

SOCIÉTÉ TUNISIENNE DE MÉDECINE D'URGENCE



December 2017 Volume 1 Issue 2

# TUNISIAN JOURNAL OF EMERGENCY MEDICINE

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# Editorial

As a scientific journal with a national dimension, the TJEM is sensitive to the experiments carried out by clinicians wishing to enlighten their action and to contribute to the collective development of emergency specialty. One of the major goals of TJEM is to become a tool, serving all emergency doctors in Tunisia and beyond. The challenge is to convince our colleagues that they are capable of raising emergency medicine in their country to a level that commands respect. Yes, they can. Not having a past is not a handicap; it is rather an advantage. Joining this important project will help us in this exciting process.

In this issue of TJEM, Dr Beltaief et al provided the results of a study aiming to test the diagnostic value of baseline C-reactive protein and its early change combined to modified Alvarado score in a cohort of 500 patients with suspected acute appendicitis. The authors should be congratulated for completing such a difficult trial and presenting it in an elegant manner. They found that these parameters are of modest value in this issue. Therefore, this report by Beltaief et al provides additional evidence to suggest that laboratory markers have very limited diagnostic utility on their own but show promise when used in combination (1). CRP is an acute phase reactant. Its diagnostic significance is largely based on both its kinetic properties and its utility as a marker for complicated/advanced appendicitis. CRP levels show an increase between 8-12 hours after the onset of inflammatory processes with a peak between 24 and 48 hours, which is later than that of white blood cells. Consequently, CRP contributes little diagnostic utility early in the case of simple appendicitis. A CRP cut-off of >10 mg/L yielded a range of sensitivity between 65–85% and a specificity between 59-73%. In a study of 542 patients the AUC of admission CRP was only 0.60 compared to 0.77 on day 2 and 0.88 day 3. In cases of perforated appendicitis, the AUC was 0.90 on day 1, 0.92 on day 2 and 0.96 on day 3 (2). Thus, CRP serves as a strong predictor for appendicular perforation but is quite limited for appendicitis in general. Virtually every diagnostic test used in medicine is susceptible to inaccuracies, false-negative and false-positive results, or a lack of sensitivity or specificity. Nonetheless, imperfect tests can still be highly

useful when applied by physicians in the proper diagnostic setting. Further studies are warranted for laboratory markers in combination and to validate potential novel markers.

In this issue of TJEM, Haj Ali et al showed the first results of Sahloul Emergency department regarding acute coronary syndrome registry (ReSCU registry). One of their main objectives is to compare their management of these patients with current guidelines in order to improve clinical practice. The authors studied 150 adults and their results were quite impressive as 130 patients had undergone primary percutaneous coronary intervention and all the others received intravenous thrombolysis. Of course, this is not the usual practice and it is not sure that this sample was not selected.

This issue of TJEM includes a study of Ghazali et al whose objective was to identify factors associated with the diagnosis of non-ST-segment elevation acute coronary syndrome in patients admitted to the ED with undifferentiated chest pain and normal EKG. They found that advanced age, history of diabetes or known coronaropathy and elevated troponin are the main markers of ACS. What should be highlighted is that all these factors are included in many available diagnostic models. It was perhaps more suitable that the authors tried to validate one of these models in their population. It should also be noted that the same study was performed in Monastir ED where a new score was proposed (3).

From its origins, point-of-care echocardiography in EDs have had 2 main challenges. The first has been convincing doubtful colleagues that emergency physicians are capable of performing an examination with acceptable accuracy after focused training. The second obstacle has been providing data of improved outcome from incorporating echocardiography into ED clinical practice. Why should an emergency physician bother learning this diagnostic method when he can simply has cardiologist or someone else to do this? This is a good question that needs to be answered. One common challenge of any new procedure in emergency medicine is overcoming the inertia of comfort with the status quo. The American College of Emergency Medicine issued a position paper in 1990 that supported the use of point of care ultrasonography (POCUS); this was followed by a similar document written by the Society for Academic Emergency Medicine in 1991 (4). With this early support for the use of POCUS by EM physicians, EM residency programs in the United States and Canada started to introduce ultrasonography as a standard part of training. The American College of Graduate Medical Education (ACGME) has established POCUS as a required part of EM training. All EM residencies accredited by the ACGME provide POCUS training that include a minimum 80 hours of dedicated clinical ultrasonography, 20 hours of didactic ultrasonography education, and accurate performance of 150 independently reviewed ultrasound studies. Accordingly, ultrasonography has become an integral part of EM over the past two decades, and it is an important skill which positively influences patient outcomes. In this issue of TJEM Ben Lassoued et al compared in their study the findings of echocardiography performed in 204 adult ED patients by emergency physicians and cardiologists. They found an excellent concordance. These results are not new; they should add an additional support to the widespread use of echocardiography in the EDs. The authors should clarify whether there was one or more physicians involved in this study and also give us more precision about the training level of the physicians included in their study.

Last but not least is the question of pain treatment in EDs. Optimal pain management is imperative in ED. Indeed, the consequences of pain on the cardiovascular and the neurovegetative systems are susceptible to aggravate the already unstable patients. In addition, anxious, agitated or aggressive behaviors frequently observed in patients with acute pain can lead to diagnostic errors and treatment failure. It is clear that beyond all these considerations, a significant obstacle to optimal pain management in ED patients would be related to the high medical and nursing workload in this setting. Some studies concluded that there is a linear correlation between emergency department overcrowding and the failure to receive adequate pain treatment (5). As a result, clinical practice guidelines have been developed with the goal of promoting effective pain treatment in ED. A simple action based on the early prescription of paracetamol could be associated with a significant decrease in pain intensity and improve patients' satisfaction. This was demonstrated in this issue of TJEM by the study of Mezgar et al conducted on 500 patients admitted to the ED. Although we apologize their effort to improve pain treatment in the emergency care setting, we suggest to the authors to conduct a randomized controlled study using the same objective.

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# **ORIGINAL RESEARCH**

# Value of early change of serum C reactive protein combined to modified Alvarado score in the diagnosis of acute appendicitis

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#### BACKGROUND

Diagnosis of acute appendicitis still challenging. The aim of this study is to test the diagnostic value of baseline and early change of C-reactive protein (CRP) concentrations, evaluated separately or in combination with the modified Alvarado score (MAS), in patients with clinically suspected acute appendicitis.

#### METHODS

This is a prospective observational study including all patients presenting to the emergency department with an equivocal diagnosis of acute appendicitis. After inclusion, clinical and demographic data are recorded and blood samples were taken at baseline and 3 hours after for serum CRP measurements (3 hour CRP). The MAS is also calculated for all patients. The ultimate diagnosis of appendicitis was based on the histologic findings of the excised appendix in operated patients and clinical follow-up in emergency department discharged patients. Diagnostic accuracy of admission CRP, early change of CRP 3 hour CRP minous admission CRP, MAS and the combination of these parameters was expressed by sensitivity, specificity, positive predictive value, negative predictive value and area under receiver operating characteristics curve.

#### RESULTS

500 patients were included from January 2010 to December 2013. Overall, 387 patients were operated the negative appendectomy rate was 8,3%. CRP concentrations were significantly higher in patients with acute appendicitis. However, the diagnostic value of admission CRP, delta CRP and MAS was moderate with area under ROC curve respectively equal to 0.63, 0.53 and 0.6. Combining admission CRP and delta CRP values to MAS did not result in a better performance. The area under ROC curve did not exceed 0.7 with the different combinations.

#### CONCLUSIONS

Early change of CRP has a moderate diagnostic value in patients with clinically suspected acute appendicitis. Combining CRP values to MAS did not improve diagnostic accuracy.

#### **KEYWORDS**

C-reactive protein, acute appendicitis, Alvarado score.

TRIAL REGISTRATION : ClinicalTrial.gov NCT02730585. Registred 31 August 2016

#### INTRODUCTION

Acute appendicitis is the most common surgical emergency and the most common source of community-acquired intraabdominal infections[1].Clinical diagnosis of acute appendicitis is still difficult. It has been estimated that the diagnostic accuracy of acute appendicitis is between 70% and 85% [2], and that up to 50% of patients hospitalized for possible appendicitis have normal appendices[3]. Misdiagnosing acute appendicitis is responsible of two types of outcomes:

Acute appendicitis is the most common surgical emergency and the most common source of community-acquired intraabdominal infections[1]. Clinical diagnosis of acute appendicitis is still difficult. It has been estimated that the diagnostic accuracy of acute appendicitis is between 70% and 85% [2], and that up to 50% of patients hospitalized for possible appendicitis have normal appendices[3]. Misdiagnosing acute appendicitis is responsible of two types of outcomes: in one hand, a delay to surgical treatmentcan that lead to perforation and peritonitis in up to 15% of the cases[4] and, in the other hand, negative appendectomywhich is associated with post-operative complications such as wound infection and adhesions[3]. Several approaches have been introduced to improve the diagnostic accuracy of acute appendicitis and therefore to reduce complications. Imaging techniques, especially abdominal ultrasonography[5] and CT scans[6], have been shown to be particularly accurate with a sensitivity and specificity overcoming 90%[7]. However, doubts have been raised about their usefulness in patients with high clinical probability of acute appendicitis associated with the need for qualified staff and medical facilities contributing to the increase of healthcare costs[8, 9]. Diagnostic scoring systems have been developed in an attempt to improve the diagnostic accuracy of acute appendicitis. The most prominent of those scores is that developed by Alvarado [10, 11]. The modified Alvarado score (MAS) is a more simplified and practical version of the original one and has been widely accepted after it was successfully tested in different studies [12, 13]. However, prospective studies have suggested that Alvarado score and MAS alone are inadequate as a diagnostic test for appendicitis[12-14]. During the evaluation of patients with possible appendicitis in the emergency department (ED), repeated physical examination of the abdomen may provide further information to help decision making. Repeated laboratory tests were also proposed to this issue without proven benefit[15].

C-reactive protein (CRP)is an acute phase protein that is often relied-on by many surgeons as a diagnostic marker of

acute appendicitis[16]. Actually, there is no strong evidence supporting its use in the diagnosis of acute appendicitis and related clinical data are controversial[2]. The purpose of this study was to investigate the diagnostic performance of initialserum CRP measurement at admission and its early variation, evaluated both separately and in combination to the MAS in patients presenting to the ED with clinically suspected appendicitis.

#### MATERIALS AND METHODS

This was a prospective observational study performed at Fattouma Bourguiba University Hospital of Monastir - Tunisia between January 2010 and December 2013. We prospectively included all patients aged more than 10 years and admitted to our ED for clinically suspected acute appendicitis. The clinical suspicion of appendicitis was made based on the presence of direct tenderness in the right lower quadrant, percussion and rebound tenderness, pyrexia, anorexia, nausea and vomiting. Patients using warfarin or heparin, pregnant women, and patients using antibioticsduring the study period were excluded. All patients were initially evaluated by the ED physician and demographic, clinical and biological findings were recorded on a specificdata form. Blood samples were obtained immediately after admission and analyzed forwhile blood cell (WBC) count and admission CRP concentrations. Three hours after, a second CRP measurement (3 hours CRP) was carried out in patients with an equivocal diagnosis of acute appendicitis. The CRP concentration was measured by immune turbidimetry (Beckman Collin, CA). The normal range of CRP concentrations, in our hospital, is between 0 and 6 mg/ml and concentrations >6 mg/L were considered abnormal. At the term of this evaluation, the MAS was calculated for all the included patients. A score above 4 was considered highly suggestive of acute appendicitis. Surgical decision was made at the discretion of senior surgeons based on medical history, clinical examination and initial blood cell count only. All appendectomies were performed by conventional methods and surgeons were blinded about the CRP values.In patients for whom the surgical treatment was decided within the 2 weeks of ED presentation, the ultimate diagnosis of appendicitis was based on histologic examination of the excised appendix.Appendicitis was defined as ulcerative, suppurative, phlegmonous, gangrenous or perforated appendicitis.Absence of appendicitis was considered if, in home discharged patients, initial symptoms has subsisted within the 2-week follow-up at the outpatient clinic; and, in operated patients, a normal appendix was found at the histopathological examination. All patients gave their written informed consent to participate in the study which was approved by our institutional ethics committee.

#### STATISTICAL ANALYSIS

Data were presented as mean  $\pm$  SD (standard deviation) or as percentages. The clinical data were compared using the student-t test for the continuous variables and the Chi-square test for categorical variables. The admission CRP and delta CRP (3 hour CRP – admission CRP) diagnostic performance was evaluated alone and in combination to the MAS by the calculation of the sensitivity, specificity, positive and negative predicted values for each category and the calculation of the area under curve (AUC) of the receiver operating characteristic (ROC) presentation. All p values < 0.05 were considered statistically significant.

#### RESULTS

During the study period, 551 patients were eligible from them 542 patients were admitted. 42 patients did not undergo a second CRP measurement and a total of 500 patients with clinically suspected appendicitis were included in the study. The patients mean age was 28±3 years with extremes ranging from 8 to85. Young subjects aged under 30-year-old and males were the most frequent (table 1).Most of the patients (n=385) underwent appendectomy within the first 24 hours of ED admission. In the operated group, negative appendectomy rate was 8,3% (64 cases). Histologic findings included 155 (40%) ulcerative, 37 (9.6%) suppurative, 60 (15.5%) phlegmonous, 41 (10.6%) gangrenous and 28 (7.2%) perforated appendices. Only two patients (1.7%) in the non-operated group had been diagnosed with acute appendicitis during their 2-week follow-up (Figure 1).

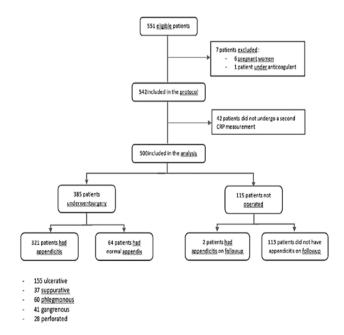


Figure 1. Patients flow chart.

