico. La disidratazione e la conseguente concentrazione urinaria sono certamente fattori determinanti, ma si considera anche l'importanza di fattori dietetici quale l'aumentato consumo di frutta, e quindi di acido ascorbico (noto acceleratore della precipitazione dei cristalli di ossalato di calcio), durante i mesi estivi.

## Endothelin-1 and nt-probnp levels in acute decompensated heart failure

Tommaso Barreca<sup>1</sup>, Ombretta Cutuli<sup>1,2</sup>, Stella Ingrassia<sup>1,2</sup>, Marco Greco<sup>1,2</sup>, Federico Catalani<sup>1,2</sup>, Paolo Moscatelli<sup>2</sup>

<sup>1</sup>Scuola di Specializzazione in Medicina d'Emergenza-Urgenza, Università degli Studi di Genova; <sup>2</sup>U.O.C Pronto Soccorso e Medicina D'Urgenza, A.O.U. San Martino, Genova

Endothelin-1 (ET-1) is a 21 aminoacids vasoconstrictive peptide, produced by the endothelium and by myocardiocytes. NT-proBNP is BNP aminoterminal portion, which is produced by myocardium in response to myocardiocyte stretching. It causes natriuresis, vasodilatation and inhibition of the RAAS. ET-1 and NT-proBNP could play an important role in the evolution of acute decompensated heart failure (ADHF); however there aren't studies that evaluated their levels in order to find a possible correlation between them and to define their physiopathological role.

### Objective

With this study we determined ET-1 and NT-proBNP levels in a

cohort of patients evaluated in our ED for ADHF to find a possible correlation between the two biomarkers, between each biomarker and haemodynamic parameters and if ET-1 could have a negative prognostic value in ADHF in a short period (7 days).

### Methods

We studied 22 patients, evaluated in our ED with symptoms of ADHF NYHA class was II for 2 patients, III for 13 patients, IV for 7 patients. Among them, 18 patients recovered, 4 died in the first week after admission. Control group was made up of 22 healthy people of the same age.

At admission we got blood samples to determine ET-1 and NT-proB-

NP levels; we also determined Troponin I and Creatinine levels (if elevated, they would have been exclusion criteria from the study). ET-1 was dosed through radioimmunological method and NT-proBNP through immunoenzymatic one. The statistical analysis was made with the analysis of variance (ANOVA); to evaluate correlation among variables we used linear regression test; instead we used multiple linear regression to evaluate the influence of ET-1 and NT-proBNP on the patient's outcome.

### Results

Levels of NT-proBNP and ET-1 was significantly higher ( $p < 0,01$ ) in patients with ADHF than control group (ET-1:  $30,9 \pm 16,9$  pmol/l vs  $2,8 \pm 0,67$  pmol/l; NT-proBNP:  $9696 \pm 10326$  ng/l vs  $743 \pm 787,1$  ng/l). We divided patients into 2 groups according to the outcome: ET-1 and NT-proBNP levels were significantly higher ( $p < 0,01$ ) in deceased patients than in those who survived (ET-1:  $46,1 \pm 18,6$  pmol/l vs  $27,5 \pm 15,1$  pmol/l; NT-proBNP:  $20468 \pm 14718$  ng/l vs  $7300,9 \pm 7751,2$  ng/l). Linear regression showed a statistically significant correlation ( $p < 0,01$ ) between ET-1 and NT-proBNP levels. We didn't find any correlation between each

biomarker and the other haemodynamic parameters (MAP, HR, SO<sub>2</sub>, NYHA class) that we have evaluated, except for heart rate (HR) and ET-1 ( $p < 0,01$ ).

Multiple linear regression showed that independent variables ET-1, NT-proBNP, HR, mean arterial pressure (MAP), but not sex, age, NYHA class and oxygen saturation, negatively influence the dependent variable outcome.

### Discussion

Our results show that ET-1 and NT-proBNP increase simultaneously in ADHF and they correlate between them. The physiological mechanism at the basis of this, how it's been demonstrated by in vitro and in vivo studies, could be multifactorial. Different factors could induce release of the two biomarkers, as myocardiocyte stretching, hypoxia, pulmonary congestion; each hormone could influence the release of the other one, but the exact mechanism are still not known.

Our study shows that ET-1 could have a good prognostic value in ADHF outcome and suggests a possible co-secretion of ET-1 and NT-proBNP.

## Pulmonary embolism risk stratification in prehospital care: is there a rule?

°Alberto Gabrieli, °Marco Calzoni, °Vittorio Schweiger, °Enrico Polati

°Scuola di Specializzazione in Anestesia, Rianimazione e Terapia Intensiva, Azienda Ospedaliera Universitaria Integrata, Ospedale Policlinico Verona

### Learning Objective

We discuss a clinical high-suspected Pulmonary Embolism diagnosis in pre-hospital setting. We use this case to update our knowledge on this disease, to understand what could help us in pre-hospital setting to choose the right level of suspect and so the correct hospitalization.

### Case Report

The prehospital medical team (Fast-Car) was sent for acute dyspnea in a rural land field used as a truck parking. A patient quick look show us a young man (30 years old) with high respiration rate (30/min). The patient was conscious, alert, free airway. We put oxygen with tape around the face mask to seal it and to avoid dust inhalation. Chest observation showed normal thorax expansion, murmur generally diminish without pathological sounds; the oxygen blood saturation was recorder of 87% in O<sub>2</sub>. Blood pressure was 100/70 with regular heart rate of 150 bpm. A 12-lead ECG showed a wide QRS and a right-shift of QRS axis, compatible with RBBB. We put 2 large-bore venous catheter and start crystalloid infusion. The GCS was 14 (E:3, M:6, V:5) and destrock was 110 mg/dL. The patient Exposure showed us a very suffering patient, moderate jugular distension, midline trachea. The lower limb exposition showed us an asymmetry on leg diameters: the left one was hard on touch, painful, swelling, with a positive Homan sign. The patient was a Bulgarian truck driver. He refer the dyspnea acute onset after a 2 day driving work. He denied chest pain. Then, we calculated the Well Criteria for the Pulmonary Embolism (PE). The result was recorded as 7.5/12.5 consequently the patients was identify in high risk level group. When the transport ambulance arrived, we choose the far hospital (35 km) because the close ones didn't have personnel and resources to manage this pathology. After 28 minutes we arrived in the Emergency Department where a pre-alerted emergency team with cardiologist support waiting us. The patient undergo promptly to a full emathochimic and cloathing screen, arterial blood sample, 12-lead-ECG, Emergency Echocardiography, and the CT Scan. The patient was admitted to ICU and he was discharge after 3 weeks in good conditions with the definitive diagnosis of Bilateral Pulmonary Embolism due to Left Deep Venous Thrombosis (DVT).

### Discussion

Pulmonary embolism (PE) is a relatively common cardiovascular emergency. PE and DVT are two clinical presentations of venous thromboembolism (VTE) and share the same predisposing factors. In most cases, in fact, PE is a consequence of DVT. PE is a difficult diagnosis that may be missed because of non-specific clinical presentation (1). Despite the limited sensitivity and specificity of signs and symptoms, the combination of these variables by the use of a prediction rule, makes it possible to discriminate suspected PE patients in categories of clinical probability corresponding to an increasing prevalence of PE. The most frequently used clinical prediction rule is the Canadian rule, by Wells et al. (2). This rule has been validated extensively using both a three-category (low, moderate or high clinical probability) and a two-category scheme (PE likely or unlikely). It is simple and based on easily collected information. However, the reproducibility was found to be variable due to the weight of one subjective item in the rule ("alternative diagnosis less likely than PE") (3).

As for Trauma, Cardiac and Stroke patients categories, we try to apply a method to transfer the patient with diagnostic suspect of PE in the hospital that can manage it better. As for EDs we use a clinical prediction rule to choose the right hospital for the right patient. We presented only a pilot case while further prospective projects to define this method on prehospital care are on the way.

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## B-type natriuretic peptide and acute respiratory failure

°Marco Calzoni, °Alberto Gabrieli, °Vittorio Schweiger, Enrico Polati, °Aldo Luzzani

°Scuola di Specializzazione in Anestesia, Rianimazione e Terapia Intensiva, Azienda Ospedaliera Universitaria Integrata, Ospedale Policlinico Verona

### Background

B-type natriuretic peptides (BNP and NT-proBNP) are elevated in patients with heart failure.

### Objective

The aim of this study is to assess the differential diagnostic and prognostic value of the N-terminal fragment of B-type natriuretic peptide (NT-proBNP) in critically ill adult patients with acute respiratory failure.

### Methods

According to standard criteria we classified acute respiratory failure in cardiogenic or noncardiogenic. Patients had NT-proBNP measurements at admission, at 24 and 48 hours after admission. NT-proBNP was then correlated with diagnosis and mortality.

### Results

Median values of NT-proBNP (IR 25-75%) were 33364 pg/ml (4838-35000) in patients with cardiogenic respiratory failure and 3822 pg/ml (1154-26662) in patients with noncardiogenic respiratory failure ( $p < 0.05$ ). The area under the ROC curve (AUC) for cardiogenic respiratory failure was 0.841. At the cut off value of 3933 pg/ml, NT-proBNP showed a sensitivity of 86.7% and specificity of 76% for the diagnosis of cardiogenic or noncardiogenic respiratory failure. The trend of NT-proBNP was not correlated with mortality.

### Conclusion

NT-proBNP can discriminate in a statistically significant way between cardiogenic and noncardiogenic respiratory failure in critically ill adult patients. Further studies are needed in order to better define its prognostic value.

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## BNP and non invasive methodic in the MANAGEMENT of acute heart failures **Verificare inglese molti errori**

R. Marino, F. Tocco, A. Giorno, S. Di Somma

Cattedra E.U.O.C. di Medicina d'Urgenza e Pronto Soccorso – Policlinico Sant'Andrea – II Facoltà di Medicina e Chirurgia, Università "La Sapienza" Roma

### Introduction

Nexfin and the techniques of BIVA, actually are used to measure respectively hemodynamic parameters as cardiac index and hydration status by non invasive method, rapidly and easily executable repetitiously. In patients with acute heart failure, because of ventricular stress by volume or pressure overloaded, there is a reduction of cardiac index and an increment of body fluids that transforming in a status of iperhydration. Objective of our study was to validate Nexfin and BIVA techniques to guide together to dosage of BNP, versus diagnosis and intrahospital management by their variations, from admission to discharge of patients with acute heart failure referring to Emergency department.

### Patients and Methods

There are enrolled: 44 patients (24 M, 20 F), mean age  $77 \pm 7,7$  (mean  $\pm$  SD) referring to Emergency Department with acute heart failure. During hospitalization ( $4,12 \pm 1,45$ , days mean  $\pm$  SD) patients underwent to serial blood samples of BNP, to admission, 0 24 hours, 72 hours and at discharge. In added, at the same times, Nexfin to evaluate cardiac index and BIVA to evaluate congestive status were performed contemporarily. Patients underwent, according guidelines of American Heart, to diuretic therapy

( $120,77 \pm 67,15$  mg mean  $\pm$  SD) independently of parameters that examined in the our study during hospitalization.

### Results

There was a reduction of BNP with statistically significant difference to 72 hours ( $357,64 \pm 193,81$  pg/ml) confirmed at the discharge ( $248,57 \pm 194,46$  pg/ml) versus admission ( $747,61 \pm 658,54$  pg/ml) ( $p < 0,005$ ) that joined to a reduction statistically significant difference at discharge ( $76,35 \pm 5,5$  %) confronting versus admission ( $79,44 \pm 6,47$  %) of iperhydration status. Cardiac index statistically significant way increased confronting with a reduction of BNP and of iperhydration status at discharge ( $3,9 \pm 1,18$  L/min/m<sup>2</sup>) versus admission ( $2,32 \pm 0,95$  L/min/m<sup>2</sup>). There was also a clinical improvement base NYAH class of patients from admission to discharge. It was highlighted also, in statistically significant difference a correlation between percentage variation of values cardiac index and hydration status from admission to discharge ( $R = 0,38$ ;  $p = 0,04$ )

### Conclusions

In patients with acute heart failure, in the Emergency department, simultaneous monitoring of cardiac index and of hydra-

tation status by non invasive method is useful to confirm clinical diagnosis together to BNP value, but moreover intraospital management of patients with acute heart failure. Particularly their variations can be considered a valuable help to identify, in easy

and fast way, the improvement of acute heart failure, not only clinically, but even in terms of reduction of congestive status and increased cardiac performance that needed for the discharge of patients with acute heart failure from Emergency departments.

## NIHI Titolo da definire Titolo da definire Titolo da definire Titolo da definire Titolo da definire

S. Farina<sup>2</sup>, L. Zileri Dal Verme<sup>1</sup>, M. Sabbatini<sup>1</sup>, D. Marsiliani<sup>1</sup>, G. Pignataro<sup>1</sup>, L. Carbone<sup>1</sup>, M. Candelli<sup>1</sup>, P. Tilli<sup>1</sup>, S. Di Giambenedetto<sup>2</sup>, N. Gentiloni Silveri<sup>1</sup>

<sup>1</sup>Dipartimento Emergenza e Accettazione, Università Cattolica del Sacro Cuore - Roma; <sup>2</sup>Clinica delle Malattie Infettive, Università Cattolica del Sacro Cuore - Roma

### Introduzione

Nel corso dei primi mesi dell'anno 2009 un nuovo virus influenzale di origine suina, Virus A (H1N1), ha rappresentato un focus rilevante nell'ambito delle patologie infettive emergenti acquisendo in poche settimane le caratteristiche epidemiologiche di pandemia. Scopo dello studio era valutare l'epidemiologia, la clinica e le caratteristiche microbiologiche della nuova Influenza A (H1N1) e di correlare la severità del quadro clinico e eventuali complicanze con differenti fattori clinici e microbiologici.

### Metodi

Tutti i soggetti giunti nei periodi maggio-agosto e settembre-novembre del 2009 presso il Pronto Soccorso del Dipartimento di Emergenza e Accettazione dell'Università Cattolica del Sacro Cuore di Roma con sintomi respiratori associati a febbre sono stati valutati in uno studio retrospettivo. Di ciascun paziente sono stati considerati la sintomatologia clinica, le caratteristiche epidemiologiche e i dati di laboratorio. Nell'analisi statistica sono stati inseriti solo i pazienti con RT-PCR assay positiva per swine-origin influenza A (H1N1) effettuata su materiale respiratorio ottenuto mediante tampone naso-faringeo. Per l'analisi comparativa tra variabili categoriche è stato utilizzato il test di Fisher's; per le variabili continue il T test di Student's. I fattori significativamente associati a diagnosi di polmonite sia all'analisi univariata che multivariata sono stati esaminati mediante regressione logistica. Tutte le analisi statistiche sono state eseguite mediante SPSS vs. 18.0 (SPSS Inc, Chicago, IL).

