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ABSTRACT BOOK

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SPEAKERS

The perspective of the Academy of Emergency Medicine and Care (AcEMC)

Ivo Casagranda (Alessandria, Italy)

To manage the troubles that presently afflict both hospital and outpatients emergency departments (ED) it is necessary to look at the National Health Service (NSH) as a system whose components need to better coordinate and integrate their actions.
ED overcrowding is mainly a consequence of the increasing number of clinical emergencies (due to elderly patient's diseases relapses) and also because of hospital wards occupied by patients that are hard to be discharged because of the lack of residential facilities. On the other hand there was a reduction of in-hospital beds. Since 2000 to 2009 there was a cut of 45,000 beds in our NHS, and there has been a shift from 5,1 to 4,2 ‰ inhabitants and now we are reaching 3 ‰
ED difficulties are not entirely due to their inadequacy but mainly because of the inadequacy of other components of the health care system that, if performing their role, would decrease the ED visits and length of stay.
To reduce ED visits it is not necessary to organize alternative emergency units outside the hospital. What is needed is a different primary care activity, adopting an active chronic care model able to prevent and decrease the need of turning to emergency care.

To shorten the ED length of stay are not needed larger departments but larger numbers of beds in nursing homes and better home care in order to allow a rapid hospital discharge and a quick turn- over of hospital beds.
To avoid ED overcrowding it is also necessary to find solution to the various forms of social emergencies that presently arise from the shortage of dedicated facilities (refectories, dormitories, homeless drop-in, etc)
Emergency medicine does not claim more resources for itself (a part from those immediately needed to overcame its actual critical state) but asks the whole health care system to investigate reasons for overcrowding in order to identify and implement more general solutions.

The practice of emergency medicine is changing (from a “passage” to a “landing space”) and consequently it is changing its position and its role in the health care system.

Its main purpose is not only to stabilize and admit patients to the hospital but it is to rapidly establish a diagnosis and start treatments that will be simply confirmed and monitored during the hospital stay.
The practice of the emergency medicine, based on dedicated professionals, has transformed the ED in an effective diagnostic place. Large part of the ED patients now reaches the hospital wards having a defined diagnosis and an ongoing treatment.

To realize this change will imply important changes also on the ground of the role and of the purposes played by ED within hospital organization and this will have relevant resource implications. The use of specialists time and diagnostic technologies by ED is far increased and new ways of financing the ED activities must be experimented (pay per episode or pay per pathway ?Attention is required not only on the role of ED in dealing with clinical urgency but also on its function in deciding hospital admissions: not just a “gate keeper” role regulating hospital admissions but the true beginning of any hospital stay. To achieve this aim ED should not be left alone, the whole hospital should be committed in achieving ED goals.

Data from one of the most overcrowded Emergency Department in Rome.

Francesco Pugliese (Rome, Italy)

Emergency Department (ED) crowding, a consequence of simultaneous increasing demand for health care and a deficit in available hospital beds and ED beds, has become an increasingly significant public health problem. Sandro Pertini Hospital ED (Community hospital in Rome - 300 bed for 700.000 inhabitants) visits about 85.000 pateints/years with about 60 patient transported by EMS and less than 20% required hospital admissions. This obviously exceeding health demand causes ED overcrowding let us organize a progressive surge plan, initially based only on the number of patients present in ED and the numbers of boarding patients. In 2009 we started to use a validated score (NEDOCS) to measure overcrowding, improve ED answer and standardize surge plan. On 2009 we verified the possibility of use NEDOCS in our setting: in this first phase NEDOCS scores was calculated by ED nurses and physicians for 3 different periods with 5 samples a days (1 am, 7 am, 1 pm, 6 pm,11 pm) for a total of 478 samples. On 2010 and 2011 Pertini ED promoted a multicentre study to monitoring ED overcrowding in Rome, to whom 6 Roman EDs participated. All NEDOCS results were compared with corresponding discharged patients, LWBS, refusing admission to hospital patients (RAHP) and patients admitted or transferred to other hospitals. From April 2011 in our ED NEDOCS scores was calculated computer-based every2 hours, together with EMS ambulance flow.

With the NEDOCS as an objective basis for mobilizing the organization, surge plan development was undertaken in an offsite retreat setting A team worked together to create a comprehensive surge plan linked to the NEDOCS Our initiative undertaken to respond to ED overcrowding passed through the development of a comprehensive organizational surge plan that took place from 2009 to 2012. The surge plan was one aspect of a multifaceted process improvement initiative that also included redesign of patient flow processes internal and external to the ED and changes to physical facilities, including the opening of a short clinical decision unit and expanded triage bed capacity; anticipated admissions in short observation Unit.

Numerous operational strategies have been proposed to provide temporary remedies to address these changes; however, few have addressed the root causes of overcrowding in the ED or have proposed system-wide solutions to address the problem.. While first undertaken as a necessary intervention during frequent periods of high census, the stated goal was to avoid reliance on the surge plan as a routine response to ED overcrowding, favoring instead the implementation of sustainable improvements designed to minimize surge conditions changes can be chosen to less the overload in ED and when is necessary to get down to surge plan.

Mass Casualty Management in the Emergency Department Lessons Learned in Beirut

Antoine Kazzi (Beirut, Lebanon)

Mass Casualty Incident (MCI) management is a special challenge to any emergency medical service, all the way from the field to the Emergency Department (ED) and to the rest of the chain of medical care. In Lebanon, emergency departments and ED providers have repeatedly faced such challenge during its various armed conflicts and wars over the last 35 years. The ED at the American University of Beirut consistently played a central role in delivering emergency care to the victims of such strife. Understandably, its ED faced the largest numbers of mass casualty incidents and its ED staff acquired significant experience and instituted special measures in the field of mass casualty management.

This session provides attendees an opportunity to acquire or polish their mass casualty management skills, with a focus on incident identification, hospital and ED leadership and staff mobilization and activation, ED staff and physical space assignment and designation, "MCI ED Triage Categories", staff mobilization and distribution, surge capacity enhancement, security issues and auto-delegation, medical records, caretakers, patient families, and crowd management, media relations, and interactions with hospital leadership, departments and staff.

Is there an overcrowding problem in the Emergency Departments in China?

Wei Jie (Beijing, China)

Emergency department overcrowding has become a global issue. It spreads quickly from the developed country to the developing country. Emergency department overcrowding results in many adverse effects. Medical therapies are delayed to use, medical error rates increase, and the death risk goes up. One of most important things is that the patient's interests are damaged. In the view of the overall hospital interest, our colleagues always do our best by our own to resolve emergency department overcrowding problem by a variety of ways. But what is the best way to really protect both our patients and our emergency system?

It is of great urgency to address this problem. Needless to say, we are saving lives every day, but do not forget that our emergency system itself get ill sometimes. We should set out to study the cause, assessment, analysis, and potential impact of emergency department overcrowding disease. Not only emergency system but also whole of public health care system need think about it, talk about it, and work together with it. All of them will contribute to find the best strategy to alleviate the daily crisis.

Acute Medicine in UK - past, present and future

Chris Roseveare (London, United Kingdom)

Acute Medicine has developed rapidly in the UK over the past decade; over 450 consultants have now been appointed to this emerging speciality, and there are 225 acute medical units (AMUs) across the UK providing multi-professional care for adult medical patients admitted to hospital in an emergency. Acute Internal Medicine is now recognised in the UK as a speciality in its own right, distinct from General Internal Medicine with a specific 4 year training curriculum. More than 300 trainees are currently undertaking this programme which is designed to deliver the competencies necessary to manage acutely unwell patients and to lead the AMU team. There is increasing evidence to support the benefits of consultant-led care provided by a trained acute physician. However, delivering this on a consistent basis, 7 days per week across all UK hospitals remains a significant challenge. The Society for Acute Medicine and Royal College of Physicians have produced guidelines which require that a consultant presence is maintained on the Acute Medical Unit for a minimum of 12 hours per day, 7 days per week. With current manpower levels this will be difficult to achieve, requiring continued involvement of general physicians for the foreseeable future. The Society for Acute Medicine (SAM) has recently published quality indicators and standards for AMUs, which will provide benchmarking data and a framework for accreditation of acute services in the future.

UK admission regulations from ED

Louella Vaughan (London, United Kingdom)

Aim:

To investigate the variability in the diagnosis and management of pulmonary embolism (PE) in the UK.

Background:

Variability of care is an increasingly pressing international issue, with studies showing that failure to adhere to results in poor patient outcomes and increased economic costs. The lack of recent UK national guidelines and the complexity of the literature surrounding all aspects of the care of PE, as well as rising rates of admission for PE, led the Society of Acute Medicine (SAM) to conduct an audit-style survey of UK hospitals.

Methods:

An on-line questionnaire was designed by members of the SAM Research Group, using the Survey Monkey platform, with the British Thoracic Guidelines for PE serving as the standard for best practice. Email invitations were sent to all SAM members. Hospitals without SAM members were approached to nominate a physician to complete the survey. Where more than one duplicate response was received, they were compared and clarification sought to reach a single agreed response. Data was then analysed (ongoing) using appropriate methods.

Initial Results:

SAM received 195 responses, of which 66 duplicates were further clarified and 2 partial responses were excluded from analysis. 127 validated responses were analysed, representing 53% of the 240 acute hospitals in the UK. There was a high degree of variability relating to all aspects of care. Of note, ~30% of hospitals do not have policies for either the diagnosis or management of PE; ~40% do not formally assess the clinical probability of PE prior to further investigation; 80% do not proceed to diagnostic imaging within 24 hours on the weekends and over 40% do not follow best practice guidelines for anticoagulation in proven PE. This data is still undergoing analysis and further results will be presented at the meeting.

Discussion:

The diagnosis and management of PE is highly variable across the UK, with only a small fraction adhering closely to national guidelines. Respondents cited barriers to care as including access to appropriate diagnostics and cost. The failure of the majority of hospitals to comply with best practice may have significant implications for patient morbidity and mortality.

Impact of the Introduction of Acute Medicine and Planning Units on Patient Flow in Australian Hospitals

Alasdair MacDonald (Launceston, Australia)

The birth of Acute Medicine Units in Australia and New Zealand dates back as long as in the UK, but without the introduction of the 4-hour rule their uptake was less rapid. They were initially called Medical Assessment and Planning Units (MAPU's) and gold standard of units was the Auckland Hospital APU opened in 2003. The remainder of the units across Australia and New Zealand have evolved over subsequent years. They were either modelled on aspects of the Auckland and other home grow models or more recently they have adopted aspects of or imported en-block NHS models, frequently accompanied by NHS executives emigrating to Australia. In this presentation I will briefly outline the diversity of Australian Models and then review data with respect both my own Hospital's Acute Medicine Unit and more broadly based Australasian Data. This data will particularly highlight the issues around length of stay, access block and unplanned readmissions. Australian Acute Physicians have had some fundamental differences from their UK counterparts and from a hospital perspective have had more in common with Hospitalist (Internist) model in the US. However, the scope of the Australian and New Zealand General and Acute Care Physician goes beyond the doors of the hospital into ambulatory care particularly focusing on the chronic co-morbid patient in the community. This focus particularly assists in early discharge and the pro-active use of Hospital Avoidance Strategies. The presentation in this way will seek to compare and contrast the various aspects of care in the Australian and New Zealand with particularly the UK acute medicine systems and practices.

Study Design and Evaluation model for Emergency Medicine

Enrico Di Stasio (Rome, Italy)

Research in Emergency Departments requires sound design and thoughtful consideration of potential biases that may influence the validity of results. It also requires careful implementation of protocols and procedures that are likely to translate from the research environment to actual clinical practice. This work is mainly directed to young researchers in order to focus principal problems related to the development of a study protocol in ED field. Methodologic features of study design, participant selection and retention, measurements and statistical analyses will be describe as well as a number of recommendations related to research methods specific for Emergency Departments.

How to manage statistical data in Emergency Medicine Research

Paul Clopton (San Diego, USA)

Research in emergency medicine is often conducted based on the assumptions of experience of active clinicians, but maximizing the productivity of the research effort requires disciplined attention to statistical design issues and the more mechanical aspects of data collection and analysis.

Once the physician identifies a critical research question, it must be translated into a testable hypothesis. Here, *testable* means not only a statement worded as a null hypothesis to be rejected, but also that the definitions of the variables are precise, the measurement tools are appropriate and valid, that the anticipated effect size is reasonable and clinically meaningful, and that such an effect can be detected with the available sample size, and that biases and confounding can be held to a minimum. Yet, successful research also depends upon execution – accurate recording of data within the prescribed time windows and diligent follow-up efforts, for example, are obvious requirements but when neglected can seriously degrade the quality of the research effort.

Beyond re-learning these lesions, emergency medicine research today needs to focus on designs that emphasize actual physician decision-making and have the potential for directly influencing outcome. Risk-stratification, for example, is most useful only if it can be shown to guide treatment in a way that improves outcomes. Research designs and statistical hypothesis testing that focuses on this goal should be emphasized going forward. Interactions with treatment effects are an example that should be explored whenever possible. Guided treatment is another. These are more challenging research designs that demand even greater care and investigator effort, but will yield more meaningful findings.

The approach to acute gastroenteritis in ED

Assumpta Ricart (Barcelona, Spain)

The approach to acute gastroenteritis in Emergency room should be focused on taking a detailed history of the patient to determine possible etiology; accurately assessment of the level of dehydration and risk of complications, start hydration, and give advice on diet and preventing measures to avoid the spread of infection. In some cases laboratory tests and notification to public health authorities will be necessary.

Even the first approach looks quite simple, and it is widely describe in guidelines, it is of paramount importance to determine which patients can be at risk of complications. On the other side, there are still some controversial aspects that make decisions at emergency room difficult. When should I send a stool sample for analysis?, Can biomarkers help me to make decisions?, when should I prescribe antibiotics? Are antimotility and enti-emetic drugs indicated?

Antibiotics are not recommended for adults with acute diarrhea of unknown pathology. Antibiotics may be appropriate when gastroenteritis is due to a known microbiological cause. Limited evidence shows that they have minimal benefits, there is a risk of serious adverse effects. Antibiotics may prolong the duration of shedding of salmonella, may increase the risk of life-threatening complications of Shiga toxin–producing E. Coli infection and the risk of harmful eradication of normal flora.

The diagnostic yield of **stool cultures** is relatively low, estimated to range from 1.5% to 5.6%. Fecal leukocytes are seldom usefull to make decision at the ED. Only id one o more of the next criteria is present, the yield of stool should be considered : patient is systemically unwell, there is blood or pus in the stool, diarrhea occurs after foreign travel to determined areas, diarrhea is persistent, patient has recently received antibiotics or been in hospital or is immunocompromised.

Biomarkers such as C-reactive protein can discriminate the inflammatory response to infection from other types of inflammation, and procalcitonin plama concentrations appears closely related to the severity and evolution of infection. With this evidence biomarkers can help us to assess patient severity and evaluate antibiotic treatment. Other clinical and epidemiological information must be taken into account and cost effectiveness must be evaluated carefully.

Antimotility agents when used with antibiotics for traveler's diarrhea or bacillary dysentery, it may reduce the duration of diarrhea by as much as one day. Because antimotility agents have been implicated in prolonged fever in human volunteers with shigellosis, toxic megacolon in patients with C. Difficile infection, and the hemolytic–uremic syndrome in children infected with Shiga toxin–producing E. coli, these agents should be avoided in patients with bloody diarrhea or suspected inflammatory diarrhea.

Even **antiemetics** can help to control the vomiting as an unpleasant symptom and vomiting by itself can bring additional complications, they shouldn't be prescribed invariably because vomiting is self-limiting, is a normal physiological reaction for ridding the body of toxic substances, and antiemetics can have adverse side effects.

Even the vast majority of cases of gastroenteritis admitted to the ED will have a good course with hydration and diet, it is essential a detailed clinical and epidemiological evaluation to find patients at risk, and be fair with the use of the diagnostic and therapeutically arsenal available.

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Ultrasound point of care echography in fast decision for patients with abdominal pain in Emergency Room

Angelo Ianni (Rome, Italy)

Abdominal pain comprises 5 to 10 percent of emergency department (ED) visits[1-3]. It represents a diagnostic challeng for emergency clinicians. Approximately 80 percent of patients discharged with undifferentiated abdominal pain improve or become pain-free within two weeks of presentation[4]. In many cases, the differential diagnosis is wide, ranging from benign to life-threatening conditions. Principal causes of abdominal pain may include medical, surgical, intraabdominal and extraabdominal ailments. Associated symptoms often lack specificity and atypical presentations of common diseases are frequent, further complicating matters. Some studies suggest that older patients with abdominal pain have increased mortality when their diagnosis is not determined in the ED[5]. Emergency ultrasound is synonymous with terms such as bedside, point-of-care, focused because it is complimentary to the physical examination but should be considered a separate entity that adds anatomic, functional, and physiologic information to care patient in ED setting. It can be applied to any emergency medical condition in any setting with the limitations of time, patient condition, operator ability and technology limitations[6]. Technological advances have led to the development of handheld, battery-powered, low weight machines like Vscan. This miniaturization of the technology has created the possibility of bringing US to the emergency department, thus gaining a potential for early diagnosis and treatment. We decided to evaluate the possible use of Vscan device in many clinical acute conditions with the aim to generate a new protocol for the management of both medical and trauma patients in ED, and we created a new acronym "USEFUL" (Ultrasound Speed Evaluation For Urgencies Level). Our aim was to demonstrate the usefulness of Vscan in an acute setting scenario such as the ED in order to evaluate the main causes of some symptoms (cardiac arrest, hypotension/syncope, chest pain, abdominal pain, polytrauma, dyspnea) and to validate the usefulness of it at different levels of urgency/emergency. An emergency ultrasound was performed for every patient complaining for abdominal pain, evaluating the presence or not of 5 important signs/pathologies: cholecystitis, hydronephrosis, abdominal aorta enlarged, peritoneal fluid, acute urinary retention. A traditional echography was later performed. We enrolled 110 patients with abdominal pain. The most frequent cause of abdominal pain was renal lithiasis or hydronephrosis (30%), followed by gallstones or cholecystitis (13%) and aortic aneurysm (1%). In 56% of patients examinated no signs were found, with a 100% correlation with traditional echography! Furthermore the mean time to perform both emergency and traditional ultrasound was calculated; it resulted in order of 4.72±1.10 minutes for the former versus 43.14±30.68 minutes for the latter.

Conclusions. Vscan POCT in ED seems to be very useful for management of patients afferred for abdominal pain. It can be performed at any time, in any place, on any patient and condition: it can be considered as an "ultrasound stethoscope". Its use can improve patient outcomes, enhance patient safety, facilitate patient management in abdominal pain and therapy optimization. Within the practice of emergency medicine, the use of point of care sonography by emergency physicians in the emergency department is an effective aid in the management of patients presenting with any one of a variety of medical and traumatic conditions.

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Use of BNP for evaluating risk in perioperative abdominal surgery patients

Paolo Mercantini (Rome, Italy)

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BACKGROUND:

Cardiovascular disease is the leading cause of perioperative death in surgical patients. A variety of clinical scoring systems have been developed to predict adverse cardiovascular events. B-type natriuretic peptide (BNP) is a sensitive and specific predictor of left ventricular systolic dysfunction and predicts first cardiovascular event and death in the general population. We present a prospective, single-center, observational cohort study of patients undergoing major abdominal surgery and evaluate the role of BNP in predicting adverse cardiac events.

METHOD:

A total of 205 patients were included in the study. All patients were assessed by a cardiological clinical evaluation, a 12-lead ECG report, and a preoperative and postoperative blood sample for plasmatic BNP assessment. The primary end point was the predictive power of preoperative BNP levels for adverse cardiac events until 30 days after discharge.

RESULTS:

Thirty-one of 205 (15%) patients had adverse cardiac events in the postoperative period up to 30 days after discharge. Five patients (2.4%) of these died of cardiac events. Preoperative BNP values were significantly increased in the 31 patients compared to the other patients in the postoperative period [mean = 112.93 pg/ml (range = 5-2,080) vs. 178.99 pg/ml (range = 5-3,980); median = 117 vs. 23 pg/ml; 95% CI = 49-181; $p < 0.0001$]. At logistic regression, a preoperative BNP value of >36 pg/ml was the only effective predictor of adverse cardiac events.

CONCLUSION:

We have demonstrated that elevated preoperative BNP levels are independent predictors of adverse cardiac events in a cohort of patients undergoing major abdominal surgery in a general surgery department, and this is the first study about this specific cohort of patients.

Hemodynamic profiling of acute CHF patients in the ED: What does it add to patient care?

Richard Nowak (Detroit, USA)

Emergency physicians currently utilize the vital signs and clinical examination of patients to estimate their underlying hemodynamic profiles. These clinically derived approximations are then used to help determine both the diagnostic and therapeutic plans for each individual. However many studies over the last 3 decades have shown that clinicians (intensivists, cardiologists, surgeons and emergency physicians) are very inaccurate when their estimates of the underlying hemodynamic profiles of acutely ill patients are compared to those obtained by either invasive or non invasive technologies.

The NEXFIN (Bmeye, Amsterdam) unit has been developed over the last 3 decades and used on the space stations to noninvasively monitor the hemodynamics of astronauts in orbit. This non invasive technology and its use in the assessment of the underlying hemodynamics of acute CHF patients in the ED will be explored. Specifically the initial results of the international PREMIUM Registry will be presented. The NEXFIN device was used to continuously monitor the hemodynamic profiles of acute CHF patients on presentation to the ED, prior to any therapy, and over the ensuing 2 to 4 hours of management. The differences in these presenting hemodynamic profiles give Emergency Physicians objective measurements that can direct a specific therapy to an individual CHF patient based on these parameters**.**

Acute Heart Failure in Brazil: Opportunities for GREAT Studies

Humberto Villacorta (Fluminense, Brazil)

A rise in the incidence of heart failure (HF) in Brazil has been observed. This has been attributed at least in part to the population ageing. To cope with this, the Brazilian Society of Cardiology founded the Heart Failure Department in 2001. In 2005 the I Latin American Guidelines for the management of heart failure was launched and was updated in 2009 and 2012. A Brazilian registry on acute heart failure, the BREATHE study, is underway and preliminary data shows high in-hospital mortality and high readmission rates. The most frequent etiology of heart failure in Brazil is ischemic heart disease (30%) but Chagas disease plays an important role, accounting for 12% of the cases. Chagasic HF patients have worse outcomes than non-chagasic. Biomarker studies have been carried out in Brazil but none has focused the acute cohort of chagasic HF patients.

A modern concept on how to clinical assess AHF patients in emergency departments

Anna Andronescu (Bucharest, Romania)

Acute Heart Failure (AHF) syndrome is one of the most frequent cardiac emergencies in the emergency department (ED). Its mortality remains high and it is the top of the list of reasons for admittance in the cardiology departments, usually in theirs intensive cardiac care unit. In the last years improving the outcome has been challenging and so far no acute therapy has proved benefits on mortality or re-hospitalizations. The current European guideline for management of heart failure underlines that the prognostic of the AHF patients is improved by a rapid and correct diagnostic carried out while the patient is being stabilized and the first measures of treatment are initiated. The possible life-threatening condition, the urgency to diagnose and simultaneously treat the AHF patient implies that those acts should be done in the ED as rapid as possible with the clinical evaluation having the most crucial role. The main objectives of the clinical assessment of the AHF patients in the ED are:

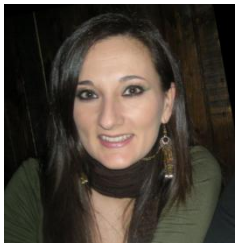
- to confirm the diagnostic;
- to establish the cause and/or the precipitating factors;
- to tailor the patient's treatment to its individual clinical profile;
- to monitor the response to therapy and to adjust it accordingly.

The clinical evaluation in the ED involves rapid but thorough anamnesis and physical examination combined with imagistic and lab work-up. It usually needs a multidisciplinary approach and collaboration.

Further research is needed to establish and validate prediction models of clinical assessment and also to find if a specialized acute heart failure unit may improve management and reduce morbi-mortality of the AHF patients.

Galectin-3: a potential novel mediator of cardiovascular dysfunction induced by aldosterone

Natalia Lopez-Andres (Nancy, France)



Background. Aldosterone (Aldo) is involved in arterial stiffness and heart failure (HF), but the mechanisms have remained unclear. Galectin-3 (Gal-3), a β-galactoside-binding lectin, plays an important role in fibrosis and HF. We here investigated whether Gal-3 is involved in Aldo-induced vascular fibrosis.

Methods and Results. Addition of Aldo in rat vascular smooth muscle cells (VSMCs) upregulated Gal-3 expression via MR. Moreover, Gal-3 over-expression specifically enhanced collagen type I synthesis. Gal-3 inhibitors or Gal-3 silencing (siRNA) blocked Aldo-induced collagen type I synthesis. Rats were treated with Aldo-salt combined with spironolactone or modified citrus pectin (MCP) for 3 weeks. Hypertensive Aldo-treated rats presented vascular hypertrophy, inflammation, fibrosis and increased aortic Gal-3 expression. Spironolactone or MCP treatment reversed all the above effects. Wild type (WT) and Gal-3 knock-out (KO) mice were treated with Aldo for 6 hours or 3 weeks. Aldo increased aortic Gal-3 and collagen type I expression in WT mice whereas no changes occurred in Gal-3 KO mice.

Conclusions. Our data indicate that Gal-3 is required for the fibrotic response to Aldo in VSMCs *in vitro* and *in vivo*, suggesting a key role for Gal-3 in vascular fibrosis.

Role of Galectin-3 in risk stratification of patients with metabolic syndrome

Philippe Rouet (Toulouse, France)

Galectin 3 (G3) is upregulated in cardiomyopathy and heart failure (HF), similarly elevated in T2D and obesity compared with normal-weight individuals and has a body mass index-dependent positive correlation with leptin, resistin, IL-6, and age. A wealth of evidence from animals and some from clinical studies has suggested that G3 is a mediator of fibrosis and remodeling. However despite accumulation of data about G3, plasma quantification of G3 as new biomarker for prognosis, diagnosis or risk stratification is not yet frequently performed. Several studies have revealed G3 level as new biomarker useful for risk stratification in patients with Acute Heart Failure Syndromes. Patients whose G3 levels went up by a factor of two during the follow up study had two times the absolute risk of short term adverse events. The risk increase was still strongly significant after adjustment for age, sex, natriuretic peptide levels, and kidney function. Patients with higher G3 plasma levels had a history of renal disease, a lower heart rate and acute kidney injury. When used complementary to B-type natriuretic peptide, G3 is associated with renal dysfunction and may predict 30-day events. For instance, G3 was evaluated in a substudy of the Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH) that comprised the inclusion of 1023 survivors of a heart-failure hospitalization. This analysis revealed that elevations in G3 pointed to an increased risk of death or HF hospitalization. Clearly the risk of death/HF hospitalization was increased >2.5 times ($p<0.0001$) for the trial's patients in the highest quartile for baseline levels of G3 compared with those in the lowest quartile, independently of age, sex, and natriuretic peptide levels. A growing number of clinical studies and mechanistic evidences based on basic research point out the relevance of G3 evaluation for risk stratification of patients with HF. Moreover, studies in the general population showed that G3 levels are raised by inflammation and the metabolic syndrome and strongly correlated with classical risk factors of cardiovascular diseases and could be used alone for risk stratification or in multi-marker strategies.

Kidney involvement in AHF patients

Paolo Menè (Rome, Italy)

Cardiorenal syndromes are a host of pathophysiological conditions in which acute or chronic dysfunction of the heart may induce dysfunction in the kidney, and *vice versa*. Parallel involvment of both organs emphasizes the tight relationship between these two key districts of the systemic circulation. Abrupt worsening of cardiac function (e.g., acute cardiogenic shock or acutely decompensated chronic heart failure) leads to acute kidney injury in the so-called cardiorenal Type I, Acute Cardiorenal Syndrome. Conversely, acute kidney ischaemia, tubular necrosis or glomerulonephritis / vasculitis may cause an acute cardiac disorder (such as heart failure, arrhythmias, ischemia) in Type III Acute Renocardiac Syndrome. Arterial hypertension is certainly a major player in this process. There is no doubt that simultaneous dysfunction or failure of both heart and kidneys greatly worsens the outcome and/or mortality in these patients. In Type V (Secondary Cardiorenal Syndrome) systemic diseases such as diabetes mellitus or sepsis may cause both cardiac and renal dysfunction, as a result of simultaneous tissue injury and/or ischemia.