Mean WBC count, mean level of admission CRP and 3 hour CRP and mean delta CRP between patients with and without appendicitis are shown in table 2. In patients with acute appendicitis mean WBC and CRP measurements were significantly higher than in the patients with normal appendix (both p<0.01). The delta CRP was positive in 73% patients with appendicitis and in 46% patients with normal appendix, the difference was significant (P < 0.001).

The diagnostic performance of both CRP and delta CRP in predicting acute appendicitis were further analyzed by using the ROC curves. The AUC for admission CRP and 3 hours CRP was respectively 0.63 and 0.65. However, for delta CRP it was only 0.53. Theperformance (sensitivity, specificity, PPV and NPV) of admission CRPand delta CRP, analyzed separately and in combination to the MAS, in the diagnosis of acute appendicitis were shown in table 3. Both admission CRP and delta CRP had a better sensitivity than MAS alone (73%, 84% and 56% respectively). Combining admission CRP or delta CRP to MAS was associated with a reduced sensitivity and a moderate increase of specificity compared to MAS alone. Moreover, applying admission CRP and delta CRP to each of MAS risk category (MAS  $\leq$  4 versus MAS > 4) did not improve the diagnostic performance (Table 4).

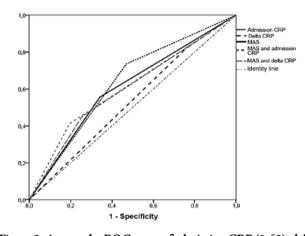


Figure 2. Area under ROC curve of admission CRP (0.63), delta CRP (0.53), modified Alvarado score (0.6), MAS combined to admission CRP (0.6) and MAS combined to delta CRP (0.59). Delta CRP = admission CRP minus 3 hour CRP.

#### DISCUSSION

The accurate diagnosis of acute appendicitis in the ED remains a challenge for the emergency physician[17]. Good clinical approach with detailed physical examination are keystones in the diagnosis of appendicitis. However, atypical clinical presentations and nonspecific findings are frequent which could delay the diagnosis leading to complications, more often perforation; or carry misdiagnosis and lead to unnecessary surgical interventions. To overcome these difficulties, many diagnostic strategies were developed including short period admission for observation, serial laboratory tests and imaging investigations [18]. Although the utility of repeated laboratory examinations may seem helpful, diagnostic yield of serial tests has not been studied thoroughly enough to be validated in this condition. Also, it is unclear which serum inflammatory markers should be used and how well the early levels changes can function as a discriminatorfactor in patients with asuspected diagnosis of acute appendicitis[19].In this prospective study we analyzed 500 patients with suspected appendicitis, and evaluated the utility of early changes in serum CRP concentrations in the diagnosis of acute appendicitis. We demonstrated that both CRPmarkers were not of significant utility either alone or in combination to MAS in the diagnosis of appendicitis.Our findings contrast with some previous studies suggesting that repeated serum inflammation tests may increase the diagnostic accuracy of acute appendicitis. Recently, Han-ping et al.foundthat the change between primary and repeated serum inflammatory markers may improve diagnostic accuracy in pediatric appendicitis[20]. ROC analysis showed that a cut-off value of serum CRP more than 4.5 mg/Lon day 2, or the increase in CRPabove 15.0 mg/L on day 3 were good predictors of acute appendicitis in children. In the same way, Wu HP et al. concluded that the change in the serum parameters could point for simple appendicitis when the increase in CRPis more than 118 mg/L; and that appendicitis could be excluded when the increase in CRP isless than 10 mg/L. For perforated appendicitis, the authors concluded thatchanges in CRP values wasnot helpful for the diagnosis[21]. In our study the second measurement of the CRP concentrations was made only 3 hours which could explain our negative results. Indeed, several studies have reported that serum CRP increase is delayed 12 to 24 hours from the onset of inflammationsymptoms [22].In Practice, repeating serum analysis more than 12 hours after ED admission would be very late especially in acute appendicitis context where complications are potentially life-threatening. Our findingshighlight the need for other new biomarkers with faster expression and kinetics.

A variable combination of clinical signs has been used together in association with laboratory tests in several scoring systems for evaluating the probability of acute appendicitis. The Alvarado score is the most widely studied score. Because counting the neutrophils as a parameter of the Alvarado score is not routine in many laboratories, a simplified version was proposed (MAS) by omitting the neutrophil count and demonstrated similar diagnostic performance[23]. Some studies have shown enhanced diagnostic potential and utility when scoring systems and inflammatory markers are combined[24]. However, our results did not confirm these findings which suggest that alternative diagnostic approach are needed. Combination of inflammatory markers or the use of novel ones combined to available scores could be of greater promise[25].

As far as we know, this is the largest study to prospectively evaluate the diagnostic value of early variation of CRP concentrations in subjects presenting to the ED with clinically suspected appendicitis. Although the important sample size we acknowledge that this trial has somelimitations. First, our study is monocentric, which could lead to a potential selection bias. Moreover, some subjects discharged home with a false diagnosis of non-appendicitis may have presented to other hospitals as for some patients contact information was lacking for followup. Finally, in our study, the diagnosis of acute appendicitis was a compromise between patient statement, physical examination and laboratory findings and no imaging tests were performed which could explain the relatively high rate of normal appendices findings at the histological examination.

#### CONCLUSION

Based on our findings, we conclude that CRP levels at admission and its early change 3 hours later, in patients with clinically suspected acute appendicitis, has a moderate diagnostic value. Combining values to the MAS added no more diagnostic utility. Other diagnostic approaches should be considered in this context.

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## **ORIGINAL RESEARCH**

# Preliminary results of ReSCUS register for the management of STEMI in Emergency Department of Sahloul

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#### ABSTRACT

Registries are an interesting tool for continually evaluation of clinical practice regarding acute coronary syndrome (ACS) which is considered as a public health problem.

#### **OBJECTIVE**

Analyzing the preliminary results of our local registry of ACS (ReSCUS registry) in order to verify our adherence to the guidelines and propose a strategy to improve patient outcomes.

Methods: Only data of patients with STEMI were selected for this study during the period from 1 February 2014 to 17 May 2016. We analyzed patients' demographic and clinical characteristics, electrical characteristics, the time of first medical contact, the delays of medical care, the delays to the balloon or thrombolysis and the overall time of reperfusion. We noted for all the patients the major cardiovascular adverse event (MACE) registered at In-hospital stay, after 1month, 6months and 1 year later. For the univariate analysis, we attempted to determine the prognostic factors associated with hospital mortality of ACS.

#### RESULTS

We included 150 patients. The average age was 61 ± 12 years with a sex ratio of 6.14. Smoking is the most common risk factor (53%). STEMI occurs anterior territory on EKG in 40% and inferior territory in 26% of cases. Only 17% of patients received medical transport to our emergency department. Complications of STEMI were detected in 47, 3% of patients. The median delay to the first EKG was Of 21 minutes. Angioplasty was the reference method of revascularization in our study. At the hospital phase, the overall mortality was 8%. The age more than 65 years, diabetes, the occurrence of a cadiogenic shock were the factors most correlated with the mortality in the hospital phase. The 12-month overall MACE rate was noted in 9.6%

#### of cases. CONCLUSION

Results of our study seem encouraging but more efforts are necessary to improve reperfusion delays and overall outcomes.

KEYWORDS: STEMI\_registry\_emergency management\_ time delays\_reperfusion\_predictive factors

#### INTRODUCTION

Coronary artery disease (CAD) remains the most common cause of mortality and loss of disability adjusted life years (DALYs) worldwide. We estimated even more than 2.5 million hospitalizations each year for this disease[1]. Despite the remarkable progress in the last few decades in elucidating the pathophysiology of acute coronary syndromes (ACS) and therapeutic advances for its management, several challenges still persist especially in emergency departments [2]. The direct relationship between good prognosis of STEMI patients and the earlier care has been well established [3]. Because of «Time is muscle» more attention is paid now to the respect of targets' time delays recommended by universal guidelines. In fact, the wealth of findings from randomized controlled trials on the diagnosis and management of ACS have been summarized in those clinical practice guidelines, almost always updated for optimising ACS' care.

It is now admitted that adherence to guidelines has been correlated with improvements in patient outcomes in ACS, including reduced mortality, improving short and long-term outcomes and so reduced health care costs [4,5]. Unfortunately, implementing guideline recommendations into clinical practice can be difficult [6,7].

The aim of our study was to analyze the preliminary results of our local registry of ACS (ReSCUS: Coronary syndrome registry Emergency service Sahloul ) in order to verify our adherence to the guidelines and propose a strategy to improve patient outcomes.

#### METHODS

This is a prospective study carried out in the Emergency Department of Sahloul, covering patients taken care for STEMI during the period from 1 February 2014 to 17 May 2016.

We analysed the data's from our local registry of acute Coronary syndrome (ReSCUS). In brief, this registry is a continually ongoing mono-center registry that prospectively collects information regarding all-comer patients with Acute Coronary Syndrome managed in our emergency department (STEMI and NSTEMI). Only data of patients with STEMI were selected for this study. For this register, STEMI and NSTEMI were considered like current universal definition. For STEMI, patients must have had persistent chest discomfort or other symptoms suggestive of ischemia, ST-segment elevation in 2 contiguous leads or a recent left bundle branch block [8]. The therapeutic strategies of STEMI and NSTEMI

depended on the practice of our institution (disponibility or not of the cath lab). Clinical and demographic informations, as well as the therapeutic management of patients entering the registry, were obtained by means of a standardized document made by our emergency team. So, the following data were collected on all patients with ACS: time courses from onset of symptoms to admission and door to therapeutic management (fibrinolysis, coronary revascularization or drugs). We noted all the cardiovascular risk factors; pre-procedural therapeutic; complications and in-hospital all-cause death. We made a follow up for all the patients after 1 month, 6months and one year by a phone call and we reported further details concerning the major cardiovascular adverse Events (MACE).

For this study, 150 consecutive patients were identified that satisfied inclusion criteria's. However, data from 3 patients was incomplete for their follow up was excluded from the final analysis.

Primary outcome was the respect of targets' time delays for the management of STEMI recommended by ESC guidelines. Secondary outcomes were the Major Adverse Cardiovascular Events (MACE) after STEMI recorded during in-hospital stay, after 1month, 6 months and 1year.

#### RESULTS

#### Patients' Demographics

There were 150 patients managed for STEMI during the study period. The demographic characteristics, cardiovascular risk factors, and baseline clinical parameters are given in Table 1. The main age was  $61 \pm 12$  years (27 years\_91years) and more than half of our population was over 60 years with a sex ratio of 6,14. Smoking was the most frequent risk factor (53%). Less than one third of patients (30%) consulted within the first hour of symptom onset. STEMI was inaugural in 70% of cases. It was an anterior territory in EKG (in 40% and inferior territory in 26% of cases. The majority of our patients (83%) arrived by their own way to the emergency department. Complicated forms were noted for 47, 3% of patients: Acute left heart failure (36%), cardiac arrhythmias (8%), cardiogenic shock (7,3%) and Cardiac arrest (4%).

#### Table 1. Baseline characteristics of the study patients

Age	61 years ±12		
		N	%
Gender		Male=129	
Cardiovascular risk			
	Tobacco	80	53
	Hypertension	51	34
	Diabetes	30	20
	dyslipidemia	21	14
	2 major Cx risk	47	31
Cardiovascular history			
	history of angioplasty	22	14.6
	previous history of MI	30	19.3
	history of angina	14	9.33
	bypass Aortocoronary	2	3
	surgery		
	chronic renal	4	2.65
	insufficiency		
	ischemic stroke	5	3
	COPD	1	1.5
	Medical transport		17
	Others way		83
Electrocardiogram data			
	Anterior		40
	Inferior		26
	Lateral		12.6
	Basal		8.7
	Left bundle block		7.8
	Circumferential		1
Complicated forms on ad		71	47.3
	Acute left ventricular Failure		36
	Rhythmic disorder		8
	Shock		7.3
	Cardiac arrest		4
Other Therapies			
	Aspirine	150	100
	Clopidogrel	150	100
	Low Molecular xeight Heparin	139	92.6
	Unfractionated Heparin	11	7.3
	Nitrate	5	3.3
	Adrenaline	4	2.6
	Dobutamine	5	3.3
	Amiodarone	4	2.6
	Atropine	2	1.3
	Furosemide	3	5.33
	Cardiopulmonary resuscitation		5.33
	External electric shock	7	4.6
	Morphine	39	26
REPERFUSION STRATEG	3Y		
	Angioplasty	130	87
	Intra hospital thrombolysis	17	11
	Prehospital thrombolysis	3	4.5

#### Management and outcomes

The average time, between the beginning of pain and the arrival of the patient at the first healthcare structure was  $210 \pm 120$  minutes. The realization of the first EKG was  $38 \pm 24$  minutes. The mean delay for door to thombolysis (D2T) was  $118\pm 63$ mn and the mean delay Door to baloon (D2B) was  $227\pm 25$ mn. The other most interesting time delays of in-hospital care were summarized in table2.

Angioplasty was the method of Revascularization of reference in our study population. Only 13% of patients undergone thrombolysis with a median delay of Thrombolysis of 106  $\pm$ 40minutes. The drug of choice for thrombolysis was Tenecteplase.