### Risultati

Sono stati arruolati 104 pazienti con infezione da virus A (H1N1).

La totalità dei soggetti riferiva in anamnesi sintomi influenzali classici, spesso associati a diarrea e vomito. Il tasso di ospedalizzazione è stato più elevato nei pazienti con età superiore a 40 anni rispetto a quelli di 15-39 anni ( $p = 0,008$ ) o ai pazienti con età inferiore a 14 anni ( $p = 0,006$ ). I segni clinici, sintomi e complicanze respiratorie sono risultati diversi tra i due periodi di studio: sul totale, 18 pazienti (17%) erano affetti da polmonite. La diagnosi di polmonite è stata più frequente nel secondo periodo (37% versus 10%,  $p = 0,002$ ). I pazienti con più di 50 anni hanno mostrato una minore probabilità di diagnosi di polmonite, rispetto ai bambini di età compresa tra 0-13 anni ( $p = 0,049$ ); una più lunga durata dei sintomi prima dell'accesso in PS è stata associata ad una maggiore probabilità di polmonite ( $p = 0,026$ ). Nell'analisi filogenetica del virus dell'influenza A (H1N1) si è riscontrata bassa variabilità sia nei geni emoagglutinina che neuroaminidasi. Inoltre, non è stata evidenziata nessuna mutazione associata alla resistenza neuraminidasi del virus.

### Conclusioni

Questo studio, con tutti i limiti di una casistica poco omogenea e retrospettiva, ha permesso di definire fattori associati alla severità clinica del virus dell'influenza A (H1N1). Molto probabilmente i quadri clinici respiratori più gravi sono correlati all'età giovane-adulta in quanto la popolazione più anziana ha avuto una precedente esposizione al virus con conseguente autoimmunizzazione. Nonostante in diverse aree geografiche (in particolare USA ed Europa del Nord) vi fosse la circolazione di quasispecie virali che hanno presentato mutazioni di resistenza alla terapia, in Italia non si sono osservati cambiamenti filogenetici rispetto al ceppo virale di riferimento.

## **Il silenziamento genico come strumento per lo studio della trasduzione del segnale in fisiopatologia cardiaca e cutanea**

V. Purpura, S. Raffa, F. Belleudi, V. Pittoni, S. Di Somma, M.R. Torrisi

Il Facoltà di Medicina e Chirurgia, UOC Diagnostica Cellulare e UOC Medicina d'Urgenza, Azienda Ospedaliera Sant'Andrea

Il silenziamento genico mediante l'uso di small interfering RNA (siRNA), in grado di interagire con uno specifico mRNA inibendone la traduzione in proteina, è una metodica ampiamente applicata per lo studio e l'analisi dei meccanismi molecolari che regolano diversi processi cellulari. La microiniezione di siRNA, in particolare, permette di interferire efficacemente con la funzione di molecole proteiche inducendone la deplezione in tempi molto rapidi.

Nell'ambito degli studi sulla fisiopatologia dello scompenso cardiaco numerose evidenze sperimentali suggeriscono che l'infiammazione possa giocare un ruolo patogenetico nella regolazione dei meccanismi molecolari coinvolti nelle risposte di adattamento cellulare alle alterazioni emodinamiche tipiche dello scompenso cardiaco. Uno dei meccanismi coinvolti riguarda la sintesi e il rilascio del peptide natriuretico (BNP) in risposta all'attivazione di specifiche vie di segnalazione innescate dal rilascio di citochine infiammatorie. Nostri studi su un modello sperimentale di cardiomiociti murini hanno dimostrato che il trattamento con IL18 è in grado di produrre un incremento dell'espressione e del rilascio di BNP (Pittoni et al. submitted). La microiniezione di siRNA per il recettore di IL18 (IL18R) e per il fattore di trascrizione GATA4, attivato durante la trasduzione del segnale IL18-mediato,

ha mostrato che la deplezione di entrambe queste proteine inibisce gli effetti indotti dal trattamento con IL18 su espressione, rilocalizzazione intracellulare e rilascio di BNP, dimostrando inequivocabilmente il ruolo di IL18R e del suo signaling PI3K, Akt e GATA4-dipendente in questi processi.

Nell'ambito dello studio del ruolo del recettore tirosino chinasi per il keratinocyte growth factor (KGFR) nel controllo del processo di differenziamento epiteliale, abbiamo utilizzato la microiniezione di siRNA per KGFR per indurre la deplezione di questo recettore in una linea di cheratinociti umani immortalizzata non tumorigenica. L'effetto sul differenziamento precoce è stato valutato mediante immunofluorescenza analizzando l'espressione del marker specifico keratinal (K1). I risultati hanno evidenziato che la deplezione di KGFR riduce la percentuale di cellule positive alla K1 dimostrando il ruolo chiave del recettore nel differenziamento precoce dei cheratinociti (Purpura et al. in preparation).

Questi nostri risultati indicano quindi come il silenziamento di specifici geni mediante microiniezione sia una metodica estremamente efficace nell'analisi del ruolo di proteine coinvolte nelle vie di segnalazione intracellulare alla base di differenti processi fisiopatologici.

## **Comparison of cardiovascular and cerebrovascular events pre and post earthquake of 6th april 2009 the abruzzo experience**

S. Sofia<sup>1</sup>, A. Melone<sup>2</sup>, E. Varrato<sup>3</sup>, R. Di Filippo<sup>4</sup>, C. Balsano\*

<sup>1</sup>U.O. di Medicina Interna, P.O. "Santissima Maria dello Splendore" di Giulianova;

<sup>2</sup>U.O.C. di Medicina e Chirurgia D'urgenza e Accettazione, P.O. "S.S. Filippo e Nicola" di Avezzano;

<sup>3</sup>U.O. di Medicina Interna, P.O. "G. Mazzini" di Teramo;

<sup>4</sup>U. O. di Medicina Interna, P.O. "S. Salvatore" dell'Aquila;

\*Dipartimento di Medicina Interna e Sanità Pubblica, Università degli studi dell'Aquila.

Each year over 500,000 earthquakes are recorded; over the past 30 years an annual average of 21 earthquakes has been reported. Although the vast majority of the shock intensity is too low to be warned, about 3000 shocks are felt by people and those from 7 to 11 result in significant loss of life.

Several epidemiological studies have been conducted on populations affected by natural disasters, so to constitute what is now called "disasters epidemiology". These studies have demonstrated the serious consequences of the earthquake on the public health from a physical and psychological point of view in the population affected by natural disasters.

However, although in our country natural disasters are frequent, few epidemiological studies have been done on the effects of disasters on public health in the Abruzzo Region.

After the earthquake of 6th April 2009 Abruzzo's area has been paid a great attention on the psychological diseases like depression, sleep and mood disorders, psychosomatic disorders too through the RAINBOW-SEPT studies, but less attention has been paid on regard of acute vascular events.

That's why our group has decided to analyze patient's accesses to the ER at the following hospitals: Avezzano - Sulmona, L'Aquila, Teramo, Giulianova, Atri and Sant'Omero.

The study will be carried out from the period between 06/04/2008 and the 31/07/2008 (preearthquake) to the period between

06/04/2009 and 31/07/2009 (post-earthquake). The aim will be the evaluation of the incidence, in the periods chosen, of ER accesses for acute vascular events, cardiovascular and cerebrovascular events etc.).

The observational clinical study will be conducted on the Abruzzo's population hit by the earthquake of 6th April 2009. Our study wants to determine the quantitative and qualitative differences among the etiology of diseases characterizing patients accessing the E.R. the pre and post-earthquake chosen periods. The data obtained will allow us to provide a practical guidance to health personnel and the Civil Protection – that will indicate the most useful and effective operations during natural disasters.

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## Identificazione precoce della nefropatia associata alla somministrazione di mezzo di contrasto: il ruolo di nuovi marcatori

Ulla Marco<sup>1</sup>, Saglio Elisa<sup>1</sup>, Bono Alessia<sup>1</sup>, Maggiorotto Matteo, Lomater Elisa<sup>1</sup>, Mengozzi Giulio<sup>2</sup>, Battista Stefania<sup>1</sup>

<sup>1</sup>S.C. Medicina d'Urgenza A.O.U. San Giovanni Battista Torino; <sup>2</sup>S.C. Biochimica Clinica A.O.U. San Giovanni Battista Torino

### Obiettivo dello studio

L'obiettivo del presente lavoro è valutare l'utilizzo di un biomarcatore precoce di danno renale, NGAL (Neutrophil Gelatinase Associated Lipocalin), nella gestione del rischio di nefropatia in pazienti sottoposti a esami radiologici con mezzo di contrasto.

### Pazienti e Metodi

Tra l'ottobre 2009 e l'aprile 2010 sono stati reclutati 40 pazienti (12 femmine e 28 maschi; età media 69,3 anni) per i quali, insieme al nuovo biomarcatore, sono stati valutati altri parametri biochimici, la diuresi e la pressione arteriosa, al momento basale (subito prima dell'effettuazione della procedura diagnostica) e dopo 24, 48 e 72 ore dall'esame contrastografico. Sono state effettuate 30 procedure di coronarografia, 8 TC dell'addome e del torace, 3 angio-TC. Solo 2 pazienti non presentavano alcun fattore di rischio, mentre 18 pazienti presentavano 3 o più fattori di rischio (fino ad un massimo di 6). Una profilassi è stata condotta prima della procedura contrastografica nella metà dei pazienti. Il dosaggio delle concentrazioni di NGAL è stato eseguito mediante un immunodosaggio a fluorescenza (Triage® NGAL, Biosite Inc.) prodotto per l'impiego come point-of-care con il dispositivo Triage Meter.

### Risultati e Discussione

Nessun paziente ha sviluppato una nefropatia riconducibile alla

somministrazione di mezzo di contrasto nell'arco di tempo considerato, come evidenziato dalla assenza di significative variazioni temporali dei parametri misurati. Nonostante non risulti statisticamente significativa, la variazione nel tempo delle concentrazioni di NGAL mostra una tendenza all'incremento a 24 e 48 ore. Tale andamento appare ancora più evidente quando si consideri solamente il sottogruppo di pazienti con valori basali di NGAL < 100 ng/mL. L'aumento delle concentrazioni di NGAL a 24 e 48 ore di distanza dalla procedura diviene statisticamente significativo nella metà della popolazione che non viene sottoposta a trattamento profilattico. Anche se la correlazione tra NGAL e creatinina e tra NGAL e GFR in condizioni basali nella popolazione studiata dimostra come NGAL possa riflettere indirettamente il grado di funzionalità renale, è presumibile che l'incremento di NGAL rilevato dopo 24 e 48 ore in questo lavoro possa riflettere un danno renale "minimo", espressione dell'evento lesivo iniziale in grado di innescare un danno renale acuto e possa essere predittivo dell'evoluzione del danno stesso, rappresentato come continuum patogenetico. Se, da un lato, l'incremento della creatinina e la riduzione del GFR sono espressione di un'insufficienza renale funzionale, che compare più tardivamente, dall'altro le concentrazioni di NGAL sembrano aumentare come conseguenza di un danno renale intrinseco, che insorge molto precocemente.

## BIC2- Biomarkers in Cardiology. Diseased state biomedical database

Anne Brüning, Andrea Pinkowski, Toni Lauterbach, Janina Stiefel, Benjamin Karow, Julia Searle, Anna Slagman, Jörn Vollert and Martin Möckel

Charité - Universitätsmedizin Berlin, Depts. of Cardiology and Emergency Medicine

### Background and conception

Each year, many patients are admitted to emergency departments with the cardinal symptoms chest pain and dyspnea. These symptoms can be caused by a multitude of differential diagnoses, both cardiac and extra-cardiac. In recent years biomarkers have greatly improved the diagnosis and risk stratification of cardiovascular diseases, but there are still unmet needs especially for a symptom-oriented early evaluation of emergency patients. Many promising biomarkers and biomarkers assays are being discovered but need to be assessed clinically.

A biomaterial database enables us to evaluate promising new biomarkers in clinically defined and consented blood samples, without the need to perform a laborious prospective study for each single marker. This allows for a prompt and cost-effective testing of multiple, diverse and relevant clinical parameters.

We set up a biomaterial database collecting samples and disease related data from Emergency Room patients who were admitted with either dyspnea or chest pain.

### Methods

Consecutive patients with chest pain or dyspnea as their leading symptom who presented to the Emergency Departments of the Charité Berlin Campus Virchow Klinikum or Campus Mitte were enrolled from spring 2008 until August 2010.

Following good clinical practice guidelines, all patients gave their written informed consent. The trial was approved by the ethics committee of the Charité (EA2/030/07).

Patients with a life expectancy below 6 months, an anaemia (Hb < 10g/dl), in a state of shock and patients serving a prison sentence were excluded from the study. Inclusion criteria were an age of above 18 years and a leading symptom of chest pain or dyspnea. Patients with dyspnea had one study blood draw within 24 hours after admission to the hospital. Patients with chest pain had a first blood draw within 2 hours after admission and a second blood draw 6 hours later. Total volume was 40ml per draw. The blood samples were stored on ice immediately, processed within two hours and then stored at -80°C latest after two weeks. All samples were collected, processed and stored obeying detailed standard operating procedures (SOPs). All collection and processing times were recorded. Samples which did not meet the standards set in the SOPs were discarded.

A telephone follow-up was made three months after recruitment with assessing death or rehospitalisation for cardiac reasons. All patient data was entered into a detailed electronic case report form (eCRF).

### Patient characteristics

We enrolled 545 consecutive patients, of which the first 509 have

complete datasets, including the follow-up.: Of these, 300 patients had a leading symptom of dyspnea and 209 of chest pain. In the chest pain group, we enrolled 133 male and 76 female patients. The dyspnea group includes 182 male and 114 female patients. To get to a full set of 200 chest pain patients with serial samples we included more than the planned 200 patients in that group, as a number of patients were discharged before the second set of blood samples could be drawn.