Pathophysiologic mechanisms and the links between disorders of heart and kidneys will be reviewed, along with a discussion of early biochemical signals and possible therapeutic strategies

Utility of ultrafiltration in AHF patients

Nadia Aspromonte (Rome, Italy)

Acute heart failure (AHF) may be characterized by rapid worsening of heart failure symptoms and signs of congestion. Hemodynamic derangements are highly variable, ranging from acute pulmonary edema with hypertension to severe peripheral fluid overload to cardiogenic shock and hypotension. Depending on the presence and severity of fluid retention, the response to withdrawal of body fluid varied from neurohumoral activation and restriction of diuresis to neurohumoral depression and extreme potentiation of salt and water excretion.

In patients with AHF the emergence of diuretic resistance is multifactorial and includes decreased solute delivery to tubules caused by decreased renal blood flow, decreased GFR, hypoalbuminemia, retention of sodium and water resulted from an interaction of hormonal and hemodynamic (renal perfusion pressure). An acute increase in serum creatinine level accompanies 21%-45% of hospitalizations for AHF, depending on the time frame and magnitude of creatinine level increase. The term cardiorenal syndrome type 1 (CRS 1) has been used to include the vast array of interrelated derangements, and reflects an abrupt worsening of cardiac function leading to acute kidney injury. Clinical outcomes in heart failure populations are poor, and concomitant decreased kidney function with eGFR <60 mL/min/1.73 m2 significantly increases the risk of mortality.

Many mainstay therapies in use for decades in the management of AHF have not been subjected to the scrutiny of proper randomized controlled trials. Treatment includes cautious and combined use of appropriate drugs or interventions to relieve congestive and/or ischemic symptoms; strict fluid management, depending on the hemodynamic and circulatory status of the patient; and following up clinical response to treatment.

A review of the pathophysiology of HF and the possible emergence of diuretic resistance highlights a possible entry point in the clinical decision-making process to institute ultrafiltration (UF) therapy. When fluid balance and congestive symptoms become increasingly difficult to manage using conventional medical therapies, intermittent (isolated) ultrafiltration (UF) or hemo(dia)filtration have been used to decrease excessive fluid overload and, in the case of significantly decreased kidney function, also correct abnormalities in electrolyte levels and acid-base status.

According to the recent guidelines, UF may be considered as an option in the volume-overloaded patient who is resistant to diuretic therapy. In addition to pharmacological advances, technology for extracorporeal UF has been introduced and is advocated for use by nonnephrologists, especially because of the marketing of small, relatively simple devices.

UF is an alternative to intravenous diuretics for the management of volume overload in AHF and centers on various aspects: faster resolution of systemic and/or pulmonary congestion, major body sodium content reduction than diuretics, recovery of sensitivity to diuretics, reduction of neuro-hormonal activation rapidity, avoidance of maladaptive renal tubular autoregulatory response. UF can remove fluid from the blood at the same rate that fluid can be naturally recruited from the tissue. The transient removal of blood ilicits compensatory mechanisms, termed *plasma* or *intravascular refill* (PR), aimed at minimizing this reduction.The rate of plasma refill is important, for if the UF rate is too aggressive intravascular volume may decrease because the rate of refill from the interstitial to the intravascular space is exceeded. This in turn may lead to hemodynamic instability and renal dysfunction.

In the RAPID-CHF (Relief for Acutely Fluid-Overloaded Patients With Decompensated Congestive Heart Failure) study, 20 patients with ADHF received ultrafiltration compared with 20 patients receiving usual care.The ultrafiltration group had a negative fluid balance with a significant improvement in heart failure symptoms, but no difference in change in creatinine levels.

The UNLOAD (Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Congestive Heart Failure) trial investigators examined this strategy in patients with hypervolemic congestive heart failure compared with usual-care patients. Weight loss was greater in the ultrafiltration group. They also found decreased need for vasoactive drugs, with fewer rehospitalizations and emergency department visits in the ultrafiltration group, but no difference in mortality. The CARRESS-HF (Cardiorenal Rescue Study in Acute

Decompensated Heart Failure) trial currently is being undertaken to further define the use of this therapy in patients with AHF and CRS 1/worsening kidney function.

Early UF is an appropriate management strategy for patients with diuretic resistance whose renal dysfunction is related to haemo-dynamic changes rather than to structural abnormalities.

Further development and wider application to clinical use of simple bedside ultrafiltration devices could provide an alternative to medication in resistant cases of chronic CRS with fluid overload.

This has led to justifiable concern regarding our ability to not only prevent and manage these challenging conditions, but also cope with the huge demands on economic resources and health care workers.

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Noninvasive ventilation: pathophysiology, trials, tips & tricks

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Noninvasive ventilation (NIV) refers to the delivery of positive intrathoracic pressure using techniques that do not need an endotracheal airway. NIV essentially requires a source of air to produce pressure, tubes to transmit the flow and an interface. There are different interfaces: masks (nasal, oranasal or total face), helmets, mouthpieces or nasal cannulas. In clinical practice there are essentially two techniques of NIV: Continuous positive airway pressure (CPAP) and bilevel pressure support ventilation (NIPSV). While NIPSV is a modality that requires some expertise and a ventilator, CPAP is a simple technique that may be also applied just with a source of air or oxygen. This particularity allows CPAP to be used in low equipped scenarios such as the pre-hospital setting.

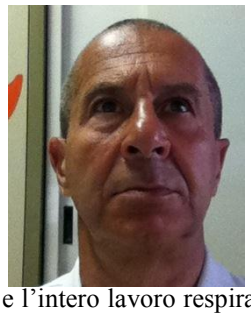
Although initially NIV was mainly used in chronic patients at home, the use of NIV in acute respiratory failure (ARF) has increased worldwide in the past 20 years and it has been associated to a decrease in nosocomial infections.

NIV reduces the intubation rate and improves more rapidly the ARF than conventional oxygen therapy in the majority of clinical settings. There is some evidence that NIV may decrease the mortality rate in acute cardiogenic pulmonary edema, in COPD exacerbations, in COPD patients with pneumonia or during weaning and in immunocomprissed patients with lung infiltrates. Indeed, NIV is useful to facilitate weaning, to prevent postextubation ARF, in do not intubate patients, in asthma and in some post-operative settings.

The appropriate selection of patients, early initial (often pre-hospital), close monitoring and asynchrony supervision, warrant the success of the technique

Ventilators interfaces for noninvasive ventilation in the acute setting

Cesare Gregoretti (Turin, Italy)



In respiro spontaneo la contrazione dei muscoli respiratori genera la pressione necessaria a superare le resistenze opposte al flusso d'aria attraverso le vie aeree (carico resistivo) e a controbilanciare il *recoil* elastico del polmone (carico elastico). Le patologie dell'apparato respiratorio, primitive e secondarie, determinano un aumento del carico elastico o resistivo o di entrambi. Inoltre, in presenza di ostruzione bronchiale, si può avere un carico aggiuntivo (carico soglia) dovuto all'iperinflazione dinamica. Supporto Ventilatorio Totale è sinonimo di Ventilazione Controllata, in cui il ventilatore insuffla il paziente con un pattern preselezionato e l'intero lavoro respiratorio viene eseguito dalla macchina. La Ventilazione Controllata può essere: 1) Volumetrica, in cui ogni atto meccanico è somministrato con Volume e Tempo predeterminati, mentre la Pressione che si sviluppa nelle vie aeree è funzione delle caratteristiche meccaniche del sistema respiratorio, 2) Pressometrica, in cui una quota di Pressione viene costantemente applicata alle vie aeree per un Tempo prefissato ed è il Volume di insufflazione a dipendere dalle proprietà meccaniche del Sistema Respiratorio. Il supporto ventilatorio totale è di difficile utilizzo in pazienti coscienti e con richieste ventilatorie variabili ed il suo impiego con modalità non invasiva (NIV) è alquanto raro nel paziente acuto. Differentemente il supporto totale si realizza molto spesso nel paziente cronico nelle fasi REM del sonno. In particolare il paziente affetto da patologia neuromuscolare si adatta molto rapidamente al pattern respiratorio impostato sul ventilatore ventilatore anche durante il giorno.

Il Supporto Ventilatorio Parziale è caratterizzato dalla interazione del paziente con il ventilatore che assiste i muscoli respiratori assumendosi una quota del lavoro respiratorio. Caratteristica comune delle forme di assistenza ventilatoria parziale è la possibilità da parte del paziente di innescare l'atto respiratorio. Ciò è reso possibile dai sistemi *trigger*, che percepiscono in vario modo (pressione, volume, flusso) lo sforzo dei muscoli all'inizio dell'ispirazione ed attivano quindi il supporto meccanico. La corretta impostazione del *trigger* prevede la scelta del livello più sensibile, tale però da evitare l'auto-innesco del supporto meccanico. La presenza di perdite aeree in ventilazione non invasiva può pregiudicare il buon funzionamento del *trigger*. La Ventilazione Assistita/Controllata (A/C) è caratterizzata dalla possibilità da parte del paziente di attivare l'atto respiratorio meccanico, che verrà erogato dalla macchina con Volume (A/C Volumetrica) o Pressione (A/C Pressometrica) e Tempo predeterminati. La ventilazione mandatoria intermittente (IMV e SIMV) è invece contraddistinta da un numero prefissato di atti meccanici al minuto che si aggiungono alla ventilazione spontanea del paziente. Con la ventilazione a supporto di pressione (Pressure Support Ventilation -PSV-) il paziente è in grado di controllare il passaggio da Inspirazione a Espirazione che non è più Tempo-dipendente, ma Flusso-dipendente. Il ciclaggio I/E avviene ogniqualvolta il Flusso inspiratorio raggiunge un valore relativo (es.: 25% del picco iniziale). La presenza di perdite pregiudica il buon funzionamento di questa funzione ed è per questo che sono stati recentemente adottati algoritmi più sofisticati atti a ridurre, se non a risolvere, l'entità del problema.

Con la Pressione Positiva Continua (CPAP) una quota di pressione viene applicata costantemente durante il ciclo respiratorio che è completamente controllato dal paziente. La CPAP si è dimostrata efficace in diverse condizioni cliniche, se pur con diverse modalità di funzionamento. Nelle riduzioni acute del volume polmonare (edema, atelettasia) la CPAP è in grado di reclutare alveoli altrimenti collassati. Nei pazienti con grave ostruzione bronchiale agisce controbilanciando il carico soglia imposto sui muscoli respiratori dall'iperinflazione dinamica.

L'associazione di CPAP e PSV rappresenta la forma di supporto ventilatorio meccanico non invasivo di maggiore uso in area critica .

Il criterio più diffuso nel classificare le interfaccia per ventilazione non invasiva è quello che le distingue secondo la parte anatomica del paziente con cui si "interfacciano" : la bocca, il naso, il naso e la bocca insieme, l'intero volto o tutto il capo. Si distinguono in questo modo interfacce orali o boccagli, maschere nasali od olive nasali, maschere facciali parziali o totali e caschi. Dai dati della letteratura per trattare insufficienza respiratoria acuta, si utilizza nel 70% dei casi interfaccia oro-nasali e nel restante 30% dei casi interfaccia nasali o caschi.

Le complicanze della NIV sono tuttavia numerose e includono scarso adattamento alla interfaccia, perdite aeree, claustrofobia e lesioni cutanee (dal semplice eritema sino a ulcerazioni facciali e a lesioni oculari) Nel contesto del trattamento di casi acuti, il comfort del paziente potrebbe apparire meno importante dell'efficacia del trattamento stesso. Al contrario è proprio il comfort del paziente, insieme all'ottimizzazione dell'interazione paziente-ventilatore, il principale determinante del successo o del fallimento della NIV

Post discharge non invasive ventilation quality assessment

Francesco Travaglino (Rome, Italy)

Non-invasive ventilation (NIV) has been shown in several randomized controlled trials to improve arterial blood gases and to reduce intubation and in-hospital mortality in patients suffering from acute exacerbations of chronic obstructive pulmonary disease (AECOPD) complicated by acute hypercapnic respiratory failure (AHRF). Patients who have received NIV for an AECOPD are a group at high risk for subsequent hospitalization and death; those at the most severe end of the spectrum are those at most risk. NIV at home for these patients might improve the long term outcome.
Home ventilation is a growth area. Rapid expansion during the 1990s was stimulated by the development of noninvasive ventilation (NIV) via a mask and the recognition that an increased number of patient groups can benefit. Evidence that individuals who develop a respiratory failure as a consequence of chest wall disease or stable neuromuscular disease benefit from nocturnal NIV is overwhelming. Patients with progressive neuromuscular disease such as Duchenne muscular dystrophy and amyotrophic lateral sclerosis can also derive prolongation of life, palliation of symptoms and an improvement in quality of life. However home ventilation in COPD patients remains controversial. Multicentric randomized controlled trials of long-term oxygen therapy (LTOT) versus NIV plus LTOT in COPD have produced mixed results, although certain subgroups, e.g. those with recurrent infective exacerbations requiring short-term NIV, patients aged more than 65 years, and those with uncontrolled hypercapnia with mild to moderate acidosis on LTOT or symptomatic nocturnal hypoventilation, may benefit. Domiciliary NIV for such patients, with recurrent admissions requiring NIV, is effective at reducing admissions and minimizes costs from the perspective of the acute hospital. In conclusion COPD patients admitted to hospital for an exacerbation with AHRF who survive following treatment with NIV have a high risk of readmission and life threatening events. These patients are to be seriously considered for discharge with home ventilation. Further studies are needed to devise strategies to reduce readmission and life threatening events in this group of patients.

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SIRS-Sepsis differential diagnosis

Nicola Fiotti (Trieste, Italy)

Background

Early diagnosis of SEPSIS in patients with SIRS is of utmost importance, since delay in sepsis treatment is deleterious and indiscriminate treatment with antibiotics leads to increased prevalence of side effects and microbial resistance, which globally reflect on healthcare cost and efficiency.New laboratory markers have been proposed in the rule-in/rule-out procedures for early discrimination of sepsis, but the studies have been conducted only on pediatric patients, so far, and little is known on their contribution in the diagnosis of SIRS/sepsis in adults.

Aims

To determine the predictive relevance of some new markers, namely IP10 and PLA_2, in ruling out non-infective sepsis (NI-SIRS) among SIRS patients, and then to develop the most accurate diagnostic model putting together clinical, routine laboratory test and these new markers.

Methods

80 patients, stratified for age and gender, were enrolled for such preliminary experience, 20 had a final diagnosis of non-infective SIRS and 60 of sepsis (20 microbiologically and 40 clinically proven). Clinical variables were those used for diagnosis if SIRS (temperature, heart rate, WBC count, and respiratory rate), laboratory variables were those of a complete Blood Cell Count plus NBU, creatinine, glucose, Na/K, and new markers were IL10 and PLA_2 as continuous variable or using a cutoff of 650 pg/mL and 7 ng/mL, respectively. Blood samples for this study were obtained at the time of diagnosis and management was carried out blind of the new markers' results.

Statistics: binary logistic regression provided positive and negative predictive values and logit models.

Results

Positive and negative predictive values (PPV and NPV, respectively) obtained combining the different groups of variables are reported in table.

Group of Markers	Binary logistic step	NPV	PPV	Overall correct
Clinical	4	94.9	84.2	92.3
Laboratory	2	96.6	20	77.2
Markers	1	96.7	60	87.5
Clin+lab	4	94.8	84.2	92.2
Clin+mark	6	96.6	89.5	94.8
Lab +mar	2	96.6	65	88.6
Clin+lab+mar	6	96.6	89.5	94.8
	9	100	100	100

When all groups of markers were combined, a complex model including temperature, cardio circulatory markers (heart rate, respiratory rate, diastolic pressure), laboratory test (with blood cells, hemoglobin, platelets and creatinine) and IP10 and PLA2 achieved the 100% of correct diagnosis. Angiopoietin, lactate, C reactive protein and procalcitonine did not add any contribution to diagnosis.

Conclusions

In our group of patients, IP10 and PLA2 were fundamental in achieving a model predicting all cases of non-infective SIRS and sepsis.

Procalcitonin and diagnosis of infection in ED

Gianfranco Cervellin (Parma, Italy)

Community-acquired pneumonia (CAP) is defined as an infection of the alveolar or gas-exchanging portions of the lungs occurring outside the hospital, with clinical symptoms accompanied by the presence of an infiltrate in the chest radiograph. Due to the high prevalence and the large request of healthcare resources, an accurate clinical and therapeutic decision making is crucial in patients with CAP. Although antibiotic policies are usually based on interpretation of national guidelines, in most cases they should be administered as soon as possible to influence the prognosis. The diagnosis of CAP is typically based on the presence of select clinical features (e.g., cough, fever, sputum production, and pleuritic chest pain) and is supported by imaging of the lung, usually by chest radiography. Microbiological studies may support the diagnosis due to an infectious agent, but routine tests are frequently falsely negative and often nonspecific. Recommendations for diagnostic testing remain thereby controversial. Due to the high prevalence and the large demand of healthcare resources, an accurate clinical and therapeutic decision making is crucial in patients with CAP. As such, there is increasing interest on the use of traditional and innovative biomarkers such as procalcitonin (PCT) and C-reactive protein (CRP). PCT is a 116 amino acid protein, precursor of calcitonin. Calcitonin is physiologically produced by the C-cells of the thyroid after intracellular processing of the prohormone PCT. The transcription of the CALC-1 gene produces a primary transcript processed into mRNA encoding a 141-amino acid protein (preprocalcitonin), which comprises a signal sequence, the N-terminal region of procalcitonin (N-PCT), the middle sequence of calcitonin (amino acids 60-91) and the C-terminal region of procalcitonin called "katacalcin". Emerging evidences attest that the measurement of the PCT might be useful in CAP because the most frequently used markers (body temperature, leukocytosis, CRP) display suboptimal sensitivity and specificity and are therefore of limited help in the clinical decision making. PCT is a relatively innovative and highly specific marker for the diagnosis of clinically relevant bacterial infections and sepsis, so that it is increasingly recognized as an important diagnostic tool in clinical practice. Localized bacterial or organ-related infections and capsulated abscesses might only trigger modest increases in PCT. It must be noted that high PCT levels are frequently observed following major surgery, after trauma injuries as well as in other severe pathological situations (i.e., PCT serum levels >0.5 μg/L usually reflect acute infections accompanied by a systemic inflammatory reaction), whereas viral infections, autoimmune disorders and malignancies do not induce significant increases of this protein. At variance with other traditional inflammatory and innovative biomarkers, PCT might help limiting unnecessary antibiotic use, reduce bacterial resistance and decrease medical costs and drug-related adverse events. PCT however carries some additional advantages over CRP, such as the greater specificity for infections and a more narrow range of normal concentrations. Nevertheless, the correct interpretation of PCT test results within the specific clinical setting as well as the accurate knowledge about the characteristics of the assay (e.g., the use of highly sensitive PCT assays and the adoption of appropriate threshold values) are essential requisites for a meaningful use of this marker.

Multimarkers approach to sepsis in emergency room

Francesco Travaglino (Rome, Italy)

Sepsis is a syndrome characterized by a systemic inflammatory response that occurs in the body as a consequence of an infection. SIRS is characterized by different clinical signs: temperatures can vary from higher than 38ºC to lower than 36ºC, heart rate may be above 90 beats per minute (bpm), tachypnea (FR > 20/min) or hyperventilation (pCO2 < 32 torr) may be present, and white blood cell count may be above 12,000 or below 4,000 cells/μL (1). Sepsis is actually a counteracting 'misresponse' of the body against infecting microorganisms (2). This uncontrolled reaction is characterized by a biased system, in favor of pro-inflammatory, pro-coagulant, and over reactive immune inflammatory response. The magnitude of the response depends on several factors, such as the virulence of the organism, host genetics, and immune status.

In the progress of the uncontrolled inflammatory response in sepsis, unpredictable cardiovascular phenomena occur, such as hypovolemia, peripheral vasodilation, myocardial depression, increased endothelial permeability, and hypermetabolism. Severe sepsis is characterized when there is association of sepsis with organ dysfunction, while septic shock, characterized by severe alterations of the cardiovascular system, occurs when resuscitation maneuvers are mandatory due to hypotension or persistent changes in tissue perfusion after conservative attempts of hemodynamic homeostasis maintenance are performed. Nevertheless, the boundaries between severe sepsis, septic shock, and multiple organ dysfunctions are not clearly defined in clinical practice (3). Sepsis is a leading cause of death in critically ill patients despite the use of modern antibiotics and resuscitation therapies (4). The septic response is an extremely complex chain of events involving inflammatory and anti-inflammatory processes, humoral and cellular reactions and circulatory abnormalities. The diagnosis of sepsis and evaluation of its severity is complicated by the highly variable and non-specific nature of the signs and symptoms of sepsis (5,6). The early diagnosis and stratification of the severity of sepsis is very important, increasing the possibility of stratify these patients in order to start prompt and appropriate treatment and to define their disposition (7).

Biomarkers can have an important place in this process because they can indicate the presence or absence or severity of sepsis, and can differentiate bacterial from viral and fungal infection, and systemic sepsis from local infection. Other potential uses of biomarkers include roles in prognostication, guiding antibiotic therapy, evaluating the response to therapy and recovery from sepsis, differentiating Gram-positive from Gram-negative microorganisms as the cause of sepsis, predicting sepsis complications and the development of organ dysfunction (heart, kidneys, liver or multiple organ dysfunction). However, the exact role of biomarkers in the management of septic patients remains undefined (8,9).

In medical literature, more than 178 different biomarkers were evaluated in many studies, classified as cytokine/chemokine biomarkers, cell marker biomarkers, receptor biomarkers, coagulation biomarkers, biomarkers related to vascular endothelial damage, biomarkers related to vasodilation, biomarkers of organ dysfunction, acute phase protein biomarkers and other biomarkers (10).

In view of the complexity of the sepsis response, it is unlikely that a single ideal biomarker will ever be found, while a combination of several sepsis biomarkers may be more effective. A multimarker pannel approach performed by rapid and accurate assays could be useful for emergency physicians to promptly identify sepsis thus managing to improve diagnosis, treatment and risk stratification (10).

In recent studies, the most commonly biomarkers showing a great diagnostic and prognostic value for sepsis are CRP, PCT (11,12), MR-proADM, copeptin and Natriuretic peptide (MR-proANP) (13-15).

In our experience, we have recently demonstrated with the publications of an observational multicentric study how MR-proADM and PCT may be helpful to the febrile patient's care in the emergency department. Our data support the prognostic role of MR-proADM and PCT in that setting, as demonstrated by the correlation with the APACHE II score, particularly in sepsis. Also of interest is the possibility that the combined use of the two biomarkers can predict a subsequent hospitalization of febrile patients accessing the ED. The rational use of these two molecules could lead to several advantages, such as faster diagnosis, more accurate risk stratification, and optimization of treatment, with consequent benefit to the patient (16).

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NGAL and procalcitonin in the management of sepsis in emergency department

Laura Magrini (Rome, Italy)

Neutrophil Gelatinase-Associated Lipocalin (NGAL) and Procalcitonin (PCT) are two biomarkers frequently increased in septic patients. PCT is a well-known biomarker of both local infections and sepsis (1-5), but NGAL, both urinary and plasma, is considered mainly a diagnostic biomarker of acute kidney injury (AKI) (6,7) even if it is released by neutrophils after activation during the course of infection or sepsis. AKI is often associated with sepsis, so it is difficult to discriminate if increased NGAL levels during sepsis are due to kidney injury or to the septic process.

PCT, a precursor of calcitonin, released and increased in the bloodstream during local or generalized infections is a known diagnostic marker of sepsis, but also a prognostic factor for outcomes in septic patients (8) and its role in the early detection of sepsis has had, recently, an increasing interest in the emergency setting (1,9).

NGAL is mainly used for AKI detection, but recently it has been studied also in the course of sepsis in ICU patients with and without AKI (10), and its plasma concentrations are significantly increased in septic patients, and among them especially in those with AKI, indicating that it is an expression of the worsening conditions of renal function during sepsis. But recent data show that it increases also in neoplasms, and inflammatory bowel diseases (7), and for this reason its role as marker of infection must be considered with caution.

We are up to publish a study in which we demonstrate the diagnostic role of PCT for sepsis and its importance in guiding antibiotic therapy (11). Moreover, our experimental data (data not published) demonstrate that plasma NGAL, and also plasma PCT, are increased in patients arriving in ED with signs and symptoms of sepsis, with or without AKI (both higher in AKI patients). In another study (data not published) we have measured plasma PCT and NGAL at arrival and after three days from the beginning of therapy, and our results confirm those of Lentini et al (10).

Plasma NGAL (as also PCT) is increased in patients with sepsis but its specific role in diagnosing it, opposite to the role of PCT that is undoubtedly clear, is still controversial because it is affected by different concomitant pathologic situations as kidney dysfunction during sepsis.

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New evidences on the pathogenic role of thrombopoietin in septic shock

Enrico Lupia (Turin, Italy)

Thrombopoietin (TPO) is a humoral growth factor mainly involved in regulation of platelet number and function. High circulating levels of TPO are detectable in septic adults and children and are related to sepsis severity [Zakynthinos S.G. et al., Critical Care Med 2004]. We have previously shown a correlation between TPO levels and platelet activation in septic burned patients [Lupia E. et al., J Thromb Haemost 2009], a phenomenon that may cause micro-thrombotic events leading to organ damage. Moreover, TPO is able to negatively modulate myocardial contractility by stimulating its receptor c-Mpl expressed on cardiomyocytes and the subsequent production of NO, and cooperates with TNF-α and IL-1β in mediating the negative inotropic effect induced *in vitro* by serum of septic shock patients [Lupia E. et al., Basic Res Cardiol 2010]. Nonetheless, it is not clear at the moment whether TPO should be considered a pathogenic mediator of organ damage during septic shock, or rather only a biomarker.

Aim of the current study was therefore to evaluate the contribution of TPO to the development of organ injury in two murine models of experimental sepsis, induced by *i.p.* injection of E.coli lypopolisaccharides or cecal ligation and puncture. To this end, we synthesized and characterized a chimeric fusion protein, named mouse TPO Receptor – Maltose Binding Protein (mTPOR-MBP), able to inhibit TPO biological activity *in vivo* in mice. The results obtained show that plasma TPO levels were significantly higher in septic animals than sham-operated mice, and correlated with the percentage of monocyte-platelet aggregates, a marker of platelet activation. Treatment with mTPOR-MBP significantly reduced monocyte-platelet aggregation, as well as the signs of organ damage in lung, as evaluated by neutrophil infiltration and thickening of alveolar-capillary membrane, and liver tissue samples, as evaluated by number of micro-abscesses.

In conclusion, our data indicate that increased circulating levels of TPO during experimental sepsis may have a role in the development of organ damage. Inhibition of TPO biological activity may represent a novel promising therapeutic approach to prevent organ failure in severe sepsis.

Adrenomedullin drug (and assay) development

Frauke Hein (Hennigsdorf, Germany)

Sepsis and sepsis-associated multiorgan failure with high mortality remain as major challenges for both scientists and clinicians. Despite extensive research in the past, the pathophysiology of sepsis in humans is still poorly understood, and hospitalization rates of septic patients have significantly increased worldwide.

Adrenomedullin (ADM) is a soluble neuropeptide comprised of 52 amino acids with a short half-life. ADM exerts its biological activity by binding of its G-protein coupled receptor CRLR, which is an association of Calcitonin-Like Receptor (CLR) with one of the receptor-modifying proteins (RAMP 2 and 3) by downstream intracellular cAMP formation. The major function of ADM is vasodilation and subsequent regulation of the vascular tone. Circulating ADM levels are highly increased in patients with sepsis and septic shock. It was found that during septic course, early supplementation of ADM is beneficial and improves microcirculation and organ function whereas in the later phase of sepsis ADM contributes to extensive vasodilation, leading to hypotension and organ failure.

AdrenoMed AG is a biotech company located near Berlin, Germany, with the mission to develop innovative drugs that reduces mortality in sepsis. We developed > 30 monoclonal antibodies against human ADM by mouse hybridoma technology and characterized them with a variety of in vitro bioassays. This screening leads to the successful identification of HAM1101, the Human Adrenomedullin Modulating antibody who combines unique drug features: We could demonstrate that binding of HAM1101 to ADM (1) stabilizes the molecule and (2) diminishes cAMP formation but does not abolish bioactivity by only partial receptor blocking. This means that in vivo:

- Beneficial effects of ADM at low concentrations are intensified due to reduced proteolytic degradation and increased bioavailability
- Potentially harmful effects of ADM at high concentrations are attenuated by reduced bioactivity of the ADM-HAM1101 complex

During sepsis course the monoclonal antibody HAM1101 is able to modulate and buffer ADM concentrations to a physiologically desired range.

In an experimental sepsis model of cecal ligation and puncture (CLP) in mice, administration of HAM1101 reduces significantly sepsis mortality from 100% down to 50% ($p<0,005$ versus controls). We could also demonstrate that HAM1101 is well tolerated by overdose in healthy mice.

HAM1101 was successfully humanized to AdrenoMed`s humanized monoclonal antibody drug candidate HAM8101. HAM8101 is currently in preclinical development of safety and toxicology studies as well as in drug substance production according GMP regulations. Clinical first-in-man studies are planned in the future.