Table 2. Summary of pre and In-hospital delays

Summary of pre-hospital delays	Average	Median
Pain-thrombolysis		155 ± 57
Pain-primary ATC		224 ± 105
(Transluminal coronary angioplasty)		
Call-thrombolysis		81 ± 37
Primary ATC		103 ± 54
((Transluminal coronary angioplasty) Call		
Summary of InHospital management	t	
Pain to the 1st care facility Delay	210 ± 120 mn	150 ± 60mn
Delay First Medical contact (FMC)	270 ± 108 mn	188± 50 mn
Delay for the 1st EKG	38 ± 24 mn	21 ± 9 mn
Delay of thrombolysis	118 ± 63 mn	106 ± 40 mn
Coro Pain Door" Delay	310 ± 270 mn	268 ± 100 mn
Delay "FMC - door coro"	167 ± 21 mn	102± 30 mn
Coro puncture Delay	15 ± 5 mn	13 ± 3 mn
Delay Door coro to Balloon (D-	38 ± 14 mn	24 ± 11 mn
coro 2B)		
Delay First Medical contact to	270 ± 108 mn	166 ± 26 mn
ballon (M2B)		
Delay Door to Baloon (D2B)	227 ± 25 mn	197 ± 38 mn

At the in-hospital phase, overall mortality was 8%. To 12 months, the overall rate of the MACE was of 14.2%. The major cardiac events (MACE) analyzed in our series were death, reinfarction, angina recurrence, left ventricular Failure and stroke. Thus, the overall MACE rate at 1 month was 19.56 %: death n=2, Angina recurrence n=17 patients. Eight patients had signs of left ventricular failure on a 1-month follow-up within 7  $\pm$  3 days after admission.

The overall MACE rate at 6 months was 20%. Four patients with an average age of  $67 \pm 15$  years re-infracted. These patients were all male and two were diabetic. None of them report poor adherence to platelet aggregation therapy. An angina recurrence was noted in 15 patients. N=9 had signs of left Acute Heart Failure on a 6 months follow-up.

The 12-month overall MACE rate was 9.6%. Only a one case of reinfarction was noted at 12 months follow up. An angina recurrence was noted in 9 patients Nine patients had signs of left ventricular failure.

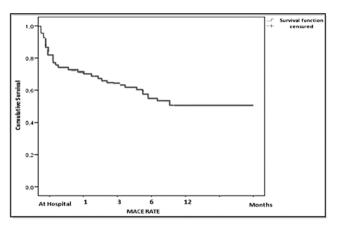


Figure 1 : Survival curve without MACE according to the Kaplan Meier method

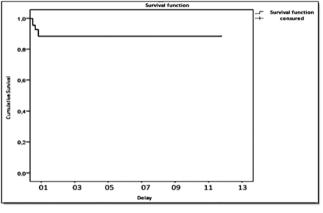


Figure 2. Long-Term Survival Curve Using the Kaplan Meier Method

#### Multivariate analysis

At the hospital phase, An age greater than 65 years, diabetes, cardiogenic shock were the most correlated factors to mortality at hospital. Time delays for angioplasty care had tendency to influence mortality. Table3

#### Table 3. predictor factors of mortality

Predictive factors by multivariate analysis	Р
Age Higher than 65 years old	0,02
Diabetes	0,03
Presence of cardiogenic shock	0,02
HTA	0,11
dyslipidemia	0,13
Pain delay to the 1st care facility	0,09
Delay D2B ( Door to Balloon )	0,08

#### DISCUSSION

Acute myocardial infarction (AMI) is a major cause of morbidity and mortality worldwide. However, in developed countries there has been an overall trend for a reduction of its mortality over the past decades [8]. Data regarding ACS in low- and middle-income countries (LIMICs) are limited. In Tunisia there is a real lack of knowledge about incidence, and management of this disease.

Registers of Acute coronary syndromes (ACS) seems to be very interesting for medical research but till now trials registries still an underutilized resource among

investigators conducting systematic reviews [9]. These registers, a mirror of real life, are reliable. They are providing continuous observation tools of professional practices and evaluation regarding adherence to the guidelines.

Our register by gathering data on the characteristics, management and outcomes of patients hospitalized for STEMI at this period can provide comparisons with future surveys and can promote our strategy of ACS management. Indeed, use of registry and its regular evaluation can change myocardial infraction's management from passivity and identify predictive factors of mortality and disability [1, 10].

Age is the most studied and most important prognostic factor found in literature and advanced age appears as independent Predictor of mortality. In our study, the average age was of  $61\pm$ 12. This result is similar to many developed countries such France (USIK Registry) United State (NRMI registry) and the result of only Tunisian FAST MI[11-13]. Although, Registry data from many LMICs support the assertion that the first ACS often occur at younger ages than developed countries [1, 14-18].

More than this, according to the most recent Global Burden of Disease study, the median age of death from CAD among males was a decade younger in LMICs in 2010 [1].

Another interesting predictive factor was the respect of target' delays for ACS' management. It is correlated with good outcomes. The in-hospital mortality in this study was not particularly low and our time delay are longer than the targets recommended by guidelines. however, 87% of patients received primary PCI which is considered as the favourite strategy for eligible patients' reperfusion[6]. But Current STEMI guidelines recommend a door-to-balloon time of 90 min or less for patients undergoing interventional strategy. Door-to-balloon time in this study was longer than that of recommended guidelines and only 38% respected this delay. This time delay is very variable between countries reported in others registers [19,20]. The lack of chest pain unit in our Emergency Department can explain the major part of this delay. Future approaches should include improving in-hospital management reducing the delay door to specific care and increasing the patients' awareness of symptoms, and shorting the transfer time between first medical contact and hospital presentation by improving pre-hospital call and transport.

#### Limitations

The present study is subject to some intrinsic limitations associated with an observational monocentric study.

We cannot apply our findings to all STEMI patients because we excluded those who were directly admitted to the cath lab by medical transport and by pass Emergency Department. National register may provide more informations about demographic, clinical and predictive prognosis factors regarding STEMI in Tunisia.

#### CONCLUSION

Use of registry for evaluation of our practice in the management of STEMI remains very helpful to identify deficiencies. More effort should be made to make our time delays shorter to adhere to universal recommendations for better outcomes. Improving patients and first line physician's awareness of ischemic symptoms must be a priority too. National strategy is necessary too to improve access to cauterization laboratories which should be continually available 24/24h.

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# **ORIGINAL RESEARCH**

# *Predictors of acute coronary syndromes in patients with acute chest pain and normal electrocardiogram*

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#### BACKGROUND

Lack of changes on an electrocardiogram (ECG) performed in patients presenting with chest pain in the emergency department (ED) is often thought to reflect less likelihood of acute coronary syndrome (ACS).

#### **OBJECTIVE**

Identify predictive factors of non-ST-segment elevation acute coronary syndrome (NSTE-ACS) in patients who presented to the ED with the chief complaint of acute chest pain and whose initial ECG was normal.

#### METHODS

Prospective, observational, over two years study. We included all patients who met the following criteria: age  $\geq$  18 years, chief complaint of non-traumatic chest pain, normal ECG, and admission for evaluation for ACS.

The diagnosis of ACS was focused on coronary angiography demonstrating >70% stenosis in a major coronary artery. Patients were divided into ACS and non ACS groups.

We performed an univariate and a multivariate analysis to identify the factors associated with ACS.

#### RESULTS

Fifty eight patients were included. The mean age was  $58 \pm 11$  years. The sex ratio was 2. 22. Comorbidities n (%): diabetic 30 (52), hypertension 20 (34), known coronaropathy 19 (33) and dyslipedemia 18 (31). Nineteen patients (33%) had elevated troponin. The median TIMI score was 2 [1, 5] and the median GRACE score was 94 [77,108]. Thirty-three patients (57%) had a positive angiography.

In multivariate analysis, age  $\geq 65$  years (adjusted OR=6.6; 95%CI [1.5-29]; p=0.01), past medical history of diabetes (adjusted OR=6.1; 95%CI [1.8–20.6]; p=0.003), known coronaropathy (adjusted OR =3.5; 95%CI [3.1-26]; p=0.02) and a positive troponin level at admission (adjusted OR=7.5; 95%IC [2.1-26]; p= 0.001) were independently associated with the diagnosis of ACS.

#### CONCLUSION

Advanced age, history of diabetes or known coronaropathy and positive troponin level at admission are the main factors associated with ACS in patients presenting with an acute chest pain and normal ECG.

The early identification of these factors by the emergency physician will improve the management of acute chest pain in patients with normal initial ECG.

#### INTRODUCTION

Cardiovascular diseases are dominated by coronary disease which is a leading cause of death worldwide (1). Chest pain (CP) is an important chief complaint at the emergency department (ED) and a common reason for admissions (2,3). It represents 5 to 20% of patients in a general ED (4). The identification of acute coronary syndromes (ACS) in case of an acute CP and ruling-out several differential diagnoses represents a challenge for all emergency physicians (EP). The diagnostic process should be quick and efficient since the prognosis improves when ACS patients receive targeted treatment as early as possible (2). The major steps in ACS identification are: reporting medical history of cardiovascular risk factors, chest pain characteristics, clinical exam findings and electrocardiogram (EKG) and biological results.

The EKG is an integral part of the work up of patients with CP (5). The resting 12-lead EkG is the first-line diagnostic tool in the assessment of patients with suspected ACS (1). It is recommended to be performed within ten minutes of the first medical contact at the ED. It should be interpreted immediately by a qualified physician in order to identify ST-segment or T-wave changes. The EKG at presentation in non-STEMI (NSTEMI) patients not only helps differentiate it from STEMI but also identify the type of ST changes which provides key diagnostic and prognostic clues (5).

In many cases, ACS diagnosis is obvious such as in ST-segment elevation myocardial infarction (STEMI). The NSTE-ACS diagnosis is a more complex setting. It is easier when the EKG shows specific abnormalities and/or when troponins serum levels are elevated. The absence of electric signs or normal biological findings cannot exclude ACS (6,7). In approximately 5% of cases, ACS is confirmed unless normal ECG or/and normal troponin dosage (4). The EP is always asked to identify high risk patients for major adverse cardiac events (MACE) and to rapidly diagnose ACS.

However, some patients with typical CP have normal or noncontributive EKG at admission. Although a normal EKG was found as an independent factor of non-hospitalization in cardiology (6,8), this subset of patients can experience complications despite the normality of EKG.

The aim of our study was to identify predictive factors of non-ST-segment elevation acute coronary syndrome (NSTE-ACS) in patients with acute CP and normal ECG.

#### METHODS

#### Study population

We conducted a prospective observational study over a period of two years (march 2012 to february 2014) in the ED of the regional hospital of Ben Arous, Tunisia. We included all adults patients aged more than 18 years old, presenting with acute non traumatic CP suggestive of ACS in whom EKG showed no significant repolarization alterations or newly-developed complete left bundle branch block and admitted to the ED for suspicion of NSTE-ACS. Patients with low clinical probability of ACS, those showing electric abnormalities (ST segment or T changes) or with findings indicating aortic dissection or heart failure at admission were not included. We excluded secondarily patients who showed EKG modifications during observation and those in whom the result of coronary angiography was not available. The study was performed according to Helsinki declaration principles; and an informed verbal consent was obtained in all patients enrolled into the study.

#### Group comparison

After the coronary angiography results patients were divided into two groups:

- Group ACS+: patients with CP suggestive of ACS, non contributive ECG and more than 70% coronary stenosis or presence of unstable significant coronary lesion in angiogram (visual estimation).
- Group ACS-: patients with CP suggestive of ACS, non contributive ECG and normal coronarography or less than 70% coronary stenosis or absence of significant coronary lesion in angiogram (visual estimation).

#### Data collection

All patients who fulfilled the above criteria where admitted to ED observation room.

Data was collected as following: personal data, medical history and treatment, comorbidities and cardiovascular risk factors, CP characteristics, time from symptom onset to ED visit, physical examination characteristics, biological findings with cardiac biomarkers, Thrombolysis In Myocardial Infarction (TIMI) (9) and Global Registry of Acute Coronary Events (GRACE) (10,11) risk scores evaluation, anti-ischemic and anti-thrombotic treatment, ED hospitalization duration, revascularization modalities, ED orientation, follow-up at six months (final diagnosis and MACE)

#### Definitions

Normal ECG definition

We defined normal ECG criteria as follow:

- normal sinus rhythm with heart rate of 55–105 beats/min,
- normal QRS interval and ST segment
- normal T-wave morphology or T-wave flattening.

"Normal" excludes pathologic Q waves, left ventricular hypertrophy, non specific ST-T wave abnormalities, any ST depression, and discrepancies in the axis between the T wave and the QRS.

The ECGs were interpreted as normal or abnormal by two senior EPs. Differences in interpretation were resolved by a third senior EP.

• ACS confirmation : The presence of coronary disease was only confirmed in patients who underwent a coronary angiography. Patient was considered to present significant coronary disease when coronary angiography showed more than 70% stenosis of a coronary artery.

• *MACEs* : Major adverse cardiac events were evaluated at six months and included: death, myocardial infarction and angina.

#### **ED** protocol

When a patient fulfilled the inclusion criteria, he/she was admitted to the observation room. Conventional troponin dosage was performed at admission and at 6 and/or 12 hours. High sensitive troponin was not available at our department during the study period. ECG was performed at 6 and 12 hours after the onset of the pain or when patients had recurrent CP and before discharge. The guidelines of the European Society of cardiology 2012 were adopted in the treatment management (12).

#### Statistical analysis

We used SPSS, version 20.0 (IBM SPSS Inc., Chicago, Illinois, USA) for data analysis. The Kolmogorov-Smirnov test was used for variables distribution. Categorical values were assessed using a chi-square test (or Fisher's exact test when indicated) and continuous variables using a Student T test or Mann-Whithney test for trends in the absence of a normal distribution. Univariate analysis of baseline variables was performed by using a backward stepwise variable selection procedure to determine the predictive factors of coronary disease in patients presenting with chest pain and initial normal ECG. To study the independent predictors of coronary disease, multivariate analysis was performed with logistic regression by backward stepwise elimination. The odds ratio (OR) was expressed with the respective 95% CI. In all tests, a p value less than 0.05 was significant.

#### RESULTS

#### Baseline characteristics of the study population

During the study period, 390 patients were admitted to our department for evaluation of suspected ACS. We didn't include 305 patients because of initial pathological ECG (n=228) and atypical CP (n=77). Eighty five patients were eligible for inclusion; however 27 patients were excluded since lack of coronary angiography results. A total of 58 patients were enrolled into the study (Figure 1).