### Summary

We set up a biomaterial database with high quality blood samples and extensive clinical data from 546 ER patients with the cardinal symptoms dyspnea and chest pain to evaluate promising cardiovascular biomarkers for early diagnosis and personalized risk stratification of future ER patients. First biomarkers studies with new molecular cardiovascular biomarkers are on their way at the moment.

## BIC6- Biomarkers in Cardiology. Cardinal symptoms and characteristics of patient population presenting to the Emergency Department

Martin Möckel, Rebecca Nordt, Julia Searle, Anna Slagman, Harald Storchmann, Phillip Oestereich, Angela Ale-Abaei, Jörn Vollert, Reinhold Müller<sup>1</sup>, Matthias Koch, and Rajan Somasundaram

Charité – Universitätsmedizin Berlin, Depts. of Emergency Medicine, Germany; <sup>1</sup>James Cook University, Townsville, Australia

### Background

The fast and safe treatment of patients presenting to the Emergency Department (ED) is of rising interest as process management in the ED is continually sought to be improved. Thus knowing the patient population presenting to your ED is essential.

Until now there is no methodically collected epidemiological data about patient populations in EDs or the connection of cardinal symptoms with diagnoses available in Germany.

Guidelines are disease-based rather than based on cardinal complaints. Patients however typically present to the ED with symptoms rather than a final diagnosis.

Symptom-oriented guidelines for first-hand use by ED doctors are necessary because an increasing number of physicians in the Emergency Room are recruited from Internal Medicine rotation programs, resulting in a constant replacement of medical staff.

For the patients as well as for the health-system it is necessary to find the right medical diagnosis and to initiate an effective therapy as fast as possible.

A prospective multicenter epidemiological study in the Emergency Departments on two of the main campuses of the Charité Berlin was initiated to characterize the patient population presenting to the ED, in particular those presenting with certain cardinal symptoms, in order to collect high-quality, symptom-oriented, epidemiological data and to establish a new model of data assessment from the hospital information system (HIS) as a tool for quality management.

### Methods

All adult patients who were admitted to the Emergency Department of Internal Medicine from February 2<sup>nd</sup> 2009 until February 1<sup>st</sup> 2010 were included. Data assessment was performed in two

steps: In step one all direct data recorded in the ED report was exported from the SAP-based hospital information system (HIS) on a daily basis. Direct data describe variables which can directly be statistically analyzed such as age, gender, type of health insurance, nationality, admission date and time, waiting times, vital signs, tests performed, laboratory test results, risk factors, and ICD-10 diagnoses. All patients were assigned to one of five groups by the attending physician according to their cardinal symptoms upon presentation to the ED: 1) chest pain, 2) abdominal pain, 3) shortness of breath, 4) headache, 5) none of the four cardinal symptoms.

In step two data of all patients with one of the four cardinal symptoms were manually extracted from free text fields of the hospital ED documentation sheet. The data was reviewed and then transferred to a CRF specially designed for this study, providing information about symptoms, patient history, medication, physical examination in the ED, diagnostic tests and therapy.

### Results

We extracted and analyzed data from 34.333 patients in total, 48,8% of them male, 51,2% female. 13.776 patients were hospitalized versus 20.557 who were discharged from ED. We will analyze the specific characteristics of these patients mainly with respect to their cardinal symptom and their in-hospital outcome.

### Conclusions

IT-regenerated epidemiological data are an essential tool for an up-to-date assessment of patient populations and the generation of symptom-oriented standardized guidelines and workflows which will improve the quality of Emergency Room processes. Furthermore these data are essential for an effective quality management in Emergency Medicine. Detailed results are submitted for presentation at ACC i2 summit 2011.

## The effect of integrating the biomarker Copeptin into the process of managing patients with suspected ACS (BIC-8)

Anna Slagman, Sönke Petrusch, Julia Searle and Martin Möckel

Charité – Universitätsmedizin Berlin, Dept. of Cardiology and Emergency Medicine

### Background

The majority of patients with suspected non-ST-elevation-acute-coronary syndrome (NSTEMI) have a negative Troponin at baseline. One of the biggest challenges for ED-physicians is the differentiation between high-risk patients who have to stay in hospital for further monitoring and low-risk patients who can safely be discharged to ambulant care.

Our study objective is to quantify the benefit of integrating the new biomarker Copeptin into the process of managing patients with suspected NSTEMI with a negative baseline Troponin test result in the Emergency Department. Our Hypothesis is that patients who test negative for Copeptin, a biomarker of severe, life-threatening stress, at admission are at low risk of ACS. This hypothesis is supported by results from clinical trials which showed a high negative predictive value for Copeptin in addition to Troponin in patients with acute myocardial infarction.

### Methods

We will conduct an interventional multicenter biomarker randomized controlled clinical trial to assess the benefit of a rule-out multimarker strategy including Troponin and Copeptin to identify low-risk chest pain patients who can safely be discharged to ambulant care.

Our aim is to enroll a minimum of 892 patients within one year in 4 study-centers in Germany.

Inclusion criteria are typical chest pain suggestive of unstable angina (UA) or non-ST-elevation myocardial infarction (NSTEMI) and a negative baseline Troponin (Cut off for standard Troponin T = 0.03 µg/L; high sensitive Troponin T = 0.014 µg/L).

Excluded from participation are patients with ST-elevation myocardial infarction (STEMI), continuing chest pain or recurrent

episodes of chest pain under appropriate therapy, high-risk ACS patients who need to be hospitalized for reasons irrespective of their initial Troponin result, patients who need to be hospitalized for other medical reasons, patients in need of urgent life-saving interventions and patients with a life expectancy < 6 months. Also excluded are patients with any condition that leads the treating physician to not consider the patient eligible for the trial. The patients will be randomized into a standard process or experimental process.

In the experimental arm of the study Copeptin will influence further patient management. Eligible patients with a negative Copeptin (cut-off: 10 pmol/L) will be considered as low-risk patients and will be discharged into ambulant care. Eligible patients with a positive Copeptin will be treated according to the current standard of care (SOC). To ensure patient safety an internet-based portal for the management of patient referrals between hospitals and resident cardiologists will be established.

Patients in the standard arm will be admitted to the CPU and will be treated according to the current guidelines for patients with suspected ACS. The Copeptin results of these patients will not be revealed to the treating physicians. Primary endpoint is the rate of major adverse cardiovascular events at 30 and 90 days. Secondary endpoints evaluate efficacy, including rate of patients with coronary angiography and PCI, safety, cost effectiveness and patient satisfaction of the new process.

### Timeschedule/Aim of the trial

First results are expected in spring 2012. If the new processes are shown to be efficient, safe, cost-effective and/or improve patient satisfaction this trial could help implementing Copeptin as a novel biomarker for the rapid rule out of NSTEMI in clinical practice.

## Management of atrial fibrillation in emergency department

M.G. D'Angelo<sup>2</sup>, P. Pitto<sup>2</sup>, P. Costelli<sup>2</sup>, F. Catalani<sup>1-2</sup>, M. Greco<sup>1-2</sup>, P. Giuntini, P. Campodonico<sup>1-2</sup>

<sup>1</sup>Scuola di Specializzazione in Medicina d'Emergenza-Urgenza, Università degli Studi di Genova;

<sup>2</sup>A.O.C. Pronto Soccorso e Medicina d'Urgenza, A.O.U. San Martino, Genova

We propose our protocol for clinical trial about treatment and management of recent-onset Atrial Fibrillation (AF) in Emergency Department.

Atrial Fibrillation remains the most common and most challenging arrhythmia. Although several new treatment modalities are available to restore and maintain sinus rhythm, the long-term success of such a strategy remains disappointing, often making rate control a good alternative.

Rhythm control of AF is generally preferred over rate control in the belief that it offers better symptomatic relief and quality of life and eliminates need for anticoagulation.

Rhythm control remains first choice for patients with initial episodes or highly symptomatic episodes of AF and for patients who have a high chance of remaining in long-term sinus rhythm (young patients, normotensive, normal left atrium size, previous short AF episodes).

### Objective

- 1) Evaluation of rhythm control in patients with AF lasting < 48h.
- 2) Evaluation of electrical cardioversion vs Pharmacological one.

3) Comparison of: a) Successful electrical cardioversions vs medical ones; b) Efficacy, adverse effects and cardioversion time of anti-arrhythmic drugs in three classes of ages; c) Adherence to internal guidelines in order to assess the destination of patients (admission or discharge from Emergency Room-ER or from Observation Unit-OU).

### Population

All patients evaluated in the Emergency Department with recent-onset AF. They can be treated electrically or pharmacologically with amiodarone, flecainide or propafenone.

### Methods

We analysed a random group of 523 patients with AF (48,6% with recent-onset AF) who were visited in the Emergency Department of San Martino University Hospital since 2006 to 2009, three months per year. Patients were divided in three age groups: 94 patients < 65 years; 117 patients from 65 to 80; 43 patients > 80 years.

We assessed the following clinical data: Sex, Age, Heart rate, Ar-

terial pressure, Oxygen saturation, Left ventricular ejection fraction, Coagulation statement.

### Results

We performed medical cardioversion in 194 patients (76,4%), electrical cardioversion in 49 patients (19,3%), 11 patients (4,3%) obtained spontaneous cardioversion.

We compared, considering their efficacy and timing in restoring sinus rhythm, Amiodarone, Flecainide and Propafenone.

Electrical cardioversion was effective in 100% of patients while medical cardioversion obtained rhythm control in 90% of patients. Cardioversion time was within 3 hours in 62% of patients using Flecainide, in 40,4 % of patients using Propafenone and in 20,7% of patients receiving Amiodarone.

Regarding the management aspects of patients with AF in the Emergency Department we used Performance Indicators:

1. Number of successful cardioversions/ number of candidates: 247/254 (0,9);

2. Successful Cardioversion performed in ER or OU/total successful Cardioversion):138/247 (0,5).

On the basis of the available data we demonstrate that:

- Most patients candidate to cardioversion obtained restoring of sinus rhythm;
- More than half of all patients evaluated were rapidly treated in the ER or in OU;
- The Adherence to Guidelines was 418/523 (0,80).

### Conclusion

As it is well known electrical cardioversion is more effective and safe in young and in older patients with normal left ventricular function without underlying heart disease.

Flecainide is effective and fast in converting recent onset AF. In older patients Amiodarone is more useful and safe according to literature. During the period of study (four years) despite of the great number of physicians of our team we observed a good adherence to guidelines both in clinical and management setting.

## Bioelectrical Impedance Vector Analysis (BIVA) for the Assessment of Peripheral Congestion in Patients with Acute Dyspnea

Marta Codognotto<sup>a</sup>, Gianna Vettore<sup>b</sup>, Mario Plebani<sup>c</sup>, Antonio Piccoli<sup>a</sup>

Departments of <sup>a</sup>Medical and Surgical Sciences, <sup>b</sup>Emergency, and <sup>c</sup>Laboratory Medicine University of Padova, Italy

### Background

There is no gold standard for the differential diagnosis of acute dyspnea. The usefulness of NT-proBNP and lung ultrasound in identification of heart failure in dyspneic patients is supported by many studies. No previous study evaluated the contribution of BIVA to the discrimination between cardiac and non-cardiac dyspnea.

### Aim

To establish the relationship between lung ultrasound (detecting lung congestion), NT-proBNP (detecting ventricular dysfunction), and BIVA (detecting peripheral congestion) in patients with acute dyspnea.

### Methods

We studied 315 patients (50-95 yrs), with eGFR  $\geq$  30 mL/min/1.73m<sup>2</sup>, presenting at emergency department with dyspnea. Dyspnea was classified into cardiac (n= 169) and non-cardiac (n= 146) based on physical examination, electrocardiogram, chest X-ray, NT-proBNP, and lung ultrasound (B-lines of lung congestion). Impedance is a vector (Z) with two components, the resistance, R (function of intra- and extracellular fluid volume) and the reactance, Xc (function of tissue cell membrane). Bioimpedance measurements at 50 kHz were transformed into standardized Z-scores, Z(R) and Z(Xc), that is  $Z(R) = (R - \text{mean } R) / \text{SD}$  and  $Z(Xc) = (Xc - \text{mean } Xc) / \text{SD}$ , with mean and SD from the reference healthy population. Z-scores are expressed in SD [Piccoli et al. Nutrition 2002; 18:153-157]. The intersubject variability of Z is represented by the bivariate normal distribution (50%, 75%, and 95% tolerance ellipses). In BIVA method, vector positions in the lower or higher

half of reference, tolerance ellipses indicate peripheral congestion or progressive decrease in tissue fluid volume, respectively.

### Results

Impedance vector components Z(R) and Z(Xc) were both significantly decreased in cardiac dyspnea group. The mean vector of the group with non-cardiac dyspnea was close to 0 SD of both components indicating a normal tissue fluid volume. The mean vector of the group with cardiac dyspnea without peripheral edema was close to the lower pole of the 50% tolerance ellipse indicating a mild increase in tissue fluid volume (i.e., latent peripheral congestion). The ROC curve indicated that  $Z(Xc) = -1$  SD (lower pole of the 50% tolerance ellipse) discriminated between cardiac,  $Z(Xc) < -1$ , vs non-cardiac dyspnea,  $Z(Xc) > -1$ , with 69% sensitivity and 79% specificity (AUC 80%). Peripheral congestion (wet BIVA) without lung congestion (negative ultrasound) was associated with an increased NT-proBNP by two-fold compared to the condition without peripheral congestion (dry BIVA). In patients with non-cardiac dyspnea, negative lung ultrasound, and dry BIVA, the NT-proBNP concentration was the lowermost of the study population. In patients with negative lung ultrasound and wet BIVA, the increase in NT-proBNP was twofold with respect to the former group. In patients with cardiac dyspnea and a positive lung ultrasound, the NT-proBNP levels were the highest.

### Conclusions

Peripheral congestion without lung congestion may result in myocardial stretch with increased NT-proBNP release. The optimal evaluation of a dyspneic patient should detect peripheral congestion with BIVA and lung congestion with lung ultrasound.