Targeting adrenomedullin - Preclinical results from a resuscitated murine septic shock model

Florian Wagner (Ulm, Germany)

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Introduction: Adrenomedullin (ADM) has been referred to as a „double-edged sword" during circulatory shock states: while genetic ADM overexpression or exogenous ADM supplementation improved organ function and survival [1] in experimental models due to maintenance of hyperdynamic hemodynamics [2,3] in otherwise hypodynamic conditions, high blood levels were associated with increased mortality in patients with septic shock [4], most likely as a result of excessive vasodilatation [5] and/or impaired systolic heart function [6].

Methods: Immediately after induction of anesthesia for cecal ligation and puncture (CLP) mice randomly received an injection of the adrenomedullin antibody HAM1101 (2 µg/g; to achieve antibody concentrations > 4 ng/mL) or vehicle via the penile vein. 15 hours later the animals were anesthetized again, mechanically ventilated and instrumented for a consecutive observation period of 5 hours. During the observation period a normotensive blood pressure (mean arterial blood pressure (MAP) > 60 mmHg) was maintained by continuous i.v. colloids and noradrenaline infusion. Plasma as well as urine creatinine were measured using gas chromatography-mass spectrometry after solide phase extraction, plasma neutrophil gelatinase-associated lipocalin (NGAL) by a commercial ELISA. Kidney hemoxygenase 1 (HO-1), cleaved caspase-3 and NF-κB were assessed by immunoblotting and EMSA respectively [7]. Immunohistochemistry was used to detect iNOS as well as nitrotyrosine expression in the thoracic aorta and kidney tissue. Plasma TNF-α and IL-6 were measured using a commercial mouse multiplex cytokine kit [7]. All data presented are median and range. After exclusion of normal distribution the groups were compared using Mann-Whitney U rank sum test. A $p<0,05$ was regarded as significant.

Results: Adrenomedullin antagonism reduced iNOS activation and nitrotyrosine expression in the aorta and the kidney tissue. This was accompanied with decreased noradrenaline requirements needed to achieve target hemodynamics (0.009 (0.009;0.012) vs. 0.02 (0.015;0.044) µg/g/h, $p<0.001$), increased total diuresis (2.6 (2.3;3.9) vs. 0.6 (0.5;2.7) mL, $p=0.028$) resulting in improved fluid balance (0.18 (0.14;0.2) vs. 0.26 (0.19;0.27), $p=0.011$) and kidney function (creatinine plasma levels at the end of the experiment: 1.3 (1.2;1.5) vs. 2.0 (1.5;2.9) µg/mL, $p=0.006$; creatinine clearance: 400 (316;509) vs. 197 (110;301) µL/min, $p=0.006$; NGAL plasma levels 11 (10;13) vs 16 (15;20) µg/mL, $p=0.008$). HAM1101 furthermore reduced plasma levels of TNF-α (1 (0;8) vs 32 (13;62), $p=0.01$) and IL-6 (43 (22;55) vs 363 (120;681), $p=0.002$) and was accompanied with attenuated expression of HO-1, activated caspase-3 and NF-κB in kidney tissue.

Conclusions: In resuscitated murine septic shock early modulation of excess adrenomedullin activity blunted the sepsis-induced aortic iNOS expression as well as peroxynitrite formation, resulting in an improved cardiovascular catecholamine responsiveness. This was ultimately associated with attenuation of systemic inflammatory response and acute kidney injury.

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Biomarkers for acute coronary syndrome early diagnosis: only troponin?

Giuseppe Lippi (Parma, Italy)

The diagnostic approach to the acute coronary syndrome has engaged for long the minds of cardiologists, laboratory as well as always busy emergency physicians. Reliable data now attests that silent or atypical presentation of an acute myocardial infarction (AMI) may be a rather frequent occurrence, especially in patients with non-ST-segment elevation MI (NSTEMI), wherein the diagnosis may be rather challenging. The recent introduction of the so-called "highly-sensitive" (HS) troponin immunoassays has remarkably contribute to enhance the diagnostic sensitivity of this marker, as well as to decrease the triage of the patients in the emergency department, since a negative diagnostic value on admission would reflect a very low risk of short, medium and long term complications. Nevertheless, the add-value of an increased diagnostic sensitivity has been counterbalanced by a substantial decrease of diagnostic specificity, so that the approach to chest pain patients now requires a much more careful evaluation of comorbidities, but also paves the way for the use of additional biomarkers, whose measurement in combination with HS-troponin may globally increase the positive predictive value and hence the global diagnostic performance. Several biomarkers have been proposed over the past decades to complement troponin testing, including myoglobin, creatine kinase isoenzyme MB (CK-MB), ischemia-modified albumin (IMA), myeloperoxidase, glycogen phosphorylase BB, Heart-Fatty Acid-Binding Protein (H-FABP), pregnancy-associated plasma protein-A (PAPP-A), HS-C Reactive Protein (CRP), procalcitonin, Interleukin-6, copeptin, neopterin, natriretic peptides, pro-adrenomedullin (pro-ADM), D-dimer, CD40 ligand, platelet-leukocyte aggregates, and even Prostate Specific Antigen (PSA) among others. Although the independent contribution of these biomarkers seem effective to slightly improve the diagnostic performance of HS-troponin alone, recent data from our group has however demonstrated that two very simple, easy and inexpensive biomarkers such as the red blood cell distribution width (RDW) and blood glucose may produce similar benefits at a much lower cost for the healthcare system.

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How to optimize rule out acute coronary syndrome for patients with chest pain in ED

Marco Tubaro (Rome, Italy)

Patients with chest pain in the Emergency Department (ED) have a variety of diseases and only a minority of them has the chest pain caused by an acute coronary syndrome (ACS). The task of the ED physician is firstly to rule out both an ACS or another serious disease, in order to discharge early and safely the patient home. In case of failure of the rule-out, rule-in is a more complex process, taking in account both the diagnosis and the prognostic stratification of the patient, in order to identify the proper hospital department where to send the patients and to delineate a meaningful diagnostic and therapeutic pathway.

The first step in chest pain diagnosis is history and careful physical examination, including an estimate of the patient probability to have an ACS, pain characteristics and the presence of risk factors for ACS. An ECG should be recorded within 10 minutes from patient's entry in ED and interpreted by an experienced health professional. In case of persistent ST-segment elevation in presence of signs and symptoms of acute myocardial ischaemia, no further diagnostic tests are useful and the patient should be immediately treated with a reperfusion strategy (primary PCI or thrombolysis as a second choice). Also in case of ST depression and/or T wave inversion, the probability of ACS is high and cardiac biomarkers are useful for differential diagnosis (between unstable angina and non-ST-elevation myocardial infarction) and prognostic stratification.

The greatest utility of cardiac biomarkers (troponin preferably) is when chest pain characteristics are inconclusive and the ECG is normal or anyway not diagnostic for ACS. High sensitivity cardiac troponin (hs-cTn) T or I have both a very high sensitivity and specificity for myocardial necrosis: high blood levels of hs-cTn(s) in a clinical situation of myocardial ischaemia yields the diagnosis of acute myocardial infarction (AMI). Due to these characteristics, a negative hs-cTn may rule-out an AMI, while a positive hs-cTn should be interpreted in the framework of the clinical and ECG data, because not only AMI causes an increase of hs-cTn(s).

In case an high suspicion for ACS would remain with respect to a non-diagnostic ECG and a normal hs-cTn, stress-imaging test can be used in the ED (stress echo or myocardial scintigraphy), while for differential diagnosis of structural cardiac or vascular diseases, a multidetector CT scan or a cardiac magnetic resonance can be of help to confirm/exclude a diagnosis of pulmonary embolisms, aortic dissection, myocarditis and others.

In conclusion, the rule-out of AMI is based on normal level of hs-cTn(s) (below the 99^{th} percentile of the distribution of the biomarker in the normal population), while the rule-out of the ACS (including unstable angina) needs a clinical judgement on history, physical examination and ECG. It should be underlined that an high blood level of hs-cTn is not diagnostic of AMI per se, because many cardiac non ischaemic diseases and some non cardiac diseases can increase hs-cTn(s): the analysis of the extent, speed and trend of hs-cTn increase can be of help in the differential diagnosis.

Finally, to exclude an ACS does not mean that the patient has not a serious disease: meaningful clinical judgement has a pivotal role for the best treatment of patients with chest pain in the ED.

Italian multicentric registry on chest pain patients in ED

Paola Ballarino (Genoa, Italy)

Chest pain is one of the most frequent symptoms of presentation in the Emergency Department, representing 5% of the total number of access in every E.D.

ESC Guidelines report that the typical clinical presentation is retrosternal pressure or heaviness (angina) radiating to the left arm, neck or jaw; however atypical presentations are not uncommon and are more often observed in older, women, and patients with diabetes, chronic renal failure, and dementia

In literature there are some studies regarding the management and treatment of selected patients with acute coronary syndromes in cardiological areas, but there aren't any studies in relation to patients with chest pain in ED

Italian Multicentric Registry on Chest Pain Patients in ED is an observational prospective study, with the aim to collect data about patients who arrive to E.D. with typical chest pain suggestive of ACS.

The hypothesis is to enroll more than 10000 patients in 10 different centers, in order to collect 2000 patients with a final diagnosis of acute coronary syndrome.

We have created an excel format with some parameters grouped in areas of interest : hemodynamic parameters, analysis of Ecg, risk factors, drugs taken at home, blood samples and in particular Troponins at time 0, 3, 6 and eventually 12 hours from the arrival of patient (other biomarkers could be added to the schedule), the collocation of the patient, additional tests, final diagnosis, re-hospitalization, medications administered in ED, scores (Timi Risk Score, Score Index, Grace Risk Score)

It doesn't exist in literature a registry in which patients who arrive to ED are treated in accordance to guidelines but with the limit of co morbidities ; the difference with other cardiological researches is that these patients aren't selected at the beginning

The objective of Italian Multicentric Registry on Chest Pain Patients in ED is to collect data about patients who arrive to ED with typical chest pain suggestive of ACS in different hospitals

The unique aspect of the study is related to give a picture of the real population of ED chest pain patients that will be selected in order to rule out patients to be discharged and to rule in patients for cardiological area

The objective of this project is to analyze these patients and to compare data regarding populations with and without a history of CAD in a large sample size and in different E.D. with various cardiological background; the primary endpoint remains however to evaluate the incidence of acute coronary syndromes in patients with typical chest pain who arrive to the Emergency Department

Exclusion criteria are age less than 18 and more than 90 years old

The sample size was estimated based on the results for expected ACS rate of 20% and a history of CAD in 35% of enrolled subjects.

The study will last 1 year, with more than 800 patients to be enrolled per month.

At the end of the first year, every center will have a month to complete its own database, and later on, the amount of data will be analyzed for an estimated period of two months.

The enrollment is not competitive and if a center does not reach the required case number, the study population will be reduced

Univariate and multivariate method will be used to explore role played by independent variables in ACS global population and in subgroups.

Acute coronary syndrome present approach in Romania in the Emergency room

Alexandru Nechita (Bucharest, Romania)

The continous improvement of ACS therapy is based on the scientific progress made both in pharmacotherapy and interventional, surgical procedures. Their practical value is seen only if applied on a mass scale . The correct diagnosis and therapy starts in the Emergency Room.

The clinical presentation of the acute coronary syndrome encompasses a very broad spectrum: most of the pacients are labeled wiith “chest pain”, others are coming for acute dispnoea, syncope and other atypical presentations.

Clinical examination is useful only when a clinical sign of value to affirm another condition is present, like the syndrome of right heart failure. The main stratificator remains the ECG, a STEMI aspect on the ECG triggers the special protocol; for such patients. A more or less aggressive scenario is also applicable to the patients with NSTEMI, for which we do not have a specific protocol. The presence of refractory ischemia and acute heart failure should trigger a more invasive scenario, but, paradoxically , sometimes the presence of AHF can focus the medical efforts in dealing with dyspnoea rather than reestablishing the patency of the culprit artery. In patients with advanced coronary artery disease and AHF it isvery difficult to establish whether there is decompensation of heart failure or thromotic occlusion.

For nearly 50% of the Romanian territory it is available the STEMI primary PCI programme. The hospital outside this area thrombolysis remains the reperfusion primary method. The patients with no reperfusion or those considered at high risk for developing cardiogenic shock are reffered by helicopter or ambulance to a PCI center. For all the Romanian territory an ECG telemetry programme is operational, the ECG data from EMS teams and also from rural medical centers is retrieved very early by doctor, who is addressing the patient to the most appropriate unit. Another voice and video system is available on some ambulances for direct guidance of therapy especially in very unstable cases. The noninterventional hospitals in the ST MI areas are reffering directly the patients with STEMI, and selectively the patients with NSTEMI, to the interventional centers.

Troponins and other biomarkers are of great help in the diagnostic workup of the ACS patients. They are useful for both the positive diagnosis and in establishing the age of necrosis in patientis with equivocal or impossible anamnesis. For some of the patients echocardiography is needed. This method can show: Ventricular wall motion disturbances, MI echo dimension and LV/RV dysfunction, concomitant and preexistant cardiac pathology, other acute cardiac conditions: aortic dissesction, acute pericarditis, APE, endocarditis, or non cardiac.

Immediate DAPT and antithrombotic therapy is given, together with the other supportive and myocardoprotective measures. A practical algorithm is discussed.

European guidelines of acute Coronary Syndromes

Massimo Volpe (Rome, Italy)

The new ESC guidelines of acute coronary syndromes (ACS), published in 2011 and 2012, focus on two main aspects of diagnosis and treatment. Primarily, the guidelines underline the need to reduce the time of recognition of disease and to start treatment as soon as possible. Afterward, specific reccomendations on newer antiplatelet drugs, such as prasugrel or ticagrelor over clopidogrel, are reported.

The guidelines of STEMI are much more demanding than the 2008 guidelines in terms of delays. The new standard for time from medical contact to ECG is 10 minutes, and the fact that you use primary PCI should not lead to complacency about the delays. You should target 60 minutes. Two hours is the limit of acceptable delay for a patient transferred from a non-PCI center to a PCI center, but the target should be 90 minutes. If PCI within two hours of presentation appears to be impossible, then fibrinolysis should be administered within 30 minutes. Therefore, the new guidelines of NSTE-ACS insist that patients suspected should be preferentially evaluated in chest pain or coronary care units, emphasizing the role of the cardiologist in this initial phase of management. Another important development is the recommendation to use ultra- sensitive troponin for the initial diagnosis of NSTE-ACS. These reactants lower the detection limit for troponin and facilitate an earlier identification of myocardial necrosis. Within 6 h of the first episode of pain, the guidelines recommend a second measurement of ultrasensitive troponin 3 h after arriving at the emergency room (the recommendation for conventional troponin was 6-9 h).

Finally, ACS guidelines focus on new P2Y2 inhibitors drugs. This recommendation is justified by the detailed analysis of the results from the TRITON-TIMI 38 and PLATO studies, showing the superiority of prasugrel and of ticagrelor over clopidogrel. Prasugrel is advised in patients with diabetes and in stent thrombosis, but with some restrictions (age > 75 years, low BMI, any previous cerebral event). Ticagrelor is a drug suitable for all patients with an acute coronary syndrome, as demonstrated by PLATO. Clopidogrel is relegated as a treatment only for patients that cannot receive ticagrelor or prasugrel.

Which antiplatelet treatment for acute coronary syndrome's patients in ED

Meinard Gawaz (Tuebingen, Germany)

Platelets play a critical role in the pathophysiology of acute coronary syndrome (ACS). For years dual antiplatelet therapy (DAPT) consisting of aspirin and clopidogrel was the cornerstone of acute treatment of patient with ACS. However, it has been increasingly recognized that platelet function is not adequately inhibited despite aspirin and clopidogrel therapy in up to 20% of patients with ACS due to clopidogrel low responsiveness. Insufficient ADP-mediated platelet inhibition with clopidogrel is mainly explained by drug interactions or genetic variants slowing the bioactivation of the prodrug clopidgrel into an active metabolite. Thus, new antagonists of the ADP-receptor (P2Y12)-mediated platelet activation pathway have been developed in the past including prasugrel (Efient) and ticagrelor (Brilique). Both new antiplatelet drugs are effective P2Y12 receptor blocker that are characterized by a fast onset after first administration and a reliable antiplatelet effectiveness. Prasugrel and ticagrelor were investigated in large prospective randomized clinical trials in patients with ACS. Based on their beneficial results in comparison to conventional DAPT (aspirin plus clopidogre)l, these agents have found their way into the recent international guidelines for treatment of patients with acute coronary syndromes. Both antiplatelet agents demonstrated superiority with respect to the primary composite endpoint (cardiovascular death/non-lethal myocardial infarction/stroke). Ticagrelor even exhibited a mortality benefit over the comparator, but both compounds also increased the risk of spontaneous major bleedings to a significant extent. Nevertheless, prasugrel and ticagrelor in combination with aspirin is strongly recommended as first antiplatelet treatment option in patients presenting with ACS in the emergency department.

Stable ischemic cardiopathy: when is it time for coronarography?

Marcello Galvani (Forlì, Italy)

Coronary artery disease is the leading cause of death and disability worldwide. An invasive approach to the evaluation and treatment of CAD is common, yet the evidence that this approach favorably influences long-term outcomes in patients with stable ischemic heart disease (SIHD) is outdated. In randomized trials conducted in the 1970s, surgical revascularization (CABG) improved survival compared to medical therapy. The benefit was most apparent in subset with high-risk anatomic features. No effective medical treatment (i.e. ASA, beta-blockers, ACE-inhibitors, statins, lifestyle interventions) was however available in those years. Optimal medical treatment alone is expected to reduce clinical events about 50%. More recently, optimal medical treatment has been compared with revascularization (both surgical and percutaneous) in several patient populations, including those with severe left ventricular systolic dysfunction (STICH trial), and those with SIHD without severe left ventricular systolic dysfunction (COURAGE trial), particularly when associated with diabetes (BARI-2D). A part from specific patient-subsets, these studies indicate that revascularization does not affect survival or the occurrence of non-fatal myocardial infarction both at short and long-term. This could, at least partially, explained by the fact that in these studies patients were randomized after, and not before, the performance of coronary angiography. This may have introduced a selection bias which may have caused the exclusion of patients with more severe and extended coronary artery disease and obscured the benefits of coronary revascularization. Retrospective analysis of the COURAGE trial, together with information provided by observational studies, shows that the outcome of SIHD patients depends by the extension and severity of myocardial ischemia as detected with stress imaging. The relief of moderate to severe ischemia by appropriate coronary revascularization may improve the outcome of patients in the case that myocardial ischemia is causally related to adverse events. On the contrary, mechanical treatment of ischemia would not translate into clinical benefit if ischemia is only a marker of vulnerability of the patient.

The hypothesis that, with the background of optimal medical therapy, coronary revascularization can improve the clinical outcome of SIHD patients with moderate to severe ischemia is currently being tested in the ISCHEMIA trial. In this study about 8,000 patients with such features are randomized, before coronary angiography, to optimal medical therapy or to optimal medical therapy and revascularization. The study hypothesis is that revascularization will improve the incidence of major adverse cardio-vascular events by 20% over an average of approximately 4 years. In patients randomized to optimal medical therapy, coronary angiography will be reserved for refractory angina symptoms, acute coronary syndrome, acute ischemic heart failure, ore resuscitated cardiac arrest. The results of the ISCHEMIA trial will have profound implications for guidelines, health policy, and clinical practice.

How to optimize coronary angioplasty pre treatment

Mehmet Birhan Yilmaz (Sivas, Turkey)

Percutaneous coronary intervention in patients with stable coronary artery disease is today's one of the most frequently performed invasive procedures, and results in improved quality of life in the selection of right patient and preangioplasty treatment.

Preangioplaty treatment generally focuses on four different domains.

1-Drugs to avoid or to stop before angioplasty such as metformin

2-Drugs to prevent contrast induced nephropathy such as hydration, N-acetyl cysteine

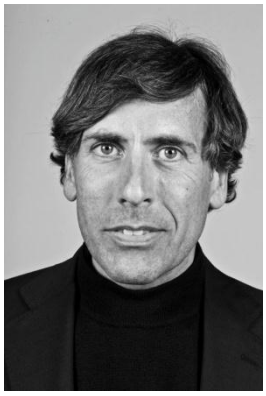
3-Drugs to improve longevity-durability of the procedure (procedural success) such as antiplatelets.

4-Drugs to improve overall prognosis of the patient such as statins

In this presentation, these four categories will in-depth be considered in order to optimize patients outcome.

Which is the best treatment for stable angina pectoris: cardiologists point of view

Francesco Pelliccia (Rome, Italy)



The objectives in treating angina are relief of pain and prevention of disease progression through risk reduction.

Mechanisms, indications, clinical forms, doses, and side effects of the traditional antianginal agents - nitrates, β-blockers, and calcium channel blockers – will be reviewed.

A number of patients have contraindications or remain unrelieved from anginal discomfort with these drugs.

Among newer alternatives, ranolazine, recently approved in the United States, indirectly prevents the intracellular calcium overload involved in cardiac ischemia and is a welcome addition to available treatments. None, however, are disease-modifying agents.

Two options for refractory angina, enhanced external counterpulsation and spinal cord stimulation (SCS), are presented in detail. They are both well-studied and are effective means of treating at least some patients with this perplexing form of angina.

Traditional modifiable risk factors for coronary artery disease (CAD) - smoking, hypertension, dyslipidemia, diabetes, and obesity - account for most of the population-attributable risk. Individual therapy of high-risk patients differs from population-wide efforts to prevent risk factors from appearing or reducing their severity, in order to lower the national burden of disease. Current American College of Cardiology/American Heart Association guidelines to lower risk in patients with chronic angina are reviewed.

The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showed that in patients with stable angina, optimal medical therapy alone and percutaneous coronary intervention (PCI) with medical therapy were equal in preventing myocardial infarction and death.

The integration of COURAGE results into current practice will be discussed.

For patients who are unstable, with very high risk, with left main coronary artery lesions, in whom medical therapy fails, and in those with acute coronary syndromes, PCI is indicated.

Asymptomatic patients with CAD and those with stable angina may defer intervention without additional risk to see if they will improve on optimum medical therapy.

For many patients, coronary artery bypass surgery offers the best opportunity for relieving angina, reducing the need for additional revascularization procedures and improving survival.

Optimal medical therapy, percutaneous coronary intervention, and surgery are not competing therapies, but are complementary and form a continuum, each filling an important evidence-based need in modern comprehensive management.

Risk assessment of head trauma patient at his arrival in the Emergency Room

Gianfranco Cervellin (Parma, Italy)

Head trauma is one of the most frequent disabling diseases, with annual incidence of approximately 250-600 patients per 100,000, and mortality of 17 cases per 100,000. The mild head injury is nearly 15 times more frequent than the moderate, and more than 20 times than the severe. Although there are still contradictions regarding the clinical significance of the term "head injury", it can not be considered synonymous with traumatic brain injury. The main challenge in the diagnosis lies in the fact that severe intracranial lesions are often associated with mild head injury, especially in the presence of specific risk factors. Despite the diagnostic gold standard is represented by CT, its systematic performance in all patients is unadvisable for limited prevalence of positivity, radiological risk, high cost and complexity. Several rules have been defined to identify patients with higher risks for CT findings and/or neurosurgical intervention. The guidelines and recommendations, which are typically based on patient history and clinical examination, include the Canadian CT Head Rule, the New Orleans Criteria, CT in Head Injury, the Scandinavian Neurotrauma Committee guidelines, and the National Institute for Clinical Excellence guidelines, and are intended to safely identify patients with intracranial complications after MHI and reduce CT usage, with very high sensitivities for ICI. However, in a recent evaluation, at least 10% of physicians reported that Canadian CT Head Rule and New Orleans Criteria guidelines were uncomfortable and approximately 5% of them misinterpreted the guidelines and did not order a CT when it was instead required. Several potential biomarkers have been proposed for the screening of patients, but protein S100B seems now the most promising for some clinical and analytical considerations. The clinical significance of S100B measurement has substantially increased throughout several areas of clinical neuroscience, from follow-up and therapeutic monitoring of neurological malignancies, to a wide spectrum of traumatic, ischaemic and degenerative diseases. The diagnostic value of S100B and its NPV in the assessment of several neurological diseases is remarkable and, importantly, is not compromised by production from extracranial sources. After performing a meta-analysis of clinical trials in patients with mild head injury, we calculated a cumulative area under the curve of 0.753 (95% CI, 0.752-0.754), a negative predictive value of 97.7% (95% CI, 97.5-97.8 %) and positive predictive value of 23.6% (95% CI, 23.2-24.0%) for brain injury. We therefore developed a diagnostic algorithm based on the preliminary assessment of the Glasgow Coma Scale (GCS). Patients with GCS <14 should be subjected to CT, those with values GCS14-15 without risk factors can be discharged, whereas protein S100B is assessed stat in those with GCS 14-15 and the presence of risk factors. According to the value of the marker, patients with a concentration below the diagnostic cut-offs can be discharged, whereas CT must be performed in those with higher concentrations. By combining the percentage of positive CT scans in patients with mild head trauma and the negative predictive value of protein S100B, this protocol would safely abate unnecessary CT by 30-50% and costs by 28%. Innovative and non-invasive diagnostic tools such as the assessment of protein S100B should hence be further promoted as safe screening tools, to support the clinical decision making to omit CT imaging in those cases of MHI that are characterized by a low-probability of brain injury.

Analgesic efficacy of orodispersible paracetamol in patients admitted to the ED, from triage to discharge.

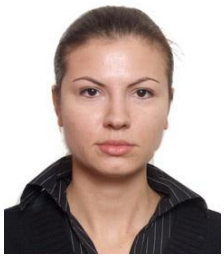
Benedetta De Berardinis (Rome, Italy)

Acute pain is the most frequent complain in emergency department (ED) admission, but its management is often neglected, placing patients at risk of oligoanalgesia. Inadequate pain management remains a major challenge for health care provides. Despite extensive research on the mechanism of acute pain, identification of factors leading to poor pain management, and development of evidence-based strategies, the transfer of this knowledge into effective clinical practices has been surprisingly slow. Oligonalagesia has been widely recognized as an issue in ED patients. Acute pain is reported by 60% to 80% of ED inpatients but is frequently undertreated. Overall, an insufficient proportion of patients with acute pain receive any type of analgesia, and pain relief remains unsatisfactory. Several factors have been associated with oligoanalgesia. First, the inaccurate assessment or lack of assessment of patients' pain is a major predictor of insufficient pain treatment. The underestimation of pain by physicians can be circumvented with the use of pain scales. Second, better knowledge of effective pain management is expected to correlate with a decreased prevalence of opiophobia and under dosing of opioid analgesics. Other factors such as sex, ethnicity, age, language, educations, and cultural and socioeconomic backgrounds are also associated with disparities in treatment. A recent study showed that poor interactions between ED physicians and patients had a negative impact on pain management. It is clear that substantial improvement in pain management in ED patients will depend on documenting pain intensity using validates scales, establishing clear strategies for use of opioid and nonopioid analgesics, and educating ED staff in this area. In our study the percentage of the patients satisfaction with pain management in ED are statistical significant but the drug use are different, in the first part of ED visit the ketorolac is the most drug used in the ED. The discharge drug is the paracetamol and its association with codeine. In particular is interesting the use of orodispersible paracetamol in patients admitted to the ED and its analgesic efficacy.

Opioids may represent a valid alternative to NSAIDs either alone or in combination with acetaminophen. In this setting we would like to underline the importance of paracetamol.

4 dimentional ecocardiography for the management of AHF patients

Aleksandra Sljivic (Belgrade, Serbia)



Acute heart failure (AHF) is defined as the rapid onset of symptoms and signs secondary to abnormal cardiac function and it is life threatening and requires urgent treatment. AHF can manifest as acute *de novo* or acute decompensation of chronic heart failure. Echocardiography is an essential tool for the evaluation of the functional and structural changes underlying or associated with AHF, as well as in the assesment of acute coronary syndromes (ESC Guidelines for the diagnosis and treatment of AHF).

4D Echocardiography (4DE) is not so new a technique in medical tehnology that can be integrated so as to improve health care. Ultrasound is now routinely used to guide therapeutic interventions, and as tehnology advances, 4DE will emerge as a standard of acquisition which should simplify the diagnostic problem.

Advantages of using 4DE allows for both qualitative and quantitative assessment of regional wall motion in a faster, more accurate and comprehensive manner, compared to 2DE, it is possible to eliminate apical foreshortening and optimize volumetric quantification, 4DE LV volumes and function do not rely on geometric assumptions about its shape and time-saving analysis of LV geometry and function can be obtained from single 3D full volume data set (volumes, sphericity, ejection fraction, regional wall motion, disynchrony, deformation and mass).