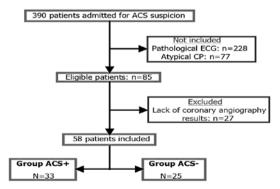


Figure 1. Inclusion algorithm

Mean age was  $58 \pm 11$  years. Seventy one percents (n=41) of patients were aged more than 65 years. Males were predominant (69%) with a sex-ratio=2.22. Median time to ED visit after CP onset was 7 hours [4-24]. Thirty eight patients (65%) had rest CP. Active smoking was found in 38% of patients (n=22). While other comorbities were as follow: diabetes (n=30; 52%), hypertension (n=20; 34%), dyslipimia (n=18; 31%), coronary artery disease (n=19; 33%), prior PCI (n=12; 21%), prior CABG (n=1; 2%). Troponins were positive at first determination in 19 patients (33%). The median TIMI risk score was 2 [1-5] where as the median GRACE score was 94 [77-108].

A significant stenosis was found in 33 patients (57%). The table 1 shows the demographic, clinical and therapeutic characteristics comparison of the two groups.

Table 1. Baseline characteristics of the suty population and group comparison

Variables	All	ACS+	ACS-	_
variables	N=58	N=33	N=25	P
Mean age years±SD	58 ± 11	62±12	52±8	<0.001
Age>65 years n(%)	41(71)	16(48)	1(4)	<0.001
Men n(%)	40(69)	24 (72)	16 (64)	0.47
Active smokers n(%)	22(38)	13 (39)	9 (36)	0.65
Median time to ED visit* (hours)	7[4-24]	7[4.5-24]	7[2-36]	0.42
Rest CP n(%)	49(84)	29(88)	20(80)	0.41
Comorbities				
Hypertension n(%)	20(34)	20 (60)	10 (40)	0.119
Diabetes n(%)	30(52)	17 (51)	3 (12)	0.002
Dyslipimia n(%)	18(31)	9 (27)	9 (36)	0.478
Coronary artery disease n(%)	19(33)	14 (42)	5 (20)	0.05
PCI n(%)	12(21)	9 (27)	3 (12)	0.2
CABG n(%)	1(2)	1 (2)	0 (0)	0.99
Positive troponins n(%)	19(33)	16(48)	3(12)	0.005
Median TIMI score	2 [1-5]	3[2-3]	1[1-2]	<0,001
Median GRACE score	94 [77-108]	100[84-116]	85[70-93]	0,004
Treatment management				
Acetylsalicylic acid n(%)	49 (84,5)	28 (84)	21 (84)	0,99
Clopidogrel n(%)	28 (48)	24 (72)	4 (16)	<0,001
Oral isosorbidedinitrate n (%)	12 (21)	11 (33)	1 (4)	0.008
IV isosorbide dinitrate n(%)	3 (5)	3 (9)	0 (0)	0.251
Enoxaparin n(%)	28 (48)	25 (76)	3 (12)	<0.001
Orientation				
Cardiology ward admission n(%)	28(48)	25(76)	3(12)	<0,001
Ambulatory assessment n(%)	30(52)	8(24)	22(88)	0.012
MACEs n(%)	17(51)	17(51)	0(0)	-
Death n(%)	1(3)	1(3)	0	-
STEMI n(%)	2(6)	2(6)	0	-
Second PCI n(%)	15(45)	15(45)	0	-
CABG n(%)	1(3)	1(3)	0	-

ACS:Acute coronary syndrome; ED:Emergency department; SD:Standard deviation; CP: chest pain; PCI:Percutaneous coronary intervention; CABG:Coronary Artery Bypass Grafting; TIMI: Thrombolysis In Myocardial Infarction; GRACE: Global Registry of Acute Coronary Events. IV: Intravenous; MACE: Major Adverse Cardiac Events. STEMI:ST-segment elevation myocardial infarction. \*Time from onset of pain to emergency room admittance.

#### Predictors of ACS

In univariate analysis, nine predictors were found to have significant association with ACS diagnosis in patients admitted to the ED with acute CP and non-contributive initial EKG as shown in table 4.

#### Table 2. Univariate analysis

Factor	OR	[95% CI]	р
Diabetes	7.8	[1.9-31.1]	0.02
Coronary disease	3	[1.1-9.8]	0.05
Aspirin use	2.5	[1.1-7.5]	0.05
Age ≥ 65 years	22.6	[2.8-18.6]	< 0.001
$SAP \ge 150 \text{ mmHg}$	2	[1.6-6.8]	0.02
DAP ≥ 90 mmHg	3	[1.8-11]	0.04
Troponins≥ 0,4ng/ml	11	[1.3-93]	0.02
TIMI score $\geq$ 4	2	[1.5-2.6]	0.008
GRACE score ≥ 140	2.9	[1.45-2.38]	0.02

OR:odds ration; CI:confidence interval; SAP:systolic arterial pressure; DAP:diastolic arterial pressure; TIMI: Thrombolysis In Myocardial Infarction; GRACE: Global Registry of Acute Coronary Events

Multivariate analysis identified four independent predictors of ACS (adjusted OR; (95% CI]; p): age  $\geq$  65 years (6.6; [1.5-29]; 0.01), diabetes (6.1; [1.8-20.6]; 0.003), history of coronary disease (3.5; [3.1-26]; 0.02) and positive troponin levels at first determination (7.5; [2.1-26]; 0.001) (Table 5).

Table 3. Factors independently associated with ACS

Adjusted OR	[95%CI]	р
6.6	[1.5-29]	0.01
6.1	[1.8-20.6]	0.003
3.5	[3.1-26]	0.02
7.5	[2.1-26]	0,001
	6.6 6.1 3.5	6.1     [1.8-20.6]       3.5     [3.1-26]

#### DISCUSSION

We studied a specific group of patients: those having acute CP suggestive of ACS with initial non contributive EKG admitted to the ED. This category of patients usually represents a diagnosis challenge. Thus, only 15 to 20% of acute CP are symptoms of ACS and only 3 to 5% of acute CP with initial normal ECG are ACS (4,8,13,14). Our study confirmed that normal initial EKG cannot exclude ACS. Troponins were determinant but did not exclude the diagnosis of ACS even if the dosage was negative as it was attested by the number of confirmed ACS with negative cardiac biomarkers (52%). Indeed, among 58 patients with normal initial ECG, 57%

had confirmed ACS with a significant stenosis. Furthermore, 17 patients of this subgroup developed MACEs during a short followup period of six months. Even though patients with initial non specific EKG are identified as group at low risk of adverse events and low rate of mortality (15), they can develop early complications (8) as it was confirmed by our results.

#### Normal ECG in ACS

St-segment depression or T wave changes are helpful signs to identify patients with ACS and to guide their management. Several studies showed that initial EKG findings were predictors of admission or discharge. Indeed Pope et al. (16) found that 2.1% of patients with confirmed acute myocardial infaction were inadvertently discharged from the ED because of a normal initial EKG. The same study concluded that non-specific EKG was the most likely predictor of discharge and thus failure to inpatient care. Among patients with acute myocardial infarction and non specific initial EKG, the 30-day mortality rate was 10.5%.

#### Predictive factors/Scores

Several risk scores has been developed for the risk evaluation of ACS patients (9,17). TIMI score is widely used (9).

This score was higher with a significant difference in group ACS+. Nonetheless, this score was described in a large population including patients with ST-segment deviation and was not specific to normal EKG patients (7). Thus, TIMI score cannot be used as the only tool in low-risk patients to identify coronary disease.

In patients with non contributive EKG, a fast diagnostic approach is adopted and tests are used to determine the ischemic risk. Identification of simple variables can reduce number of inadequate hospitalizations. We identified four independent predictors associated with the diagnosis of ACS: age  $\geq$  65 years, diabetes, history of coronary disease and positive troponins at first determination. These factors were also found in other reports.

Martinez-Sellés et al. (4) analyzed data of 365 consecutive patients admitted to the chest pain unit. All of them had a non-contributive EKG. Independent predictors of coronary artery disease were: typical chest pain, aspirin use, diabetes and age>64 years.

Otherwise, Sanchis et al. (7) developed a risk score for patients with CP, non-ST segment deviation EKG and normal troponin levels. The variables used in the score were: Chest pain score, more than 2 episodes of CP, age  $\geq$  67 years, insulin-dependent diabetes mellitus and prior PCI.

#### Chest pain units in the ED

Utility of CPU is well described and accepted. One of their fundamental objectives is not only to identify rapidly and efficiently

low-risk patients who do not require hospitalization (4) but also to determine patient who have the potential to benefit from inpatient care (6).

#### Study limitations

Our study has some limitations. First, no chest pain unit (CPU). In a CPU, other tests can be performed such as stress echography or treadmill test (18,19).

Second, the number of patients included was relatively limited to generalize the findings. Finally, we perform a monocenter study; multicenter protocol may increase the number of patients to better identify ACS patients among those with non contributive EKG.

#### **Conflicts of interest**

We declare no conflicts of interests.

#### CONCLUSIONS

Normal electrocardiogram during chest pain does not rule out acute coronary syndrome. We identified four factors (three anamnestic variables and one biological result) independently associated with ACS in patients presenting with CP and normal initial ECG.

A specific score derivated from these results would be elaborated and integrated to a diagnosis algorithm.

There has been no large multicenter study addressing the prognostic value of normal or non contributive initial ECG during assessment of ACS in the ED. Launching a national registry of NSTE-ACS collecting data about ECG findings and other characteristics will be an opportunity to assess major cardiac events risk.

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# **ORIGINAL RESEARCH**

# *Benefit of paracetamol early analgesia during emergency triage:a 500 patients tunisian study*

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#### BACKGROUND

The implementation of analgesia facilitates the management of the patient. Pain relief should be a part of the therapeutic priorities in emergencies departments.

#### AIM

To demonstrate the value of early and systematic pain management with oral Paracetamol in emergencydepartement.

#### **METHODS**

In this prospective observational study, one gram of oral paracetamol was administered to 500 consultants at the emergency department of Farhat Hached University Hospital in Sousse, Tunisia. An evaluation of the pain at 0, 30, 60 and 120 minutes was performed by the visual analog scale.

#### RESULTS

During the observation period 433 patients (86.6 %) experienced a decrease in pain. A favorable pain outcome was observed in 415 patients (83%). No significant difference in pain pattern was found for the reason for consultation. Diagnostic concordance was greater than 95% for most consultation reasons except for chest pain.

#### CONCLUSIONS

Early systematic analgesia with oral paracetamol reduces pain with favorable change in pain in 83% of patients. This favorable development is correlated with the young age and the delay between the onset of pain and consultation. Early Analgesia in triage does not interfere with diagnosis.

KEYWORDS : Analgesia ; Paracetamol ; Triage ; Emergency department

#### INTRODUCTION

Pain is a common reason for consultation in the Emergency Department. More than two-thirds of Emergency Department consultants are algic patients [1,2,3]. Currently, pain is seen as vital distress that needs to be addressed quickly and although doctors in the emergency room have a varied therapeutic arsenal for treating pain, observing daily life in these units and analyzing the medical literature show that its management is still an important problem. Apart from the obvious ethical necessity of relieving any pain for the comfort of the patient, the implementation of an Analgesia facilitates the management of the patient without compromising the diagnostic analysis contrary to the preconceived ideas. On the other hand, the harmful consequences of the pain on the organism have been amply demonstrated, which can precipitate an already precarious clinical state, largely justifying the early introduction of analgesia [6].

Pain relief must be part of the therapeutic priorities in emergencies. The goals of pain management include recognition, appropriate treatment, systematic and regular re-assessment.

The objective of the study is to demonstrate the value of early and systematic pain management with oral Paracetamol in emergency rooms.

#### MATERIAL AND METHODS

This is a prospective observational study carried out at the Emergency Department of the University Hospital of Hached, Sousse between March 1st 2014 and December 31st, 2014 which covered a population of 500 consultants. We included all patients aged 15 years or older who are consultants in Emergency Departments for acute pain, with no consciousness disorder and who have agreed to participate in this study. Parents' consent was sought for under-aged of under 18 years of age.

The procedure consists in orally administering to the patient in the triage a gram of Paracetamolafter examination and evaluation of the pain. Patient-follow-up is done by re-evaluating pain at 30 minutes, 60 minutes and 120 minutes. The pain was assessed by the Visual Analog Scale (VAS).

The patient's socio-demographic characteristics, antecedents, reasons for consultation, diagnosis of the first trials after triage, pain assessment after administration of paracetamol (1 g) at 0, 30, 60 and 120 min were analyzed, retained diagnosis at the end of the explorations and orientation of the patient. All calculations were carried out using the Statistical Package for Social Sciences (SPSS) software 18.0 for Windows.

#### RESULTS

The average age of our patients was 40 years, the most affected age range was between 21 and 40 years. A female predominance of about 60%. Headache was the most frequent reason for consultation (20%). The average time between onset of pain and consultation time was 64 hours. More than 90% of our population have no immediate emergency (priority 3 or 4). All the characteristics of the population are presented in Table 1.