## Neutrophil gelatinase-associated lipocalin (NGAL) e cistatina C come marker precoci di AKI (Acute Kidney Injury)

Cristina Bongiovanni

Neutrophil gelatinase-associated lipocalin (NGAL) è un nuovo marker precoce di AKI (Acute Kidney Injury). Molti studi clinici ne hanno dimostrato l'utilità attraverso la misurazione dei livelli di NGAL nelle urine in pazienti con danno renale acuto. La cistatina-C è una proteina di basso peso molecolare, prodotta in quantità pressoché costante da tutte le cellule nucleate liberamente filtrata, riassorbita e catabolizzata per il 99% circa nel tubulo rappresentando quindi un ottimo marker endogeno di funzionalità renale. Il nostro studio si prefigge di verificare l'utilità di ripetute misurazioni di NGAL plasmatico e cistatina C in tutti i pazienti giunti in Pronto Soccorso e successivamente ammessi nel Reparto di Medicina d'Urgenza al fine di: stratificare il rischio di danno renale precoce (AKI), valutarne la severità, impostare rapidamente una terapia adeguata, stabilire la prognosi. Nella fase preliminare nel nostro centro sono stati arruolati 200 pazienti (123 M - 77 F), con un'età media di  $73,5 \pm 13,7$  anni, le patologie più frequenti in anamnesi sono risultate ipertensione arteriosa, BPCO, diabete mellito, cardiopatia ischemica cronica. 47 pazienti erano affetti da AKI (valutato attraverso i criteri RIFLE). Sono stati effettuati 6 prelievi

ematici rispettivamente a tempo 0, 6 ore, 12 ore, 24 ore, 48 ore e 72 ore misurando nel plasma NGAL, creatinina e cistatina C. In conclusione, dai risultati preliminari del nostro studio si evince quanto segue: l'incidenza di AKI nei pazienti che giungono in Pronto Soccorso e, successivamente, necessitano di ricovero, è elevata (20%); tra le cause principali da considerare come determinanti per lo sviluppo di AKI in tali pazienti, lo scompenso cardiaco acuto e le BPCO riacutizzate rappresentano le patologie predominanti (soggetti maggiormente a rischio); la preesistenza di ipertensione arteriosa sembra determinante nell'incidenza di tale patologia. La valutazione del nuovo biomarker, NGAL, sembra realmente promettente per valutare tali pazienti al momento dell'ammissione in Pronto Soccorso, infatti da questi dati preliminari appare evidente che valori di NGAL inferiori a 110 ng/dl correlano con una scarsa probabilità di sviluppare AKI (VPN 89%). L'elaborazione dei campioni di plasma per il dosaggio della cistatina C è ancora in corso ma a breve valuteremo la reale correlazione tra cistatina C ed AKI e l'efficacia della misurazione combinata di NGAL e cistatina C nella diagnosi precoce di danno acuto renale.

## Audit Clinico sulla Durata della TAO nei pazienti con E.P. idiopatica

Casarsa C, Orso D, Perich D, Mariza S, Mearelli F

Scuola di Specializzazione in Medicina d'Emergenza-Urgenza, Università degli Studi di Trieste

### Background

La durata della terapia anticoagulante orale nel paziente con embolia polmonare discende dal rischio della ricorrenza dell'evento, dal rischio di sanguinamento e dalla stessa preferenza del paziente<sup>1</sup>. I pazienti con embolia polmonare unprovoked (idiopatica) e quelli con embolia polmonare ricorrente sono candidati alla terapia anticoagulante a lungo termine con una periodica rivalutazione del rapporto rischio/beneficio<sup>2</sup>. In tali condizioni i fattori di rischio per sanguinamento maggiore sono molti, e tra questi: l'età avanzata (>75 anni), il pregresso sanguinamento gastrointestinale; inoltre, dalla compresenza di: pregresso ictus non cardiogeno, insufficienza renale cronica, malattia epatica, terapia antiaggregante ed altre malattie acute o croniche severe. Una particolare menzione merita lo scarso controllo della terapia anticoagulante<sup>3-11</sup>.

### Disegno dello studio

Studio retrospettivo tra i pazienti affetti da embolia polmonare unprovoked trattati con anticoagulante che abbiano presentato, durante il loro trattamento, un evento emorragico maggiore, definito come un episodio che abbia richiesto il ricovero e/o il trattamento con vitamina K.

### End point

Valutare la prevalenza dei fattori di rischio per sanguinamento per definire uno "scoring" che assista la valutazione del rapporto rischio/beneficio nella durata della terapia anticoagulante. I risultati ottenuti, in questa fase preliminare, saranno oggetto di una successiva validazione prospettica.

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## Epidemiology and Treatment of Atrial Fibrillation in Emergency Department: Preliminary Results of the Cardioversion of Atrial Fibrillation in Emergency (CAFÉ) Study

Francesco Buccelletti<sup>a</sup>, Salvatore Di Somma<sup>b</sup>, Alberto Galante<sup>c</sup>, Francesco Pugliese<sup>d</sup>, Filippo Alegiani<sup>e</sup>, Giuliano Bertazzoni<sup>f</sup>, Nicolò Gentiloni Silveri<sup>a</sup>, Francesco Franceschi

<sup>a</sup> Department of Emergency Medicine, Catholic University of the Sacred Heart, Rome - Italy; <sup>b</sup> Department of Emergency Medicine, Sant'Andrea Hospital, La Sapienza University, Rome - Italy; <sup>c</sup> Department of Emergency Medicine, University of Tor Vergata, Rome - Italy; <sup>d</sup> Department of Emergency Medicine, Sandro Pertini Hospital, Rome - Italy; <sup>e</sup> Department of Emergency Medicine, Fatebenefratelli-Isola Tiberina Hospital, Rome - Italy; <sup>f</sup> Department of Emergency Medicine, Umberto I Hospital, La Sapienza University, Rome - Italy

### Background

Atrial Fibrillation (AF) management is still matter of debate. Research is largely based in cardiology setting and few data exist on management of AF in Emergency Department (ED). This study investigated which factors drive different AF treatments in ED, describing their use in different hospitals. Finally, efficacy of different strategies in terms of cardioversion in ED is analysed.

### Methods

Charts of patients treated in 6 EDs in Italy for "atrial fibrillation", in a 24 consecutive months period, were reviewed and analysed. Demographics, comorbidities, treatment strategy and ED outcome were collected. Inclusion criteria were symptoms onset <3 weeks and hemodynamic stable conditions at presentation. Propensity score was used to adjust for baseline clinical characteristics and to compare different treatments efficacy.

### Results

3085 patients were included in the analysis. Variables associated with a rhythm control strategy were symptoms onset <48 hours, age, dyspnea, palpitations, renal failure and mechanical valve. Different EDs applied different strategies in terms of drugs used and electric cardioversion, showing heterogeneity in AF management. Adjusting for propensity score, electric cardioversion and antiarrhythmic drugs of class Ic were more effective than wait-and-watch in ED.

### Conclusion

Despite international guidelines are respected, AF management is heterogeneous in different ED settings. Rhythm control strategy with electric cardioversion and Class Ic drugs is more effective than wait-and watch approach during ED visit. Further research, toward an evidence-based, approach to AF in ED, is warranted.

## Role of Gas6 protein in thromboembolic diseases: effects on human platelets activation

Luigi Castello, Alessandra Bertoni, Clara Di Vito, Federica Alciato, Elena Ranza, Claudio Michelone, Pier Paolo Sainaghi, Gian Carlo Avanzi

Dipartimento di Medicina Clinica e Sperimentale. Università del Piemonte Orientale "A. Avogadro"

The identification of new molecules involved in the regulation of platelet activation represent an important goal in order to decrease mortality and morbidity due to acute thromboembolic events as myocardial infarction, stroke and pulmonary embolism.

Gas6 is a vitamin K-dependent protein produced by many cells types and it binds to one of three receptors of the TAM family (Tyro3, Axl or Mer). Gas6 has been showed to be involved in widespread physiologic roles, such as cell adhesion, migration, growth and survival. Moreover, Gas6 and its receptors seem to have a role in the pathogenesis of thrombosis. The current hypothesis indicate Gas6 as an amplifier of the platelet response to other agonists being unable to evoke any activation per se. Therefore the inhibition of Gas6 might constitute a promising therapeutic strategy to prevent thromboembolic events avoiding

bleeding side effects. Dicumarolics act as vitamin K inhibitors leading to a reduction in gamma-carboxylation of many proteins including several blood coagulation factors and Gas6.

The objective of our project is to clarify if dicumarolics affect platelet aggregation and whether the effect may be due to the Gas6 inhibition. For this purpose we recruited 19 patients treated with dicumarolics (with stable INR values) and 19 controls at the Emergency Unit of "Maggiore della Carità" Hospital in Novara. We evaluated different aggregation tests in different experimental conditions on both washed platelets and platelet rich plasma (PRP). For each agonist (i.e. U46619, ADP) we analyzed the aggregation curve lag time, slope and amplitude.

We found a statistically significant reduction in the PRP slope of the patients treated with dicumarolics with respect to controls.

In particular 5  $\mu$ M ADP generated a slope of 96.32° ( $\pm$ 16.18°) in patients and of 122.45° ( $\pm$ 22.33°) in controls: this difference is statistically significant ( $p < 0.01$ ). In the presence of 3  $\mu$ M ADP there was a statistically significant difference ( $p < 0.05$ ) since there was a slope of 96.5° ( $\pm$ 12.88°) in patients and of 112.5° ( $\pm$ 19.04°) in controls. Finally, also in the presence of ADP 1  $\mu$ M the slope showed significant changes between the two populations ( $p < 0.01$ ) with values of 56.28° ( $\pm$ 15.41°) in patients and 89.07° ( $\pm$ 18.45°) in controls. In the presence of 2  $\mu$ M U46619 it was observed a slope of 105° ( $\pm$ 22.66°) in patients and 127.38° ( $\pm$ 22.82°) in controls with a  $p < 0.05$ . We also compared all the slopes obtained by stimulation with 1  $\mu$ M U46619. In the patients we observed that the slope on washed platelets was of 71.00° ( $\pm$ 22.75°), while on the PRP it was of

94.50° ( $\pm$ 4.78°); in the controls the slope obtained on washed platelets was of 56.66° ( $\pm$ 10.96°), while on the PRP it was of 146.33° ( $\pm$ 5.77°). The slope value of the control PRP is significantly higher than that obtained in other experimental conditions, that are PRP of patients treated with dicumarolics and washed platelets ( $p < 0.01$ ). This evaluation leads us to observe that in the control PRP, which is the only one in which Gas6 is present in the gamma-carboxylated form, the slope assumed higher values; however, where the protein is not present (washed platelets) or it is inhibited by dicumarolics (PRP of patients) the slope was lower. In conclusion, in our model, dicumarolics seem to modulate platelet aggregation by lowering the rate of platelet aggregation through inhibition of plasma Gas6 and not through a direct action on platelets.

## Immigrati e PS: una nuova sfida. Dati 2008-2009 Pronto Soccorso Ospedale Sandro Pertini

F. Paglia°, M. Salim°, A. Celestini\*, A. Revello°, F. R. Pugliese°

°DEA Ospedale S. Pertini Roma; \*Cardiologia Ospedale Sant'Andrea Roma/Ospedale San Paolo Civitavecchia

### Background

La sempre maggiore presenza di persone di nazionalità non italiana, presenti sul nostro territorio nazionale, rappresenta per la Medicina d'Urgenza una nuova sfida per affrontare patologie vecchie e nuove in contesti socio-culturali spesso non conosciuti. Per avere l'opportunità di conoscere più a fondo questa nuova realtà, abbiamo effettuato un'analisi retrospettiva dei pazienti di nazionalità non italiana che sono stati curati presso il PS del nostro ospedale.

### Materiali e Metodi

Abbiamo analizzato retrospettivamente l'accesso al Pronto Soccorso dell'Ospedale Sandro Pertini dei pazienti stranieri negli anni 2008 e 2009. Oltre ai parametri demografici (età, sesso, nazionalità), sono stati presi in considerazione i seguenti parametri: livello di triage, disciplina di competenza, modalità d'arrivo e esito. In ultimo è stata analizzata la diagnosi di ricovero o di dimissione.

### Risultati

Nel periodo 2008-2009 sono stati visitati presso il PS dell'Ospedale Sandro Pertini 21.342 pazienti di nazionalità non italiana, che corrispondono quindi a circa il 13% del totale degli accessi in Pronto Soccorso (2008-12,8%; 2009-13,1%). L'età adulta (>14 anni) rappresentava il 94,5%, il 57,1% era di sesso femminile; nell'età pediatrica invece il sesso più rappresentato è quello maschile (51%). La nazione più rappresentata è stata la Romania (28,9%), seguita da Egitto (4,4%), Bangladesh (4,1%), Serbia-Montenegro (3,9%), Perù (3,6%), Polonia (3,4%), Albania (3,1%) e Filippine (2,9%). I pazienti di nazionalità cinese sono risultati l'1,7% del totale dei pazienti stranieri. Il 47,4% degli accessi era di competenza medica, mentre il 33,4% di pertinenza ortopedica o chirurgica. Per il sesso femminile il 34,5% degli accessi era di

competenza ginecologica, in linea con i dati nazionali. La valutazione di triage ha assegnato il codice verde al 74% dei pazienti, mentre il 9,7% è stato valutato come giallo o rosso. Il 76% dei pazienti ha raggiunto il PS con mezzi autonomi ed il 15,3% è stato ricoverato o trasferito presso un altro nosocomio.

Le patologie d'accesso rispecchiano i dati del Ministero: la diagnosi più frequente è relativa al decorso di una gravidanza (8,8% del totale e 15,4% dei pazienti di sesso femminile), seguita da dolore addominale (5,6%), sifilide (3,9%), dolore toracico (3,5%), colica renale (2,2%) e cefalea (1,7%). Interessante è l'andamento di presentazione settimanale: per gli adulti la massima frequenza di accessi è il martedì e giovedì; mentre per l'età pediatrica il martedì e la domenica.

### Conclusioni

I pazienti di nazionalità straniera rappresentano sempre più una parte consistente della totalità degli accessi di Pronto Soccorso. La popolazione straniera che si rivolge al nostro PS appartiene ai cluster etnici relativi a 8 paesi a basso reddito, di cui la maggioranza proviene dalla Romania. Le varie nazionalità non sono rappresentate in maniera proporzionale rispetto alla loro presenza sul territorio italiano: ad esempio, i pazienti provenienti dalla Cina, sono solo l'1,7% del totale, benché la comunità cinese sia una delle più numerose in Italia. Gli stranieri non sembrano ancora sufficientemente informati sulla possibilità di usufruire del 118 (più dei tre quarti degli accessi avviene con mezzi propri). La diagnosi di dimissione ci dimostra come il PS venga spesso utilizzato per controlli durante la gravidanza, che in molti casi potrebbero avvenire in un ambulatorio dedicato. Infine, il fatto che il 3,9% dei pazienti sia giunto in PS per la sifilide, induce a pensare come il mosaico delle patologie nei nostri PS, potrebbe nel giro di qualche anno cambiare radicalmente.