Limitations of this technique, especially in patients with AHF is that good image quality is a prerequisite for LV quantitation, which is often difficult in these patients, because they often do not have regular cardiac rhythm and because cooperation of patients for breath holding is essential, there is often poor quality acqusition soon after the stabilization of a patient. There is limited evidence regarding the reference values for LV parameters and the relatively low temporal resolution of 3DE limits the assessment of regional wall motion .

Advances in acquisition and post processing continue to evolve and may lead to more routine utilization of this tehnology .

Combination for high sensitivity troponin and Heartscape ECG

Irene Lalle (Rome, Italy)

Acute myocardial infarction (AMI) is a major cause of death and disability worldwide. Coronary artery disease (CAD) is estimated to affect 16.3 million people in the USA; of these, nine million have angina pectoris and nearly eight million have had an acute myocardial infarction (AMI). Delayed 'rule in' increases morbidity and mortality, particularly in patients with pre-existing CAD, while delayed 'rule out' prolongs the time spent in the emergency department (ED), increasing patients' uncertainty and anxiety and resulting in a significant cost to the healthcare system.
ECG and cardiac troponin (cTn) form the diagnostic cornerstones of clinical assessment in ED. Troponin levels peak at 12 hours, and stay elevated for 10 days or more. The 12-hour wait for the levels to peak remains the Achilles heel of this biomarker. Newer, more sensitive troponin assays have been introduced to rectify this weakness. Lowering troponin cutoff to the 99th percentile can increase the number of false-positive results, on the other hand, the absence of detectable hs-TnT levels rules out acute myocardial infarction with very high negative predictive value.
Particularly challenging in ED is distinguishing AMI from cardiac non-coronary artery diseases (CNCDs) such as hypertensive urgency/ emergency, myocarditis, pericarditis, acute heart failure and cardiac arrhythmia that have been reported as potential causes of elevations in conventional troponins and even more novel more sensitive assays. Haaf et al demonstrated that the combined use of hs-cTn at presentation and its early absolute change, as low as 0.005 mcg/L in the first hour, excellently discriminates between patients with AMI and acute CNCD (98.4% of all patients with AMI had either presentation values >0.028 mcg/L or absolute changes of >0.005 mcg/L in the first hour).
According to the recent guideline for the management of acute coronary syndromes, blood samples should be obtained at the time of presentation and 3 h after admission when using hs-cTn assays. There is recent evidence suggesting that patients with an AMI can be reliably identified within 3 h after admission with up to 100% sensitivity and up to 100% negative predictive value using a hs-cTn assay indicating that observation time may be reduced for the rule-out of AMI. Furthermore, recent studies suggest that an absolute increase of hs-cTnT values (e.g. >7 ng/L over 2 h) is superior to a relative percentage changes from the baseline.
Despite historically poor sensitivity for non–ST-elevation MI (NSTEMI) and unstable angina (UA), the 12-lead ECG remains the main technology for the initial diagnosis of MI. ECG alone is often insufficient to diagnose AMI because significant ECG changes are absent in numerous AMI patients and it is severely limited in detection of inferior, right sided, lateral, and posterior MI and has an especially low sensitivity for MI in patients with bundle branch blocks.
The Heartscape system utilizes 80 data collection points that provide a 360-degree view of the electrical activity of the heart and has been developed to detect acute myocardial ischemia in cases the traditional 12-lead ECG is inconclusive. The increased spatial view of the heart can assist emergency physicians to better risk stratify and manage difficult to diagnose chest pain patients in the hospital emergency department and can reveal important information that may reduce time to intervention while avoiding unnecessary delay associated with the need to conduct more costly and invasive diagnostic tests.
OCCULT-MI trial revealed a significant 8.7% absolute and 81% relative increase in sensitivity for MI (19.4% vs. 10.7%) and a 5.2% absolute and 73% relative increase in sensitivity for ACS (12.3% vs. 7.1%), for 80L mapping compared to the 12L. This increase in 80L sensitivity occurred without a substantial decrease in specificity.

Research proposal:
Aim of our study is to evaluate the diagnostic and prognostic role of combination of high-sensitive troponinT and HeartScape 80-lead ECG in patient referring in ED complaining chest pain, in order to evaluate the possibility of a safe and rapid rule-out, or a faster petients' selection for revascularization procedures.

Anticoagulant treatment for acute atrial fibrillation patients: past and future

Raffaele De Caterina (Chieti, Italy)

Drugs that interfere with blood coagulation are a mainstay of cardiovascular therapy. Until recently, vitamin K antagonists (VKA) were the only available orally active anticoagulants. Although effective, VKA have numerous limitations, which complicate their use. These limitations have prompted the introduction of new oral anticoagulants that target thrombin or factor Xa, key enzymes in the clotting pathway. The new oral anticoagulants, which can be given in fixed doses without coagulation monitoring, overcome most of the problems associated with VKA.

We will review the mechanism of action, pharmacological properties, and side effects of these new anticoagulants; and describes and comments the results of recently completed clinical trials in atrial fibrillation, where initial experience has been gathered. Four such new anticoagulants (dabigatran etexilate, rivaroxaban, apixaban, edoxaban) have undergone or are currently undergoing experimentation in phase III trials in such conditions. Dabigatran etexilate, rivaroxaban and apixaban have already proven to be viable alternatives to VKA in atrial fibrillation. Overall, new anticoagulants are exciting new therapeutic options, providing new treatment opportunities, but also with relevant challenges ahead.

Pharmacological or electrical cardioversion for acute atrial fibrillation patients?

Mehmet Birhan Yilmaz (Sivas)

Rapid ventricular rate and irregularity of the rhythm can cause symptoms and severe haemodynamic distress in acute AF. Patients with a rapid ventricular response usually need acute control of their ventricular rate. Atrial fibrillation usually terminates spontaneously within the first hours or days. In the case of a hemodynamic disturbance or in patients who remain symptomatic despite adequate rate control, or in patients in whom rhythm control therapy is pursued, pharmacological or electrical cardioversion of AF may be achieved by an antiarrhythmic drug or DC cardioversion. Although, the conversion rate with antiarrhythmic drugs is lower than with DC cardioversion, which requires sedation, drugs are deemed to be more comfortable or less painful to the patient. On the other hand, patients who undergo pharmacological cardioversion require continuous medical supervision and ECG monitoring during the drug infusion and for a period afterwards to observe proarrhythmic events. Herein, drugs versus devices in the context of acute AF will be

How to prevent stroke in acute atrial fibrillation patients

Maurizia Rasura (Rome, Italy)

The morbidity and mortality associated with atrial fibrillation (AF) are related mainly to ischaemic stroke and the prevention of thrombo-embolism is an important component of the patient management. The pravalence of AF is 1 % of American population and it expected to increase by 2.5 fold by 2050. The choice of optimum antithrombotic therapy depends on the risk of thrombo-embolism, and the assessment of thrombo-embolic risk using validated stratification schemes, such as the $CHADS_2$ score, is a critical step. The pattern of AF (paroxysmal, persistent, or permanent) should not influence the selection of antithrombotic treatment. Several clinical trials have demostrated that anticoagulant treatment, antagonist of vitamine K (VKA), is the best therapy to prevent stroke in patients with AF. Furthermore the goal to prevent stroke in AF is not only the choise of VKA , but the time within terapeutic range. Despite this relevant evidence most patients with AF are not treated with VKA for several reasons: difficulty to mantain therapeutic INR, physicians understimate risk of stroke and overstimate risk of bleed.

The development of new antithrombotic agents, presented as “ideal anticoagulant”, that are easier to use and have a superior benefit-to-risk ratio will extend treatment to a greater proportion of the AF population at risk.

Clinical experience with Vernakalant in ED

Juul-Möller Steen (Malmö, Sweden)

Background:

In patients with acute atrial fibrillation, requiring rhythm control, it is important to perform the conversion without delay. This in order to minimize remodelling of the atrium and avoid prolonged atrium fibrillation-related symptoms. The treatment includes drug treatment and/or electrical cardioversion.

Electrical cardioversion is a highly effective treatment modality, with an acute cardioversion rate of 90 % or more. However, it requires anaesthesia, and unstable hemodynamic patients may be exposed to serious side effects including proarrhythmia and hypotension. The patient has to be in a fasting condition for at least four hours prior to the electrical cardioversion attempt.

Until now, the drugs used for fast atrial fibrillation conversion includes Class 1c drugs. The conversion efficacy is lower compared to that of electric cardioversion, 65-80 %. These drugs all expose the patient to risk for proarrhythmia, including ventricular tachycardia and ventricular fibrillation, mostly within the first 24-72 hours. This risk is related to concomitant coronary artery disease and reduced left ventricular function and probably also related to the patients hemodynamic state. The proarrhythmia risk is a consequence of the drug-effect on the ventricular myocardium besides the required antiarrhythmic effect on the atria.

Vernakalant:

Vernakalant is a novel drug entity with a pronounced atrial selectivity. This reduces the risk of proarrhythmia. Clinical trials with vernakalant have demonstrated conversion efficacy of 50 %. The conversion was fast, with 11 minutes time to conversion (median). The atrial selectivity has been confirmed in several clinical trials where the QRS-duration and the QTc intervals have been unaffected by the drug. Also the RR-intervals have been unaffected, demonstrating lack of effect on the His-bundle and the Sinus Node.

Clinical efficacy in Malmö, Sweden:

Vernakalant (Brinavess ^{TM}) has been approved in Europe for conversion of acute atrial fibrillation since late 2010. From January 2011 it has been used for this purpose at the Emergency Department at the Skåne University Hospital in Malmö, Sweden. The treatment at this hospital has been in accordance with a set of rules, specifying that the patients are identical to the group of patients with acute atrial fibrillation normally undergoing electrical cardioversion. Electrical cardioversion is the preferred treatment for these patients in the Nordic countries. Added contraindications are severe aortic stenosis and hypotension (SBT lower than 90 mm Hg). Also, we have aimed for treating patients with a short duration of the acute atrial fibrillation, preferably less than 12 hours.

For the period January 2011-March 2012 we have treated 179 patients with vernakalant. In all, 222 patients were evaluated for this treatment, but 45 were rejected because of contra-indications: Six patients due to hypotension (SBT < 90 mmHg), 1 patient with severe Aortic stenosis, 3 patients with acute coronary syndrome and 32 patients with ongoing per oral Class 1 or 3 treatment. This was a contraindication at our hospital for the first 6 months. After that period, the patients with ongoing per oral Class 1 or 3 antiarrhythmic treatment could also be treated with vernakalant.

The efficacy of vernakalant conversion was 69 % for the first period (january-august 2011). It was 81 % for the period september-december 2011, and 85 % for the period january-march 2012. This indicates that the treatment efficacy is higher than in the clinical trials and that it may be affected by the handling of the patients at the Emergency Room.

Among the patients who did not respond to vernakalant treatment, spontaneous conversion occurred in 5 % while waiting for electrical cardioversion. The efficacy of electrical cardioversion in the remaining patients was unaffected by earlier Vernakalant treatment, and was found to be 95 %.

The mean period from the start of Vernakalant infusion to sinus rhythm was 10 minutes (1-90 minutes). The mean period from the patient presenting themselves at the Emergency Room to vernakalant treatment was 1,5 hour (0,5-3,0 hrs). The mean monitoring period after vernakalant conversion was aimed at 2,0 hrs and was found to be 2,5 hrs. The measured mean duration from the patient presenting at the Emergency Department to discharge after successful Vernakalant conversion was 3,5 hrs (2,3-6,2 hrs).

The estimated time period from start of atrial fibrillation symptoms to presenting at the Emergency Department was 3,5 hrs (0,5-6,0 hrs). This is in contrast to the time period for patients treated with conventional electrical cardioversion, 8,0 hrs (0,5-32 hrs).

The side effects were rather frequent, but none were serious. The side effects were transient, and none had duration of > 3 minutes. In 24 % the patients experienced sneezing, in 10 % metal taste and in 1 % hypotension. The two patients with hypotension were both dehydrated. This is a reminder of the importance to avoid treating dehydrated patients and a recommendation to pre-treat patients with saline infusion.

Conclusion:

Vernakalant treatment of patients with acute atrial fibrillation was found to be effective and fast, and the patients did not experience serious side effects. No proarrhythmic event was seen. Also, remaining patients could be treated successfully with electrical cardioversion.

The Finnish experience with Vernakalant in AHF patients in ER

Harri Hyppölä (Kuopio, Finland)

In Finland, we have used Vernakalant (Brinavess) from the beginning of year 2011. Kuopio University Hospital was one of the first hospitals that begun to use Vernakalant in Finland. We have now used Vernakalant for more that hundred patients with very good result. The overall success rate for cardioversion is almost as high as 80 %. The reason for high success rate is obviously that we have used pharmacological cardioversion in Emergency Department with patients whose AF has lasted mainly for only 12 to 24 hours. Most common side effect has been taste disturbance, affecting about 15-20 percent of the patients. This has been reversible and mostly mild.

Our experiences are encouraging and the use of Vernakalant in acute AF patients seems to be good option for those who are eligible for pharmacological cardioversion. Patients can be discharged after two hours observation and there is no need for overnight stay as is the case for patients with electrical cardioversion who live alone. In Finland, the use of Vernakalant has also spread to smaller hospitals where there are no anesthesiologists available.

The Austrian experience with Vernakalant in AHF patients in ER

Anton Sandhofer (Innsbruck, Austria)

Vernakalant is used in the emergency department of the Medical University in Innsbruck since April 2011. Meanwhile Vernakalant was administered to 64 patients aged 34 to 83 years with recent onset atrial fibrillation. In the beginning only relatively young and healthy subjects were selected. As experience is growing we also choose patients with higher age and more comorbidities. The success rate was initially about 80%, but decreased due to treatment of patients with more cardiac comorbidities. However, we experienced clinical significant adverse events in only three patients: The first was broadening of the QRS-complex to a transient left bundle branch block accompanied by heavy sneezing and coughing. The second patient experienced a self-terminating ventricular tachycardia of 10 beats, and the third an asystole of 6 seconds. Remarkably in all three patients no intervention was needed and all three patients converted to a stable sinus rhythm.

In summary, we use Vernakalant in an increasingly broadening cohort of patients with recent onset AF, as in our

Spanish guidelines for the management of Atrial Fibrillation in ED

Alfonso Martín Martínez (Madrid, Spain)

Atrial fibrillation is the most frequently sustained arrhythmia managed in emergency departments, and accounts for a high and increasing prevalence in Spain. Atrial fibrillation increases mortality, is associated with substantial complications and, therefore, has a relevant impact in running of the health care system. Management requires consideration of diverse clinical variables and a large number of possible therapeutic approaches, justifying action plans that coordinate the work of medical staff in the interest of providing appropriate care and optimizing resources. These evidence-based guidelines contain recommendations for managing atrial fibrillation in the special circumstances of hospital emergency departments, and have been developed together by the Arrhythmia Division of the Spanish Society of Emergency Medicine (SEMES) and the Electrophysiology and Arrhythmia Division of the Spanish Society of Cardiology (SEC). Atrial fibrillation usually affects elder people, with a high risk of stroke, structural heart disease and co.morbidity, and that attend emergency departments mainly due to acute symptomatology, all of them critical decision factors for management. Moreover, recent onset episodes are usually managed at emergency departments, and that highlights the importance of an accurate management in this setting, in order to increase the chance of achieving sinus rhythm restoration and to prescribe an early stroke prophylaxis. In this presentation (and in the related consensus document) are discussed in detail Stroke prophylaxis (the mainstay of management, either during sinus restoration as a long term prophylaxis after acute management), rate control (the heart rate to be achieved, the drug regimes to be used-with a special emphasis on beta-blockers), rhythm control (the benefits of this strategy in acutely symptomatic recent onset episodes, the decision factors for management and the procedures either pharmacological or electrical depending on patients' profile), and related diagnostic and logistic issues. [For further information the consensus document is available at Emergencias 2012;24:300-324]

Syncope and pseudo-syncope: from doubt to clinical certainty

Fabrizio Ammirati (Rome, Italy)

New Guidelines on the Diagnosis and Management of Syncope of the ESC 2009 present the following new features:

1. inclusion of syncope in the large group of blackouts and its definition as a "loss of consciousness due to transient cerebral hypoperfusion characterized by rapid onset, short duration, spontaneous and complete resolution"
2. detailed classification of various forms of orthostatic hypotension

3. New data on the epidemiology useful for differential diagnosis

4. diagnostic approach based on risk stratification also by "scores" (OESIL SCORE, SCORE EGSYS) aimed to identify patients with good prognosis compared to patients with cardiac syncope with worse prognosis

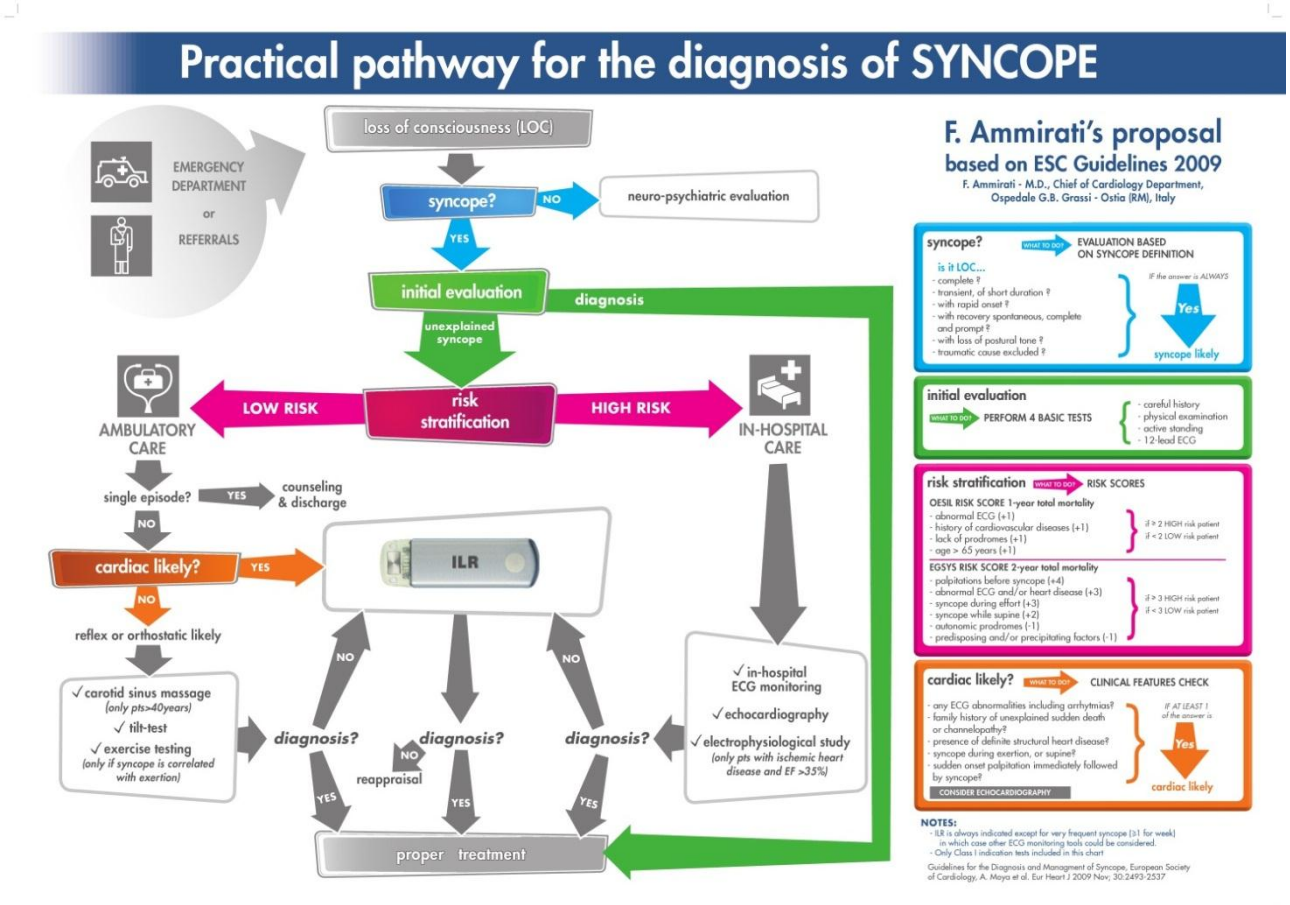
5. important diagnostic role of ECG monitoring is not extended by devices such as implantable and implantable loop recorder

6. An update of evidence-based therapy

7. special attention for syncope in the elderly and in children

8. particular attention to the quality of life for therapeutic purposes and for any limitations on normal daily activities

The flow-chart (in attachment) is a practical pathway for the diagnosis of SYNCOPE



Risk stratification: between logic and intuition

Clifford Mann (London, United Kingdom)

Logic is often regarded as a key aspect of the rational mind. However this assertion ignores the fact that logic provides no new information; instead it constructs valid arguments from given facts. In consequence logic is susceptible to misinformation and consequent poor decision making. Intuition rejects rational thought and analysis and as such is contrary to the principles of scientific enquiry and evidence based medicine. Expert clinicians in complex situations use a system of professional intuition based upon inference and empirical data derived from previous outcomes.

Clinical decision rules are a method of distilling professional intuition into aids for the inexperienced

Diagnostic paths in Short Intensive Observation

Pietro Lentini (Rome, Italy)

Per O.B.I. si intende un' area del dipartimento di emergenza dedicata a pazienti che necessitano di ulteriore osservazione clinica dopo la breve osservazione del pronto soccorso.

Una commissione di esperti riunita dalla regione Lazio esprime che l' OBI è una modalità di gestione delle emergenze urgenze dei pazienti con problemi clinici acuti, ad alto potenziale di reversibilità che richiedono assistenza intensiva di norma non inferiore alle 6 ore e non superiore alle 36 ore con l' obiettivo di pervenire ad un rapido inquadramento diagnostico e terapeutico e di valutare le reali necessità di ricovero appropriato e di dimissione sicura. L' obiettivo di tale struttura è quella di dare valutazione diagnostica, osservazione long-time e terapia a breve termine di patologie urgenti e di determinare il miglioramento dell'appropriatezza dei ricoveri.

E' fondamentale che in ogni Azienda vengano redatti opportuni percorsi diagnostico-terapeutici per le patologie più frequenti, condivisi dopo la opportuna contestualizzazione nella singola realtà. E' nostra esperienza che proprio in quest' ambito possono esprimersi più compiutamente le potenzialità che tale modello organizzativo fornisce. La patologia più presente nel reparto di OBI del Vannini è la sincope. Una recente revisione delle linee guida della sincope ha introdotto alcune novità emerse dalla letteratura internazionale. La più importante riguarda la definizione stessa. Si parla infatti di "perdita di coscienza transitoria dovuta ad un'ipoperfusione cerebrale globale, caratterizzata da rapida insorgenza, breve durata, recupero completo e spontaneo". Innovativo è l'approccio diagnostico focalizzato sulla stratificazione del rischio: basso e alto rischio. Il secondo necessita di osservazione in OBI. Nella più recente letteratura, inoltre, sono stati pubblicati alcuni metodi di stratificazione del rischio nel paziente con sincope. I più affidabili sono quelli emersi nello studio EGSYS 2 (Evaluation of Guidelines SYncope Study) e nello studio OESIL (Osservatorio Epidemiologico della Sincope nel Lazio). Notevole importanza ha assunto nella diagnostica il monitoraggio elettrocardiografico prolungato con dispositivi impiantabili. Lo studio ISSUE 2 (International Study of Syncope of Uncertain Etiology 2) ha infatti ipotizzato che il presupposto per la selezione dei pazienti con sincope neuromediata, che possano trarre beneficio dall'impianto di pacemaker, dovrebbe essere la dimostrazione di un'asistolia spontanea e non rilevata al tilt test. Nei pazienti anziani, per l'alta incidenza di sincopi neuro riflesse ed ortostatiche, è sempre importante eseguire la prova di ipotensione ortostatica, un test semplice ed economico. L'approccio in OBI alla sincope mette in evidenza l' importanza di una "Sincope unit" che coinvolga varie figure professionali e unità operative di ricovero ed ambulatoriali che possano seguire il paziente in un percorso diagnostico e terapeutico che non si esaurisce in ospedale.

In un periodo caratterizzato dalla tendenza alla deospedalizzazione e alla riduzione del numero di posti letto per acuti , l'O.B.I. offre peraltro un setting assistenziale alternativo al ricovero tradizionale, garantendo all'utenza prestazioni qualitativamente ottimali con minore utilizzo di risorse per varie condizioni patologiche spesso complesse e di estrema diffusione come la sincope.

Sudden Death: the experience from the territory.

Fedele Clemente (Campobasso, Italy)

In tutte le regioni d'Italia sono attualmente attivi ed operativi i Servizi di Emergenza Territoriale "118", per un totale di 103 Centrali Operative 118. Il principale elemento per la valutazione della loro efficacia è rappresentato dalla verifica della sopravvivenza nell'Arresto Cardiaco, causa di Morte Improvvisa, in cui è necessario un ottimale compromesso tra Risorse impiegate e Qualità della prestazione.

L'epidemiologia della Morte Improvvisa, secondo diversi studi internazionali, colpisce 1 paziente ogni 1000 abitanti ed in Europa le vittime della Morte Improvvisa sono approssimativamente 375.000 all'anno. L'OMS riferisce che i maschi colpiti sono 90 ogni 100.000, mentre le femmine sono 60 ogni 100.000. Lo studio MONICA riporta che su 100.000 persone 88 hanno un'età compresa tra 55 e 64 anni, mentre 286 hanno un'età compresa tra 65-74 anni. Il principale metodo di ricerca epidemiologia è rappresentato dall'UTSTEIN Style, adottato dall'International Liaison Committee on Resuscitation (ILCOR).

Anche la Società Italiana Sistema 118 (SIS118) ha condotto una ricerca sull'argomento, adottando lo schema dell'Utstein Style modificato. Lo studio ha interessato il 23% delle Centrali Operative italiane ed ha riguardato una popolazione di 13.297.387 soggetti (circa il 23% della popolazione italiana). Il periodo di studio è durato circa 3 anni, dal 2008 al 2011.

La ricerca ha rilevato n. 3.780 arresti cardiaci confermati (0,03% della popolazione - 1 ogni 3.517 soggetti). Dei 2.517 arresti cardiaci, hanno ricevuto un tentativo di rianimazione il 60% dei casi (2.264) e di questi, quelli che avevano un'eziologia cardiaca, sono stati l'80% (1.805). Di questi ultimi, quelli testimoniati dai mezzi di soccorso avanzati, dai mezzi di soccorso di base e dagli astanti sono stati il 91% (1.647). I ritmi defibrillabili sono stati riscontrati nel 28% dei casi (503) e la ripresa del circolo spontaneo (ROSC) è avvenuta nel 19% dei casi (353).

Per quanto vanno riconosciute alcune limitazioni alla ricerca, dovute alla discontinuità della raccolta dati, ai tempi di raccolta e, in alcuni casi, ad una parziale incompletezza dell'inserimento dei dati nel database, sono stati ottenuti risultati decisamente significativi che spingono ad effettuare una rivalutazione dei dati attualmente riportati dalla letteratura internazionale. Sicuramente, sono da programmare ulteriori studi più accurati e più ricchi di dettagli.

In ogni caso, l'avvento di un Sistema di Emergenza Territoriale organizzato e professionalizzato, adeguatamente presente su tutto il territorio nazionale, può permettere un più puntuale inquadramento della tematica e può fornire maggiori suggerimenti per le decisioni terapeutiche che ne seguono.

From Syncope to Sudden Death

Cinzia Sighieri (Rome, Italy)

Syncope represents a symptom; when evaluating it, on one hand a precise cause must be looked for in order to allow a precise treatment and on the other a correct stratification of the risk must be carried out so as to identify patients in whom a cardiac origin is most likely.

The most common cause of cardiac syncope are arrhythmias; they may cause an haemodynamic instability which may determine a critical fall of the cardiac output and cerebral hypoperfusion. There is no doubt that syncope recognizes a multifactorial mechanism based on the cardiac rate, on the type of arrhythmia and on the adequate vascular response (for example baroreceptor response to orthostatic hypotension induced by the arrhythmia). A sinus atrial node dysfunction and the tachy-brady syndrome may be a cause of syncope especially when the arrhythmia is brusquely interrupted; another cause may be atrio-ventricular blocks (Mobitz type II, high grade or complete block). A bradycardia with prolonged repolarization may induce polymorphic ventricular tachycardia such as torsades de pointes.

Normally, the patients regain consciousness before the arrhythmia terminates. If the haemodynamic condition remains inadequate for the tachycardia, the loss of consciousness persists. In this case the regain of consciousness is not spontaneous and the event cannot be classified as a syncope but represents a cardiac arrest.