#### Table 1. Characteristics of the population

Age Average $\pm$ SD, y 39.61 $\pm$ 16.0	)6
Age group, n° (%) 15-20	CO (40 C)
21-40	63 (12,6) 217 (43.4)
41-60	162 (32.4)
80	8 (1.6)
Sex, n (%)	0(1.0)
Male	198 (39.6)
Female	302 (60.4)
History, n (%)	502 (00.4)
Yes	108 (21.6)
No	392 (78.4)
Consultation reasons, n (%)	002 (10.4)
Headache	100 (20)
Abdominale pains	94 (18)
Thoracic pains	60 (12)
Post traumatic pains	49 (9.8)
Nephritic Colic	36 (7.2)
Lumbosciatalgia	27 (5.4)
Odynophagies Odynophagies	20 (4)
Dismerrohea	19 (3.8)
Otalgia	17 (3.4)
Lower Back Pain	14 (2.8)
Cervicalgia	14 (2.8)
Epigastraly	11 (2.2)
Arthralgia	9 (1.8)
Flu syndrome	8 (1.6)
Other	80 (16)

There was an average decrease in VAS at the first hour of 1.2 cm. The overall decrease during the 120 minutes of observation was 1.87cm. During the observation period, 433 patients (86.6%) experienced a decrease in pain. A favorable outcome was observed in 415 patients, or 83% of the study population. No significant difference in pain pattern was found for the reason for consultation. The course of pain is shown in Table 2

#### Table 2. Level and evolution of Pain

Average decrease in VAS	pain 30 min	1.08 ± 1.12 cm
Average decrease in VAS	pain 60 min	1.2 ± 1.24 cm
Average decrease in VAS	pain 180 min	0.94 ± 1.42 cm
Pain average decrease in	(VAS 60), Ave	erage ± SD, cm
Dysmenorrhea		1.94 ± 1.79
Post-traumatic		1.82 ± 1.32
Thoracic pain		1.98 ± 1.63
Headache		1.80 ± 1.46
Abdominal pain		1.90 ± 1.64
Cervicalgia		2.22 ± 1.48
Nephritic Colic		1.55 ± 1.59
Favorable pain course	Yes	Not
Total, n° %	415 (83)	185 (17)
Male	162 (81.8)	
Female	253 (83.8%)	49 (16.2)
Age, average ± SD, y	38.9±16.2*	43±1799
Consultation time		
Average limite, h	58.2±129**	92.8±178.3
Consultation reason, n%		
Headache	89(89)	11(11)
Thoracic pain	48(80)	12(20)
Abdominal pain	77(81.9)	17(18.1)
Dismenorrhia	16(84.2)	3(15.8)
Post-traumatic	36(73.5)	13(26.5)
Nephriticcolic	31 (86.1)	5 (13.9)
Lumbosciatalgia	23(85.2)	4(14.8)
0	. ,	

y : years ; h : hours ; \*p=0,04 ; \*\* p=0,048

Diagnostic concordance was greater than 95% for most consultation reasons except for chest pain (p = 0.006). In fact, chest pain is significantly different from other patterns in terms of diagnostic agreement (p = 0.006). Additional analgesia in combination with paracetamol was required for approximately 10% of patients. 40 patients, or 8% of the study population, were hospitalized.

#### DISCUSSION

In this work, an initial evaluation of triage pain followed by an early prescription of analgesics followed a systematic and repeated follow-up of the pain evolution in patients were done. The mean decrease in VAS for all of our study population regardless of the reason for consultation is 1.2 ± 1.24 cm. Kelly et al. have established a clinically significant minimal difference of 0.9 cm in their 1998 study in Australia for traumatic and non-traumatic pain [7]. Powell et al. determined a minimal variation in clinically perceptible VAS of the patient equal to 1 cm in their study in 2001 in the United States [8]. We found an average VAS decrease of 1.82 cm for posttraumatic pain. In a study by Eliza M. Wong et al. In China (Hong Kong) in 2006, there was a decrease in mean VAS equal to 1.3 cm for minor trauma [9]. In another study conducted in France in 2007, administering 1 g of paracetamol for osteo-articular trauma, A. Viallon et al. demonstrated that the 2 cm gain on the EVA scale had a positive predictive value of 93% pain relief [10].

For our study population, there was an average VAS decrease of 1.98 cm for chest pain and an average decrease of 1.9 cm for abdominal pain. Karcioglu et al. have established in their study in Turkey in 2004 that the minimal difference in clinically significant VAS for thoraco-abdominal pain is 2.42 cm [7]. The correlation between pain evolution and the reason for consultation shows that the mean decrease in VAS varies according to the reason for consultation, the maximum decrease was seen in consultants for neck pain (2.22 cm) and the minimal decrease was seen in consultants for renal colic (1.55cm). Nevertheless, no significant difference was found for a given reason in relation to the rest of the population.

AVAS decline of less than or equal to three centimeters was considered favorable for the first 60 minutes, otherwise the evolution was considered unfavorable. A favorable outcome was observed in 415 patients, i.e. 83% of the study population. The mean age of patients with a favorable outcome was  $38.9 \pm 16.2$  years, and for patients with an unfavorable change, the mean age was  $43 \pm 17.9$  years. A significant difference was noted (p = 0.04). It can thus be seen that the favorable trend is correlated with the youngest age. The average time between the onset of pain and the consultation time for patients with a favorable course the average time was 93 hours. The noted difference was significant (p = 0.048). It can be deduced that a longer delay in suffering may be an indicator of adverse change after analgesia.

The evolution of the patients was also studied according to the reason for consultation and no significant difference was observed for any reason. It can thus be said that the evolution of the patients is independent of the reason for consultation, in other words the evolution of the patient after analgesia can be favorable or unfavorable regardless of the reason for consultation In the literature, the retained diagnoses for emergency hospitalized patients vary according to the studies [11-13] and the rates of concordance between the presumed diagnosis and the ultimately retained diagnosis are also variable [14-17].

In our study population, there was a general agreement between the diagnosis referred to and the diagnosis made in 94.2% of the cases. The evoked diagnosis was different from the retained diagnosis in 5.8% of cases. The factors that may influence the occurrence of a diagnostic error are stress, number of patients per physician, and severity of patients. Systematic analgesia is also considered to be an influencing factor.

The diagnostic concordance varies according to pattern, 95.5% for headache and abdominal pain, while 82.8% for chest pain (p = 0.006). Romain Tack confirms this finding and found in a study carried out in 2012 that the main diagnostic discrepancies are noted for cardiac and pulmonary pathologies and he stresses the difficulty that the emergency physician can experience in making a precise diagnosis in this setting [18] .For abdominal pain, there was a diagnostic agreement of 95.5%. This concordance rate is similar to that of a study by H. Oguzturk et al. in Turkey in 2012 [13], where 94% diagnostic accuracy was demonstrated with paracetamol in acute abdominal pain. It has also been demonstrated in this same study that the early administration of paracetamol or tramadol hydrochloride helps to reduce pain without interfering with the diagnosis [13].

During the management of the patients, the early analgesia component was considered as much as the diagnostic investigation component. It is thus stressed that early analgesia does not interfere with the diagnosis and, on the contrary, allows a better diagnostic approach

#### CONCLUSION

This study showed that early systematic analgesia with oral paracetamol reduces pain with an overall decrease in EVA over 120 minutes and a favorable change in pain in 83% of patients. This favorable development is correlated with the young age and the delay between the onset of pain and consultation. There is no significant difference in the evolution of pain according to the reason for consultation. Diagnostic concordance is greater than 95% for most reasons for consultation, except for chest pain. Analgesia does not interfere with diagnosis. Early analgesia is required whenever the patient expresses pain on the self-assessment scales

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# **ORIGINAL RESEARCH**

# Transthoracic echocardiography performed at the patient's bedside by the emergency physicianversus the cardiologist : A concordance study about 204 patients.

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#### BACKGROUND

Transthoracic echocardiography (TTE) is practised in emergency departments by emergency physicians at the patient's bedside as a routine special investigation procedure following a detailed physical examination. The purpose of our study is to evaluate the performance of TTE in emergency departments by emergency physicians by comparing the findings obtained to those given by an echoDoppler proficient cardiologist.

#### METHODS

A randomised prospective study of consecutive patients older than 16 years in whom there was an urgent need to practise a TTE. Each patient had to undergo a double echocardiographic examination: an investigation carried out by an emergency physician followed by an echocardiographic examination achieved by a cardiologist. An inter-rater agreement analysis was performed between the emergency physician and a board-certified cardiologist.

#### RESULTS

There were 204 patients enrolled during the study period. Mean age was  $52 \pm 1.13$  years, sex ratio 5 males/7 females. The concordance of the findings obtained by the emergency physician and by the cardiologist for the visual estimation of the LVEF was Kappa = 0.82 [95% CI 0.63-1] with an agreement = 0.90 [95% CI 0.74-0.99].

The concordance for measurement of the diameter of the IVC was Kappa = 0.95 [95% CI 0.63-1] with an agreement = 0.95 [95% CI 0.64-0.99] and for assessment of its compliance Kappa=1 with an agreement = 1. The concordance of the findings obtained for the diagnosis of pericardial effusion was Kappa=0.86 [95% CI 0.71-1] with an agreement = 0.92 [95% CI 0.64-0.99] and the concordance for the detection of echocardiographic signs of compressive effusion was Kappa = 1 with an agreement = 1.

#### CONCLUSION

The concordance of the findings obtained by both operators was excellent. Emergency physicians should then be encouraged to practise TTE at the patient's bedside. A prior training of 3 months in Doppler echocardiography is nevertheless necessary.

KEY WORDS : Transthoracic echocardiography -emergency physician -cardiologist

#### INTRODUCTION

Emergency physicians (EPs) are routinely called on to manage critically ill patients who may present with an indeterminate or changing hemodynamic status. Early in the patient's course, it may be difficult to firmly identify the underlying etiology. Bedside echocardiography offers a noninvasive, brief, rapid method of evaluating cardiac function. It should be practised by EPs physicians as a routine special investigation procedure following a detailed physical examination. In fact it has been shown that bedside echocardiography helps emergency physicians make the correct diagnosis, treatment and enhanced disposition decision, and significantly improve patient care. [1,2,3] This study aimed to evaluate the performance of tranthoracic echocardiography (TTE) in emergency departments by emergency physicians by comparing the findings obtained to those given by an echoDoppler proficient cardiologist.

#### METHODS

This was a randomised prospective study carried out in the emergency department of the military hospital of Tunis (Tunisia) during the period going from 1 January 2016 to 31 December 2016. It included all patients aged > 16 years in whom there was an urgent need to practise a TTE. The patients in the study had to undergo a double echocardiographic examination: an initial echocardiographic investigation carried out by an emergency physician who had previously received a three-month training in Doppler echocardiography, followed by a subsequent investigation performed by an echo-Doppler proficient cardiologist.

An inter-rater reliability analysis using the K statistics with 95% CI<sup>10</sup> was performed to determine the degree of agreement between the emergency physician and the cardiologist for each echocardiographic parameter. The evaluation considered the global visual estimation of the left ventricular ejection fraction (LVEF), the presence or absence of pericardial effusion (independently of the site), and the diameter and compliance of the inferior vena cava (IVC).

#### RESULTS

Two hundred and four patients were involved in the study. Mean age was 52 + 13 years, sex ratio 5 males/7 females.

The concordance of the findings obtained by the emergency physician and the cardiologist for the visual estimation of the LVEF was Kappa = 0.82 [95% CI 0.63-1] with an agreement = 0.90 [95% CI 0.74-0.99].

The concordance for measurement of the diameter of the IVC

was Kappa = 0.95 [95% CI 0.63-1] with an agreement = 0.95 [95 % CI 0.64-0.99] and for assessment of its compliance Kappa=1 with an agreement = 1.

The concordance of the findings obtained for the diagnosis of pericardial effusion was Kappa=0.86 [95% CI 0.71-1] with an agreement = 0.92 [95% ICI 0.64-0.99] and the concordance for the detection of echocardiographic signs of compressive effusion was Kappa = 1 with an agreement = 1.

#### DISCUSSION

#### LV systolic function

Visual estimation of global LV systolic function by the EPs in this study showed substantial agreement with that made by the cardiologist (90%, K=0.82, n=44). This degree of agreement is comparable with those found in previous studies of emergency physician-performed echocardiography. [1,4,5]

This study suggests that, even with limited training, EPs were able to use visual estimation n for global LV function with reliable accuracy. Similarly, Moore et al [4] concluded that emergency physicians with focused training in echocardiography could accurately determine left ventricular function in hypotensive adult patients.

Another study conducted by Eherman et al founds that agreement between EP-sonographers was good with 95% agreement on normal vs abnormal diastolic function, with K= 0.66 (95% CI,0.39-0.92) and weighted K = 0.77 (95% CI, 0.56-0.96) for grade of diastolic dysfunction(DD). There was also 95% agreement on presence of clinically significant DD. This demonstrates the high reliability of the EP-performed diastolic examination, which is important because it shows that EPs were able to consistently follow a multistep protocol and reach similar conclusions. [6]

Similarly to the study conducted by Bustam et al [1] our study directly compared echocardiography examinations performed by the EPs and the cardiologist immediately after one another. This provides a more direct and real-time comparison.

Furthemore, the visual technique to estimate LV function by EPs is not only accurate but also quicker to perform. In addition it saves time and costs.

#### Pericardial effusion

Pericardial effusion was identified by the presence of an anechoic stripe within the pericardium surrounding the heart, and was categorically assessed as either absent or present.

It is also important for emergency physicians to be able to accurately diagnose the absence of pericardial effusion, as it can be mistaken for pericardial fat, other pericardial abnormalities or the more common pleural effusion. [1,7,8] False positive findings of pericardial effusion might lead to inadvertent pericardiocentesis. [9]

The detection of pericardial effusion when comparing when comparing the findings of the EPs with those of the cardiologist was Kappa Kappa=0.86 [95% CI 0.71-1] with an agreement = 0.92 [95% CI 0.64-0.99] and the concordance for the detection of echocardiographic signs of compressive effusion was Kappa = 1 with an agreement =1. These results are compared to other studies which reported sensitivities of emergency physicians-performed focused echocardiography in detecting pericardial effusion of between 88% and 100%. [10,11]

#### IVC assessment for fluid volume status

IVC assessment in this study involved measuring the changes in the diameter of IVC during inspiration and expiration. The degree of collapsibility of the inferior vena cava provides information regarding the central venous filling volume and the right atrial pressure represented by the CVP. This is done by viewing the vena cava below the diaphragm in the sagittal plane and observing the change in the IVC diameter during the respiratory cycle. During inspiration, negative intrathoracic pressure causes negative intraluminal pressure and increases venous return to the heart. The compliance of the extrathoracic IVC causes the diameter to decrease with normal inspiration. In patients with low intravascular volume, the inspiration to expiration diameter ratios change more than in those patients who have normal or high intravascular volume, and therefore a quick assessment of intravascular volume can be made. [1,12,13,14]

IVC evaluation can be particularly helpful in those patients with a significant respiratory collapse during inspiration, permitting prompt identification of the hypovolemic patient. [15]

In our study, the concordance for measurement of the diameter of the IVC was Kappa = 0.95 [95% CI 0.63-1] with an agreement =0.95 [95% CI 0.64-0.99] and for assessment of its compliance Kappa=1 with an agreement =1. Whereas, in the studies conducted by Bustom and Randazzo the IVC diameter and collapsibility assessment by the trainees showed only a moderate agreement with that made by the cardiologist (64.2%, K=0.45, n=95) and (68.1% K=0.41, n=94) respectively. [1,5]

#### Limitations

One of the limitations of our study was the small number of patients. Besides, the emergency physician was not blinded to the study. As he knew he was being evaluated, he may have been more motivated to diagnose and enhance his performance on the criteria being studied. Another limitation of our study is that we enrolled a sample of patients at a single institution, which likely introduced selection bias.