## HRTC role in the diagnosis of H1N1 Pneumonia

M. Vinciguerra, A. Pallavicino, E. Teti, M.V. Tomassi, L. G. Vismara, C. De Dominicis

Radiodiagnostic Department – S. Andrea Hospital (Rome); Infectious Diseases Department – S. Andrea Hospital (Rome)

### Background And Objectives

A/H1N1 flu originally appeared in Mexico in March 2009 and later it quickly extended all over the world. The first cases in Europe dated at May 2009 and, at June, WHO declared the pandemic emergency. The study includes patients examined from October to Decem-

ber 2009 and it wants to point out an essential multidisciplinary management (clinical and imaging) of the A/H1N1 infection. In particular it underlines the imaging role as initial approach to the patient (chest x-ray) and as fundamental way to identify any complications (HRTC) stimulating following therapeutic choices.

**Patients And Methods**

18 patients have been screened, 10 males and 8 females in a range between 21 and 65 years old, hospitalized at S. Andrea Hospital since October to December 2009. All of them presented signs and symptoms of A/H1N1v flu described in the CDC guide lines (fever, headache, weakness, dry cough, sore throat, rhinitis, myalgia, stomach pit's pain), RT-PCR positive for H1N1v and concomitant chronic diseases or responsible of immunitary depression. The patients have been evaluated with chest x-ray at the beginning of the symptoms and then HRTC in case of no response to the antiviral therapy with Oseltamivir.

**Results**

4 of the 18 patients examined, presented a rapid improvement with antiviral therapy, whereas others 14 patients have been submitted to in-depth examinations HRTC (2 of them initially presented negative radiography) and to further antiviral therapeutic cycle because of the persistent case history. The lesions presented in the 14 cases at HRTC were: small consolidated areas especially in peripheral sites (75%), patchy ground glass opacities (75%), thickening of inter-intralobular septa (87.5%), pleural effusion (50%). Pulmonary involvement has been bilateral in all patients except for one; pulmonary zones more interested were lower presenting a diffuse distribution of the lesions (87.5%). All of the patients showed clinical and imaging improvement at the follow-

up except for one patient dead during the admission for ARDS complication and bilateral alveolar interest.

**Conclusions**

Chest radiograph confirms itself as an adequate tool for identifying A/H1N1 related pneumonia, according to clinical-serological findings. However, in few selected cases, HRTC results more sensible in diagnosis of pulmonary's complications, above all in clinical radiological mismatch and in those case histories seriously compromised by interstitial and small airways' interest, not evident at x-ray. Finally our study points out a new localization of thickening of interstitial septa in the subpleural site followed by the appearance of ground glass opacities in short time, which has never described in Letterature earlier.

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## Cocaine abuse in patients referred to the Emergency Department: the Policlinico Tor Vergata experience

Guarino S., Legramante J.M., Gallù M., A. Galante

Medicina d' Urgenza, PTV Dipartimento di Medicina Interna, Università di Tor Vergata

**Introduction**

The rise of cocaine use in Europe, as well as in many countries outside Europe, has increased the number of emergencies and hospitalizations due to emergency situations related to the abuse.

**Objective**

1) provide information about the extent of the phenomenon with reference to the reality of Policlinico Tor Vergata, over the period May 2004-April 2007, 2) to identify the distinctive characteristics of those who come to the emergency department for conditions related to cocaine abuse, 3) identify the causes that most often push these patients to seek emergency department and the codes assigned priority, 4) evaluate the impact of the phenomenon in the emergency room trying determining which are the periods of more crowd and therefore more workload within 24 hours, 12 months, and days of the week.

**Materials and Methods**

Patients included in the study were tested for urinary screening based on clinical and / or medico-legal criteria (request of the Judicial Authority). The screening test was also used to search for the positivity to other drugs. Ethanol was searched by determining plasma. Urinary levels of cocaine metabolites greater than or equal to 300 ng / ml were considered positive. Sex, age, nationality, date of access (time, day of week, month, year), access code, diagnosis, acceptance, positive to cocaine, alone or multiple drugs of abuse, were analyzed.

**Results**

The study included 141 subjects, 119 (84.4%) male and 22 (15.6%) female, 136 (96.5%) of Italian nationality and 5 other countries. 36 subjects (25%) in age between 15 and 24, 90 (64%) between 25 and 44 years, 15 (11%) between 44 and 64 years. The month with the highest turnout was in August (17 patients) with a slight predominance of the accesses in the late afternoon (around 19.00). The more crowded day was Thursday with 27 hits, followed by Saturday with 25. The most accesses were caused by a car accident (46 patients 36%), followed by cardiovascular causes (25 patients, 20%), aggression (15 patients, 12%), abdominal pain (5 patients, 4%), seizure (4 patients, 3%), other (32 patients, 25%). Most of the patients were assigned a green code (60 patients, 42.5%), to 51 (36.2%) a red code, 30 yellow codes(31.3%). Among the 141 patients enrolled in our study, 92 (65.3%) were positive only to cocaine, whereas 49 (34.7%) positive results simultaneously in more than one abuse substance (9 of these 49 patients positive at the same time at more than two drugs). The most frequent association was with alcohol (24 patients, 48.9%), followed by opioids (12 patients, 24.5%), benzodiazepines (10 patients, 20.4%), the cannabis (3 patients, 6.2%).

**Conclusion**

the distinctive features of those who come to the emergency room for illnesses related to cocaine abuse are male, Italian nationality, on average 32 years. Such patients go to the ER mostly in the late afternoon after a car accident, they get a green code and are positive for at least another abuse substance.

## Management of Cancer-related pain in Emergency

Legramante J.M.

Medicina d'Urgenza, PTV – Dipartimento di Medicina Interna, Università di Tor Vergata

More than 930 thousands people die every year due to cancer-related diseases in the 15 EU countries accounting for about 40% of the overall deaths (about 2.5 million/year). Moreover, cancer has a great social impact representing the second death cause in Europe after cardiovascular diseases and due to the progressive aging population this social impact is gradually increasing. Despite epidemiologic studies of cancer are substantially developing in Italy after the activation of the Banca Dati Italiana dei Registri dei Tumori, data concerning patients affected by cancer presenting in Emergency Department (ED) are still lacking. A study performed in Piemonte (Italy) shows that about 0.4% of the patients presenting in ED are affected by cancer-related diseases representing twice the rate of yellow and red code as compared to the total number of patients presenting to the ED. Also the number of patients who die in ED (1.2% vs 0.1%) and charged in the hospital (53.6% vs 12.2%) are greater for cancer-related patients as compared to the total number of patients presenting in ED. In line with these observations a study performed in the Emergency Department of our University Hospital (Policlinico Tor Vergata) is noteworthy. We have evaluated the number of patients presenting in ED who were diagnosed for a previously ignored cancer-related disease. In two years about 332 patients received a novel diagnosis of cancer-related disease in the Emergency Department. Therefore these indirect data clearly show that cancer represents a real challenge for Emergency Department. Moreover, about 80% of cancer-related patients suffer from chronic pain and ED is often a place of refuge. There are significant barriers to optimal pain management in the emergency setting, including lack of knowledge, inexperienced clinicians, myths about addiction, and fears of complications after discharge. These factors contribute to unnecessary suffering not only for the patient but also for family and caregivers. Malignant pain is highly responsive to medication. Adequate malignant pain control is possible in more than 90% of patients if established therapeutic approaches are applied systematically in any practice setting, including the ED. It has been suggested that management of an acute pain crisis in a patient with advanced cancer "is as much a crisis as a code," and

emergency clinicians should, and can, become comfortable caring for patients with cancer in acute pain. Patients with cancer often present to the ED because their pain is unmanageable. Although there are multiple physiologic possibilities for inadequate pain control, the emergency clinician should also be aware of the many psychosocial factors contributing to oligoanalgesia in the cancer patient. Depression, unresolved spiritual or social concerns, and misconceptions of prescribed medications may interfere with adequate treatment. With a properly focused evaluation, the treatment of unresolved pain in the cancer patient can be performed rapidly and effectively in the ED.

General principles of good pain assessment are particularly important in the patient presenting to the ED with malignancy and are not different from those used in an outpatient pain unit. The problem is the setting, completely different from an outpatient ambulatory. ED crowding, the need to see the patient as soon as possible, the great number of patients to be managed by one doctor, make the assessment of pain not always feasible. Accordingly, the definition of severity, character, likely etiology, timing and location, exacerbating and relieving factors, and associated symptoms which usually provides essential information for proper management, becomes a difficult task in ED. Moreover, to collect details of the clinical history may reveal particular cancer pain syndromes, some of which require urgent diagnosis and intervention to prevent permanent functional impairment. Therefore by attempting to reach a compromise between the ED frenetic activity with the need for an adequate pain assessment, effective therapy can be quickly implemented in the ED. Also because a rapid response to a pain crisis is essential for patients both with early stage disease and, particularly, those at the end of life. Failure to adequately manage a pain crisis early in the disease course encumbers both the patient and family with the fear that escalating pain and lack of effective treatment will dominate their final days of life. This issue is well explained by the sentence tracked in a recent paper "Managing acute pain crisis in a patient with advanced cancer. This is as much of a crisis as a code" (JAMA 2008; 299 (12): 1457-1467).

## Venous Thromboembolism Prophylaxis In Medically Ill Patients. Policlinico Tor Vergata Emergency Medicine Experience

Di Lecce V.N., Gallù M., Gravina A., Legramante J.M., Galante A.

Medicina d'Urgenza, Policlinico Tor Vergata, Dipartimento di Medicina Interna, Università di Tor Vergata

Available data indicate that the frequency of deep vein thrombosis in medically ill patients, in the absence of prophylaxis, varies from 10% to 26%. Pulmonary embolism is responsible for up to 10% of deaths that occur in hospital, and 75% of fatal pulmonary emboli are in medical patients. Evidence-based guidelines recommend that acutely ill hospitalized medical patients who are at risk of venous thromboembolism (VTE) should receive prophylaxis. Despite the existence of these guidelines, VTE prophylaxis remains underused (IMPROVE and ENDORSE study). The first reason appears to be a lack of awareness of both the disease and the evidence based guidelines. Physicians' fear of potential bleeding

complications is the second reason for not using prophylaxis. The aim of this study was to assess the prevalence of patients at risk of VTE in our Emergency Medicine Division, to determine the proportion of these hospital setting at risk patients who received prophylaxis as recommended by the American College of Chest Physician (ACCP 2008) evidence based consensus guidelines, and to analyze the reason of an eventual prophylaxis underuse in these populations of patients. Patients were considered at risk for bleeding, and for this reason not eligible for an anticoagulant prophylaxis, if they present with or developed during hospitalisation any of the following: intracranial haemorrhage, hepatic impairment,

bleeding at hospital admission, gastroduodenal ulcer, thrombocytopenia. Of the 436 patients admitted into our department between January and September 2009, 283 patients met the criteria of the 2008 ACCP guideline recommendations. In total 155 patients (55%) received pharmacologic VTE prophylaxis. These data are consistent with previous studies. The prophylaxis was carried in 75% of patients with congestive heart failure, 67% with respiratory failure, 55% with immobility  $\geq 3$  days, 100% with prior VTE, 52% with cancer, 52% with sepsis. When two or more VTE risk factor were present 63% of patients received ACCP recommended prophylaxis even if one bleeding risk was present. In our study 122 patients (43%) were considered to have a sufficient risk for

bleeding to present a contraindication to anticoagulant prophylaxis, even though one half of these patients received prophylaxis. The type of bleeding risk and not its simple presence have had a role in the decision to provide VTE prophylaxis; excluded from prophylaxis: platelet count  $< 50000$ , ICH, INR  $> 2$ , active bleeding, esophageal varices F3. Only few patients without risk factor for bleeding not received prophylaxis. Our data show that a large proportion of acutely ill hospitalized medical patients are at risk for VTE and that recommended VTE prophylaxis is underused not for a lack of awareness of the evidence based guidelines, but for the presence in the same patient of one or more bleeding risk; in this patients subset guidelines are not clear.

## The anti-coagulant oral therapy and his complications. The effects on the Policlinico's Emergency Department in Tor Vergata

Verga V., Forte E., Brandi A., Giovagnoli G., Santucci L., Legramante J.M., Galante A.

Medicina d' Urgenza, PTV Dipartimento di Medicina Interna, Università di Tor Vergata

The increase of number of patients treated with oral anti-coagulants drugs in Italy, as well as in many other world countries, has determined an increase of their side effects leading to an increase of hospitalizations, huge use of Emergency Departments (ED) and consequently increase of the costs of the entire Health System.

The aim of our research is to estimate this phenomenon from a particular point of view represented by the Policlinico's Emergency Department in Tor Vergata in order to consider the impact on it, during the period between January 2006 and December 2007. The total number of patients treated by our Emergency Room, during the above mentioned period, has been 98570. Among them, 137 patients (0.13% of the interested population) have been included in this research to have a countercheck of the INR $>5$  values. The analysis has been conducted dividing the people according to sex (51.8% males and 48.8% females), age (45.2% of them were belonging to a range between 75 and 89 years), acceptance code (59.1% were yellow code, 34.3% were green, 5.8% were red and 0.7% white), INR's values at the beginning (54% of them reported values between 5 and 6.9), indicators of the anticoagulant oral therapy (51.8% of them were suffering FA), kind of consumed medicine (51.8% of them were consuming sintrom), eventual kind of haemorrhage (30.6% of the patients were going to the ED because of haemorrhages and among

them 22.7% for gastrointestinal ones, 21.4% for haematomas, 16.6% for haematuria, 10% for brain haemorrhage, 10% for epistaxis, 10% for ecchymosis, 6.8% for gingival problems, 4.7% for haemoptysis, 2.3% for conjunctival haemorrhage), administered therapy (mostly konakion), outcome at discharge (most of them were hospitalized again), admission's date (the most crowded month has been August).