Many drugs may cause brady and tachycardias. Many antiarrhythmic drugs may cause bradycardia especially for their effect on the sinus-atrial function or on the atrio ventricular node. Syncope due to torsades de pointes is not infrequent especially in women and is often due to drugs which prolong the QT interval. This occurs more often in patients who have a long QT syndrome. Drugs which prolong the QT interval belong to different categories and are continuously monitored.

Structural heart disease may also cause syncope when the cardiovascular demand exceeds the reduced heart capacity to increase cardiac output. Multiple mechanisms may be involved; not only the reduced cardiac output which is observed in the hypertrophic cardiomyopathy but also an inappropriate baroreceptor response, an orthostatic hypotension or an arrhythmia may lead to a cardiac arrest (i.e.aortic stenosis). Further on, also arrhythmias such as atrial fibrillation are frequently associated with the other causes so that the mechanism of the syncope must be considered multifactorial. The recognition of a cardiac cause of a syncope is important so as to adequately intervene when possible.

The syncope represents about 1% of the reasons of access to an emergency department and a cardiovascular cause is more frequent in the elderly population. A structural heart disease and a primary electrical disease are the main risks factors for sudden death. Different factors are able to predict outcome and have been identified and validated in prospective studies.

When the cause of a syncope remains uncertain after an initial evaluation, the following necessary step is to evaluate the cardiovascular risk score for sudden death.

The evaluation of the risk is carried out considering simple parameters such as the history, the presence of ECG abnormalities, age etc (OESIL score and EGSYS2 score) and is able to recognize patients with worst prognosis who require hospitalization once they arrive at the emergency department, patients with a moderate risk for whom a prolonged observation for 24-36 hours is warranted or those patients with a low risk who can be dismissed rapidly after a short observation period.

The presence of a structural heart disease does not imply that the syncope necessarily correlates with the underlying disease. Some of these patients have a typical reflex syncope or in others the underlying disease such an inferior myocardial infarction or an aortic stenosis may act as stimuli for a vasovagal syncope. Often in these patients, supraventricular or ventricular arrhythmias may occur which may cause syncope. The treatment varies according to the underlying disease. In the acute cardiovascular events, treatment must be aimed at the acute event (acute myocardial infarction, pulmonary embolism, cardiac tamponade etc). In case of unexplained syncope in patients at high risk of sudden death, ICD implant does not protect from syncope episodes (SCD-HeFT Sudden cardiac death in Heart failure trial); this induces to try to search for a possible cause so as to introduce a specific treatment when possible.

The evaluation of a syncope in an emergency department has two goals: to try to understand the underlying mechanism and to stratify the risk. In this way it is possible to identify those patients who do not need further exams or treatment and who can be rapidly dismissed, to recognize those cases at high risk of sudden death who must be hospitalized and those at low risk who can be addressed to an out patient evaluation and to further diagnostic investigations when the initial evaluation is not conclusive.

Sudden Death in the airport

Carlo Racani (Rome, Italy)

M.Cesario MD, L.Cerisano MD, L.Poggipollini MD, A.Russo MD*and C.Racani MD
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"Leonardo da Vinci" Fiumicino International Airport is the largest and busiest airport in Italy and the seventh busiest airport by passenger traffic in Europe. The whole airport area covers approximately 3 hundred square kilometers, which is indeed a very large area, even larger than the city of Florence.

Every day more than twenty thousand people work here and every month approximately 3 million passengers travel through this airport. Of course such a crowded airport has a Medical Center available seven days a week, twenty-four hours a day. Fiumicino Airport Medical Center is located next to Terminal 3, in a place that allows rescuers quick access to both of the restricted area (runways, aircrafts, boarding gates, etc.) and the free-access area. This is the last annual report on our activity: approximately 10 hundred medical care and more than 1 hundred stretcher services for a total number of nearly 10 thousand health services and 8 sudden cardiac arrests occured at Fiumicino airport last year and 5 of these were associated with shockable rhytms. When our dispatchers receive a request for emergency assistance, they send out a Mobile Intensive Care Ambulance with 1 physician, 1 nurse and 2 drivers/professional rescuers on board. The average time needed to arrive on scene is 4 minutes, but unfortunately, if the rescuers have to reach the farthest areas of the airport, it can take up to 8 minutes for our team to reach the patient... and this time is too long to save cardiac arrest victims. That's why Aeroporti di Roma has provided publicly accessible defibrillators throughout the entire airport area. Actually automated defibrillators allow bystanders to deliver lifesaving shocks several minutes earlier than professional rescuers can arrive on scene. And we know that each minute saved increases the victim's chance of survival by ten percent. At Fiumicino airport Automated External Defibrillators (AED) units are visibly located in cabinets throughout the airport terminals and linked to the Airport Medical Center. Removing an AED from a wall cabinet automatically notifies the Airport Medical Center's Coordinator that immediately dispatches the rescue team to the area.

Case report.

Sudden death is defined as a natural death, preceded by sudden loss of consciousness, which occurs within 1 hour of onset of symptoms, in patients with or without known pre-existing cardiopathy, but in which the time and mode of death are unexpected. Ventricular fibrillation is the cause of 85% of cardiac arrests. In this case report a 33 years old man with no history of syncope and a family history of sudden cardiac death while was in line at the check-in, syncopal episode occurred with falling, decisive stab wound in the occipital region.The check-in staff immediately contacted the operations room communicating the presence of "syncopal episode in patients with tonic-clonic contractions. The Medical personnel arrived on site finding the patient in cardiopulmonary arrest, with isocoriche, isocicliche pupils and with stab wounds in the occipital region. For this reason we started the cardio-pulmonary resuscitation following the international protocol and applied DAE which identified a shockable rhythm (ventricular fibrillation). Five DC shock were carried out but ineffective.

Sinus rhythm was obtained after dispensing the 6th DC shock and after administration of amiodarone 2 phials and adrenaline 2 phials. Also we obtained the restoration of spontaneous respiration (SO_2 95%).

At this point we proceeded to administration of O_2, and maintaining the patient under ECG monitoring graph transfer of the same at the nearest hospital where the patient underwent endotracheal intubation for signs of hypoxic coma and was admisted at the intensive care unit and then transfer in cardiology. There were no significant morphological alterations in the echocardiography and so the patient underwent coronary angiography study that documented coronary free from injury. Then they decided to proceed to ICD (implantable cardioverter-defibrillator) implantation. After three days the patient was discharged in stable clinical condition.

POSTERS

A NEW METHOD FOR MICROBIOLOGICAL ANALYSIS

THAT COULD BE USED FOR POINT-OF-CARE TESTING (POCT).

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Standardized microbiological methods used in clinical analysis are based on traditional microbial enrichment on selective media, possibly followed by characterization of bacteria with molecular methods. These techniques present several difficulties, such as the subjectivity in the interpretation of genetic, biochemical or morphological tests and the possible interference of biological matrices, specially when low levels of contamination are present. In addition, standardized microbiological analyses are characterised by the high cost of the method, both in terms of labor and supplies, and above all, by the long time needed to obtain definitive results (from 3 to 7 days). These reasons have led to the development and refinement of microbiological POCTs which are now available for several microorganisms, even thought no microbiological POCT was up to now developed for the count of total viable bacteria (TVC) in serum, urine or other biological fluids.

MBS srl (a spin-off of Roma Tre University, Rome, Italy) has developed and patented an alternative method for selective counting of bacteria, called Micro Biological Survey (MBS) method. The MBS method is based on colorimetric survey performed in mono-use disposable reaction vials in which samples can be inoculated without any preliminary treatment. The analyses can be carried out by untrained personnel and anywhere where they are necessary, without the need for any other instrumentation than a thermostated optical reader that can automatically detect the colour change providing the number of bacteria present into the sample. The MBS method measures the catalytic activity of the redox enzymes in the main metabolic pathways of bacteria, allowing an unequivocal correlation between the observed enzymatic activity and the number of viable cells present in the samples. The time required for a color change is inversely related to the log of bacterial concentration; like an enzymatic reaction, the greater the number of bacteria, the faster the color change.

The objective of this study was the primary validation, in accord with ISO 13843:2003 (Guidance on validation of microbiological methods), of the quantitative Micro Biological Survey (MBS) method for Total Viable Count (TVC). Validation aims to compare the results obtained with an alternative method, in this case the MBS method, with the results obtained with the reference method. To verify the equivalence between the two methods different parameters were analyzed: selectivity, linearity and accuracy. The validation has shown that the MBS method gives similar results and is in agreement with the reference methods. The MBS method could therefore represent a worthy aid in microbiological analysis as POCT device without replacing the analysis carried out with traditional methods which are very precise though often long and complex.

Research proposal:

EKG 80 leads and new biomarkers for physiopathological process on the myocardial cells.

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Introduction

Chest pain is one of the most common reasons of patients admission to the emergency room. Acute coronary syndrome (ACS) needs to be distinguished from a variety of other cardiac and noncardiac diseases that cause chest pain. ACS is divided in ST-Elevation (STEMI) and Non ST-Elevation/ Unstable Angina (NSTEMI/UA).

Around 2.5 million hospital admissions worldwide are due to NSTEMI/UA, a major cause of death and morbidity in Western countries. In-hospital death and re-infarction occur in 5% to 10% of patients and, even after antiischaemic and antithrombotic drugs are used, 5% to 10% of patients die or have a recurrent episode in the following month (1). In 2002, the WHO estimated that one third of all deaths worldwide were attributable to cardiovascular disease (CVD), and 12.6% of all deaths were caused by ischaemic heart disease. About 1 on 3 Americans have underlying CVD, and NSTEMI accounts for 1.5 million admissions to hospital each year (2, 3). It is estimated that two-thirds of acute coronary syndromes present as NSTEMI, and the remaining one third are attributable to STEMI. It is thought that patients with non-ST segment elevation may have a higher long-term risk of death and recurrence of MI than do patients with ST segment elevation (4). Coronary heart disease is decreasing in many developed countries, but is increasing in developing and transitional countries, partly as a result of increasing longevity, urbanisation, and lifestyle changes. Trends from the world's largest database of patients with acute coronary syndrome show that the percentage of patients with a diagnosis of NSTEMI/UA is rising dramatically (5). This is likely to be due to the advent of more sensitive assays for myocardial injury, earlier pharmacotherapy, and reperfusion (and prevention) of STEMI (5, 6).

Objective

Aim of this study is first of all to evaluate the diagnostic and prognostic role of new biomarkers such as : Copeptin, a plasma osmolarity and hemodynamic stress marker (7); Galectin 3, a protein is associated with heart failure, including myofibroblastic proliferation, fibrogenesis, tissue repair, inflammation and cardiac remodelling (8, 9); and Troponin T HS a specific and early protein expression of necrosis myocardial cells (10, 11). Our aim is to discover a direct correlelation between physiopathological processes and clinical signs in patients with ACS. Secondary, to demonstrate the diagnostic and prognostic validity of Heartscape 3D EKG System, the first EKG with 80 leads which ensures a complete interpretation of the cardiac function. Than, we could build a prognostic score to recognise very quickly the cause of chest pain, in specific ACS, to reduce duration of management in the emergency room.

Materials and Methods

We will enroll 100 patients presenting to ED with chest pain. Patients will be divide into four different groups: STEMI or NSTEMI at high risk (TIMI score) or Haemodynamically unstable group, NSTEMI group at low risk (TIMI score), chest pain at high risk and chest pain at low risk (low and high risk is calculated on the basis of the HEART score). We will monitor these four groups of patients with a new group of three biomarkers (Copeptine, Troponin T HS and Galectine 3), TIMI score, HEART score, EKG 80 leads, Case Report Form, ambulatory follow-up after 30 days from the hospital discharge and phone follow-up after 180 days from the hospital discharge.

Endpoints

To obtain valid and quik information on acute myocardial injury due to physiopathological process on the myocardial cells in order to direct patients to an adequate therapy which consider rapid recovery of damaged tissue. Moreover based on this study results the ED physician will have a short time decision making for the management and to rule out patients with chest pain at low risk, to reduce duration of dwell time in the ER, to avoid overcrowding and saving resources.

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Hints for Therapeutic Prospectives in Slow-Release Valproate Overdose: a Case Report.

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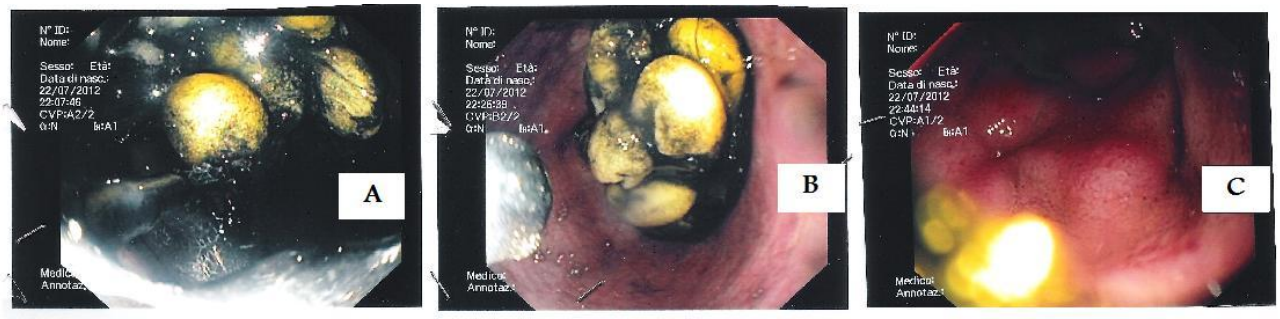
CASE REPORT: F.G., a 39 year old woman, presented herself at our Emergency Department (ED) for the consumption of high doses of slow-release sodium valproate (VPA), with suicidal intention. First, gastrolusis was performed. No improvement, rather a slow progression was observed in her state, with increasing deterioration in her mental status (GCS 15 → 12). In accordance with toxicological consult, emergency gastroscopy (EGDS) was performed, and numerous colliquated tablets were removed from the stomach (Image 1). As a result, 16 hours after her admission, she started improving and the blood level of VPA, although remained above the therapeutic range, markedly decreased. Liver function remained unaltered during the observation. Her state of consciousness improved slowly until full recovery (GCS 15). Arterial blood gas parameters, initially showing slow, continuous ascent, returned to normal range within 65 hours after her admission. Blood ammonium level, reaching its maximal value of 82 μg/dl 40 hours after admission, also started decreasing (Table 1). Taking the patient's stable clinical condition into consideration, she was referred to Psychiatric Service for Diagnosis and Treatment (PSDT), and finally emitted 8 days after her admission.

DISCUSSION: Severe acute VPA toxicity can be characterized by several biochemical abnormalities, including hyperammonemia, hypernatremia, hypocalcemia, alteration in blood pH and increased transaminases activity. In the case presented in this paper, a fundamental role was attributed to the EGDS in the treatment of slow-release VPA intoxication, which, as supported by serial blood sampling and laboratory measurements, resulted in the prompt removal of the toxic agent from the site of absorption. This constitutes a real breakthrough in the therapeutic approach of the overdoses of slow-release drugs; until now, pharmacological detoxification (such as carnitine treatment in VPA intoxication) was suggested as a first-line measure, together with hemoperfusion as Ultimum Refugium resulting in a 30 day long clinical treatment on average. In contrast, our patient was emitted in a good condition 8 days after her admission. Furthermore EGDS also allows the direct evaluation of the local damage caused by the toxic agent and the accurate estimation of the dose of the drug taken by the patient, thus aiding in planning the supportive therapy, if required.

IMAGE 1: The image illustrates the EDGS performed 6 hours after the patient's admission to the ED. In the anterior-pyloric portion and fundus of the stomach, many tablets, grouped together are visible (A). Activated carbon administered upon the patient's ED admission could only be partially removed by washing, causing remarkable difficulties in visualization of the gastric mucosa (B). About 40-50 tablets (and their remnants) were removed in multiple steps during EDGS. Deformed duodenal bulb with hyperemic mucosa – as a consequence of the previously documented peptic ulcer - was also visible during the examination (C).

TABLE 1: Results of sequential blood tests performed from the patient's admission until her transfer to PSTD.

MAIN REFERENCE: Andrew S. Davison et al. The Consequences of Valproate Overdose. *Clinical Chemistry* September 2011 vol. 57 no. 9 1233-1237.



SUDDEN DEATH IN THE AIRPORT

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Sudden death is defined as a natural death, preceded by sudden loss of consciousness, which occurs within 1 hour of onset of symptoms, in patients with or without known pre-existing cardiopathy, but in which the time and mode of death are unexpected. Ventricular fibrillation is the cause of 85% of cardiac arrests. In this case report a 33 years old man with no history of syncope and a family history of sudden cardiac death while was in line at the check-in, syncopal episode occurred with falling, decisive stab wound in the occipital region.The check-in staff immediately contacted the operations room communicating the presence of "syncopal episode in patients with tonic-clonic contractions. The Medical personnel arrived on site finding the patient in cardiopulmonary arrest, with isocoriche, isocicliche pupils and with stab wounds in the occipital region. For this reason we started the cardio-pulmonary resuscitation following the international protocol and applied DAE which identified a shockable rhythm (ventricular fibrillation). Five DC shock were carried out but ineffective.

Sinus rhythm was obtained after dispensing the 6th DC shock and after administration of amiodarone 2 phials and adrenaline 2 phials. Also we obtained the restoration of spontaneous respiration (SO2 95%).

At this point we proceeded to administration of O2, and maintaining the patient under ECG monitoring graph transfer of the same at the nearest hospital where the patient underwent endotracheal intubation for signs of hypoxic coma and was admisted at the intensive care unit and then transfer in cardiology. There were no significant morphological alterations in the echocardiography and so the patient underwent coronary angiography study that documented coronary free from injury. Then they decided to proceed to ICD (**implantable cardioverter-defibrillator**) implantation. After three days the patient was discharged in stable clinical condition

Clinical usefulness of copetin, MRproADM and suPAR in patients admitted to the emergency department with acute infections.

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Background

The aim of this study was to establish whether the outcome of patients admitted to the emergency department (ED) with acute infections may be predicted by a panel of innovative biomarkers, including copetin, mid-regional pro-adrenomedullin (MRproADM), soluble urokinase plasminogen activating receptor (suPAR) and high-sensitive C reactive (hsCRP). The variation of serum procalcitonin (PCT), which is the most reliable biomarker of active infections, was used as surrogate measure of clinical outcome.

Materials and Methods

Venous blood samples (serum and EDTA plasma) were collected at patient admission to the ED and immediately before hospital discharge. PCT, MRproADM, and copeptin were determined by immunofluorescent assays on KRYPTOR (BRAHMS AG, Hennigsdorf, Germany). The concentration of suPAR was assayed with suPARnostic® Standard ELISA (Virogates, Birkerød, Denmark), whereas hsCRP was tested by a commercial immunonephelometric assay (Behring Diagnostics, Marburg, Germany). To establish whether variations of PCT were correlated with those of other biomarkers (primary endpoint), the results (mean and 95% CI) were expressed as ratio between the second (discharge) and the first (admission) measurements.

Results

The study population consisted on 23 patients (15 males and 8 females; mean age 68 y; 95% CI, 59-77 y), who received final diagnoses of pneumonia (n=11), chronic obstructive pulmonary disease (n=9) and erysipelas (n=3). The main findings of this study are shown in table 1. PCT was significantly correlated with all biomarkers except hsCRP. However, hsCRP exhibited the highest sensitivity and NPV, whereas suPAR had the best specificity and PPV. The better agreement (k) was found for copeptin. Analysis of diagnostic performance by receiver operator characteristic (ROC) analysis, revealed that hsCRP had the best area under the curve (AUC), followed by copeptin and suPAR, although the differences were not statistically significant (all $p>0.05$). It is noteworthy that in multivariate linear regression analysis were PCT was entered as dependent variable, significant associations were only found for copetin (coefficient, 0.36; $p=0.018$) and suPAR (coefficient, 1.56; $p=0.024$), but not with MRproADM (coefficient, 0.74, $p=0.14$) and hsCRP (coefficient, -0.06; $p=0.50$). A significant association was also found between copeptin and suPAR ($r=0.662$; $p=0.001$), between suPAR and MRproADM ($r=0.429$; $p=0.041$), but not between copeptin and MRproADM ($r=0.348$; $p=0.103$).

Discussion

The aim of this study was to verify the clinical usefulness of a panel of innovative and promising biomarkers in the management of patients admitted to the ED with various types of infection, using PCT variation as surrogate measure of clinical outcome. Multivariate linear regression analysis confirmed that copetin and suPAR, but not hsCRP and MRproADM, may be accurate and independent predictors of PCT variations and thereby prognosis in patients admitted with acute infections to the ED. The lack of correlation between MRproADM and copeptin also suggests that these biomarkers target different clinical pathways, and their use may hence be complementary. The good correlation found with all other biomarkers suggest that suPAR may be a promising biomarker for monitoring multiple clinical pathways in the ED.

Table 1. Correlation and diagnostic accuracy of biomarkers for prediction of clinical outcomes reflected by variations of serum procalcitonin.

	Univariate correlation	Sensitivity	Specificity	NPV	PPV	k	AUC
Copetin	r=0.775; p<0.001	0.87	0.75	0.75	0.87	0.62; p=0.003	0.89 (95%CI, 0.74-1.00)
MRproADM	r=0.510; p=0.013	0.87	0.63	0.71	0.81	0.51; p=0.015	0.74 (95%CI, 0.53-0.96)
SuPAR	r=0.774; p<0.001	0.73	0.88	0.64	0.92	0.56; p=0.005	0.85 (95%CI, 0.69-1.00)
hsCRP	r=0.364; p=0.087	0.93	0.63	0.83	0.82	0.59; p=0.004	0.92 (95%CI, 0.79-1.00)

Evaluation of the current prognostic implications of cardiogenic syncope and of pre-existing heart diseases in syncopal patients.

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Background: Historical studies about the prognosis of syncopal patients, performed in the 1980s, showed that the 1-year mortality was consistently higher in cardiogenic than in non cardiogenic or unexplained syncope. Ten years later, further studies questioned these evidences, showing that the risk of death was only predicted by the underlying heart disease and not from syncope. Aim of this study was to evaluate the prognostic implications of both the etiology of syncope (cardiogenic vs. non-cardiogenic), and the pre-existence of structural heart disease.
Methods: This is a prospective cohort study aimed to compare the prognosis of cardiogenic vs. non cardiogenic syncope and of syncope in patient with vs. without heart diseases. We studied 200 syncopal patients consecutively admitted into the ED of the University Hospital of Parma. At 1 month and 1 year after discharge we compared the incidence of syncopal recurrences, readmission for non-syncopal events, major procedures, cardiovascular events, cardiovascular death, death for any reason, in patients with cardiogenic vs. non cardiogenic syncope and in patients with vs. without heart diseases.
Results: Cardiogenic syncope was associated with the presence of at least one adverse event at short term and with death for cardiovascular diseases, major procedures, cardiovascular events, syncopal recurrences, readmission for non-syncopal events, at long term; Kaplan-Meier analysis (see Figure) reveals that survival in patients with cardiogenic sincope was significantly lower than in cases with non cardiogenic syncope. The presence of cardiovascular disease (in broad sense) was associated only with readmission for non-syncopal events at long term; after a more restrictive selection of cardiovascular diseases (coronary heart disease, heart failure, primarily arrhythmogenic diseases), we found a strict association with the presence of at least one serious event at 1 month and with cardiovascular death at 1 year.
Discussion: Despite significant advances in the treatment of cardiovascular diseases over the past decades, cardiogenic syncope continues to be associated with a significantly worse prognosis as compared with non-cardiogenic syncope. As regards the role of the presence of cardiovascular disease in syncopal patients, we suggest to adopt a strict definition of cardiovascular variables considered at risk, in order to avoid an excessive hospitalization.

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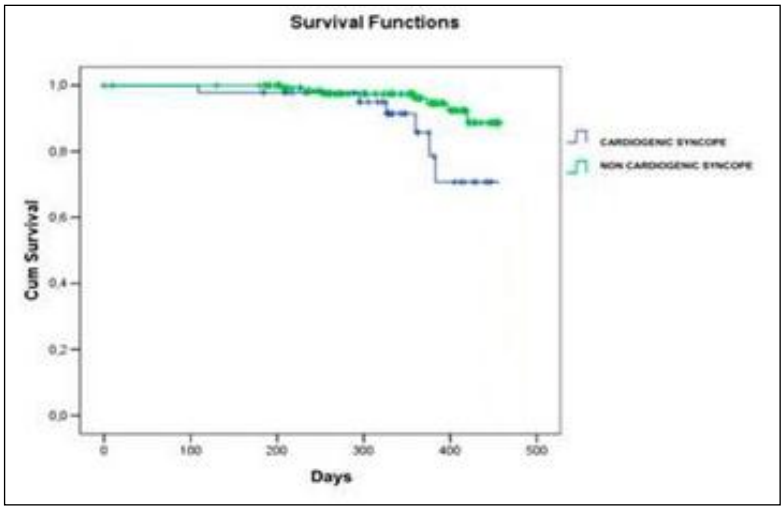
Survival Functions
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
100
200
300
400
500
Days
CARDIOGENIC SYNCOPE
NON CARDIOGENIC SYNCOPE

Sometimes they come back!! The forgotten diseases too. A case of Beri-beri Shoshin in Parma in year 2012.

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A 78-years-old man, born and living in a little village into the mountains surrounding Parma, presented to our Emergency Department on March 12th, 2012 complaining for exertion dyspnoea, peripheral oedemas and mild dysuria. The symptoms lasted for a long a time, but they were worsening in the last two weeks.
The patient lived alone, reported no major health problems in the past, and no psychiatric history. He worked for forty years as employee in a post office with good results and his sister says he was a solitary guy.
Only after a long talk we discover inappropriate dietary habits, due to both low quality and quantity of food. In particular he has been eating, for over 20 years, only few strictly selected foods (i.e., chestnut honey and chestnut jam produced by himself). He refused, in an obsessive way, to eat protein-rich foods, fruits and vegetables, justifying such behaviour with the fear to be poisoned, thinking that most of the food was contaminated by petrol.
The patient was conscious, well oriented , apyretic and slightly dyspnoeic. The main physical findings were: PA 130/80 mmHg, Sp02 97% on air, HR 75 bpm, BMI 21.
His ideation was focalized only on matter of contamination and poisoning, and also on politic, philosophic and religious themes.
The patient was undernourished, he has columnar peripheral oedemas, poor respiratory sounds, and a bladder globe. With insertion of a catheter we obtained about 400 ml of clear urine.
Haematological and biochemical profile, together with urinalysis, were normal. Serum albumin was 2,4 g/dL, and BNP 2470 pg/ml. The EKG was normal. On chest X-rays we found bilateral pleural effusion, and on abdomen echography some free liquid in the perisplenic and perihepatic space and between the intestinal loops. The echocardiography showed mild aortic and mitral insufficiency, and mild pulmonary hypertension (PaPs 50 mm/hg).

Diagnostic evaluation, treatment and discussion:

Chestnuts contain 0.238 mg of Vitamin B1 per 100 gr. of product, but the chestnut honey contains only traces of it and the other chestnut products, as the jam, lose at least 25% of vitamin B1 after cooking. The recommended dietary allowance for Vitamin B1 is 1 mg a day. Taking into consideration the history and the clinical findings, we have suspected a case of wet Beri-beri and then the patient was given a low dose of furosemide together with nutritional supplements and Vitamin B1 100 mg i.m. We also persuaded the patient to begin to have a proper diet. In a few days we observed a rapid and progressive weight loss and complete remission of the dyspnoea and the oedemas.
After psychiatric evaluation, a therapy with olanzapine has been set and the patient has been transferred in a nursing home with caring of social services.
The lack of Vitamin B1 (also known as thiamine, a water-soluble vitamin, related to glucose metabolism) is the cause of the disease generally known as Beri-beri, common in underdeveloped countries, particularly in the Southeast of Asia. Generally, Beri-beri is classified into two main forms: 1) wet Beriberi, or Beriberi Shoshin, affecting the cardiovascular system, with oedema due to heart failure, 2) dry Beriberi, causing loss of muscle tone and peripheral neuropathy. Alcohol also affects both the absorption and the metabolism of thiamine, and Wernicke's encephalopathy in chronic alcoholics, mainly due to thiamine deficit, is well known in western countries. On the other hand, the true Beri-beri, still common in poor countries, is now very rare in the western world. As such, considering Beri-beri in the differential diagnosis of oedema syndromes can be of basic importance, and an accurate and thorough history is fundamental for this purpose.

"A certain very troublesome affliction, affecting men, is called by the natives Beriberi (which means sheep). I believe that people who are affected by this disease, whose knees shake and the legs bend, it's a kind of paralysis, or it's better to say trembling, and all this sometimes affects the movement and sensitivity of the hands and feet and of the whole body…."