#### CONCLUSIONS

Emergency physicians are able to perform and interpret focused echocardiography with reliable accuracy. Emergency physicians should then be encouraged to practise TTE at the patient's bedside. Nevertheles a practical training seems necessary.

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# **ORIGINAL RESEARCH**

# *Evaluation of Anticoagulation therapy in Atrial Fibrillation in the emergency department*

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#### BACKGROUND

The vitamin K antagonists (VKAs) are currently the most effective therapeutic class for the prevention of cerebrovascular events in atrial fibrillation (AF) patients. However, several studies showed an under-prescription of this therapy.

The aim of the study was to assess the prescription of VKAs in non-valvular AF (NVAF) patients and factors influencing the non-prescription of such treatment.

#### METHODS

We conducted a prospective, observational study in an emergency department (ED). Patients with high thromboembolic risk NVAF and not receiving VKAs beforehand were included. Calculation of CHA2DS2-VASc and HAS-BLED scores was performed. An analytic study was conducted in order to identify independent predictors of the under-prescription of VKAs.

#### RESULTS

During study, 176 patients were enrolled, the mean age was  $67\pm13$  years and 66% were women. The mean CHA2DS2VASc and HASBLED scores were  $2.88 \pm 1.55$  and  $1.52 \pm 1.05$ , respectively. Among our cohort, VKA was prescribed in 36% of cases. Age >70 years (OR=1.59, 95%CI[1.11-2.21],p<0.001), creatinine level  $\geq 110 \mu$ mol/l (OR=2.54,95%CI[1.20-5.37],p=0.01) and aspirin use (OR =1.7,95%CI [1.08-2.67],p=0.02) were independently associated with under-prescription of VKAs. Bedside, the main causes reported by the emergency physicians (EP) were: factors related to patient characteristics (n=38,34%), factors related to emergency physician (n=62,55%), factors related to the patient environment (n=20,17%) and factors related to the drug (n=22,23%).

#### CONCLUSIONS

Our results showed that the prescription of VKAs was low in ED. The reasons of VKA under-prescription are linked usually to several factors inherent to patient and to the adherence of EP to new recommendations.

KEYWORDS : Non valvular atrial fibrillation - Anticoagulation - Underuse - Emergency Departments.

#### INTRODUCTION

Atrial fibrillation (AF) is the most common significant cardiac rhythm disorder encountered in emergency departments (EDs) being present in 3.6 to 7% of general emergency visits (1, 2). It affects 2 to 5% of the general population, and increases substantially with age (3-5). Patients with AF have at least a 5-fold increased risk of ischemic stroke (6).

Approximately, 15% of all strokes are associated with this dysrhythmia, and the association increases with age (7,8). Stroke prevention is therefore crucial to reduce mortality and disability in patients with AF, and especially in those with the highest risk of embolic events (9).

Major randomized primary prevention trials conducted in patients

with AF have shown that oral anticoagulation (OAC), reduce the risk of embolic events (9-13).

The vitamin K antagonist (VKA) is currently the most prescribed therapeutic class for the prevention of embolic events. However, hemorrhagic stroke is the major complication of VKA, it come to the forefront of iatrogenic accidents and are responsible for approximately 1.1 to 7.4% per year independently of age and from 1.1 to 13% per year in elderly patients (14). It is therefore essential to accurately assess the benefit / risk ratio of VKA to each patient to whom anticoagulation is proposed.

Diverse studies conducted in the hospital setting, in general practice, and in EDs have found that anticoagulation is prescribed to less than 55% of eligible patients [14]. The reasons of this underuse remain unclear. EDs play a substantial role in AF management, notably, concerning stroke prophylaxis. On the other hand, a significant proportion of AF patients attending EDs are at high risk of stroke and are not receiving anticoagulants (15). Therefore, these patients may benefit from adequate prescription to improve their prognosis and long-term quality of life.

In this perspective, we conducted this study whose objectives were to assess the prescription of VKAs in non-valvular AF (NVAF) patients and factors influencing the non-prescription of this therapy.

#### METHODS

We conducted a prospective, observational and mono-centric study in an ED over a period of two years (April 2013 to April 2015).

#### **Patient Selection**

We included consecutive patients older than 18 years, attended to the medical area of the ED during the study period, with the diagnosis of AF eligible for anticoagulation by VKA according to guidelines of the European Society of Cardiology (ESC) (3).

AF was documented in an electrocardiogram (ECG) obtained when the treating physician considered it necessary during clinical evaluation. Exclusion criteria for the study were valvular AF, patients receiving OAC, low risk of stroke (CHA2DS2-VASc=0), contraindications to VKA and hemodynamic instability.

#### Data collection

Data collected from patients included demographic data, comorbidities, disability, type of AF (first episode, paroxysmal, persistent and permanent), risk factors for stroke according to theCHA2DS2-VASc scores, bleeding risk–prediction factors according to the HAS-BLED score, symptoms that caused ED consultation, clinical presentation and ED evaluation, arrhythmia management (rhythm or rate control), patients' outcome (symptom relieving and type of cardiac rhythm at discharge), final disposition (discharge, admission, or death) and stroke prophylaxis prescribed in the ED (anticoagulation, antiplatelet therapy, or both).

Patients with a CHA2DS2-VASc score  $\geq 1$  are classified as at high risk of stroke, and therefore anticoagulation is recommended in patients without contraindications. VKA was prescribed in a doseadjusted approach to achieve an international normalized ratio (INR) target of 2.5 (2-3). If anticoagulation was not prescribed, the treating physician was asked to explain the reason for not prescribing it. Patients were divided into two groups: VKA+ Group: patients received VKA and VKA – Group. The two groups were analyzed and compared in order to identify factors independently associated with VKA under-prescription.

Finally, the reasons why physicians did not give VKA were described with detailed arguments on the benefit/ risk of OAC.

Follow-up for adverse events (ischemic stroke, hemorrhagic complications) and death was performed during a three months period. We used telephone follow-up, in addition to record review.

#### **Data Analysis**

Statistical analysis was carried out with SPSS (version 18.0) statistical software package. Continuous variables are presented as means ± standard deviation (SD) and discrete variables as absolute values and percentages. An univariate analysis comparing the two groups was performed, with the chi -square test with Yates' correction or Fisher's exact test when appropriate, odds ratio (OR) with 95% confidence intervals (CI), and the unpaired t-test.

The logistic regression analysis with no prescription OAC as dependent variable was there run. The analysis was performed with a binary logistic regression and "enter" method, with an entry criterion of 0.05 and a removal criteria of 0.10. Differences were considered to be statistically significant with P<.05 or when the 95% confidence interval (CI) of the odds ratio (OR) excluded the value of 1.

#### RESULTS

Characteristics of the study population:

Between April 2013 and April 2015, 126,800 patients were presented to the ED, 249 of these patients were found to have AF and 176 patients were included in the study (Figure 1)

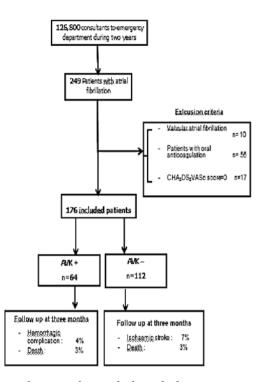


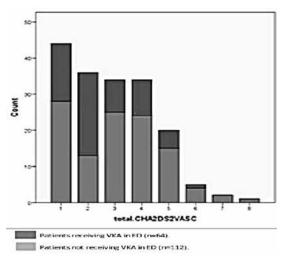
Figure 1. demographic and clinical characteristics of the study population.

Table 1. Baseline characteristics of the study population

	Group	Group	Total	
Characteristics	VKA+	VKA-	(n=176)	
	(n=64)	(n=112)		
	36%	64%		
Demographics				
Age, mean (SD),years*	61±12	69±13	$67 \pm 13$	
Age≥75 years n(%)*	9 (14)	47 (42)	56 (32)	
Male gender n(%)	17(26)	42(37)	59 (34)	
Sex ratio	0.36	0.6	0.5	
Risk factors (%)				
Hypertension	38 (64)	72 (64)	110 (62)	
Congestive heart failure*	7 (11)	27 (24)	34 (19)	
Coronary disease	3 (5)	16 (14)	19 (11)	
Diabetes	19 (30)	28 (25)	47 (27)	
Dyslipidemia	9 (14)	11 (10)	20 (11)	
Previous AF*	8 (12)	35 (31)	44 (25)	
Previous stroke	3 (4)	7 (6)	10 (5)	
COPD	11 (17	13 (11)	24 (13)	
Dysthyroidism	1 (1)	4 (3)	5 (3)	
Renal failure	1 (1)	4 (3)	5 (3)	
Type of AF (%)				
Paroxysmal (<48 hours)	30 (47)	38 (34)	68 (38.6)	
Paroxysmal (>48 hours)	21 (33)	25 (22)	46 (26.2)	
Persistent	5 (8)	10 (9)	15 (8.5)	
Permanent	8 (12)	39 (35)	47 (26.7)	
More than 3 drugs per day*	13 (20)	42 (37)	56 (31)	

COPD: Chronic obstructive pulmonary disease, \*Significant difference between the groups

The mean CHA2DS2-VASc score was  $2.88\pm1.55$ . The mean HAS-BLED score was  $1.52\pm1.05$ . A high bleeding risk (HASBLED score  $\geq 3$ ) was found in 18% of patients. Only sixty-four patients (36%) were received VKA at ED. Anticoagulation prescription according to the CHA2DS2-VASc score was illustrated in figure 2.



# Figure 2. Oral anticoagulation according CHA2DS2 - VASc score.

Performed in 17% of patients and rate control (in patients with AF >48 h) in 40% of patients. Eighty-eight percent (88%) of patients were discharged home from ED.

Factors associated with the non-prescription of VKA:

Patients who were not receiving VKA were older (69 vs. 61 years, p<0.001), more likely to have permanent AF, their HAS-BLED score was higher ( $3.09 \pm 1.64$  vs.  $1.17 \pm 0.8$ , p<0.001) and had more than three drugs per day in their medication prescription (37 vs. 20%, p=0.01).

The prevalence of ischemic stroke at three months was higher in the VKA- group (7 vs. 0%, p=0.02), and the incidence of hemorrhagic complications was higher in VKA + group (4 vs. 0%, p=0.04). The rate of death was similar in the 2 groups (3 vs. 4%, p=0.5).

Factors independently associated with lack of oral anticoagulation prescription in eligible patients on logistic regression analysis were showed in table 2.

# Table 2. Factors Independtly associated with lack of oral anticoagulation prescription

	Adjusted OR	CI 95%	Р
Age ≥ 70years	1.59	[1.11-2.21]	<0.001
Creatinine level ≥ 110µmol/L	2.54	[1.20-5.37]	0.01
Aspirin use	1.7	[1.08-2.67]	0.02

Table 3. Reasons given by physicians to explain why patients were not receiving oral anticoagulation

Reasons given by physicians to explain why patients were		%
not receiving VKA		
Factors related to patient characteristics :	38	34
. cognitive impairment	12	32
. physical dependence	26	68
Factors related to EP:	62	55
. concept of "clinical inertia" (old age)	24	38
. fear of side effects interesting the fear of bleeding	16	26
. ignorance of recommendations	22	36
Factors related to patient environment:	20	17
(social isolation and poor socioeconomic conditions)		
Factors related to drugs:	22	23
(polymedication and adherence to treatment)		

#### DISCUSSION

Our study has shown that the prescription rate of VKAs was low (36%). Factors independently associated with the prescription were related to the characteristics of the patients (advanced age, using aspirin and past medical history of renal failure).

The leading reason why patients were not receiving OAC was a «potential contra-indication» (especially advanced age), followed by «lack of knowledge of recommendations», cognitive impairment and physical dependence of patient and «fear of bleeding».

The medical management of AF (other than antiarrhythmic drugs) is primarily focused on reducing the risk of stroke. The prevention of thromboembolic events is based on the establishment and monitoring of anticoagulation now mainly based on the use of VKA.

This preventive treatment is a well codified theory, based on the thromboembolic risk assessed by the CHA2DS2-Vasc score (3).

Although the VKA prescription rates increased over time since the publication of AFASAK, BAATAF, SPAF, CAFA, SPINAF studies between 1989 and 1992, an under-prescription of VKA has been observed in patients with NVAF at high thromboembolic risk (11-13,16).

VKA prescription rates in patients with AF vary from 28-64%. In elderly patients (from 75 to 80 years), it vary from 35 to 46% (17,18).

We found that despite a mean age of patients more than 65 years, with high risk of thromboembolism, the prescription of VKA was around 36%. These data were consistent with the results of many recent studies (19-21).

Patients not receiving VKA were older (69 vs. 61 years, p<0.001),

had higher prescription medication including more than 3 drugs per day (37 vs. 20%, p=0.01) and higher HASBLED score (3.09  $\pm$  1.64 vs. 1.17  $\pm$  0.8, p <0.001).

The number of ischemic stroke was higher in the VKA- group, and bleeding events were more frequent in the VKA + group. The mortality rate was similar in both groups.