From our estimate, it appears clear and needs an afterthought the fact that the number of patients that, thought haematochemical exams, have got INR $>5$  values, represented an important/huge portion of all Policlinico's First Aid Department's users during the considered period ( $p=0.00001$ ). Furthermore, among all patients, those who really needed a prompt intervention, with assigned red code, has been those with INR $>5$  values without clearly haemorrhagic development ( $p=0.01203$ ).

The experience gained inside the Emergency Department and the data analysis allow us to state that, for the majority of the observed patients, a good and correct health education, a good check (including indications and contraindications to the therapy, the elapsed therapeutical time, the good management of the intercurrent illnesses), a medium and discrete knowledge of the patient's skills, an accurate and serious anamnestic collection, could reduce the risk of complications that would also mean a less waste of resources and efforts for the entire Health System.

## Neodiagnosis of cancer in Emergency Room: three years of observation in the Emergency Department of Policlinico Tor Vergata

Tamburri R., Legramante J.M., Gallù M., Minetola L., Galante A.

Medicina d'Urgenza, Policlinico Tor Vergata, Dipartimento di Medicina Interna, Università Tor Vergata, Roma

Cancer is one disease which produces more worry all over the world since it causes worsening of life quality and weighs heavily on population's premature mortality besides requiring a lot of resource investment to allow the diagnosis and promote the treatment of patients.

The aim of the present study was to evaluate patients who refer

to the Emergency Room of Policlinico Tor Vergata (PTV) from January 2005 to December 2007 and were discharge with a new diagnosis of cancer.

We enrolled 332 oncologic patients who were diagnosed in PTV ED from 2005 to 2007. Most of patients belong to cluster who were 75-79 years hold or 70-74 years hold. Both patient with

underhand clinical symptoms (asthenia, abdominal pain) and patients who present more important symptoms (Thoracic pain, gastroenteric bleedings) indifferently referred to ED, which is deputed to manage the emergency. According to the site the most frequent cancer diagnosed in ED were: the Gastroenteric. Breast, hemopoietic and Reproductive System cancer were not represented in our sample. This difference maybe justified by different way of hospital admission for this kind of patients for which the diagnostic suspect comes out during ambulatory visits or in day hospital regimen. For 169 pts the cancer was discovered during the recovery in the Emergency Department, that was, in average, 2 days for patients who have medical problems and 4 days for patients with surgical one's. 179 pz (54%) undergone a specific surgical operation, 153 (46%) undergone only a medical treatment in Medical Divisions, both Internal Medicine and Specialistic. No one patient was enrolled in a chemiotherapeutic treatments. At the end of hospitalization 78% of patients was discharged at home,

12% died during the recovery, 6,4% were admitted in different structures (only 9 were admitted in Hospice).

The study shows how Emergency Department is a privileged observatory which allows to estimate the efficiency of the oncologic screenings plans. Prevention and precocious diagnosis had drastically reduced the numbers of admittance in Emergency Department for patients who show disease diffusion. It's extremely important to sensitize the whole population in screening plans for a prompt diagnostic strategy which allow an early cancer diagnosis. Unfortunately, our results show that too frequently the first diagnosis of cancer is done too late as compared to the cancer exordium. The missing diagnostic timeliness reveals both the lack of valid and sensible instruments which can discover some kind of cancer, which are available only during hospitalization regimen and the failure of Territory Medicine which seems to be inattentive and inadequate when it has to face oncologic disease.

## Study of cardiovascular autonomic regulation during early phase of acute myocardial infarction: an experimental model in conscious, freely moving rats

Crobeddu P., Sacco S., Pallante M., Galante A., Legramante J.M.

Medicina d' Urgenza, PTV Dipartimento di Medicina Interna, Universita' di Tor Vergata

Ischemic heart disease includes illnesses with different etiology. These have in common the imbalance between demand and supply of oxygen to the myocardium. One of the most frequent clinical expression of ischemic heart disease is the myocardial infarction which is caused by myocardial ischemia inducing cell necrosis. During myocardial infarction an alteration of the Autonomic Nervous System occurs, in particular of the Arterial baroreflex System.

Therefore there is an increased activity of the Sympathetic Nervous System associated with a reduced functionality of the Parasympathetic Nervous System. It has been widely reported that the Baroreflex sensitivity is reduced after acute myocardial infarction and this reduction represents an adverse prognostic significance.

Currently few studies describe these mechanism during the early phases of Acute Myocardial Infarction (IMA) in vivo. Therefore the aim of the present study was to evaluate the feasibility of the cardiovascular autonomic study in the early phase after IMA and to report preliminary data. The technique of spontaneous sequences allow the study of the autonomic cardiovascular regulation in a noninvasive and nonobtrusive way. The total study have been performed on 11 rats of both sexes (8 in the IMA group and 3 in the control group). Eight rats were part of the myocardial infarction group, three rats were part of the control group.

Our team implants a transducer in the abdominal aorta to continuously record blood pressure. From the blood pressure time series calculation of baroreflex and non-baroreflex sequences is performed as expression, respectively, of negative and positive feedback neural mechanisms of cardiovascular regulation.

The myocardial infarction have been induced by cauterization of the left anterior descending coronary artery. Preliminary data show an increase in the occurrence of baroreflex sequences along the 24 h both in the IMA and in the control group (from 91 in control condition to 120 after 24 h for IMA group and from 63 in control condition to 125 after 24 h for the control group). This increased baroreflex engagement is related to a reduced baroreflex sensitivity (BRS) in the IMA group (from 3.3 msec/mmHg in control condition to 1.9 msec/mmHg after 24 h) but not in the control group (from 3.3 msec/mmHg in control condition to 3.0 msec/mmHg after 24 h).

Nonbaroreflex sequences show no substantial changes along the 24 h in the IMA group (from 37 to 43) whereas a trend to decrease is evident for control group (from 39 to 16). Similarly to BRS the sensitivity of nonbaroreflex sequences shows a trend to decrease fro IMA group (from 3.2 msec/mmHg to 1.8 msec/mmHg after 24 h) whereas no substantial changes are evident in the control group (from 4.7 msec/mmHg to 3.6 msec/mmHg).

According these preliminary data, instability of the cardiovascular system seems to occur after the experimentally-induced IMA. We see an increase in the baroreflex engagement with a corresponding trend to BRS decrease after IMA as compared to control animals. Even though the small sample reported in this preliminary report need to be increased in order to have more definite results, we can suggest that this first demonstration of a BRS decrease in the first 24 h after IMA add a pathophysiological mechanisms supporting the widely reported increased risk for life threatening arrhythmias in the first hours after IMA.

## Early versus Late Recurrence of Panic Attack in the Emergency Department

Francesco Buccelletti, Davide Marsiliani, Annarita Carroccia, Emanuele Gilardi, Giuseppe Merra, Nicolò Gentiloni Silveri, Francesco Franceschi

Department of Emergency Medicine, Catholic University of the Sacred Heart, Rome – Italy

### Introduction

Panic Attack Disorder (PAD) is a very common diagnosis in the Emergency Department (ED). Although it is a benign disease in terms of mortality, recurrence is almost the rule and therefore it represents an economic burden [1]. Moreover, PAD often mimics more serious conditions such as acute coronary syndrome and the work-up in the ED might be expensive, long and difficult [2]. There are programs and tools in the ED to screen for PAD but none is validated and recognized as gold standard [3]. Identifying patients at high risk for early recurrence (i.e. within 90 days) might help to plan education treatment for PAD preventing further ED visits. This study investigated clinical characteristics of patients diagnosed with PAD in ED with recurrence within 90 days.

### Materials and Methods

ED electronic database, GIPSE® (Public Health Agency, Italy) was searched for patients discharged or admitted with primary ICD-9 diagnosis of panic attack, from 2001 to 2006 in a tertiary care, university, hospital. Exclusion criteria were age <18 and acute coronary syndrome. Search was performed between January 2001 and December 2006. All selected patients were tracked for recurrence until December 2009 (at least 3 year of follow-up). Charts were manually extracted in a dedicated database and blindly reviewed by two authors (FB and DM) for diagnosis accuracy. Cohort was then divided into “early recurrence” (i.e. patients who presented for PAD a second time within 90 days) and “late recurrence” (patients who experienced a second attack and visit in more than 90 days). The two groups were compared for demographics, symptoms patterns and intervention received (pharmacologic treatment and psychiatry consult) using logistic regression with a forward likelihood (inclusion and exclusion thresholds respectively 0.05 and 0.1) to improve model fitting and to select only significant variables. P values <0.05 were considered significant.

red significant.

### Results

One-thousand-three-hundreds-one (1301) patients had a primary diagnosis of PAD and met inclusion/exclusion criteria. 214 patients (16.5%) had at least a recurrence in the next 3 years. Median time for recurrence was 6.5 months. 31.8% of the patients had more than one recurrence. 59 patients (27.2%) had a recurrence within 90 days (early recurrence). Table 1 summarizes demographics and clinical characteristics. Logistic regression including predictors shown in table 1 identified age (OR 0.80 [0.65-0.98]) and shortness of breath at presentation (OR 0.47 [0.22-1.00]) as the only significant factors associated with early recurrence (omnibus model test  $p=0.016$ ). Intervention such treatment with benzodiazepines and psychiatry consult performed in the ED were not significant ( $p=0.11$  and  $0.88$  respectively).

The most important limits of this study were: single hospital and a possible underpower issue since panic attacks are often diagnosed with alternative codifications (i.e. unspecific chest pain etc.).

### Conclusions

PAD is common in the ED because symptoms at presentation mimic more serious conditions. Despite a precise diagnosis is made, patients presents to the ED with recurrence in a high percentage of cases (within 6.5 months in 50% of the cases). Patients who experience a new ED access within 90 days are generally younger (<40 year old) and experienced shortness of breath as chief complain compared to those who returned to the ED later in time. This group might require a specific and more aggressive intervention in terms of education and medical/psychological referral. Even though we cannot exclude to be underpowered, psychiatric consult in the ED did not seem to prevent early recurrence.

Table 1 - Demographics and clinical characteristics of PAD

	Early Recurrence (N=59)	Late Recurrence (N=155)	Univariate P-Value
Age	35 (12)	41 (14)	0.05
Female	34 (57.6)	92 (59.4)	0.81
Shortness of Breath	10 (16.9)	33 (21.3)	0.44
Chest Pain	7 (11.9)	22 (14.2)	0.67
Palpitations	12 (20.3)	33 (21.3)	0.88
Self Reported Anxiety	23 (39.0)	56 (36.1)	0.75
Tremors	16 (27.1)	42 (27.1)	0.99
Headache	2 (3.4)	10 (6.5)	0.38
Pharmacologic treatment in ED	34 (57.6)	74 (47.7)	0.19
Psychiatric Consult in ED	11 (18.6)	21 (18.1)	0.91

All cells are numbers (%) except age expressed as mean (standard deviation). Univariate P-values are based on chi-squared test except for age (Mann-Whitney U test).

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# Clinical Presentation, Microbiological Features And Correlates Of Disease Severity Of 2009 Pandemic Influenza A (H1N1) Infection

S. Farina<sup>1</sup>, L. Zileri Dal Verme<sup>2</sup>, M. Sabbatini<sup>2</sup>, D. Marsiliani<sup>2</sup>, G. Pignataro<sup>2</sup>, L. Carbone<sup>2</sup>, M. Candelli<sup>2</sup>, P. Tilli<sup>2</sup>, S. Di Giambenedetto<sup>1</sup>, N. Gentiloni Silveri<sup>2</sup>

<sup>1</sup>Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart; <sup>2</sup>Department of Emergency Medicine, Catholic University of Sacred Heart

## Purpose

To describe epidemiological, clinical and microbiological characteristics of confirmed novel influenza A (H1N1) infection, investigating factors associated to disease severity.

## Methods

We retrospectively selected patients seeking care for respiratory symptoms in two periods (May-August and September-November 2009) with different epidemiological characteristics. Only patients with swine-origin influenza A (H1N1) detected from respiratory specimens by RT-PCR assay were considered for this analysis.

## Results

A total of 104 patients with H1N1 infection were evaluated. Subjects mostly complained of classic influenza symptoms; in addition, diarrhea and vomiting were often referred. The hospitalization rate was higher in patients older than 40 years when

compared to those aged 15-39 (p=0.008) or to those under 14 years (p=0.006). Clinical signs, symptoms and respiratory complications seemed to differ between the two study periods. On the total, 18 patients (17%) had pneumonia. A pneumonia diagnosis was more frequent in the second period (37% versus 10%, p=0.002). Patients older than 50 years showed a lower probability of pneumonia diagnosis when compared to children aged 0-13 (p=0.049); a longer duration of symptoms before medical care was associated with a higher probability of pneumonia (p=0.026). Phylogenetic analysis showed a low variability both in hemagglutinin and neuraminidase genes. In addition, no neuraminidase mutation associated to antiviral resistance was detected.

## Conclusions

A detailed description of respiratory diseases associated with H1N1 infection was provided and factors associated with its severity were investigated, thus contributing to the insight into epidemiological, clinical and microbiological knowledge of the disease.

# Left Ventricle ultrasound evaluation agreement between different expertise operators in Emergency Department

Pivetta E<sup>1,2</sup>, Balcet L<sup>3</sup>, Lorenzati B<sup>4</sup>, Esposito G<sup>5</sup>, Di Bella S<sup>6</sup>, Laurita E<sup>2</sup>, Goffi A<sup>7</sup>, Cibinel GA<sup>2</sup>

<sup>1</sup>Cancer Epidemiology Unit and Piedmont Oncology Prevention Center, AOU S. Giovanni Battista - Turin, and University of Turin;

<sup>2</sup>Emergency Medicine Department – “E. Agnelli” General Hospital – Pinerolo, Torino;

<sup>3</sup>Geriatrics and bone metabolic diseases, AOU S. Giovanni Battista – Turin, School of Specialization in Geriatrics, University of Turin;

<sup>4</sup>General Medicine 3, AOU S. Giovanni Battista – Turin, School of Specialization in Internal Medicine, University of Turin;

<sup>5</sup>V division of Internal Medicine and Immunoallergology, School of Specialization in Internal Medicine, II University of Naples;

<sup>6</sup>Geriatrics and bone metabolic diseases, AOU S. Giovanni Battista – Torino, School of Specialization in Internal Medicine, University of Turin;

<sup>7</sup>Critical Care Medicine Department, Saint Michael's Hospital, Toronto, Ontario, Canada

## Introduction

First level ultrasound evaluation (US) is often used in Emergency Medicine Department (ED) as a diagnostic tool in chest, abdomen, venous and heart examination. A recent study has highlighted a high agreement in the evaluation of the left ventricle function between intensivists inexperienced in echocardiography and expert echocardiographers.