Jacobus Bonitus, written in Java, 1630

First episode of seizure in adults in the ED of Parma: epidemiology, clinical presentation, differential diagnosis and management. Observational study.

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Background: Seizure is a common problem in the Emergency Department (ED), accounting for 1% of all ED visits in the United States. The differential diagnosis is broad and challenging for the Emergency Physician because many conditions can mimic a seizure. Moreover, it is often difficult to establish the need of diagnostic testing for patients presenting with a first episode of seizure. Aim of this study was to determine the main characteristics of the adult population presenting to our ED with a complaint of first episode of seizure and to analyse the principal aetiologies, together with the clinical management of these patients.

Methods: All the cases of seizure, syncope, loss of consciousness, or mental confusion were retrieved from the database of our ED during a period of 365 days (January to December 2011). For each patient demographic (sex, age, race) and clinical data (medical history, physical examination, laboratory testing, EEG, neuroimaging, acute treatment and hospital admission) were collected. The statistical method was simply descriptive.

Results: Our ED registered 85.958 patient visits over the observational period, with an average of 235.5 patients per day. A total of 1,949 (2.2%) cases of altered mental status as chief complaint were observed during the same period. Among these, 1473 (76%) were discharged with a diagnosis of syncope, 86 (4%) with a diagnosis of confusion and 390 (20%) with a diagnosis of seizure. Seizures (both first episodes and already known) then accounts for 20% of all consciousness disturbances and 0,4% of all ED visits. The patients with a first episode of seizure were 136 (7% of patients with consciousness disturbances and 0,1% of all ED visits); males were 78 (57.3%); the mean age was 62 years (range: 16-96). The main clinical presentations were: tonic-clonic seizures (n=70), tonic seizures (n=3), partial seizures (n=15), convulsive loss of consciousness (n=22), confusion (n=22) and status epilepticus (n=4). Lab tests were performed in almost all the patients (n=133). Computed Tomography (CT) of the brain was obtained in 125 patients; it was normal in 43 cases, but showed lesions in 85 patients: 7 acute strokes, 13 old strokes, 9 new brain tumors, 11 known brain tumors, 19 lacunar infarcts, 18 diffuse vascular encephalopathy, 2 diffuse cerebral atrophy and 3 undetermined lesions. EEG was performed in 32 cases and it was clearly altered in 14 patients, showing 3 cases of status epilepticus and 11 cases of paroxysmal brain activity. Notably we found that the majority of seizures (n=104; 76.5%) were symptomatic, as follows: 4 metabolic disorders, 8 infections, 6 ethanol/drugs- related, 4 brain injury, 20 brain tumors (9 formerly unknown), 7 acute stroke, 50 chronic cerebrovascular disorders, 2 cerebral venous thrombosis, 2 diffuse cerebral atrophy and one of cardiac origin. In 32 patients no apparent cause was identified (possible unprovoked seizure). 34 patients received acute treatment with benzodiazepines because of early recurrence of seizure in the ED and 19 began specific therapy with antiepileptic drugs in ED. 71 patients (52%) were admitted to hospital and 65 (48%) were discharged, 42 after an observation period in ED (minimum 8 hours).

Discussion: Patients presenting in the ED with a first episode of seizure are more likely to be middle-aged and old males and to have a symptomatic event. Among provoked seizures, cerebrovascular disorders are responsible for most cases. As such, we recommend a liberal use of urgent cranial CT in all patients with a first seizure, while there is less evidence for perform EEG in the ED, except in case of suspected status epilepticus. The need for hospital admission must be considered for patients with status epilepticus, but also for patients who present early recurrence of seizure, for elderly patients with comorbidities, and for those with history of cancer, with CT focal lesions and with EEG paroxysmal activity.

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Lack of correlation between Acute Atrial Fibrillation incidence and microclimatic variations. Results of a 9-year survey, including 3633 cases, in Parma Emergency Department.

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Background
Some diseases show a correlation with microclimatic variations. Among these, renal colics (1), stroke (2), and myocardial infarction (3) have been well documented. Some Authors have shown a correlation between incidence of Acute Atrial Fibrillation (AAF) and seasonality, being higher the incidence during wintertime (4), but the data are poor and conflictual . Aim of this study was to assess the influence of day-by-day climate changes on the number of visits for AAF in our Emergency Department (ED).

Methods
All the cases of AAF (both first-diagnosed AF and Paroxysmal AF) episodes were retrieved from the database during a period of 3286 days (January 2002 to December 2010). Only the cases whose onset was within 48 hours from ED visit were selected. For all the 3286 observed days, the meteorological data about the Parma Province were obtained from ARPA (Agenzia Regionale Prevenzione e Ambiente; Environment and Climate Regional Agency). We therefore checked for correlation between ED visits for symptomatic AAF and variation of air temperature and humidity. With this purpose, the chronological data of all the visits for AAF were interfaced with the climate data in univariate and multiple linear regressions analysis using the program Mathematica7®.

Results
Our ED registered 725,812 patient visits over the observational period, with an average of 221 patients per day. A total of 3,633 AAF cases were observed during the same period, being males 52% (mean age 63±14 yrs) and females 48% (mean age 71±11 yrs). During all the observational period a significant increase of visits for symptomatic AAF has been recorded (Fig.1). We didn't find any significant correlation between average daily visits for AAF and daily change of average temperature($P>0.05$, Fig.2) and humidity ($P>0.05$, Fig.3). A limiting factor of this study is represented by the inclusion of some repeated visits of a few patients referred for recurrent AAF. Moreover, it was not possible to record the comorbidities, such as structural heart disease, thyrotoxicosis, gastroesophageal reflux disease, sepsis, recent surgery etc …potentially capable of elicit AAF.

Conclusions
Our study shows that the incidence of symptomatic AAF is not significantly related to changes of the considered microclimatic variables. We therefore can not confirm the results of some previous studies. It is however possible that a seasonal increase of incidence of AAF (including asymptomatic forms), related to comorbidities prevailing during wintertime (i.e., pneumonia, exacerbation of COPD), may happen.

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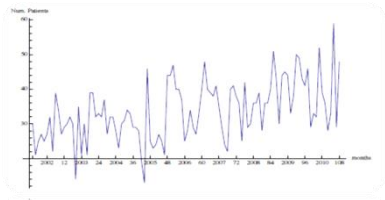

Fig. 1

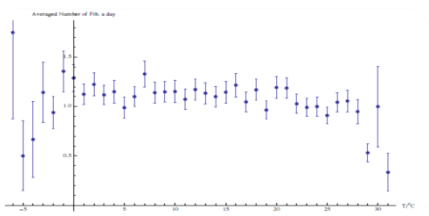

Fig. 2

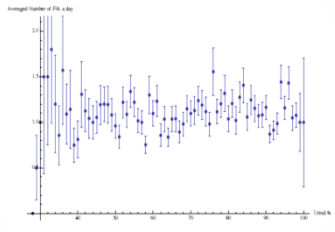

Fig. 3

Biomonitoring and Cardiorenal Syndrome in Heart Failure (BIONICS-HF) trial: preliminary results

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Introduction

When evaluating patients with suspected acutely decompensated heart failure (ADHF) in the emergency department (ED), prompt diagnosis and appropriate treatment is the key to superior outcome. Part of the intricacy of caring for patients with ADHF is managing the past, present, and future medical co-morbidities that may complicate management. While medical issues such as anemia or hyponatremia are common and often challenging to manage in patients with ADHF, a dreaded situation is that of confronting severe HF in the setting of renal dysfunction. In this context, patients with both cardiac and kidney failure not only represent a diagnostic challenge but they present among the most considerable therapeutic conundrums as well. Thus, patients suffering from this combination of organ failure have a considerable risk for adverse outcome, which has been well studied and reviewed by our research group (1-4). Indeed, heart disease and kidney dysfunction are so intricately interrelated from an etiologic and pathophysiologic perspective and are so important clinically that the term "cardiorenal syndrome" has been coined to describe this deleterious intersection of cardiac and renal failure (5-7).

Materials and Methods

We enrolled patients from April to July 2012. This study was conducted in two sites in Rome and in Boston. Inclusion criteria: Dyspnea thought to be due to ADHF, NYHA Class III or IV symptoms. Exclusion criteria were: Renal failure requiring renal replacement therapy prior to enrolment, Unable or unwilling to participate, >6 hours from first dose of intravenous diuretic.

Data Collection

Baseline demographics, vital signs, and results of physical examination was recorded after informed consent. A 10 mL sample of blood was drawn into a tube containing ethylenediaminetetraacetic acid, spun for 15 minutes, and aliquoted to freezer tubes for biomarker measurement following the completion of the trial. BIVA measurements was taken after phlebotomy.

Clinicians were not provided the results of the biomarkers or BIVA. In-hospital events, including WRF, initiation of renal replacement therapy, or death were noted. For those with event-free survival to discharge, following completion of a 180 day follow up period, patient records were reviewed for events subsequent to release from the hospital, including all-cause death, all-cause re-hospitalization, and initiation of renal replacement therapy. All medical information were de-identified, coded with a study number, and stored in a locked cabinet.

Blood analysis

Blood samples were remain frozen at -80 degrees C until the completion of study procedures. The samples were thawed and analyzed for respective biomarkers. NT-proBNP were measured using the Roche Elecsys ProBNP method on a Cobas e411 modular analyzer. A highly sensitive method for sST2 (Presage ST2, Critical Diagnostics, San Diego, CA) were analyzed using a two-step enzyme linked immunosorbent assay (ELISA) on a Grifols instrument. NGAL were analyzed using a commercially available method (Alere, San Diego, CA) using standard techniques.

Outcome

The primary outcome measure of interest is the onset of Worsening Renal Function (WRF) following admission, as defined as a rise of serum creatinine by 0.3 mg/dL (or rise ≥25% from baseline) (8). In those patients meeting the criteria of WRF, the cause (CRS Type 1, 2, 3, 4, or 5) were judged by two study physicians blinded to the results of biomarkers and BIVA using standard criteria (5). Additional outcomes included initiation of renal replacement therapy

(continuous veno-venous hemofiltration, percutaneous ultrafiltration, hemodialysis, or peritoneal dialysis), all-cause mortality, and all-cause rehospitalization.

Results

100 of the 103 patients (mean age 74.59 ± 11.49: 38 M;) enrolled were included in the statistical analysis. The incidence of WRF was higher in patients with pleural effusion and interstitial edema ($p=0.04$ and $p<0.05$ respectively). WRF was confirmed in 25 cases (25%) on the basis of RIFLE criteria (a rise of serum creatinine by 0.3 mg/dL). The mean (± 1SD) blood BNP was 1001.58 ± 1076.75 pg/ml in WRF group vs 602.91 ± 667.48 pg/ml in NO WRF group ($p<0.05$). The mean (± 1SD) blood NGAL was 309.35 ± 258.47 pg/ml in WRF group vs 256.15 ± 270.04 pg/ml in NO WRF group ($p=0.38$). The mean (± 1SD) length of stay was 12.16 ± 12.73 pg/ml in WRF group vs 5.32 ± 5.36 pg/ml in NO WRF group ($p<0.05$). The AUC (area under the curve) of NGAL

Conclusions

Our study reconfirm WRF in patients admitted from ED for ADHF were associated bad outcome: our results showed that in these patients the incidence of in-hospital death and the length of stay is increased.

The BNP measurement is increased in patients that have ADHF and concomitant WRF for more congestive fluid. The NGAL measurement is increased in patient that have more events during the follow-up period 30 days.

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Tuberculosis in emergency department

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Purpose. To evaluate clinical and radiological features of tuberculosis (TB) patients hospitalized at Sant'Andrea Hospital Emergency Department (ED).

Methods and Materials. Using the International Classification of Diseases, ninth revision (ICD-9) we elaborated a medical record review of 188 (120 male, 68 female, mean age 52, ds 21) TB patients admitted to Sant'Andrea HospitalED in a period ranged from 2006 and 2011, with symptoms of acute disease. Most of these patients had multiple ED visits (29% two visits, 9% three visits). 4% of these patients were excluded because their admission were not primarily connected to TB (trauma, renal colic or non-specific abdominal pain).

Results. The most frequent clinical presentation was characterized by signs and symptoms of pulmonary acute disease (fever, cough, dyspnea). CXR and CT patterns upon the observed cases had the following findings: lobe/diffuse interstitial infiltrate (49%), cavitary lesions (22%), calcific lymphadenopathies (5%), pleural effusion (20%), mass or coin lesions - not cavitary (20%), calcific fibrothorax (4%), bronchial ectasia (17%), tree-in-bud (18%), ground-glass (8%), parenchymal scar (14%) and normal pleuro-parenchymal pattern (29%). Only two patients were admitted because of bone tuberculosis and peritoneal localization; 4% developed TB pericarditis.

Conclusion. As already observed in literature it is frequently hard identifying TB patients during ED visits, given that patients are often affected by atypical and nonspecific signs and symptoms.

The emergency department is a determinant point of contact of TB patients and radiologist needs a training in recognize pleuropulmonary TB.

THE ROLE OF PHYSIOLOGICAL AND OPERATIVE SEVERITY SCORE FOR THE EVALUATION OF MORTALITY AND MORBILITY IN THE STRATIFICATION OF ABDOMINAL AND EXTRABDOMINAL SURGERY PATIENTS

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BACKGROUND
Adequate stratification and scoring of risk is essential to optimize clinical practice; the ability to predict operative mortality and morbidity is important to choose the gold therapy and a proper use of resources. The Physiological And Operative Severity Score For The Evaluation Of Mortality And Morbility (POSSUM) has been proved to be the most appropriate scoring system in providing an estimation of postoperative mortality for patients undergoing abdominal surgery. The aim of our study was to verify the predictive accuracy of POSSUM in patients undergoing elective extrabdominal surgery.

PATIENTS AND METHODS
Our study included 189 patients, all admitted to Intensive Care Unit (ICU) at S.Andrea Hospital in Rome. The sample was divided in 2 groups: group A, abdominal surgery; group B, extrabdominal surgery.
All types of surgery were included except for cardiac surgery, pediatric surgery and urgent surgery. For each patient was determined the POSSUM score. Age, sex and preoperative information, surgical diagnosis, severity of the procedure , time of hospitalization, post operative complications were also recorded.
The two groups were divided in classes, based on the rate of morbidity and mortality. For each class was calculated the relation between predicted and observed deceases, and the relation between predicted and observed complications, scoring 1 if present and 0 if not present, in order to assign a reliability score to each group. Furthermore, basing on the length of stay, were individuated three subgroups of patients: hospitalization < 3 days, between 4 and 7 days, > 7 days. For each group was evaluated the correlation between observed and predicted morbidity.

RESULTS
Above 189 patients, 49 developed postoperative complications, with a real morbidity rate of 25,9% (95%CI: 20%-32%) and a predicted rate of 51,3%; the relation between observed and predicted complications (O/P ratio) was 0,50. For the A group the O/P ratio was 0,45, with a real morbidity rate of 25,53% (95% CI: 17%-34%) over a predicted rate of 56,4%. In the B group the O/P ratio was 0,53, with a real morbidity rate of 26,31% (95%CI: 17,2%-34,8%), and a predicted rate of 49%. Above 189 patients, 5 deceased, with a real mortality rate of 2,64% (95% CI: 0,4%-4,8%), over a predicted rate of 16,4%; the relation between observed and predicted deaths (O/P ratio) was 0,16. For the A group, O/P ratio was 0,11, with a real mortality rate of 2,1% (95% CI: 0-5%) over a predicted rate of 18,08%; for the B group, O/P ratio was 0,25, with a real rate of 3,16% (95% CI: 0-436,7%) over a predicted rate of 12,63%. Correlation between time of hospitalization and POSSUM morbidity has an average strength expressed by a ρ value = 0,4.

CONCLUSION
Observed data confirm the possibility to extend the POSSUM score in the stratification of patients undergoing extrabdominal surgery. Even though it overpredicted the value of morbidity and mortality, as widely known, POSSUM score shows an impressive uniformity and concordance between the main groups A and B. Furthermore, there is a good correlation between time of stay in ICU and the POSSUM morbidity.
Our results suggest that POSSUM can be an adequate perioperative mean, recommended to evaluate the real condition of a patient after surgery and to determine the requirement of an admission to the postoperative ICU.

Prognostic indicators in patients with SIRS: contribution of the new biomarkers.

Authors: **De Roia Marina**, Orso Daniele, Perich Daniele, Fernandes Giovanni, Burekovic Ismet, Valentini Denis, Marizza Silvia, Iudicello Alessandra, Occhipinti Alessandro, Montanari Giulia, Biolo Gianni, Giansante Carlo.

Background

Mortality in Systemic Inflammatory Response Syndrome (SIRS) reaches 10% per week, and organ failure is a common finding in this syndrome. Indicators of worse prognosis are eagerly needed in adult population while some biomarkers have been studied in pediatric population. Moreover, combinations of markers in predicting death or organ failure are also scarcely investigated.

Aims

To assess the association of new biomarkers namely IP10, PLA2, Procalcitonin and Angiopoietin, with organ failure and death in a population of patients admitted in medical ward with SIRS and look for a model predicting those outcomes.

Methods

In eighty patients, 20 with a final diagnosis of NI-SIRS and 60 with SEPSIS (20 microbiologically documented) IL10, PLA2, Procalcitonin and Angiopoietin plasma levels as well as SOFA score at admission or at diagnosis of SIRS were compared according to their prognosis: death, organ failure or good outcome. Management of patients was carried out blind of the markers' results. Moreover, binary logistic regression, was used to look for an array of clinical and biomarker indicators of unfavorable outcome in SIRS.

Results

Death rate was 11% (9 events) during 1 week of observation. Clinical features associated to mortality were hypothermia and SOFA score. Patients who died had higher plasma values of IP10, PLA2, angiopoietin and lactate. Organ (lungs, emocoagulative, liver, cardiocirculatory, central nervous system, kidney) dysfunction occurred in 32% of patients: those with hemostasis dysfunction, lung, liver or kidney failure had higher IP10, PLA2 and angiopoietin plasma levels (<0.05). IP10, angiopoietin and, at a lesser extent, SOFA score, correlated with the number of organ failures for each patient (all <0.01).

Binary logistic regression confirmed the data obtained with univariate analysis both on death and organ failure.

Conclusion

The use of biomarkers is a promising strategy in identifying adult patients at higher risk of developing fatal outcome or organ damage and possibly plan a strategy to counteract those events. Larger population would allow more firm conclusions.

Early predictors of success or failure of Non-invasive Ventilation for Acute Hypercapnic Respiratory Failure in the Emergency Department

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INTRODUCTION AND BACKGROUND: Emergency physicians often face the challenge of predicting short-term outcomes for patients with acute respiratory failure (ARF) in the emergency department (ED)

AIMS AND OBJECTIVES: To identify early and objective clinical parameters and laboratory biomarkers for severity assessment and predicting outcomes in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) requiring noninvasive mechanical ventilation (NIV)

METHODS: Three-months observational prospective single-centre study in real life practice of the acute setting of the ED of a university teaching hospital, including every consecutive non-selected patient emergently admitted for ARF due to AECOPD and treated by NIV according to EP's early clinical indication referring to an institutional protocol. Treatment failure defined as hospital mortality and/or need for tracheal intubation (TI) and invasive mechanical ventilation (IMV) at any time

RESULTS: 124 patients (media 1.38/day). Failure (23 cases, 18.5%) and success (101; 81.5%) patients were different in: neurologic status score (Kelly-Matthay scale), urea, creatinin, AST, ALT, CPK, CPK-MB, troponin T, LDH, PCR, pH, and arterial blood gas analysis parameters after 1-2 hours of NIV (PaO_2, pH, $PaCO_2$, HCO_3^-, SaO_2, PaO_2/FIO_2)

CONCLUSIONS: NIV is a cost effective intervention even outside intensive care units for the treatment of ARF caused by AECOPD. We showed the possibility to identify in the ED early predictors of outcome: some clinical parameters, biomarkers and arterial blood gas analysis data to recognize severe conditions and the response to treatment. Appropriate patient selection and timed intervention are required for optimal administration of early NIV in haemodynamically stable patients, not meeting criteria for IMV, closely monitored in an environment where TI is promptly available, with medical and nursing motivated team, with extensive training and experience in NIV. A main unresolved question in the ED is about selection criteria and early choices for patients with ARF having preset therapeutic-prognostic limits and acutely reversible processes for which NIV should be considered as “ceiling” treatment

Acute asthma presentation to the Emergency Department

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BACKGROUND: The incidence and the complexity of asthma and its acute exacerbations are widely growing. Hospitalizations and Emergency Department (ED) visits account for a large proportion of the health-care cost burden of asthma

AIMS: Our aim was to define the epidemiological and clinical impact of Acute Asthma (AA) at presentation to the ED and the role of the Emergency Physician (EP)

METHODS: We conducted a 6 month (from 1/1 to 30/6/2009) observational, prospective clinical study including every consecutive AA patient who presented to the ED of a university teaching hospital, collecting data easily accessible to the EP in the early phases of evaluation and treatment

RESULTS:

Patients: 209 (media 1.15 cases/day).

Data part 1 - Rates %: females 63.5; Italian nationality 70.2; general practitioner's request for ED visit 6.0; current therapy for asthma 83.1; known risk factors 63.5; previous physician's visit 15.9; chest X-rays in ED 72.1; ABG analysis in ED 21.6; therapy in ED 79.5; mechanical ventilation in ED 2.9; hospitalization 18.2; therapy at discharge 77.9; follow up at discharge 65.9; second visit to ED 4.3.

Data part 2 - Media (median, minimum, maximum), respectively: age 41 years (39, 14, 100); waiting time in the ED 48 minutes (18, 0, 310); time for evaluation and treatment in ED 104 minutes (93, 1, 482); total time spent in ED 153 minutes (136, 9, 552); systolic blood pressure 127 mmHg (123, 90, 220); diastolic blood pressure 78 mmHg (80, 60, 125); pulse rate 94 bpm (90, 60, 147); pulsoxymetry 97% (98, 72, 100); body temperature 36.9°C (36.7, 36.0, 39.7); symptoms debut before ED visit 7 days (3, 0, 90); time between second and first ED visit 50 days (19, 8, 144)

CONCLUSIONS: The characteristics at presentation of AA to the ED are recently deeply changing. The majority of asthma exacerbations has a window of opportunity in which deterioration can be recognized and reverted, and severe asthma attacks can be prevented by currently available strategies. The subgroup at main risk for very severe or near-fatal AA seems to be represented by patients with poorly controlled disease whose condition gradually deteriorates over a period of days before the life-threatening event. Of concern was the dependence of most patients on the ED for initial care, and the small number of cases in which patients visited a physician before presenting to the hospital. The EP plays then a key role in AA: emergency management; medical treatment; diagnosis; prevention; maintenance and follow up; education about self-management. Nowadays the EP must be involved in approaching all the typical most frequent and relevant causes of inadequate asthma control in AA patients: late, inaccurate or wrong diagnostic assessment; lack of information and prevention about awareness of risks; inadequate therapy prescription; low adherence to therapy; inadequate follow up

Noninvasive Ventilation in the Emergency Department: the role of Arterial Blood Gas Analysis to predict the outcome in Acute Cardiogenic Pulmonary Oedema

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Background: Noninvasive positive pressure ventilation (NIPPV) is considered a first line intervention in Acute Cardiogenic Pulmonary Oedema (ACPO): robust evidence support the efficacy and safety in reducing the need for endotracheal intubation (ETI) rates, mortality and other adverse events. Emergency Physicans (EP) need some objective measures and parameters as an adjunct to clinical judgement when deciding on managing Acute Respiratory Failure (ARF). Arterial Blood Gas Analysys (ABG) is largely available in clinical practice in the Emergency Department (ED) and showed some promises to predict outcome in ARF treated with NIPPV and medical therapy

Aims: We aimed to assess the role of ABG, since the early phases in the ED, in recognizing severe conditions and the response to treatment of carefully selected and controlled patients with ACPO treated by NIPPV, and so to predict the outcome

Materials and Methods: Outcome as treatment failure was defined as hospital mortality and/or need for ETI and invasive mechanical ventilation at any time. We conducted an observational, prospective clinical study in the real life practice of the acute setting in the ED of a University teaching Hospital, during five months, including every consecutive patient emergently admitted for ACPO according to EP early clinical indication to first-line NIPPV (referring to an institutional protocol). We prospectively analyzed and then abstracted ABG data at presentation and the outcome at the end of hospitalization; blood gas samples were evaluated at baseline just after admission, and in the early (1 to 6 hours) phase of follow up after beginning treatment

Results: 214 patients (media 1.42 / day) were included. Failure rate was 15,5% and success 85,5%. Our data shows that, in patients with ARF due to ACPO and treated with NIPPV, ABG at presentation (at study entry) is not able to predict the outcome (in terms of need of ETI and / or death during hospitalization). After 60 minutes of NIPPV both groups (success versus failure) improved in ABG parameters without any significant difference and with a similar delta. After 120 minutes patients in the failure group stop sustaining the correction in gas exchange and the improvement in ABG parameters; we showed a significant delta increment in the success group. This trend is confirmed after 3 and 6 hours

Conclusions: In a vast majority of well selected ACPO patients NIPPV improves gas exchange and avoids ETI and ventilator-associated complications. The improvement of ABG after 2 hours initiating NIPPV is associated with success in ACPO; these patients will likely benefit from continuation of NIPPV. The inability to improve gas exchange after 120 minutes of NIPPV is predictor of failure; these patients should be closely monitored with a low threshold for ETI

IL-18 plasma levels correlate with BNP in Acute Heart Failure patients, and it stimulates BNP synthesis by cardiomyocites

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Introduction: Interleukin 18 is known to display inflammatory, hypertrofic and proapoptotic properties. There is evidence of an altered IL-18 secretion in Heart Failure patients. IL18 plasma levels are increased in these patients, and recent experimental studies have proven that the administration of IL18 causes myocardial dysfunction.The aim of the study was to verify the ability of Il-18 to induce Brain Natriuretic Peptide (BNP) synthesis in vitro and to analyse the relationship between these two molecules in plasma from acute heart failure (AHF) patients.

Patients and methods: 38 patients (M:F=19:19, mean age: 76,2±1,9 years) arriving in our Emergency Department (ED) with AHF were enrolled. BNP plasma levels were measured by an immunofluorescent assay and the point-of-care device Triage meter (Alere, San Diego, CA, USA). IL18 plasma levels were determined by a sandwich ELISA immunoassay (Human IL18 ELISA kit, Medical & Biological Laboratories Co, Naka-ku, Nagoya Japan). A murine cardiomyocyte cell line HL-1 (JRH Biosciences, Lenexa, KS, USA)was cultured and used for IL18 treatment (recombinant mouse IL18, R&D System, Minneapolis, MN,USA) from 1 to 24 hours.

Results: We demonstrated the ability of Il-18 to directly stimulate a murine cardiomyiocyte cell line to express BNP gene, with the subsequent induction of a cell secretory phenotype and BNP release. A correlation between Il-18 (AHF 293,4±204,9 vs controls 283,9±163,7 ng/ml, $p<0,8$) and BNP (AHF 969±643,5 vs controls 44.7±41,6 pg/ml, $p<0,001$) plasma levels was found in AHF patients ($r=0,47$,$p<0,007$), and in a subgroups of AHF patients with diabetes ($r=0,67$, $p<0,02$) and coronary artery disease ($r=0,65$, $p<0,09$). AHF patients with renal failure had significantly higher IL-18 plasma levels than patients without ($p<0,03$).

Conclusion: Our study provides the first evidence of the ability of IL-18 to induce BNP synthesis in vitro and outlines the relationship between the two molecules in AHF patients with an ongoing inflammatory status.

RDW and Acute Coronary Sindrome

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RDW (Red Blood Cells Distribution Width) is a measure of the variation of red blood cell width, reported as part of standard complete blood count. High RDW values indicate greater variation in size of red blood cells. Normal reference range in human red blood cells is 11.6-14.6%.

In literature there are several articles dealing with the theme of the role of RDW in Acute Coronary Syndromes (ACS). Particularly, it's described a higher mortality in patients with RDW values beyond the normal range.

Our goal was to study the role of RDW in the acute phase of an ACS.

We enrolled 173 consecutive patients, admitted to the Coronary Care Unit of our hospital, with a diagnosis of obstructive ACS, documented by the evidence of obstructive coronary lesions on coronary angiography.

We divided patients into two Groups: Group 1,104 patients with normal values of RDW; Group 2, 69 patients with RDW values higher than normal range. The prevalence of high values of RDW in our population was 39,9%. We studied ventricular systolic function, measuring Ejection Fraction (EF) with echocardiography. We found a significant difference between groups, observing a greater EF in patients of Group 1 (Group 1: Mean ±SEM= 47.9±0.95; Group 2: Mean±SEM: 43.9±1.5. P value=0.017).