Advanced age (>70 years) was independently associated with the lack of anticoagulant prescription to eligible patients. These data are consistent with those in other studies in which the elderly population was often excluded from anticoagulant treatment (15, 22-27).

The fear of bleeding is one of the main barriers in these patients, and may override the perception of these patients' risk of stroke (28-30). It was provided as one of main explanations by our physicians. They probably consider that it is more serious to have severe bleeding because of properly prescribed and managed OAC, than to have severe embolic events in the absence of OAC. These explanations had already been suggested (3,28,30).

But different studies have demonstrated that anticoagulation in this population reduces the risk of stroke without a significant increase of bleeding and that the net benefit of anticoagulation is greater than in younger patients (31-35).

One of the major reasons provided in SAFE II by GPs, and sometimes cardiologists, not to prescribe OAC, was that they thought there was no indication (28,29). This reason was provided by 36% of physicians in our study.

This finding supports the hypothesis that the main reason why NVAF patients are not receiving OAC in practice is a lack of knowledge of trials and guidelines.

Because the guidelines' recommendations have been demonstrated to be widely applicable in daily practice (3,27,32), and previous studies in local settings have demonstrated the usefulness of specific training to improve management's adequacy, educational efforts to increase physicians' adherence to the guidelines appear warranted (36).

Previous cognitive impairment, falls or gait disturbances and living conditions were often considered as major contra-indications for OAC. These factors have not been clearly evaluated until now and should be only considered on an individual basis when the risk of such a condition appears higher than that of the natural history of the disease.

Because stroke is the major risk of AF and because OAC can drastically reduce this risk, primary and secondary prevention of ischaemic stroke among patients with AF by an appropriate use of OAC is a crucial issue to improve quality of care.

#### **STUDY LIMITATIONS**

The main limitation of this study is the small number of patients; this does not reflect the real rate of the VKA prescription in the other ED and cardiology department. Another limitation is that our data lack objective assessment of cognitive status, falls or gait disturbances and living conditions.

#### CONCLUSION

In This study, the prescription of VKA in patients with high thromboembolic risk NVAF was low in ED. The reasons of VKA under-prescription are linked usually to several factors inherent to patient and to the adherence of EP to new recommendations.

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#### **CASE REPORT**

# *Hypertrophic cardiomyopathy (HCM) mimicking acute myocardial infarction: a case report and review of literature.*

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#### INTRODUCTION

Electrocardiogram (ECG) is the most commonly used diagnostic tool for recognizing and triaging of patients with symptoms suggestive of acute myocardial infarction (AMI) [1]. ST elevation (STE) represents common electric sign of acute transmural ischemia caused by an occlusion of an epicardial coronary artery by a blood clot. Especially in pre hospital care and without other investigations, urgent therapy for patients with chest pain and STE must be considered to reanalyze the occluded artery by percutaneous coronary intervention or fibrinolysis when cat lab is unavailable or far away. However, many patients presenting with typical symptoms have elevation of the ST segment due to non ischemic etiologies (NISTE) [2]. We report here a case of hypertrophic cardiomyopathy mimicking a ST elevation myocardial infarction (STEMI) in patient with chest pain in pre hospital care.

#### CASE REPORT

A 37-year-old male patient presented to emergency room in primary centre, complaining of chest pain, acute coronary syndrome was suspected. Our emergency medical system received call for this patient and activated pre hospital emergency team for transfer.

Without any medical history, the patient suffered from a continuous angina chest pain one hour before our intervention. The patient was not on any regular medication. The patient vital signs included the following: blood pressure was 150/80 mmHg, heart rate 70 beats/min, respiratory rate was breaths/ min, oxygen saturation was 97% and temperature was 37°c. Cardiac auscultation was normal. There were no congested neck veins. Neither lower limb edema nor signs of pulmonary congestion was observed. The initial ECG showed a sinus rhythm, undetermined QRS axis in both frontal and precordial leads, a Q wave with concave STE was observed in D2 D3 AVF, in V6 V7 V8 V9 and in V3R V4R with reciprocal changes

in leads D1 and AVL, as well as inverted biphasic T wave in anterior leads. The initial diagnosis of STEMI was established. After initiating treatment by Aspirin (250 mg), Clopidogrel (300 mg) and intravenous heparin, the patient was transferred to cat lab. Coronary angiography performed thirty minutes later, however showed normal coronary arteries without significant stenosis. Transthoracic echocardiography concluded to hypertrophic cardiomyopathy with normal left ventricle systolic function, and no resting wall motion abnormalities.

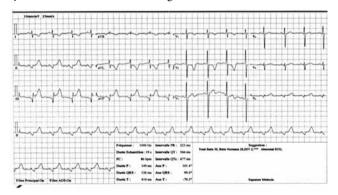


Figure 1 : ECG patient



Figure 2 : Coronary angiography

#### DISCUSSION

Today, the ECG still has a major role in diagnosing and triage of patients presenting with chest pain [3]. The current American college of cardiology/ American heart association (ACC/AHA) guidelines for STEMI recommend that patients with suggestive symptoms of myocardial ischemia who have STE at the J point in (2 contiguous leads or more of 0.2 mV or more in males or 0.15 mV or more in women in leads V2 V3 and/o of 0.1 mV or more in all other leads in threshold) should undergo immediate reperfusion therapy [2]. In Emergency department, STE ins seen in approximately 20 % of patients presenting with chest pain, but only minority of them have a true Acute coronary syndrome (ACS) [4]. Otto Found that 63 among 123 (59%) with chest pain and STE in pre hospital care had diagnosis rather than AMI [5]. In another study, Brady found that 157 among 212 (74%) patients presenting with chest pain had NISTE [6]. NISTE is very common in emergency department (ED): in up to 29% of ECG [5]. This condition is challenging for emergency physicians and even cardiologists. Jason found a rate of 3 to 29 % of false positive STEMI with expert ECG reader (cardiologist), whereas the false negative rate was between 0 and 50 % [4]. The differential diagnosis of elevation of the ST segment is wide including conditions with secondary of the myocardium (for example dissection of aortic wall), pre existing STE without acute ischemia and instances with new ST with chest pain and without evidence of ischemia (for example myocarditis or pericarditis, pulmonary embolism, electrolyte imbalance, rate related repolarization changes etc.) [1]. Wang described twelve conditions of mimicking STEMI, and highlighted the electrocardiographic clues that can be used to differentiate them from AMI [7].

Some criteria can be useful to differentiate STEMI from NISTE. The most sensitive is reciprocal changes, it support the diagnosis of AMI with a positive predictive value more than 90 %. Reciprocal changes were present in our case and it induced diagnosis error. Therefore over diagnosis STEMI STEM caused false activation of PCI protocol and also unnecessary indeed unsafe administration of fibrinolytic therapy. Another criterion was also studied: concavity versus convexity. Brady and all reported 77 % sensitivity, 97 % specificity, 94% PPV and 88% NPV for a non concave STE morphology in acute MI diagnosis [8]. But the most specific distinguishing criterion is changes in time of ischemic electrical signs [6].

Previous papers reported similar cases of HCM mimicking AMI [9,10,11,12,13,14] and from those cases, many instructive keys should be emphasized. First HCM can mimic AMI in all points. Chest pain is common particularly in young patients [15]. This symptom may be caused by cardiac ischemia secondary to imbalance between oxygen supply and demand in the thickened ventricle or by compromised coronary arteries filling during diastole. Then,

ECG in HCM shows frequently "pseudo ischemic" signs. The most common abnormality is High QRS voltage in precordial leads due to left ventricular hypertrophy. Our case is the first report with biventricular hypertrophy and consequent T wave changes. Deep and narrow Q wave in inferior and lateral leads are also common in HCM [9]. In the other side, ECG of our patient showed wide Q waves particularly in D2 D3 and AVF mimicking myocardial necrosis. Moreover, reciprocal changes were present and were in favor of STEMI diagnosis. Several abnormalities should alert physicians on the hypothesis of HCM. They include: high QRS voltage, concave morphology of STE, absence of reciprocal changes and non modification of electrical signs. Echocardiography must be performed before any therapy and coronary angiography should be considered early when patient present continuous chest pain.

#### CONCLUSION

Emergency physician must be aware of the importance to differentiate between STEMI and NISTE in patients presenting with symptoms suggestive of MI in order to avoid unsafe treatment. Chest pain is common in HCM and a sensible ECG analyze can detect specific signs and indicate echocardiography in order to confirm diagnosis.

### Table 1. Etiologies of STE according to Wang (N Eng J Med 2003; 349: 2128-35)

QT commont Elevation in	normal circumstances and various conditions
·	
Condition	Features
Normal (so-colled male	Seen in approximately 90 percent of healthy young
pattern)	men therefore,
	normal elevation of 1-3 mm most marked in V2
	concave
Early repolarization	Most marked in V4 with notching at J point
	Tall, upright T waves
	Reciprocal ST depression in aVR, not in aVL, when
	limb leads are involved
ST elevation of normal	Seen in V3 through V5 with inverted T waves
variant	Short QT, high QRS voltage
Left ventricular	Concave
hypertrophy	Other features of left ventricular hypertrophy
Left bundle-branch block	Concave
	ST-segment deviation discordant from the QRS
Acute pericarditis	Diffuse ST-segment elevation
	Reciprocal ST-segment depression in aVR not in aVL
	Elevation seldom >5 mm
	PR-segment depression
Hyperkalemia	Other features of hyperkalemia present: widened QRS
	and Tall, peaked, tented T waves
	Low-amplitude or absent P waves
	ST segment usually downsloping
Brugada syndrome	rSR' in V1 and V2
	ST-segment elevation in V1 and V2 typically
	downsloping
Pulmonary embolism	Changes simulating myocardial infarction seen often in
	both inferior and antero-septal leads
Cardioversion	Striking ST-segment elevation, often > 10 mm, but
	lasting only a minute or two immediately after direct-
	current shock
Prinzmetal's angina	Same as ST-segment elevation in infarction, but
-	transient
Acute myocardial	ST segment with a plateau or shoulder or upsloping
infarction	Reciprocal behavior between aVL and III

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#### **CASE REPORT**

# *Kounis syndrome: an allergic acute coronary syndrome case report*

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Kounis syndrome (KS), also known as allergic angina syndrome, was described in 1991 by Kounis and Zafras as "the coincidental occurrence of chest pain and allergic reactions". In the literature three variants of KS are described, this classification is based essentially on the coronary angiography data.

KS related allergen are continuously increasing, therefore the awareness of its manifestations in a patient diagnosed with an allergic reaction and the understanding of its pathophysiology can be lifesaving. In fact, the management of KS should follow the evidence-based guidelines for the treatment of a regular acute coronary syndrome, in addition to the antiallergic treatment.

KEY WORDS : allergic reaction, chest pain, vasospasm, acute coronary syndrome

#### **INTRODUCTION**

Kounis syndrome (KS), also known as allergic angina syndrome, was described in 1991 by Kounis and Zafras (1) as « the coincidental occurrence of chest pain and allergic reactions ». Vasospasm of the coronary arteries has been suggested to be the main pathophysiologic mechanism.

It is important to appropriately recognize and treat KS in patients with exposure to a documented allergen. Therapeutic management may be challenging because the epinephrine which is currently used for the treatment of the hemodynamic impairment must be used with caution as it can worsen the coronary vasospasm.

We present two cases of patients diagnosed with KS.

#### CASE 1

A 40 years old female presented to the emergency (ED) department with acute dyspnea after she inhaled a chlorinated product. She was a heavy smoker, without previous history of allergy.

She was sweating and agitated but conscious, she had a cutaneous rush, her respiratory rhythm was equal to 40 cycles per minute, with the use of accessory muscle and wheezing on auscultation. Her blood pressure was 140/85 mm Hg, and pulse of 120 beats/minute.

The initial electrocardiogram (ECG) demonstrated a complete left bundle branch block (Figure 1).

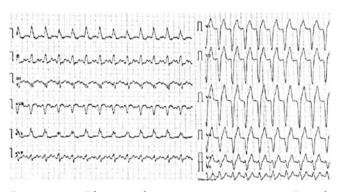


Figure 1. Electrocardiograms in case 1. Initial electrocardiogram demonstrates a complete left bundle block.

Diagnosis of stage II anaphylaxis was made. Treatment for anaphylaxis was initiated with nebulization of epinephrine, intravenous hydrocortisone and diphenhydramine with improvement in pruritus and dyspnea. Repeat ECG showed an incomplete left bundle branch block with ST segment deviation. Her blood cell count and basic chemistry panel were unremarkable except for a troponin I levels of 0.50 ng/mL (normal <0.04 ng/mL). She received an anti-ischemic and antithrombotic treatment. An emergent coronary angiogram was performed and it showed normal coronary artery. She was discharged home in a stable condition.

#### CASE 2

A 53 year old man presented to the ED with a cutaneous rash which occurs soon after he ate a tuna sandwich. He was a heavy smoker, with a history of hypertension, diabetes mellitus, and coronary artery disease but without previous history of allergy.

On arrival, he had a generalized erythematous rash over the face, neck and thorax accompanied by itching. His blood pressure was 100/60 mm Hg and the pulse 100 beats/minute. Examination of the heart, lungs, abdomen and central nervous system revealed no abnormalities. An ECG performed initially was normal. An antihistamine and steroid therapy were given to the patient. During admission in the ED, he felt unwell, started sweating, became pale and complained of severe retrosternal pain radiating to both arms associated with nausea and vomiting. His blood pressure fell to 70/40 mm Hg and his pulse increased to 120 beats/minute. An ECG performed immediately demonstrated ST-segment elevations of 1 mm in leads I and aVL with a specular reflection on leads II, III and aVF (Figure 2).