## Objectives

The aim of this study is to evaluate the agreement between inex-

perienced operators and a single expert echocardiographer (used as reference) in evaluating the left ventricle function and the ejection fraction in ED.

## Methods

Medical resident physicians have been involved as inexperienced US operators: at the moment of the study their only experience consisted in participation in an advanced US course (9 hours of theoretical and practical echocardiography).

Patients evaluated in Pinerolo General Hospital ED, triage codi-

fied as green or yellow, were recruited if presenting with syncope, acute dyspnoea, chest pain or palpitations.

We collected demographic and clinical data for each patient, including ED evaluation cause, medical history, physical examination, EKG, chest X-ray evaluation, details on US evaluation (echocardiography, possible compression vein US, lung US and evaluation of inferior cava vein (ICV)) provided by resident physician and by an expert operator, an emergency physician and a cardiologist with a level 3 American Heart Association expertise. Cohen's kappa was used as the agreement measurement for each US variable.

### Results

At this time, 23 patients have been enrolled: 9 women (39.1%) and 14 men (60.9%). Median age was 85 years (range 78-97 years) and 73 years (range 60-100), respectively. 4 patients were positive for chronic obstructive pulmonari disease, 6 for ische-

mic cardiopathy, 5 for cardiomiopathy and 7 for hypertensive cardiopathy. ED evaluation causes were: syncope in 5 cases, acute dyspnoea in 14, chest pain in 3 and palpitations in 1 case. The expert operator categorized 13 US evaluation as "low complexity", 1 as "medium", and 4 as "high". Cohen's kappa was 0.62 for left ventricle evaluation (categorized as "normal" or "dilated/hypokinetic"), 0.51 for estimated ejection fraction ("normal", "small/moderate/large reduction") and 0.86 for ICV dimensions evaluation ("normal" or "dilated").

### Conclusions

Our study found a moderate agreement between inexpert operators and a reference echocardiographer in evaluating left ventricle function and ejection fraction in ED. We expect to find an increased agreement in learning curves for each inexpert operators as the number of evaluations increases. Finally, we found a high agreement for ICV dimensions evaluation.

## Lung Ultrasound for acute dyspnoea in Emergency Department – a multicenter study protocol

Pivetta E<sup>1,2</sup>, Goffi A<sup>3</sup>, Baldi I<sup>1</sup>, Lupia E<sup>4</sup>, Ciccone G<sup>1</sup>, Cibinel GA<sup>2</sup>, Merletti F<sup>1</sup>

<sup>1</sup>Cancer Epidemiology Unit and Piedmont Oncology Prevention Center, AOU S.Giovanni Battista - Turin, and University of Turin;

<sup>2</sup>Emergency Medicine Department – "E. Agnelli" General Hospital – Pinerolo, Turin;

<sup>3</sup>Critical Care Medicine Department, Saint Michael's Hospital, Toronto, Ontario, Canada;

<sup>4</sup>General Medicine 5, AOU S.Giovanni Battista – Turin and University of Turin

### Introduction

Dyspnoea is one of the most frequent symptoms in patients evaluated in Emergency Departments (ED) and yet often difficult to interpret by emergency physicians. Early and accurated differential diagnosis is essential for efficacious therapy. Several studies have assessed the utility of ultrasound (US) for disпноic patient evaluation. Lung US has proven to have good accuracy and reproducibility, although estimates show large variability due to the different reference used (i.e. lung x-ray, lung computed tomography, an expert physician...) and to the small number of cases.

### Objectives

The aim of this study is to describe the protocol for the evaluation of accuracy and diagnostic impact of lung US performed by emergency physicians to identify interstitial syndrome and pleural effusion as US signs of cardiogenic dyspnoea. The reference will be the "a posteriori" diagnosis by a panel of expert emergency physicians. The protocol was approved by the Ethical Committee of the AOU San Giovanni Battista in Turin, and has been submitted for registration on clinicaltrials.gov.

Moreover, the study will evaluate reproducibility between operators in interpreting US images and will define a clinical-US flow chart for acute dyspnoea management in ED.

### Methods

The design of this study is a multicenter prospective cohort, with a six months recruitment period in each center. Adult patients will be considered eligible if they refer acute dyspnoea, an emergency physician with lung US experience is present, and US examination is possible within 30 minutes after the start of the clinical evaluation. Dyspnoea cases clearly due to neither cardiogenic nor respiratory etiology will be considered not eligible.

After the initial diagnostic work-out (medical history, physical examination, EKG, arterious blood gas), the emergency physician will classify dyspnoea in cardiogenic or respiratory dyspnoea

and write it down in a specific form (clinical form). Immediately after this, lung US will be performed: the physician will describe it and evaluate the etiology again (integrated evaluation form). Then a chest X-ray evaluation will be performed for each patient. A final diagnosis ("a posteriori" form) will be determined after discharge by a panel of expert emergency physicians using all available information.

Patients will be investigated in supine or semi-recumbent position, following a scanning protocol modified by Volpicelli et al. [Bedside lung ultrasound in the assessment of alveolar-interstitial syndrome. American Journal of Emergency Medicine, 2006. 24(6)] in which eight zones of the lungs are scanned.

The study intends to recruit 1000 patients. Such a study sample size will allow us to test absolute differences of 10% in sensitivity and specificity between standard and US-integrated evaluation, with 90% study power and 5% alpha (two-samples test), assuming: a cardiogenic dyspnoea prevalence in the cohort ranging from 45% to 55%, and traditional evaluation sensitivity and specificity ranging from 70% to 85% and from 75% to 85%, respectively.

A pilot study is ongoing to test feasibility and the data collection tools. Recruitment for the main study is planned to start on November, 2010, with a one-year estimated study duration, and the involvement of six EDs.

### Conclusions

The study will define lung US sensitivity, specificity, positive and negative predictive values in the identification of interstitial syndrome and pleural effusion; positive and negative likelihood ratios to determine how diagnosis probability may change with lung US result; the impact of US diagnostics. Furthermore it will be possible to assess inter-observer agreement in interpreting US images (expert vs inexpert, blinded evaluations). Further analyses will be performed by subgroups for other tests regularly used in dyspnoea diagnosis (i.e. BNP dosage).

## A “double-coding triage system” to re-organize the patient pathways in the Emergency Department: the experience of an Italian Hospital

Mana E<sup>1</sup>, Civita M<sup>1</sup>, Sfasciamuro C<sup>1</sup>, Goffi A<sup>2</sup>, Odetto C<sup>1</sup>, Pivetta E<sup>1,3</sup>, Cibinel GA<sup>1</sup>

<sup>1</sup>Emergency Medicine Department – “E. Agnelli” General Hospital – Pinerolo, Turin;

<sup>2</sup>Critical Care Medicine Department, Saint Michael's Hospital, Toronto, Ontario, Canada;

<sup>3</sup>Cancer Epidemiology Unit and Piedmont Oncology Prevention Center, AOU S. Giovanni Battista - Turin, and University of Turin

### Introduction

As stated by the Italian law, the priority of admission to the Emergency Department (ED) is triaged according to a colour code that can be red, yellow, green, and white, in descending order of priority. This system allows the stratification of patients on the basis of the main complaints. After a careful review of the procedural protocols and an adequate training of the nurses, as established by the Italian law n°43-15182 of 23/03/05, a new triage system has been developed in the ED of the Pinerolo General Hospital. It results in the combination of a numerical code with the previous and more traditional 4-colour code.

### Objectives

The aim of this study was to evaluate waiting time (WT) for medical examination with the new 6-codes based triage system in a first level general hospital ED.

### Methods

The numerical code stratifies patients in four different categories according to the potential rapidity of clinical deterioration on the basis of clinical signs and symptoms: 4) immediate threat to life and/or severe alteration of at least one of four specific vital signs, 3) remarkable risk of short-term alteration of vital signs 2) low-risk of short-term alteration of vital signs 1) no alterations of vital signs.

The triage steps are: first evaluation (taking vital signs), second evaluation (general suffering signs, pain intensity, bleeding, vomiting, temperature, primary specific signs, related to the main symptom, and secondary specific signs, indirectly related to the main symptom, i.e. allergy, medicaments, history of past illness, last meal, age, risk factors...), code definition and continuous re-evaluation (no re-evaluation for 4 red but immediate medical evaluation, after 5 minutes for 3 yellow, after 10 minutes for 2 yellow,

after 45 minutes for 2 green, after 90 minutes for 1 green, after 240 minutes for 1 white).

The double-coding triage system was applied to all patients during the first trimester of 2008.

### Results

With the new triage system the WT decreased from 48 to 14 minutes for 3 yellow, from 49 to 15 for 2 yellow, from 60 to 38 for 2 green, whereas it increased from 50 to 55 for 1 green and from 76 to 95 for 1 white.

The analysis of data led to the re-organization of the patient pathways in the ED: before the study, our ED was organized in three different working lines, differentiating patients having surgical issues (one dedicated medical doctor, MD), medical issues (two dedicated MDs) and patients with low severity codes (green and white – one dedicated MDs). After this study, a four pathways system has been introduced in the daily clinical practise of the ED, as follows: two pathways for newly admitted patients with high priority code (3 - 2 Yellow and 2 Green), one pathway for patients admitted to the ED during the previous clinical shift (each shift lasting 6.30 or 12 hrs) and for patients requiring immediate assessment (4 red), and finally one pathway for patients with low priority codes (1 Green and 1 White). This last pathway runs only during daytime (8 a.m. - 8 p.m.).

### Conclusions

Overall, the new triage system resulted in a significant reduction of the WT for patients with high priority codes and just a moderate WT increase for low priority codes.

This study found that the implementation of a procedural reorganization of the ED may result in a more efficient health service, even if further investigations are needed to define better the potential impact of this novel system on patient care.

## Utility Of A Multimarkers Approach In The Diagnosis And Prognostic Stratification Of Patients With Chest Pain In Emergency Department

Valerio Pittoni M.D., Emiliano Salvatori M.D., Gabriele Tavani M.D., Salvatore Di Somma M.D.

Department of Emergency Medicine, S. Andrea Hospital, La Sapienza University, Rome-Italy

### Introduction

The evaluation of patients with acute chest pain in Emergency Department (ED) is often a diagnostic challenge to physicians. Undetected acute coronary syndrome (ACS) remains a serious public health issue and represents a major cause of malpractice in the emergency setting. A common work up in these patients' evaluation includes clinical history, physical examination, ECG, laboratory tests. Most widely accepted are the WHO criteria for ACS diagnosis which comprises ECG evidence, symptoms of chest discomfort, biochemical evidence (myocardial necrosis/

ischemia markers). The measurement of troponins have helped to shorten and improve the diagnostic workup. Strategies combining troponin measurement with already known such as myoglobine or CKMB or newly discovered markers remains to be elucidated.

The aim of the study is to evaluate the use of a point-of-care measurement of a combined panel of four markers: troponin I, CKMB, Myoglobine, BNP (Triage Point of Care Triage POCT Bio-site, San Diego USA), in patients admitted to ED for chest pain.

**Patients & Methods**

523 patients referring to ED for chest pain have been enrolled (in our ED and in "Vittorio Emanuele Hospital" of Catania (Italy), "Hospital de la Santa Creu i Sant Pau" of Barcellona (Spain), and "Emergency Department University Hospital" of Jena (Germany), from April 2008 to November 2009), 323 Men, 179 Women, mean age 64 ( $\pm 14$ ) yrs. 18 patients have been excluded, 6 due to enrollment exclusion criteria and 12 because diagnosis was missing. We performed at arrival in ED anamnestic data, TIMI risk score, physical examination, ECG 12 leads, chest X-ray and blood tests analyzed by POC system at the admission (T0) and after two hours (T1) for BNP, TnI, CK-MB and Myoglobin.

**Results**

First draw BNP for prediction UA showed the most significative

AUC ( $0.613 \pm 0.074$ ): BNP 20 pg/ml cut-off has best odds ratio (3.64, p-value  $< 0.0001$ ). The sensitivity and specificity for diagnosis of UA improves when we combine BNP (0 hr) + TIMI + TnI (2 hr).

The same model showed the most significative AUC ( $0.751 \pm 0.094$ ) in the prognostic stratification for major cardiac events at 30 days.

**Conclusions**

Our data show that baseline sample of BNP seems to be a better predictor of UA than CK-MB, TnI and Myoglobin. (the cut-off 20 pg/ml is superior than 80pg/ml and 200 pg/ml) and of major cardiac events at 30 days from discharged. Moreover the diagnostic value of BNP improve in association with TnI and TIMI score.

## Serum procalcitonin and S.Viridans endocarditis: case report

Buccelletti F, Zileri dal Verme L., Marsiliani D, Carroccia A., Merra G., Gilardi E., Calcinaro S., Franceschi F, Gentiloni Silveri N.

Department of Emergency Medicine, Catholic University of the Sacred Heart, Rome – Italy

**Introduction**

Procalcitonin (PCT) is considered a biomarker sensitive and specific for bacterial infection [1]. It is particularly useful in the differential diagnosis of undifferentiated dyspnoea in the Emergency Department (ED) and it has been proposed as guide in severe sepsis/septic shock treatment and prognosis [2;3]. Although its high sensitivity and specificity, in literature certain classes of pathogens do not elevate PCT.

**Clinical case**

A 67 year old male, affected by coronary artery disease, hypertension, paroxysmal atrial fibrillation and previous cholecystectomy presented to the ED complaining of one-month fever and sweating. During his out-of-hospital work-up a cardiac ultrasound was performed showing a medium aortic valve insufficiency and no vegetations.

Patient was admitted to the hospital for immunological and rheumatic workup together with serology for viruses. PCT was measured 3 times all times along with blood cultures. PCT was negative in all determinations while Streptococcus Viridans was isolated in the blood..

After this last data a new echocardiogram was performed, which showed a lesion of anterior aortic cusped; lesion confirmed by a transesophageal echocardiogram.