Therefore, we investigate whether there was a relationship between RDW and proBNP: we find a correlation between this two parameters: P=0.0007; r Pearson: 0.27; 95%CI: 0.1184-0.4120). Moreover, patients of Group 2 had proBNP levels higher than patients of Group1 (P=0.0005).

We also analyzed the Killip Class in two Groups of patients, but we didn't find significant difference between the groups.

We found a relation between elevated levels of blood creatinine and RDW values beyond normal range: P value: 0.0002; Creatinine in Group1: Mean ±SEM 0.95±0.03mg/dl; in Group2: 1.66±0.22 mg/dl.

Our results suggest that RDW can provide information concerning severity of clinical condition in acute phase of an ACS, both as regards the cardiac contractility, both with regard to renal function. These variables are important prognostic factors in patients after ACS.

Since this measurement is included in the routine tests to which every patient admitted to the hospital should be submitted, as part of peripheral blood counts, RDW appears to be a variable that should be taken into account in the overall assessment of the patients.

The role of Procalcitonin in Acute Coronary Sindrome

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Procalcitonin (PCT) is a peptide precursor of the hormone Calcitonin; it's composed by 116 amino acids and is produced by parafollicular cells of thyroid and by euroendocrine cells of the lung and the intestine. Normal levels in human blood samples are lower than 0,05 ng/ml, but they can raise in response to inflammatory stimulus, especially bacterial infections. PCT may also raise during stress condition for organism, like surgical intervention, trauma, and during other conditions like acute pancreatitis or cardiogenic shock.

Despite there are many articles in literature investigating the role of PCT, the mechanism by which this peptide is produced is not yet clear. Similarly it's not clear if PCT plays some important role in Acute Coronary Syndrome (ACS): some authors describe an increase of its levels during acute coronary syndrome, associated with an increase of CRP levels. Others didn't confirm these results.

The aim of our study was to evaluate role of PCT in ACS. We enrolled 221 consecutive patients, admitted to the intensive coronary care unit of our institution, with the diagnosis ACS, confirmed by presence of at least one coronary lesion greater than 75% at the coronary angiography. In addition to routine tests, we assayed PCT and CRP levels of each patient. We divided the population in two groups: Group1, composed by 131 patients , with PCT values within the normal range (<0.05ng/ml); Group2, composed by 90 patients, with PCT values beyond normal range (>0.05ng/ml). CRP mean value in Group 1 was 1,086mg/dl and 5.776 mg/dl in Group 2. Prevalence of high value of PCT is 40,7%.

A positive correlation between PCT and CRP values was found (P value: 0.0061; r Pearson: 0,18; 95% C.I.: 0.054-0.316). Moreover we sought to determine whether there was a correlation between PCT levels and markers of myocardial necrosis, particularly Troponin I. A correlation between PCT and Troponin I: P<0.0001, r Pearson: 0,29; 95%CI: 0.1646-0.4072. T-test didn't show a significant difference between Troponin I levels in patients of Group 1 vs Group 2. A correlation was not found comparing PCT and CK-MB. Patients of Group 2 had proBNP levels higher than patients of Group1 (P<0.0001). Moreover patients of Group 2 have a greater Killip Class than patient of Group1 (P=0.0061).

Therefore, we divided entire population in three groups according to the type of ACS: Unstable Angina, NSTEMI, STEMI to assess whether PCT values were dependent on kind of diagnosis;

we didn't find a significant difference between three groups (P value= 0.435).

Finally we sought to determine whether greater levels of PCT were associated with a worse coronary pathology. We don't find an association between PCT and severity of coronary lesions (analyzing number of coronary artery affected by atherosclerotic lesion greater than 75%): P value =0.25.

In conclusion, our data don't show an additional value of PCT as compared to other inflammatory markers, in patients affected by ACS. Particularly, relationship between CRP and PCT suggest a common ability to indicate an inflammatory state. Several articles in literature indicates a role of CRP in determining risk profile of patients, suggests that the measurement of the CRP may be sufficient in acute phase of patient affected by ACS. Probably, PCT can suggest a worse left ventricular function, as suggested by our results.

USEFULNESS OF CLINICAL PRE-TEST SCORES FOR A CORRECT DIAGNOSTIC PATHWAY IN PATIENTS WITH SUSPECTED PULMONARY EMBOLISM IN EMERGENCY ROOM.

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Background: Pulmonary Embolism (PE) is a disease characterized by not specific signs and symptoms. In Italy, there are about 65,000 cases per year; mortality is about 30% if PE is not identified and decreases to 2-8% if PE is recognized and treated. International guidelines include several strategies for diagnosing the disease with confidence.
The diagnostic pathway includes a clinical approach with the Wells and Revised Geneva scores, the use of D-dimer and, eventually, a Computed Tomography (CT). The CT seems to be the ideal investigation to confirm or exclude PE but it is not free from complications. Sometimes in medical practice clinicians tend to order CT more frequently than necessary, reflecting a defensive behavior instead of an evidence based behavior. This practice exposes patients to some risks, especially for kidney.
Objective: To identify the efficiency of the use of clinical scores and diagnostic algorithms following the latest guidelines in patients with suspicious of PE. To analyze how many CTs could be avoided using the right approach and to evaluate the importance of any clinical variable. Eventually, to apply a new algorithm.
Methods and materials: A retrospective, single centre, cohort study was performed from January 2011 to April 2012. All patients who made a CT in the Emergency Room for suspicion of PE were collected and classified in two groups: PE - and PE +. In all patients Wells Score and Revised Geneva Score were calculated.
Results: 111 patients (64% female; mean age 72±16 years) were studied. There were no differences in anamnestic, clinical and laboratory variables between the two groups. With the classic pathway 6 patients could have been safely ruled out without performing a CT. With the Wells score one PE+ patient had a low pre-test probability; with the Revised Geneva score actually 7 PE+ patients had a low pre-test probability. These results were source of doubt about the reliability of the scores. So a new algorithm was tested, in fact it was noticed that applying both the scores led to a better result: in 7 patients PE could have been safely excluded without even using CT scan.
Conclusions: The study focuses on the clinical approach to PE. The clinical scores proposed by guidelines (Wells score and Revised Geneva score) are unreliable if used alone, out of a pathway. We propose to apply a new algorithm with both the scores together to exclude PE safely without performing CT when not necessary.

Matrix remodeling as index of microorganism diffusion in patients with sepsis

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BACKGROUND

Diffusion of microorganisms in blood during an infection leads to sepsis, thus reducing survival and, in general, worsening the patient's prognosis. A positive blood culture shows diffusion of the microorganism from the site of infection to the blood. Some microorganisms exploit host's matrix metalloproteinase (MMP) production to spread: circulating levels of specific matrix metalloproteinases (MMP-7 and -9) correlate with blood-brain barrier permeability, and MMP-1 is required for the degradation of tubercular granuloma. Microorganisms induce inflammation and, in turn, unbalanced MMP increase in the sites of infection, but mechanisms of bacteria spreading are not much investigated. The expression of MMPs and of their natural inhibitors, TIMPs (Tissue Inhibitors of Matrix Metalloproteinases) is in part under genetic control and there is no information on the relationship between genetic variants of these proteins and susceptibility or resistance to the spreading of microorganisms.

AIMS

We aim at assessing the association of genetic polymorphisms of MMP-1, -2, -3, -8 and -9, of TIMP-1, -2, and -3 with the development of bacteremia documented by positive blood culture, and measure the plasma levels of these MMPs and TIMPs at enrollment, i.e. when a patient is diagnosed with infection/SIRS.

METHODS

In this pilot study we plan to enroll around 800 patients with sepsis, either clinical or with positive blood culture, and compare the prevalence of these polymorphisms between these two groups. A blood sample is taken at enrolment, and plasma and buffy coat are immediately separated and stored for batch analysis. Clinical workout is carried out independent of the results of the test.

ANALYSIS

Genetic association will be carried out with □2 test, after stratification for site of infection and other clinical variables and laboratory (infection/inflammatory) markers. For plasma levels, immunoenzymatic determination will be also carried out and compared to genotype and according to the blood culture results.

EXPECTED RESULTS

About 30% of SEPSIS can be documented by blood culture. This allows a 2:1 comparison between the two goups of patients and with such ratio, it is possible to detect a 10% difference in allelic frequency between the two populations.

PERSPECTIVES

Control of microorganism diffusion during infection could prevent many fatal complications. The results should allow to develop a model to individualize therapy in patients with infection, stratify the risk of patients undergoing surgical procedures and, in the long term, suggest a strategy to reduce bacterial invasion within tissues.

Use of antibiotics for epidermal wounds in emergency room: correct prophylaxis and right choice of the treatment

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Background: antibiotic therapy and prophylaxis of epidermal wounds in emergency room are often made empirically in case of clinics due to infective complications, although there are no scientific evidences supporting their validity yet. Furthermore, resistance to many antibiotics is a constantly growing problem, especially in Lombardy, Italy. When needed, better prefer beta-lactams or macrolides for their large-spectrum activity.

Methods: We identified all patients (pts) treated to our emergency room for epidermal wounds in a period between 1st and 31st july 2012. Then, we performed a retrospective, observational analysis of epidemiological, clinical and therapeutic features of those pts. $\leq$12 years old individuals were exluded. We considered at high risk of infections pts with at least one of the following comorbidities: diabetes, neoplastic disease, therapy with corticosteroids, immunodepression.

Results: A total of 201 pts were evaluated, 143 males (71.1%) and 58 females (28.9%). The median age was 46,3 yrs. Among the pts 101 (50.2%) needed treatment with suture. 13 (6.5%) pts came after at least 12 hrs after the accident. 107 (53,2%) pts did not need therapy, while in 82 (40.8%) cases antibiotic prophylaxis (89% beta-lactams, 9.8% macrolides, 1.2% others) has been prescribed; 4 (2%) were adviced to start antibiotic therapy only in case of acute epidermal infection development at home; we don't have this information about 8 pts (4%). In 185 (93.5%) pts clinical signs of acute epidermal infection were missing. 15 (7.5%) pts had an high risk of developing infections in history taking; 3 of them received antibiotic prophylaxis, 8 didn't, 4 not known. In 143 individuals (71,1%) the history taking has been insufficient.

Conclusions: Even if acute local infection is possible in wounded pts, only subjects at high risk should be closely screened and monitored to detect early infection, in order to evaluate the necessity of specific antibiotic therapy. Clinical evaluation should also include comorbilities as valvulopathy or immunosuppression.

PLASMA LEVELS OF THROMBOPOIETIN IN PATIENTS WITH ACUTE PANCREATITIS

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Background: Thrombopoietin (TPO) is a humoral growth factor that stimulates megakaryocyte proliferation and differentiation. Furthermore, it favors platelet aggregation and polymorphonuclear leukocyte activation.

Elevated plasmatic concentrations of TPO have been shown in patients with critical diseases, including acute coronary syndrome, burn injury and sepsis. In particular, clinical severity is the major determinant of elevated TPO levels in patients with sepsis.

Acute pancreatitis is a relatively common disease whose diagnosis and treatment are often difficult, especially in the clinical setting of Emergency Department. In addition, about 20% of patients with acute pancreatitis develops a severe form of the disease, which is associated with a mortality rate as high as 30%.

In order to identify patients affected by severe acute pancreatitis, many clinical score systems (Ranson's criteria, APACHE II, …) and several biomarkers (C-reactive protein, procalcitonin, …) have been studied, although without conclusive results.

No data regarding TPO plasma levels in patients with acute pancreatitis are available.

Aim: **a) To investigate TPO plasma levels in patients with acute pancreatitis; b) To assess the accuracy of TPO as a biomarker for clinical severity in these patients.**

Methods: We enrolled patients with acute pancreatitis at the moment of the first clinical evaluation in the Emergency Department. 10 healthy volunteers were used as controls. TPO concentrations were determined by ELISA. An internist physician, unaware of the aim of the study, reviewed patient charts in order to classify the patients as having "mild" or "severe" forms of the disease.

Results: We studied 22 patients with acute pancreatitis (5 severe and 17 mild pancreatitis). No difference for gender and age were detected either between patients and controls or between patients with mild and severe disease. TPO plasma levels were not significantly higher in patients with acute pancreatitis (54.37±9.1 pg/ml) than in controls (41.96±6.51 pg/ml). However, patients with severe acute pancreatitis had higher TPO concentrations (78.48±33.38 pg/ml) than those with mild acute pancreatitis (47.28±6.66 pg/ml), although the difference was not statistically significant.

ROC curve led to calculate a cut-off value of 40.95 pg/ml. This value identified correctly 4 out of 5 patients affected by severe pancreatitis, with a sensitivity of 80%, a specificity of 65%, a +PV of 40%, a –PV of 92%, and a +LR of 68%, similarly to what obtained using APACHE II and Ranson's Score systems.

Conclusions: Our results may indicate TPO as a useful biomarker of clinical severity in patients with acute pancreatitis. Further studies, involving larger numbers of patients, are needed in order to validate these preliminary data.

Microcirculatory effects of analgosedation measured by Near-Infrared Spectroscopy (NIRS) in patients with and without sepsis.

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INTRODUCTION

It is widely known that microcirculation dysfunction characterizes the manifest sepsis[1] and that this dysfunction underlies the multiorgan dysfunction syndrome (MODS), which is the main cause of the high rate of mortality in Intensive Care Units (ICUs) [2]. In most of the patients admitted to ICUs analgosedation is used to ensure mechanical ventilation and reduce psychomotor agitation and risk of self-injurious events. Althoug the effects used for analgosedation on microcirculation have been largely studied in healty subjects[3,4],it is still unknown if these drugs exert their action on microcirculatory regulation in patients with sepsis. The aim of our study is to evaluate if long-term infusion of Propofol and Remifentanyl modify skeletal muscle microcirculation, in particular we evaluate changes of compliance, in patients with sespsis condition and in critical patients without manifest sepsis.

METHODS

The study was conducted in the ICU of Sant'Andrea University Hospital, Rome, and included 18 critical patients, 9 in a sepsis condition (according to 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference defining criteria), (Sepsis Group), and 9 without sepsis (No Sepsis Group), as controls. Near-Infrared Spectroscopy (NIRS) was used to investigate the microvascular function in the brachioradial muscle during a series of four venous occlusions. The protocol provided one measurement during contemporary Propofol and Remifentanyl infusion, and subsequent measurements were performed halving and interrupting the infusion of Remyfentalyl first, and then the Propofol one. The study was interrupted whenever occurred psychomotor restlessness with superior limbs movements or significant respiratory and hemodynamic parameters modifications, that were recorded.

RESULTS

Microvascular compliance was the only variable that differed between the two groups during double sedation; in fact it resulted considerably lower in the Sepsis Group. (See the table)

compliance	T0	T1	T2	T3
sepsis	0,188	0,204	0,248	0,195
no sepsis	0,311	0,28	0,269	0,286
P-value	0,015	ns	ns	ns

DISCUSSION:

The study was interrupted in most patients before halving the propofol dose, thus we did not obtain results about its effects on microcirculation. Instead, effects of remifentanil were different between the two groups. In fact, emerged that remifentanil acts differently on microcirculation functions in the Sepsis Group and in the Non Sepsis Group: this suggests that sepsis has an additive effect compared to drug only.

The consequences of propofol and remifentanil in the induction of anesthesia are known, but their effects in continuous sedation are controversial. Certainly remifentanil has an effect on basal levels of reduced and oxygenated hemoglobin in critical patients without sepsis, probably due to vasodilatation, but there is no variation of blood flow and tissue oxygen consumption during venous occlusions: it can be stated that the drug has an effect in basal condition of micro vascular bed, but it does not influence the microcirculatory auto regulation. Finally, it's not clear if the effects of sedation and sepsis are additives, and which is the relative importance of these two factors, but it seems possible that the effect of sepsis is predominant on microcircolatory function.

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Multicenter Study: Monitoring with NEDOCS score Overcrowding in Roman ED.

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Background - EDs overcrowding is a worldwide crisis that has many root causes both internal and external to the ED. ED overcrowding can harm patients, impair the patient care experience, and lead to negative operational and financial performance.. In the last decade most Italian EDs declared to be frequently overcrowded; the most common results are: blockade or diversion of EMS ambulances, and inability to transfer ED patients to an inpatient bed once the decision to admit is made. **Aim** – Verify if NEDOCS score can fairly estimate and monitoring the degree of Roman ED overcrowding, helping to find suitable strategies to manage it. **Methods and Materials** – Prospective multicenter study, to which 7 roman hospitals (university, community, rural community), situated in 4 areas of roman health system, participated. Hospitals measured ED crowding with NEDOCS score for the first 6 months in 2010 and 2011, calculated 5 times a day. For each hospital and area the data of NEDOCS, ED pts rate, pts by ambulance rate and flow, hospital admission; %LWBS; time to medical visit, time of boarding were compared. **Preliminary results** – As reported in Literature metropolitan hospitals constantly present a higher degree of overcrowding. In Roman experience University ED resulted never better than "very busy" condition, usually "dangerously overcrowded" and "disaster"; with the longest time for inpatient admission. Only the rural community hospital is rarely overcrowded; while urban community hospital has more difficulties to recover from disaster level. Pertini Hospital (metropolitan community) has the highest ED pts/yr and pts by ambulance/yr; even if the multiareas' ED organization proves to have better resilience. EMS ambulance flow shows poor communication with hospitals about ED crowding. **Conclusions** Overcrowding diminishes the capability of the ED to manage these emergencies effectively. NEDOCS score seems capable to estimate overcrowding also in Roman ED; moreover, it can be used to monitor the evolution of overcrowding, as it is a user-friendly score. The analysis of the other parameters had permitted to point out the most important issues for each hospital, that are peculiar for each area.

RABIES DISEASE: epidemiology, guide-lines and Emergency-department organization.

An update.

Autori:

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Background

Rabies is a zoonotic disease caused by a RNA virus belonging to the family of Rhabdoviridae. All mammals are susceptible and are able to transmit rabies virus. The rabies virus belongs to the family of Rhabdoviridae, has a single-stranded of RNA genome with negative sense. The genetic information is packed as a ribonucleoprotein complex in which RNA is tightly bound by the viral nucleoprotein. The RNA genome of the virus encodes five genes: nucleoprotein (N), phosphoprotein (P), matrix protein (M), glycoprotein (G), and the viral RNA polymerase (L). Once within a muscle or nerve cell, the virus uses the acidic environment of that endosome and start the local replication. This virus is neurotropic, and after infection and first local replication it can start travelling, by the point of entry, quickly along the neural pathways, until the central nervous system and other organs.

Human rabies: clinical manifestations

Approximately 55,000 people die from rabies virus infection worldwide every year and 95% of reported cases occur in Asia and Africa. Rabies is endemic in about 100 countries[1]. Human exposures are most frequently associated with bite or scratch by rabid animals and transmission of virus from animal secretions (mainly saliva). Rabies virus replicates within the muscle and connective tissues and after affecting the central nervous system can cause acute and progressive encephalitis. Human rabies is characterized by a variable incubation: from two to twelve weeks. Most important and frequent symptoms are partial paralysis, anxiety, insomnia, confusion, agitation, abnormal behavior, paranoia, hallucinations, delirium and hydrophobia. The clinical course of rabies encephalitis is characterised by two possible forms that have a first common phase: generic symptoms involving respiratory, gastrointestinal and nervous systems. While subsequently, the disease develops in two acute forms: furious (encephalitic), which is characterised by episodes of excitement and hallucinations and often hydrophobia and aerophobia; or dumb (paralytic), which is characterised by flaccid muscle weakness. Both forms are progressive and lead to death, usually within 7 days and 2 weeks in patient with encephalitic or paralytic rabies respectively.

Rabies in Italy

Italy was declared free from urban rabies since 1973, but a periodic reintroduction of rabies in wild animals from north-east may occurs. In fact, in October 2008, animal rabies cases reappeared in some place of the northeast region of Friuli Venezia Giulia. It should be keep in mind also that cases of imported rabies[2], mainly due to international travellers, are increasing during the last year. Recently a case of imported human rabies has been described in Italy (the fourth since 1975 and the 23rd case in EU in the last 20 years).

An Indian man of fourty years old[3], living in Italy, was admitted to a ED in Mantova on 23 October 2011, with a clinical picture of rabies infection (fever 40.4°C, malaise, headache, diplopia, whole body paraesthesia, ataxia, myalgia and flaccid paresis of the arms, anxiety and agitation). The patient reported an extensive bite on his left arm and right leg by a dog showing marked aggressiveness (occurred 1 month before) while he was in a suburban area of the city of Manpur, north-east India. Immediately after the accident, he had received post-exposure prophylaxis (PEP), four vaccine injections respectively on day 0, 3, 6 and 14, but rabies immunoglobulin was not administered. The patient died after 22 days of intensive care and rabies was confirmed post mortem.

Prevention strategies and treatment of human cases

Animal prevention of rabies can be carried out by controlling both in domestic and in wild animals, including the use of animals vaccination programs. For human prevention the pre-exposure immunization can be taken into account, specially for travellers in rabies-endemic countries. In cases of animal bite potentially infected by rabies virus an incorrect or partial post-exposure prophylaxis (PEP) can be related to a fatality rate of nearly 100%.

In fact, PEP is highly successful in preventing the disease if administered promptly, in general within 10 days of infection. Correct PEP consist in wound cleaning with soap, water and a virucidal agent associated with vaccine/immunoglobulin administration according to WHO guidelines based[1] on the category of exposure to a rabid animal.

Despite the availability of international guidelines for PEP we register a lack of both procedures *ad hoc* and drugs for patient presenting in Emergency Department (ED) with a positive history for bite or scratch with potentially rabid animals.

A survey aimed to provide information about the protocols used in the early management of patients bitten by animals potentially affected and the availability of specific immunoglobulins or vaccines in ED has been recently conducted by Pavia Poison Control Centre.

Preliminary Results

Preliminary data analysis suggests a lack of specific protocol for rabies management in most of EDs. Except for the northeast, an inhomogeneous presence of specific immunoglobulins or vaccines has been evidenced, that results absent in 60% of the EDs.

Conclusion

These prelimary data requires a critical revision of procedures for urgent treatment of potentially rabies affected patient presenting in ED and a proposal for preventive storage of specific immunoglobulins or vaccines (e.g. Poison Centres and some EDs selected on the basis of geographical criteria).

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Diagnostic and 30-day prognostic value of admission quantitative body-fluid evaluation by Hydration Index obtained by Bioelectrical Impedance Vector Analysis in patients with acute heart failure in the Emergency Department

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Background:

Acute Heart Failure (AHF) is characterized by a combination of clinical, haemodynamic and neurohormonal abnormalities that lead to sodium and water retention (1) with consequent total body fluid congestion. The bioimpedance vector analysis (BIVA) is a non invasive technique to estimate body water content whose utility in evaluating total fluid congestion in AHF patients has been recently demonstrated**.** Quantitative assessment of congestion by BIVA could be useful in the management of AHF patients. No data are available on the diagnostic and prognostic role of quantitative fluid retention evaluated by BIVA in AHF patients at the moment of their ED presentation.

Objectives:

Our aim was to evaluate in patients referring to Emergency Department (ED) for acute heart failure (AHF) the diagnostic and 30-day prognostic value of quantitative body fluid assessment by bioelectrical impedance vector analysis (BIVA).

Methods:

AHF patients, presenting to the EDs of Sant'Andrea University Hospital, Rome and of Novara University Hospital from January 2011 to December 2011 were enrolled. Inclusion criteria were: patients referring to the EDs for dyspnea or other symptoms raising a suspicion of AHF by ED clinician.. Exclusions criteria included: inability to provide informed consent, unconsciousness, presentation secondary to trauma, acute coronary syndrome, ascites and peripheral edema secondary to vein disorders, lymphedema, or hypoalbuminemia.

Point vectors and Hydration index (HI) were obtained by BIVA in 280 patients at ED arrival. In order to evaluate cardiovascular (CV) events, 30-day follow-up was performed.

Results:

Based on final clinical diagnosis, patients were divided in: AHF group, (n=146; 52.2%) and control group with other acute diseases, (n=134; 47.8%). Compared to controls, HI mean value resulted significantly higher in AHF group (82.6%±6.9 versus 74.5±5.3%, $p<0.001$). Apart from BNP, HI showed a significant diagnostic power in AHF (cut-off 73.5%, AUC 0.83, sensitivity 90%, specificity 49%). 30-day HI prognostic value was evaluated by the univariate analysis (HI >74.3%: OR 3.09, 95% CI 1.17-8.18, $p =0.023$) and it was confirmed at the multivariate analysis.

Conclusions:

In AHF patients a quantitative evaluation of fluid congestive status by HI obtained by BIVA at arrival in ED provides significant diagnostic and 30-day prognostic value. This could lead to a better management of these patients with possible improvement in reducing subsequent CV events.

Verifying Emergency Room Dyspnea: *the VERDI study.*

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INTRODUCTION

Dyspnea is an unpleasant or uncomfortable sensation of difficult breathing experience by an individual. It is difficult to grade dyspnea, because this is caused by a variety of physiological, pathophysiological, psychological and environmental factors, 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 (PCT, MR pro-ANP, MR pro-ADM). The enrolment was carried out between December 2010 and December 2011.

Primary endpoints of the study are:

1) Diagnostic accuracy of PCT for low respiratory tract infections (differential diagnosis)
2) Diagnostic accuracy of MR pro-ANP for acute heart failure (differential diagnosis)
3) Correlation between MR pro-ADM levels with events (rehospitalization and death) at 30 and 90 days from discharge (prognostic value).

MATERIALS AND METHODS

We studied patients admitted to the Emergency Department with acute dyspnea and hospitalized. 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. 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.

RESULTS

We enrolled 501 patients with shortness of breath arrived at ED, but statistical analyses was performed on 441 patients. Mean age was 77.8 (SD 10.84) years, 209 (47.4%) were males and 232 (52.6%)females. 162 (36.7%) patients had a cardiogenic dyspnea (final diagnosis of acute heart failure), 239 (54.2)patients had a respiratory dyspnea (final diagnosis of COPD exacerbation, LRTI-low respiratory tract infection, asthma), 40(9.1%) patients had a mixed dyspnea (caused by both cardiac and respiratory diseases). A subgroup of 128(29%) patients with infection (LRTI) was identified. 343(77,8%) patients were discharge at home, 57(12.9%) were transferred to other institutions and 41(9.3%) patients died in hospital. At 30 days follow-up we recorded 69 events (50 rehospitalizations and 19 deaths); at 90 days follow-up we recorded 88 events (67 rehospitalizations and 21 deaths).

For the diagnosis of acute heart failure, MR-pro ANP had a significant value: AUC 0.664 ($p<0.0001$) with a sensitivity of 60.9% and specificity of 66.55% (LR- :0.59, LR+:1.82; cut-off value:327.7 pmol/L). For the diagnosis of infections, PCT had a significant value: AUC 0.65 ($p<0.0001$) with a sensitivity of 68.93% and specificity of 56.92% (LR- :0.55,

LR+:1.6; cut-off value:0.09 ng/mL). As a prognostic indicator, MR-proADM demonstrated a significant value in predicting mortality at 30 and 90 days from discharge in all patients with a superiority in predicting 90-day mortality and with a more relevant role for values of 72 hours (30 days deaths: ADM 72 h, AUC 0.68, p=0.0065; 90 days deaths: basal ADM, AUC 0.668, p=0.0015, ADM 72 h, AUC 0.713, p<0.0001.) Furthermore, PCT values show a significant prognostic value in the infection subgroup in predicting mortality at 90 days, both at admission and at 72 hours (basal PCT, AUC 0.749, p<0.0001; PCT 72 h, AUC 0.751, p=0.0003).

CONCLUSIONS

The use of a panel with these three biomarkers can ameliorate the diagnosis (PCT and MR-proANP) and can improve the risk stratification (PCT and MR-proADM) and the treatment of adult patients admitted to the emergency department for acute dyspnea. Additional measurements of MR-proADM during hospitalization have more relevance in predicting mortality than a single admittance value.

"Usefulness of Bioelectrical Impedance Vector Analysis (BIVA) to evaluate dehydration status in Emergency Department."

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Background:

Dehidration is the loss of water and salts essential for normal body function. Hydration status is a very important tool in medical examination so to ensure good health in various clinical situations; at the same time it is very difficult to assess due to the inaccuracy of clinical evaluation and lack of techniques. In fact, severe dehydration can develop with minimal clinical signs and there are not validated laboratory methods to estimate total body water. Actually, the most widely used markers of hydration are plasma osmolarity, urine osmolarity and urine specific gravity, and between techniques Bioelectrical Impedance Vector Analysis (BIVA), is one of the most used.