**Discussion**

PCT is a relatively new marker and for this reason we do not know all its characteristics. In fact in a brief report of Cuculi et

all: "Serum Procalcitonin has the potential to identify S.Aureus endocarditis" [4] PCT is not able to identify an infection from Streptococcus Viridans but at the same time it has optimal results with Staphylococcus Aureus. Our case confirmed previous observations in a endocarditis. This issue needs to be considered when PCT is ordered and results interpreted. The reason why Str. Viridans do not alter PCT is unknown.

**Conclusions**

Normal levels of PCT are not a sufficient data to rule out the patient from the diagnosis of a bacterial infection in the setting of Streptococcus Viridans infection.

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## Analisi Epidemiologica Degli Accessi Per Dolore Addominale Acuto Non Traumatico In Abruzzo: Valutazione Della Conformita' Della Diagnosi Tra P.S. E Reparto

E., Varrato<sup>1</sup>, G. Cretara<sup>1</sup>, A. Melone<sup>2</sup>, S. Sofia<sup>3</sup>, R. Di Filippo C. Balsano\*

<sup>1</sup>U.O. di Medicina Interna, P.O. "G.Mazzini" di Teramo;

<sup>2</sup>U.O.C. di Medicina e Chirurgia D'urgenza e Accettazione, P.O. "S.S. Filippo e Nicola" di Avezzano;

<sup>3</sup>U.O. di Medicina Interna, P.O. U.O. di "Santissima Maria dello Splendore" di Giulianova, Medicina Interna, P.O. "S. Salvatore" dell'Aquila;

\*Dipartimento di Medicina Interna e Sanità Pubblica, Università degli studi dell'Aquila

Negli Stati Uniti ogni anno accedono ai Dipartimenti di Emergenza/Urgenza 5 milioni di persone per dolore addominale acuto. La percentuale di ricovero varia dal 18% al 42%. È interessante notare come al momento dell'accesso in P.S. dal 5 al 10% dei pazienti presenti già le complicanze.

Leziopatogenesi del dolore addominale acuto rimane misconosciuta in oltre il 30% dei casi; infatti, la causa più comune è rappresentata dal "dolore addominale non specifico" (dal 24 al 44,3%), seguita dall'appendicite acuta (15,9 - 28,1 %), dalla patologia biliare acuta (2,9 - 9,7 %) ed, infine, dall'ostruzione intestinale e dalla diverticolite.

In Italia, ed in particolare nella regione Abruzzo, non esistono dati statistici relativi agli accessi in P.S. e ai ricoveri per dolore addominale acuto non traumatico.

Il nostro gruppo intende condurre uno studio osservazionale sui pazienti con addome acuto, che accedono ai Dipartimenti di Medicina di Emergenza/Urgenza sottoriportati, in modo da determinare l'epidemiologia relativa alla Regione Abruzzo e stilare le raccomandazioni per l'istituzione di percorsi diagnostico-terapeutici-assistenziali e di profili integrati di cura nelle Aziende Sanitarie della Regione Abruzzo.

Inoltre, visto che il quadro clinico del dolore addominale richiede una grande esperienza e capacità di giudizio nell'interpretazione dei segni, il secondo obiettivo sarà quello di verificare se l'utilizzo dell'ecografia in emergenza da parte del clinico possa migliorare l'accuratezza diagnostica della prima valutazione in Pronto Soccorso rispetto alla diagnosi di dimissione dal reparto.

Lo studio verrà effettuato nei Presidi Ospedalieri sotto elencati: Unità Operativa di Emergenza-Urgenza del P.O. di Teramo Unità Operativa di Emergenza-Urgenza del P.O. di Avezzano Unità Operativa di Emergenza-Urgenza del P.O. dell'Aquila Tra gennaio 2011 e gennaio 2012 si valuterà il numero di accessi totale per dolore addominale acuto, si stratificherà il campione di popolazione in relazione alla casistica etiologica osservata ed in rapporto all'età dei pazienti. Verrà, quindi, valutata la conformità della diagnosi effettuata in P.S. rispetto a quella formulata in reparto di degenza.

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## Prognostic value and therapeutic implications of Hyperdensity Middle Cerebral Artery Sign (HMCAS) in hyperacute ischemic stroke

F. Biraschi, F. Di Lisi, A. Romano, A. Bozzao, L. Fantozzi, M. Rasura

Dipartimento Neuroscienze/Stroke Unit – Neuroradiologia Ospedale Sant'Andrea/Sapienza II facoltà di Medicina – Roma

### Objectives

Aim of our study is to evaluate patients with evidence of HMCAS at CT multi-detector performed within the 6 hours from stroke onset by analyzing neuroimaging and clinical features in order to assess the prognostic value of HMCAS, site of HMCAS and possible therapeutic implications.

### Methods

We retrospectively reviewed the records of 41 patients admitted to our Emergency Room with the diagnosis ischemic stroke in the vascular territory of the MCA within 6 hours after the symptoms onset. We evaluated CT scan, determined the site of the hyperdense middle cerebral artery sign (HMCAS), performed the Alberta Stroke

Program Early CT Score (ASPECTS) on MRI at 24 hours to the onset. Baseline clinical characteristics were analyzed with the NIHSS at the admission, risk factors, stroke aetiology and therapeutic measures. Clinical outcome was evaluated with 3 months modified Rankin Scale (mRS). According to the site of HMCAS we identified three groups: proximal (M1), middle (M2), distal (M3). For each group we correlated the average ASPECTS with NIHSS at the admission and 3 months mRS. Further analysis was performed for the subgroup of patients who underwent to intravenous thrombolysis.

### Results

We identified 15 (36.6%) patients with M1 hyperdensity, 14 (34.1%) patients with M2 hyperdensity and 12 (29.3%) patients

with M3 ("dot sign") hyperdensity. Baseline characteristics do not show significant differences among the 3 groups. Mean NIHSS at the admission among the three groups was 15.2 in M1, 10.4 in M2 and 6.8 M3 group (p 0.001). The ASPECTS average in the three groups was M1 4.8, M2 6.5, M3 7.0 (p 0.006). In logistic regression analysis the HMCAS is independently associated with an unfavorable outcome (modified Rankin Scale mRS > 2) at 3 months. However average mRS shown significant differences among the groups (p 0.02). Ten patients (24,4%) were treated with intravenous thrombolysis and no significant differences were found in clinical outcome. Five of these patients, 50%, therefore, belong to the M1, and even within this subset there are differences in prognosis.

#### Conclusion

HMCAS is the most easily accessible predictor of MCA occlusion (1). Hyperdensity sign is related with high stroke severity

and the 3 months unfavourable outcome. In accordance to site of hyperdensity, proximal tract (M1) is related to the worst prognosis even in patients who received rt-PA treatment. We, therefore, suggest that patients with M1 tract hyperdensity can be early addressed to alternative procedures such as endovascular treatment or intra-arterial thrombolysis.

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## The Use Of A New Automatic Device For Patients' Assessment At Triage In Emergency Department

Gori Chiara Serena, De Berardinis Benedetta, Salvatori Emiliano, De Nuzzo Daniele, Tranne Caterina, Ferri Enrico, Di Somma Salvatore

Second Medical School, "Sapienza" University, Sant'Andrea Hospital Emergency Department, Rome, Italy

#### Objectives.

To assess time saving in an Emergency Department arising out of the introduction of automatic devices (Carescape™ V100) to measure vital signs compared to the manual devices.

#### Methods

We performed a prospective, observational study of eligible patients referring to Sant'Andrea Hospital Emergency Department during the entire month of October 2009, randomly assigned into two groups. In the first group of 476 patients vital signs measurements were detected with manual devices, while in the second group of 477 patients with automatic device Carescape™ V100.

#### Results

Data indicated that the comparison of the total time between the two groups gave a significant difference (1993 vs 1518 min, p<0,001). No differences were found with respect to age, sex and priority codes. Significant differences were also found when comparing the subgroups of the same acuity categories: white codes 4,33 vs 2,27 (min), p<0,05; green codes 4,28 vs 3,37 (min), p<0,001, yellow codes 3,92 vs 2,72 (min), p<0,001.

#### Conclusions

Our data demonstrated a statistical significance between the two groups with a difference of 475 minutes spent in Triage procedures including vital signs measurements. In conclusion time saved by vital signs automatic device could allow ED physicians to make a qualified approach with an earlier diagnosis and a more rapid and effective therapy, possibly improving patients' outcomes.

## Utilità dell'ABCD<sup>2</sup> score nel processo decisionale del TIA in Pronto Soccorso

Efrem Iascone, Augusto Tricerri, Stefania Cerrai, Luigi Zulli

UOC Medicina d'Urgenza e Pronto Soccorso ACO San Filippo Neri, Roma

#### Introduzione

I pazienti affetti da Attacco Ischemico Transitorio (TIA) costituiscono un gruppo eterogeneo in termini di fattori di rischio, sintomatologia, comorbidità, prognosi.

L'importanza di riconoscere questa frequente condizione è legata all'alto rischio di stroke ischemico precoce correlato al TIA (8% a 30 giorni).

Studi recenti suggeriscono l'utilità dell'ABCD<sup>2</sup> score nella stima del rischio di stroke dopo un TIA. Questo score si basa esclusivamente su parametri clinici di semplice rilevazione (tabella 1), particolarmente attuabile in quelle circostanze in cui non sia possibile un immediato supporto diagnostico strumentale.

Lo scopo del nostro studio è stato quello di calcolare l'ABCD<sup>2</sup> score in una popolazione di pazienti affetta al nostro DEA per TIA.

#### Metodi

Sono stati presi in considerazione tutti i pazienti consecutivamente visitati nel periodo gennaio-agosto 2008 presso il DEA del San Filippo Neri per sospetto TIA e successivamente ricoverati per osservazione ed approfondimento diagnostico.

#### Risultati

In 12 pazienti, 8 uomini e 4 donne, la diagnosi di TIA è stata confermata al termine dell'iter diagnostico-osservazionale (tabella 2).

Tabella 2 - Risultati preliminari

	DONNE					UOMINI							
	M.S.	FB.	E.N.	E.F.	L.R.	N.M.	A.S.	A.B.	M.V.	R.I.	G.S.	E.G.	FB.
TC senza m.d.c.		*	*	*	*	*	*	*	*	*	*	*	*
ECG	*	*	*	*	*	*	*	*	*	*	*	*	*
Ecodoppler TSA	*	*		*	*	*	*	*	*	*	*	*	*
RM encefalo + DVW	*	*			*	*		*		*			
Ecocardiogramma			*	*			*						*
EEG				*		*				*	*	*	
ABCD <sub>2</sub>	3	7	5	5	4	2	4	5	5	6	4	5	3

Periodo di riferimento gennaio-agosto 2008

### Conclusioni

Le principali linee guida internazionali raccomandano l'ospedalizzazione dei soli pazienti affetti da TIA con un ABCD<sub>2</sub> score almeno di 3 (American Heart Association) o di 4 (National In-

stitute of Clinical Excellence, UK) e seguire ambulatorialmente quelli con punteggio inferiore.

La nostra casistica, nonostante il crescente ricorso ad atteggiamenti clinici di tipo difensivo, si conferma essenzialmente in linea con le attuali strategie internazionali di sfruttamento delle risorse sanitarie.

## Verifying Emergency Room Dyspnea: the VERDI study

V. Russo, B. De Berardinis, F. Travaglino, E. Salvatori, CS. Gori, C. Bongiovanni, V. Mura, O. Piras, S. Di Somma

Emergency department Azienda Ospedaliera Sant'Andrea, II School of Medicine "La Sapienza" University, Rome, Italy

### Introduction

Recent literature demonstrated the diagnostic and prognostic role of several biomarkers in critically ill patients referring to Emergency Department (ED). Patients with acute dyspnea may have more than one underlying aetiology but ED physician must identify acute and serious life threatening causes.

Recent studies identified biomarkers which increase in patients with shortness of breath. Procalcitonin (PCT) and Mid Regional pro-Adrenomedullin (MR pro-ADM) plasma concentration can increase in several diseases such as bacterial infections, Acute Myocardial Infarction (AMI), unstable angina, Community Acquired Pneumonia (CAP), Chronic Obstructive Pulmonary Disease (COPD), Acute Respiratory Distress Syndrome (ARDS), pulmonary hypertension and Systemic Inflammatory Response Syndrome (SIRS). Mid Regional pro-Atrial Natriuretic Peptide (MR pro-ANP) is equivalent to BNP (Brain Natriuretic Peptide) or NT pro BNP (N terminal pro Brain Natriuretic Peptide) in the diagnosis of Acute Heart failure (AHF) in patients with dyspnea. The use of a multi-biomarkers panel could be the optimal strategy to promptly diagnose and treat patients with acute dyspnea.

### Study design

The study is no profit, competitive, observational, prospective, multicentric, directed to value diagnostic and prognostic care of a biomarker's panel. The enrolment was carried out between June 2009 and June 2010. This study use biomarkers panel (PCT, MR pro-ANP, MR pro-ADM) to permit accurate and rapid diagnosis of acute heart failure, pneumonia or sepsis and stratify patient's risk.

Primary endpoints of the study are:

PCT to value bacterial infections of respiratory tract (differential diagnosis)

MR pro-ANP to value acute heart failure (differential diagnosis)

Correlation between MR pro-ADM levels and rehospitalisation at 90 days (prognostic value).

### Materials and methods

We studied 50 patients admitted to the Emergency Department with acute dyspnea. All patients were hospitalized. Exclusion criteria: psychogenic dyspnea, post-traumatic dyspnea, cardiogenic dyspnea, pulmonary embolism, pneumothorax, coronary acute syndrome, major surgery, burns, haemodialysis treatment, vital prognosis <24 hours, patients transferred, age <18 years. The withdrawal was effectuated three times for measurement of plasma PCT, MR pro-ANP, MR pro-ADM. The first blood sample was obtained on admission to Emergency Department, the second blood sample was obtained after 24 hours; the third blood sample was obtained after 72 hours. If hospitalization exceeded 72 hours fourth blood sample was obtained at the discharge. A Case Report Form was filled up with clinical history, vital signs at the time of each blood sample. Patients were contacted by phone to evaluate outcomes 30 and 90 days after discharge.

Conclusions. The study confirmed the PCT value to diagnosis of bacterial infections, the MR pro-ANP value to diagnosis of acute heart failure. VERDI study demonstrated that patients with higher levels of MR pro-ADM underwent to rehospitalisation at 90 days.