BIVA is a non invasive analysis of impedance measurements (Resistance and Reactance) plotted as a vector in a coordinate system. Resistance (R) and Reactance (Xc) are obtained from an alternate current passing through tissues. Reference values, adjusted for gender, are plotted as so-called "tolerance ellipses" in the coordinate system. On this basis, a statement of the hydration status can be made with regard to water balance (normo-, hypo-, hyper- hydration) and body cell mass (nutritional status).

Study Design:

The Emergency Department (ED) setting is a particular context in which it is necessary to have a quick estimate of hydration status. The aim of our study is to validate BIVA accuracy in assessing hydration status in patients arriving in our ED, and the possibility to apply this technique in this complex setting as an easy and safe instrument.

Materials and Methods:

This is a prospective, descriptive, non intention to treat study. We enrolled patients arriving to our Emergency Department, using as major criteria of inclusion clinical dehydration, and excluding patients in state of unconsciousness. For each patient we analysed BIVA measurements at different times (arrival, 4, 24, 48 hours and discharge), and we registered vital signs, fluid balance, and haematological parameters.

Results:

We enrolled 71 patients (37 F and 34 M, with a mean age of 81.5 years old). We analysed:

1) correlation between BIVA values and conventional markers of dehydration: plasma osmolarity, urine osmolarity, urine specific gravity, hematocrit (diagnostic value);
2) correlation between BIVA values and incidence of adverse events with a 30 days follow up: days of hospitalization, rehospitalization, mortality, (prognostic value).

Conclusion:

BIVA can ameliorate clinical evaluation and could help Emergency Physician to detect patient's hydration status quickly and easily. Also, we found that patients who arrived in ED with an important dehydration status have a worse prognosis at 30 days.

Research proposal: Advanced management of patients with acute respiratory failure using noninvasive mechanical ventilation combined with biomarkers.

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Introduction:

Acute respiratory failure (ARF) is a common emergency department (ED) presentation. Patients with ARF may have more than one underlying aetiology to their clinical condition.

Over the last 20 years, in addition to invasive mechanical ventilation , a great deal of clinical research has shown that non-invasive ventilation (NIV) too, is a valuable form of treatment for ARF and nowadays NIV has radically changed the management of ARF. NIV is preferable to invasive ventilation whenever possible, because it has been shown to reduce mortality and hospital length of stay, reducing risk of endotracheal tube and ventilator associated pneumonia; furthermore it reduce markedly costs.

According to several randomized controlled trials, NIV has gained acceptance as the preferred ventilatory modality to treat ARF due to acute exacerbations of chronic obstructive pulmonary disease (AECOPD), cardiogenic pulmonary edema, respiratory failure in immunocompromised patients, and it's benefits are more evident when early application of NIV occurs.

During NIV, the most important parameters of clinical course are PaCO2 (the arterial partial pressure of carbon-dioxide), PaO2/FiO2 ratio, pH, respiratory rate, dyspnea, and alertness: these must be monitored frequently in the first hour (every 30 minutes) and their improvement in the first two hours is the best predictor of NIV success. They represented also the main criteria for stop NIV: NIV can be stopped when RR (respiratory rate) < 24/min, HR (heart rate) < 110/min, pH > 7.35, SpO2 > 90% with FiO2 30%.

Therefore, there aren't specific parameters that indicate NIV's interruption, but in emergency setting, physicians require optimizing resources and time in the diagnostic and prognostic evaluation of patients.

Recent literature demonstrated the diagnostic and prognostic role of several biomarkers in critically ill patients referring to ED and new peptides are emerging that may give additional information about prognosis and treatment options, such as Adrenomedullin (ADM) and copeptin.

The role of MRproADM and copeptin as a prognostic biomarkers was examined in different conditions frequently observed in ED, where their plasma concentration is increased, such as acute myocardial infarction, congestive heart failure, sepsis and septic shock, lower respiratory tract infections, community-acquired pneumonia, AECOPD, hypertension, chronic renal failure, stroke and traumatic brain injury.

Aim of the study:

First Aim is to evaluate the individual and collective ability of MR-proADM and copeptin for predicting outcomes (ARDS, all-causes death, all-causes rehospitalization) in patients presenting in ED with ARF, treated with NIV and hospitalized.

Second Aim is to compare the individual and collective ability of MRproADM and copeptin with hemogasanalytic parameters (pH and PaO2/FiO2) to assess if the multimarker assessment will be more accurate to identify pulmonary gas exchange improvement and it could be superior or at least non inferior to clinical variables for indicate when stop NIV.

Inclusion criteria*:*
Patients >18 years of age, presenting to the ED with dyspnea with hemogasanalytic diagnosis of ARF due to cardiogenic pulmonary edema, AECOPD, pneumonia, acute respiratory distress syndrome (ARDS), requiring noninvasive mechanical ventilation and hospitalization (expected need >48h), with possibility to take informed consent and a blood sample for biomarkers before starting NIV.

Exclusion criteria:
- unconscious patients
- dyspnea secondary to trauma
- life expectancy less than 48 hours or patients requiring early intubation and invasive ventilation.
- chronic respiratory failure treated with domiciliary NIV
- patients unable to provide informed consent

Materials and methods:

The study is a prospective, observational one, enrolling 50 patients admitted to our ED for acute respiratory failure, requiring noninvasive mechanical ventilation and hospitalization; as ventilation's mode, pressure support ventilation (PSV) will be used. If the patient is willing to enroll, informed consent will be signed.

Baseline demographics, vital signs, results of physical examination, values of blood gas analysis and ventilation's parameters will be recorded using a specific case report form (CRF). Antibiotics and steroids administration will be also noted.
Two tubes 4.5 ml sample of blood will be drawn in tube containing ethylenediaminetetraacetic acid (EDTA) for the measurement of MRproADM and copeptin at admission and Blood Gas analysis will be performed also before starting NIV (T0). Furthermore, blood samples for serial biomarkers measurements and serial blood gas analysis will be performed: 24 hours (T1) after the start of mechanical ventilation, after 48 hours (T2) and at the moment when the physician will stop NIV (T3). MR-proADM and Copeptin will be measured using an automated sandwich chemiluminescence immunoassay on the KRYPTOR system (B·R·A·H·M·S AG, Hennigsdorf/Berlin, Germany).

Moreover, at 30 and 90 days after discharge a phone follow up will be performed for death or rehospitalization, to evaluate the prognostic value of MRproADM and copeptin.

PREVALENCE AND MANAGEMENT OF PAIN IN THE EMERGENCY ROOM IN VENICE: IMPLEMENTATION OF GUIDELINES.

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BACKGROUND AND AIMS: Pain is frequently observed in the Emergency Department (ED). Awareness of the need of prompt and appropriate pain evaluation and treatment, regardless of its causes, is rapidly emerging, because of the negative consequences that symptoms may have on patients. However, pain is often underestimated, analgesics are underused and delay in treatment is common. Aim of the study was to assess prevalence and management of pain in ED.

PATIENTS AND METHODS: The study was conducted in the SS. Giovanni e Paolo Hospital, Venice city center. A sample of patients with pain accessing ED during working days was asked to fill in a form reporting pain severity and pain perception during the whole observation period (first aid, triage..), before and after analgesic treatment. After seven days (Follow-up) we asked them to fill out a questionnaire reporting pain perception. The pain was evaluated following the VAS (Visual Analogic Scale) and the NRS (Numerical Rating Scale) scale, assigning the highest score for the highest pain intensity.

RESULTS: One third of the sample complained of pain caused by burns and trauma due to accidental falls (41%). Only 40% underwent analgesic therapy. The average waiting time between patient admission (triage) and medical examination and treatment was 80 minutes in keeping with the priority code initially assigned by the triage nurse. The correlation between algometric measurements and triage nurse evaluation was good ($r=.65$, $p<0.0001$). The waiting time did not correlate with the pain intensity evaluated by the NRS scale. None of the patients took analgesic drugs before the first medical assessment. The guidelines were followed in patients with mild pain, but only 26% of patients with severe and acute pains got a course of analgesic treatment according to relevant guidelines, due to underestimation of pain severity by the medical staff. After analgesic treatment, the pain disappeared in 50% of the sample and strongly weakened in the other 50%. Seventy five per cent of the sample treated with analgesic therapy manifested a substantial relief. At follow-up, 60% of the out-patients reported following therapy and the pain vanished in 44%. None reported side effects.

CONCLUSION: Pain evaluation and treatment are common procedures in ED. However, pain severity is underestimated during emergencies by the medical staff and/or overestimated by the patient. Correct implementation of the procedures and guidelines for acute pain and its constant monitoring will permit better pain evaluation and treatment and greater patient satisfaction.

SEPSIS, SEVERE SEPSIS AND SEPTIC SHOCK IN VENICE: IMPACT OF AWARENESS CAMPAIGN ON MANAGEMENT AND CLINICAL OUTCOME

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BACKGROUND: Sepsis is a remarkably widespread disease. Its incidence is growing and its mortality is high and increases with severity: 25-30% for severe sepsis and 40-70% for septic shock. In the elderly sepsis has an even higher incidence and it is more difficult to diagnose as its apperance is often atypical. Moreover, the risk of death is higher because of comorbidities. Improvement of patient outcome has been observed after implementation of specific guidelines and awareness campaigns among health professionals. Venice has an old population and only one hospital. Therefore, it offers a good opportunity for studying sepsis in the elderly and for evaluating the impact of awareness campaigns on health staff.

OBJECTIVES: The main goal of the study was to assess epidemiology and presentation of sepsis, severe sepsis and septic shock in the population of Venice. A secondary goal was to monitor improvement in the patients' management and outcome after awareness campaigns on the implementation of guidelines for sepsis diagnosis and therapy for physicians in emergency and non-surgery Departments.

PATIENTS AND METHODS: The study was organized into two phases of six months each, separated by a professional seminar. In the first phase patients were chosen through DRG, while in the second one through reporting by treating physicians on the basis of the Surviving Sepsis Campaign criteria. Collected data include clinic and demographic characteristics, the parameters needed to calculate MEDS, SOFA and APACHE II scores, empirical therapy characteristics, cultural isolations, performed procedures and outcome.

RESULTS: The mean age of the patients was 71 ± 19 years and the disease presentation showed no difference from the literature. Even though the most frequent origin of the infective episode was pneumonia, consistent with those reported in previous studies, the aetiology was different: a prevalence of Gram+ germs was found in blood cultures, and not of Gram- bacteria, which more often led to sepsis in elderly patients according to the literature. The variables that have the greatest impact on mortality were age ($P<0,0001$), Charlson's comorbidity index ($P=0,0001$), MEDS, SOFA, APACHE II scores, evolution in severe sepsis and septic shock ($P<0,0001$). The awareness intervention allowed a larger percentage of patients to receive the empirical therapy within 1 hour from reaching the hospital, and it reduced mortality, but it did not influence the length of hospital stay.

CONCLUSIONS: The population of Venice is an excellent cohort for studying sepsis in elderly patients, without differences in presentation if compared with the known data from literature. Aetiology differs from international data and deserves further investigations. Raising awareness among health professionals is useful to improve management and outcome of patients with sepsis. Such campaigns need to be repeated periodically to improve the implementation of guidelines and to test new written protocols.

Mind your step! A pilot study on geriatric patient profile in a Dutch academic emergency department.

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Background: Current Dutch emergency care system focus on rapid emergency department (ED) management with 4 hour completion times (1), which may not meet specific needs of the older emergency patient.

Objective: This pilot study was conducted to assess profile and patterns of use in geriatric patients presenting to a rural ED in the Netherlands.

Design, study population and setting: Observational pilot study in patients aged 70 years presenting to the ED of VU University Medical Centre (VUmc), Amsterdam, Netherlands.

Outcome measures: Patient characteristics (age, gender, presenting complaints, medication, comorbidity, delirium) and patterns of use (specialists involved, length-of-stay, disposition, 30-day return visit).

Results: 100 patients were included. Median age was 81.0 (70, 97) years, 35% male. 86% (86/100) lived independently at home. Fall-related injuries were the most common reason for ED presentation (36%, 36/100). Of the patients with a current outpatient medication list, 50% (42/84) used five or more prescription drugs. Overall admission rate was 42% (42/100). Delirium prevalence rate was 9% (9/100). Mean ED length-of-stay was 181.3 ± 84.1 minutes. Involvement of more than one consecutive medical specialty significantly prolonged ED length-of-stay ($p = 0.001$). Of the patients discharged home from the ED, 21% (11/53) had an unplanned ED return visit within the next 30 days, of which 45% (5/11) initially presented with fall-related complaints.

Conclusions: Our study showed that the majority of the 70+ patients were discharged home from the ED. Noticeably, patients who initially presented with fall-related complaints accounted for nearly half of the patients with an unscheduled 30-day ED return visit, suggesting that fall (risk) assessment was not adequately performed. Current Dutch ED care systems focus on rapid patient management with care being delivered by many specialities. As a result, care is fragmented, leading to poor care coordination. We believe geriatric and fall risk assessment training for emergency physicians or adding a geriatrician to the acute care team would improve care for the older ED patient.

BIVA monitoring predictive value for death and re-hospitalization in patients with dyspnea in E.D.

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Introduction

Dyspnea is one of the most frequent causes of admission to the ED. It is a non specific symptom and it can be caused by different pathologies such as acute heart failure, re-exacerbation of chronic obstructive pulmonary disease (COPD), lower airways tract infections, pulmonary embolism. Generally patients with dyspnea are in critical conditions and, from a prognostic point of view, it is important to make a correct risk stratification. In this scenario Bio-Impedance Vector Analysis (BIVA) could be a new parameter useful to formulate a proper diagnosis and prognosis. BIVA is a non invasive analysis of impedance measurements (Resistance and Reactance) plotted as a vector in a coordinate system. Resistance (R) and Reactance (Xc) are obtained from an alternate current passing through tissues. Reference values, adjusted for gender, are plotted as so-called "tolerance ellipses" in the coordinate system. On this basis, a statement of the hydration status can be made with regard to water balance (normo-, hypo-, hyper- hydration) and body cell mass (nutritional status).

Aim of the study

The aim of the study was to verify if the use of BIVA could help emergency physicians in the management of patient with dyspnea and in formulating a correct prognosis.

Materials and methods

This was a prospective, descriptive, non intention to treat multicentric study. We enrolled patients arriving to the Emergency Department with dyspnea,. For each patient we analysed BIVA measurements at different times (at arrival, at 24 hours and at discharge), and we recorded anamnestic data, vital signs, physical examination, chest X-ray and laboratory tests (including BNP and Copeptin). Each patient was followed-up by phone call after 90 days to check the clinical condition.

Results

290 patients (135 males (46%),155 females (54%); mean age 78.2± 10,5 years) with dyspnea were enrolled: 175 diagnosed as cardiogenic dyspnea and 115 diagnosed as respiratory dyspnea;; mean Hydration index value in cardiogenic dysnea group 81.9% ± 6.7%, mean hydration index value in respiratory dyspnea group was 75.7% ± 4.6%;in the follow-up the events were 87 (35.2%). Our results showed that considering the entire population the more the vector (both at arrival and at discharge), is placed far from the 50^{th} percentile elipse, the more the prognosis is worse.

Conclusions

Our data confirm that hydration index can identify ED patients with dyspnea due to congestive heart failure because the difference between the mean value of the hydration index of the two groups is statistically significant ($p<0.0001$). Furthermore it seems that there is a correlation between the position of the vector and the prognosis but it is not statistically significant. This correlation is presente both at admission and discharge: maybe we need an intention to treat trial based on the biva monitoring to improove the outcome. Further analyses are needed to confim our data, and to better understand the prognostic role of BIVA in ED.

HOSPITAL DISASTER PLAN: EFFICACY OF SIMULATION AS A TRAINING TOOL FOR HOSPITAL STAFF MEMBERS.

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Introduction

Recently San Raffaele Hospital set up a plan to for response to both internal and external major incidents. Since in disaster medicine we cannot have "on job training", a one day-course was organized for the hospital staff members involved in the response to different threats.

Method:

109 professionals were enrolled in four editions of the course: 36 doctors, 60 nurses, 13 employees.

In the first part of the day the trainees were introduced to the details of the hospital disaster plan, principles of triage in disaster medicine and damage control surgery.

In the second part of the day they performed a drill, a full scale simulation exercise with active participation of all delegates in the position they would have in real disaster situation (emergency room, Operating theatre, Command Center, ICU.).

The drill was performed on the base of MACSIM system; it uses "simulated patients", taken from real scenarios regarding recent terroristic attacks. The basic element in MACSIM system is the "patient card"; it illustrates patient's initial position, sex, age, initial clinical condition according to ATLS terminology. The cards are magnetized and can be moved on different magnetic whiteboards representing the parts of the hospital The patients have real injuries that have to be known and treated by the trainees within a certain time, in order to avoid mortality or complications. The outcome is analyzed in terms of avoidable deaths related to Injury Severity Score (ISS).

To assess the efficacy of the training in improving the trainees' knowledge of the hospital plan and their skills in disaster medicine, we asked them to answer 15 questions at the beginning and at the end of the course.

Results:

All the participants increased their knowledge of the topics under training.

Before training, 39,8% of the participants were aware of the general organization of the hospital during a major incident; they were 76,4 at the end of it (+95%); 46,7% previously knew how to set the different areas in the emergency room after the alert, then they were 79,5% (+74%); 40,4 of the trainees were conscious of the Incident Command Center; they increased to 80% (+101%) after the training; 43,5% of the applicants knew the chain of activation of the alert inside the hospital; after the course, 79% of them knew it (+83%). The knowledge of the emergency management (alert, preparation, action) increased after the drill (40% vs 77,9%: + 97%). Only 37% of the applicants were aware of the role of HDM (hospital disaster manager), but after the course they were 82,2% (+123%). 49,6% of the trainees were skilled in primary triage; they rose to 64% at the end of the day (+60%). Data were comparable for secondary triage: 37,4% vs 64,5% (+77%). The use of action cards was previously known by 52,7% of the applicants, it was 88,9% later (+72%). 43% of the trainees were aware of activation of on call staff, then they were 77,3% (+82%). Little knowledge was shown about surgical triage and damage control surgery before the course (33,8% and 27,2% respectively), with improvement after it (60% and 58,6% respectively): + 85% and +128%. Only 22,8% of the trainees were conscious of the disaster clinical chart, but the number rose to 60% at the end of the drill (+176%). An increased knowledge of the number of disaster victims to be accepted by the hospital and of the actions to discontinue disaster plan was achieved during the course (27,5% vs 66,9%; + 145% and 24,6% vs 66,9%; + 186% respectively).

Conclusion:

These data show that training based on MACSIM system is a good method the improve hospital staff's knowledge of the hospital disaster plan.

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CARDIOVASCULAR EVENTS IN PATIENTS WITH HYPERTENSIVE EMERGENCIES AND URGENCIES ADMITTED TO AN ED: A 2 YEAR FOLLOW UP

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Background: at present, few data are available on the prognostic significance of hypertensive emergencies and urgencies admitted to Emergency Departments (ED). The aim of our study was to evaluate the incidence of total and cardiovascular events (CV) during follow-up in hypertensive patients admitted to an ED of the Brescia Hospital (Northern Italy) with hypertensive emergencies (HE) or urgencies (HU). **Methods**: between January and December 2008, medical records of patients aged > 18 yrs, admitted to the ED of the Spedali Civili di Brescia with blood pressure values >180 mmHg (SBP) and/or >120 mmHg (DBP) were collected and analysed in 1551 patients with either an ”hypertensive emergency” (n=317) or ”hypertensive urgency” (n=1234). Follow-up data were analysed on 947 patients (”hypertensive emergency” (n=201) or ”hypertensive urgency” (n= 746)(44% males, mean age 71±13 years); the mean duration of follow-up after admission to the ED was 2 years. **Results**: a first fatal or non fatal CV event occurred in 226 patients (62 cardiovascular events, 45 cerebrovascular events, 42 hospital admissions for heart failure, 46 cases of new onset kidney failure and 31 cases of new-onset diabetes). Patients with CV events were older, more frequently males, with a higher prevalence of diabetes mellitus and previous CV disease, and a greater proportion of inadequate BP control. During the follow-up a new episode of “hypertensive crisis” was recorded in 203 pts (24%). The incidence of hypertensive crises was significantly higher in patients with hypertensive emergency in comparison with hypertensive urgency ($p=0.03$). The incidence of fatal and non-fatal CV events was 14.5 vs 4.5 per 100 patient-years in patients with hypertensive emergency and urgency respectively ($p<0.001$). Similar results were obtained when we considered separately the occurrence of cardiac, cerebrovascular or renal events. **Conclusions**: admission to the ED for hypertensive emergencies identifies hypertensive patients at increased risk for fatal and non fatal cardiovascular events. Our results underline the need for a strict and accurate follow-up in patients with hypertensive crises.

ASSESSMENT OF CHEST PAIN IN AN EMERGENCY DEPARTMENT (S. ORSOLA-MALPIGHI HOSPITAL- BOLOGNA) - 2011 DATA

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Chest pain accounts for up to 5% to 10% of the consultations in emergency departments [1]. A prompt, correct diagnosis is crucial, as misdiagnosed chest pain can result in serious health damages [2]; furthermore, a correct diagnosis and an early rule-out in Emergency Department (ED) for low risk patients allow a significant reduction of inappropriate hospitalizations.

In the present study, we aimed to verify the amount of patients complaining for chest pain admitted in 2011 in our ED and their final destination (discharge or hospitalization); in 20% of patients we also analyzed high sensitivity Troponin T values and final diagnosis. Value of Troponin T minor to 14 ng/L were considered negative, border-line between 14 and 53 ng/L and positive above 53 ng/L. Relative increasing values observed in consecutive determinations of Troponin T were considered significant for acute coronary syndrome [3].

In 2011 the total amount of patients admitted to our ED complaining for chest pain (keyword used to select patients: "Dolore toracico", "Toracoalgia", "Precordialgia") was 2751 (54% male, 46% female, main age 57, range 14-111); 1337 patients (49%, main age 54, range 14-96) were discharged, 1414 (51%, main age 71, range 20-111) were hospitalized. Out of the discharged patients, 70% were discharged directly from ED, whereas 30% were discharged after intensive short observation (OBI). Diagnosis at discharge resulted as follows: 1% of discharged patients obtained a cardiologic "coronary" diagnosis, 5% a cardiologic "non coronary" diagnosis, 61% a non cardiologic diagnosis and 33% only a descriptive diagnosis. In 20% of the discharged patients Troponin was not determined at all whereas in 80% at least one Troponin determination was performed, resulting negative in 95% patients, border-line in 5% patients, positive in no patients.

As for the hospitalized patients, 45% were admitted to a cardiology ward or intensive care unit (ICU), 52% were admitted to a general medicine or geriatric ward and 3% to other wards. The final diagnosis for the hospitalized patients resulted as follows: a cardiologic "coronary" diagnosis in 30% of patients, cardiologic "non coronary" in 17%, non cardiologic in 41% patients and descriptive in 12% of patients. In 15% of these patients, Troponin was not assessed at time of hospitalization whereas in 85% Troponin was determined (negative in 36% cases, border-line in 37%, positive in 27% patients).

Our data confirm that chest pain represents a frequent cause of ED admission and hospitalization (more than 50% of cases). Unfortunately, quite often patients receive either a descriptive diagnosis (12%) or a non cardiologic diagnosis (41%) even after hospitalization. On the other hand, a short observation in OBI unit often allows a faster patient rule-out, avoiding useless hospitalizations.

We think that chest pain unit, characterized by the collaboration between the ED physician and the cardiologist together with the early use of cardiac imaging and provocative tests, represents an extremely useful model for a better management of chest pain patients. In fact, this model allows an early rule-out of chest pain patients and helps to determine the appropriate need of hospitalization.

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Ultrasound Speed Evaluation for Urgencies Level (USEFUL) in the emergency room: A new protocol with pocket-sized ultrasound technique (Vscan) in managing acute diseases.

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Background

Ultrasound techniques in Emergency provide the possibility to rapidly evaluate critical patients in life threatening conditions and to screen patients needing hospitalization or immediate therapeutical decisions. The use of new ultrasound devices with a small size and used at bedside would allow to accelerate these processes. ACEP guidelines for use of Ultrasound in emergency medicine provide a policy statement on the usefulness of ultrasound in emergency, and ultrasound has become an attractive useful diagnostic tool in a growing number of situations in the acute settings.

Objective:

Our aim was to demonstrate the usefulness of Vscan in an acute setting scenario such as the Emergency Department in order to exclude the diseases cause of symptoms (cardiac arrest, hypotension/syncope, chest pain, abdominal pain, polytrauma, dyspnea), and to validate the usefulness of it at different levels of urgency/emergency, that is to validate it not only in the very acute setting but, also, in lower levels of emergency. The second aim was to estimate the reduction of timing diagnosis, therapy and, eventual, hospitalization.

Materials and Methods:

This was a n observational study. We enrolled 404 patients (222:182/M:F; mean age 64±19 years) Fig 1, arriving to the Emergency Department of a 450-beds University hospital (Sant'Andrea Hospital) in the period between 1st November 2011 and 29 February 2012. All standard diagnostic radiological examinations were made in the radiology examination room by a specialist radiologist prior the ultrasound pocket-sized test, while Vscan examination was performed bedside in the emergency room by trained EP residents or registrars who underwent a six months didactic and practical training about the techniques of ultrasound in emergency and of the Vscan pocket device. The exclusion criteria was age <18 years, unavailability to give informed consent.

Results

Total time used to perform imaging examinations was, for traditional imaging, 43.14±30.68 minutes, and, for Vscan, 4.72±1.10 minutes ($p<0.0001$) [Fig 2]. The global inter-rater agreement between Vscan and traditional imaging was K=0.739 (95%CI 0.665-0.812). Correlation between Vscan and traditional imaging was r=0.74 (95%CI=0.69-0.78). Perfect correlations ($r=1.00$, $p<0.0001$) were found for the signs of "aortic dilation" and "cholecystic thickening". When Vscan was compared to the traditional imaging the specificity was always higher than sensitivity for each studied sign. High sensitivity and specificity of Vscan was recorded in all the different final diagnoses.

Conclusions:

Our results show that Vscan examination in patients with different acute diseases offers a high–quality and affordable diagnostic assessment integrated in the initial physical examination especially in excluding, rather than in including, specific acute conditions. This could lead to a significative reduction of health costs for the hospital by decreasing LOS and costly imaging. Other studies should be performed to confirm the usefulness of pocket-sized, not invasive ultrasound examination evaluation in ED.

Platypnea-orthodeoxia syndrome: an unusual case of dyspnoea.

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F.M., a 65-year-old-woman was admitted to our hospital for rapidly progressive shortness of breath over 2 week's duration. She reported also cough and chest pain, but no fever. The patient's medical history was otherwise notable only for essential hypertension treated with amlodipine and lisinopril/hydrochlorotiazide.
The physical examination revealed a woman with moderate distress and dyspnea, with heart rate of 68 bpm, blood pressure of 120/70 mmHg, respiratory rate of 22 breaths/min and peripheral blood oxygen saturation (SpO_2) level of 87% on room air and 96% on 15 L/min per nasal cannula. Bilateral basal rales and muffled heart sounds were present at auscultation. There was left leg edema, but no calf pain. During the physical examination it was noted that, while sitting upright, the patient became intensively dyspneic and SpO_2 decreased to 75% despite supplemental oxygen administration.
Arterial blood gas analysis obtained at admission (on room air) revealed respiratory alkalosis and hypoxemia, with a pH of 7.47, an SpO_2 of 86%, and with oxygen and carbon dioxide partial pressures of 49 mmHg and 31 mmHg, respectively. The hemoglobin level was 14,9 g/dl, the platelet count 296 $x10^{3/}\mu L$, the white-cell count 9.8 $x10^{3/}\mu L$. Renal and liver tests were normal. Troponin I was negative. A chest x-ray showed the absence of focal abnormalities. A transthoracic echocardiogram showed right ventricular dilatation and an interatrial septal aneurysm.
A computed tomography (CT) of the chest was negative for pulmonary embolism. A ventilation-perfusion scanning was interpreted as medium probability for PE. The patient was anticoagulated with heparin and transitioned to oral warfarin. Lower-extremity ultrasonography was negative for deep vein thrombosis.
A transthoracic and trans-esophageal echocardiogram was performed, showing the presence of a patency of the foramen ovale (approximately 19 mm), with interatrial septal aneurysm, and a right-to-left shunt, confirmed by the administration of saline contrast. In upright position the right-to-left shunt became more evident and was associated to severe hypoxia.
A second ventilation-perfusion scanning, performed after one week of anticoagulation therapy, was interpreted as a probable previous PE, in a resolution phase. After 2 weeks the patient's conditions had only slightly improved and it was decided for surgical correction of PFO. A transesophageal echocardiogram performed after surgery confirmed the successful closure of the foramen ovale, with a minimum residual shunt on the supero-posterior ridge of the fossa ovalis. The patient had no further episodes of hypoxia in supine and/or upright or lateral position and was discharged.