# Figure 2. Electrocardiogram in case 2. Electrocardiogram demonstrates ST-segment elevation of 1 mm in lead I and aVL with a specular reflection on leads II, III and aVF

The diagnosis of ST-segment elevation acute myocardial infraction (STEMI) was made and the patient received a dual anti-platelet (Aspirin and Clopidogrel) and anti-thrombosis (subcutaneous low molecular-weight heparin) medications. After administration of isotonic saline infusion (1000 ml) without epinephrine use, the patient became hemodynamically stable. An emergent coronary angiography was performed and showed a tight thrombotic stenosis of the anterior interventricular artery figure (3). An intracoronary stent was implanted with good **Outcome**.

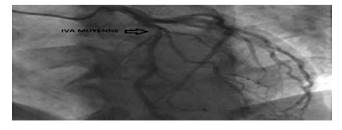


Figure 3. Coronary angiogram in case 2. The coroangiography of the second case shows a significant thrombosis of the anterior interventricular artery.

#### DISCUSSION

The ischemia in allergic reaction is secondary to the release of inflammatory mediators, including histamine, tryptase, chymase, platelet-activating factor, cytokines, prostaglandins and leukotriene synthesis, which leads to coronary vasospasm (2). These mediators are mainly located between myocardial fibers and in the arterial intima especially in the sites of coronary plaques (3). It has been demonstrated that they have a higher density in ischemic heart (4). Three types of KS have been previously described (5).

Type I includes patients with normal coronary arteries without predisposing factors for coronary artery disease in whom the acute allergic insult leads to coronary artery spasm with normal cardiac biomarkers or infarction with positive cardiac biomarkers. This variant represents a manifestation of endothelial dysfunction or microvascular angina (6).

The type II variant includes patients with culprit but inactive preexisting atheromatous disease, in whom the allergic insult leads to plaque erosion or rupture, leading to acute myocardial infarction or coronary vasospasm with normal cardiac enzymes (5)

The type III variant includes coronary artery stent thrombosis secondary to allergic reaction

Based on this classification, our first case was a form of type I KS and the second case represented a form of type II KS (5).

Since 1991, multiple allergens have been implicated as the main trigger factors for KS including drugs, food and environmental factors. New agents are recently described (7) but there is no case of KS related to chlorinated product exposure was reported before.

In the first case, our patient didn't have chest pain. The acute coronary syndrome was diagnosed on the bases of the ECG findings and the troponin screening. Therefore, ECG should be considered in patient presenting anaphylactic reaction even in the absence of chest pain.

In the second case, the KS occurred after fish ingestion. Tuna induced KS has been described previously in the literature (8). The therapeutic management of our patient presented a real challenge as he developed a hemodynamic impairment.

It is now proved that hypotension related to anaphylaxis is successfully treated with intravenous epinephrine. However, in the context of acute coronary syndrome (ACS) this drug may prolong the QTc interval, induce arrhythmias and worsen the coronary vasospasm, especially when administered intravenously.

In this case, it is a challenge to distinguish between a global myocardial hypoperfusion due to peripheral vasodilatation and a primary cardiac myocardial ischemia due to mast-cell mediator activity. The quick efficiency of fluid resuscitation to restore a good hemodynamic status suggests that the systemic vasodilatation reduced venous return which may cause coronary hypoperfusion. However, the necessity of undergoing a coronary angioplasty denotes that the ACS was more likely caused by the activation of local coronary mast cells resulting in atheroma rupture and coronary vasospasm.

It is important to recognize these forms of KS to provide appropriate management and care.

The diagnosis and treatment of KS can be indeed challenging, requiring attention to both the cardiac and anaphylactic pathophysiology concurrently.

Treatment of KS requires thoughtful use of several common drugs. Morphine, an important drug for treating acute chest pain, should be avoided in KS, as it may potentially stimulate histamine release and exacerbate the pathologic cascade in KS.

Beta-blockers also may potentiate coronary vasospasm if used in an acute exacerbation of KS due to an unopposed alpha adrenergic action. Epinephrine, which is used routinely for the treatment of anaphylaxis, should also be used with cautionary monitoring, as it may potentially worsen coronary vasospasm and aggravate coronary ischemia in KS (9).

The primary focus of treatment of KS should be directed towards the allergic insult and removal of the off ending allergens.

#### CONCLUSION

There are many allergic agents involved in KS and the number is continuously increasing. KS should be always kept in mind while managing anaphylaxis, even in the absence of chest pain.

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#### **BRIEF REPORT**

# Wellens' syndrome: about two cases

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#### SUMMARY

Wellens' syndrome is a pattern of electrocardiography T-wave changes associated with critical proximal left anterior descending artery lesions. Patients with Wellens' syndrome are at high risk of developing extensive myocardial infarction of the anterior wall and death. Thus, it becomes crucial that Emergency Department physicians recognize these patients promptly. In this article, we report cases of Wellens' syndrome to study its epidemiological, clinical, electrical and therapeutic characteristics.

KEY WORDS: wellens' syndrome, electrocardiographic changes, emergency, myocardial infarction

#### INTRODUCTION

Wellens' syndrome was first described in 1982 by H J WELLENS. «It is characterised by episodes of unstable angor associated with an inverted T wave in the anterior derivations». This presentation is associated with a higher risk of anterior myocardial infarction (M I) and/or sudden death related to a critical stenosis of the proximal left anterior descending (LAD) artery lesion.

#### CASE 1

This case is about a 44-year-old female smoker at 10 packs/ year, with no medical history. She presented to the Emergency Department with a crushing chest pain of one month duration which radiated to the back. The pain occurred in attacks lasting a few minutes at rest. The attacks were getting more and more frequent and increasingly painful. The patient also complained of increasingly severe dyspnea on exertion. On physical examination, the patient was afebrile; her BP 100/50 mmHg in both arms, her heartbeat at 82 bpm, her respiratory frequency at 16 cpm and her SpO2 at 100% on room air. There were no signs of acute heart failure. ECG showed anterosepto-apical negative T waves. (Figure 1)



Figure 1. Deeply inverted T waves in antero-septo-apical leads

The patient ws diagnosed with Wellens' syndrome. She was given a dual anti-platelet (aspirin and clopidogrel) and antithrombosis (subcutaneous low molecular-weight heparin) treatment. She was referred to the Cardiology Department where a coronary angiography revealed double-vessel-coronary lesions, a subocclusive stenosis of the medium anterior interventricular artery, an important short stenosis of the ostium of the second marginal branch involving the origin of a collateral branch. (Figure 2)

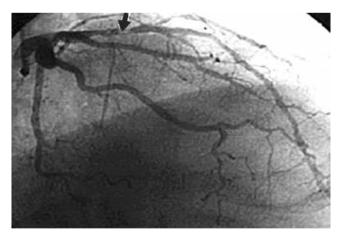


Figure 2. Coronagraphy showing a stenosis of the medium anterior interventricular artery

Primary PTCA of the medium anterior interventricular artery was performed consisting in the implantation of a radioactive stent without prior dilatation.

#### CASE 2

This case is about a 73-year-old hypertensive female with newly diagnosed hypertension and who had been complaining of chest pain and exertional dyspnea for 2 months. She was referred to our Emergency Department by a cardiologist in private practice for electrocardiographic abnormalities of recent onset. On admission, the patient was not in pain, Her BP 140/80mmg Hg, heartbeat at 75 bpm with no signs of acute heart failure. Her ECG revealed an antero-septal sub-epicardial ischemia. (Figure 3)

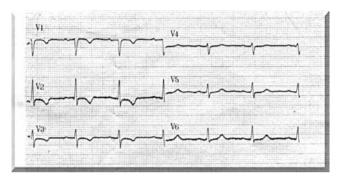


Figure 3. ECG showing antero-septal sub-epicardial ischemia

Cardiac laboratory tests were negative. A coronary angiography performed at hour 12 showed an occluded anterior interventricular artery in its proximal portion with a tight ostial circumflex (Figure 4)

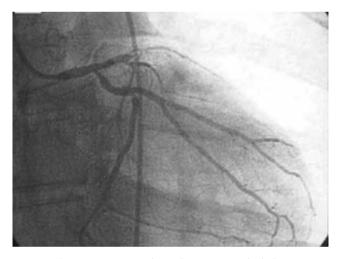


Figure 4. Coronarography showing occluded anterior interventricular artery in its proximal portion

The management consisted in a double by-pass of IVA and of the circumflex. The echography did not show any segmentary kinetic disorders. The obtained ventricular ejection fration (LVEF) was estimated at 50%. The patient was discharged free of complications.

#### DISCUSSION

Initially described by Gerson and al in 1980 then by Wellens in 1982, this syndrome is defined by the inversion of the T waves. It is the expression of a severe stenosis of the proximal LAD leading in 75% of cases to anterior myocardial infarction within a few days [1]. The pathophysiology of Wellens' syndrome ECG manifestations in relation to proximal LAD lesions is not fully understood, and it has been suggested that the development of T-wave inversion with a resolution of symptoms represents a phase of reperfusion [2]. In Wellens first study, in 26 out of 145 patients admitted for unstable angina (18%), ECGs showed changes which developed during the pain-free period [1]. In the later prospective study, 180 out of 1,260 hospitalized patients (14%) showed the characteristic electrocardiographic changes [3]. An urgent coronary angiography was implemented, and all of the 180 patients with electrocardiographic changes were found to have blockage of the LAD, varying from 50% to complete obstruction [3]. The diagnosis was established by the evidence of inverted T waves on ECG performed in the intercritical period. The characteristic electrocardiographic pattern often develops when the patient is not experiencing angina. This electrical sign is the expression of the resumption of the myocardial perfusion. ECG changes in V2-V3 only, reveal a lesion in the segments 1 and 2 of the septal branch of LAD. However, when the lesion is more proximal, the changes involve the precordial derivations. Diagnostic clues of Wellens' syndrome are given in table 1.

#### Table 1. Criteria for diagnosis of Wellens' syndrome

Criteria for diagnosis	comments
Chest pain with normal ECG or with	Represents critically narrowed or
T wave with either ST elevation or	occluded vessel
depression	
Progressive symmetrical deep T-	Represents reperfusion
wave inversion in V2-V3 during pain	Not necessarily limited to V2-V3
free periods	
Little or no enzyme elevation	If not treated early $\rightarrow$ extensive
	anterior MI
No loss of precordial R waves	
Tight proximal LAD stenosis	Typically between 1 <sup>st</sup> and 2 <sup>nd</sup> septal
	branches

There are two types (A and B) of ECG changes occurring in Wellens' syndrome (figure 5): Biphasic T waves in leads V2 et V3 (type A) and deeply inverted T waves in leads V2 and V3 (type B), both suggesting substantial "preinfarction" lesions.



Figure 5. Types of Wellens' syndrome

Type A occurs in 75% to 80% cases of Wellens' syndrome; the remaining 20% to 25% represent type B and show much more subtle findings of smaller biphasic T waves across the anterior leads, most commonly leads V2 to V3 and occasionally leads V1 and V4 to V6 [4]. While the differential diagnosis for T-wave inversions is broad, abnormalities found in Wellens' syndrome are particularly of concern because they often occur in asymptomatic patients, they might pseudonormalize in those presenting with cardiac chest pain or dyspnea, and they will not typically elevate cardiac enzymes. The concern is that ECGs might be interpreted as "nonspecific ST-segment or T-wave changes" in patients with identified risk factors for coronary artery disease who are then sent for outpatient Stress Test [5]. Numerous cases in the literature describe patients with these ECG abnormalities sent for stress test experience fatal myocardial Infarction during testing.[4, 6, 7]. In fact, performing exercise stress tests for these patients can be fatal due to severe stenosis that might lead to infarction at the time of increased cardiac demand [8]. As cardiac enzyme test results are often negative or within the upper limit of normal, ECG interpretation might be the only clue to the safest disposition of these patients. These ECG abnormalities can be found in a range of patients, including those aged 39 [9] and those with previously stented LAD lesions or recurrent Wellens' syndrome [10]. Emergency physicians should be able to recognize these ECG changes and must be aware of their importance so that they can prescribe the correct treatment.

#### CONCLUSION

Wellens' syndrome is a clinico-electrocardiographic entity which reveals precise anatomical lesions in AIV in its proximal portion that must be recognized by the emergency physician. An accurate identification of patients with Wellens' syndrome allows more rapid and appropriately aggressive management. It becomes crucial that Emergency Department physicians recognize these patients to prevent prolonged stays in the Department and inappropriate conservative therapy.

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#### **BRIEF REPORT**

# *Anomalous circumflex coronary artery: A rare cause of acute myocardial infarction : A case report*

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#### SUMMARY

The circumflex branch originating in the right coronary artery is the most common anatomical variations of the coronary artery. Although some authors have considered such a finding as an anatomical variation and a rare cause of ischemia or myocardial infarction, we report a case in which the circumflex branch originated in the right coronary artery was occluded causing a myocardial infarction.

KEY WORDS : Anomaly, coronary angiography, circumflex coronary artery, myocardial infarction

#### INTRODUCTION

About 0.6 to 1.55% of patients who undergo coronary angiography have coronary artery abnormalities (1, 2). Difficulties may occur in the diagnostic procedure but recognition and adequate visualization of the anomaly is essential for proper patient management especially in patients undergoing evaluation for percutaneous coronary intervention (3). We present a case of an aberrant origin of the circumflex coronary artery (Cx) from the proximal right coronary artery (RCA) diagnosed in percutaneous coronary intervention (PCI) in a patient who had an inferior myocardial infarction.

#### CASE REPORT

A 65-year-old male patient presented to the Emergency Department (ED) one hour after experiencing a typical acute angina chest pain. He had a 50 packs-year history of cigarette smoking, with a history of hypertension and diabetes mellitus. His vital signs were as follows : blood pressure 130/70 mmHg, pulse rate 72 beats/min, respiratory rate 20 breaths/ min and oxygen saturation with pulse oximetry 98%. An electrocardiogram showed an ST-depression from leads V1 to V6. Troponin assay performed at six hours from the onset of chest pain was positive at 1.69 µg/l (normal: < 0.05 µg/l :). A dual anti-platelet and anti-thrombosis medication was given. A PCI showed a narrow stenosis of the circumflex artery (Cx) arising directly from the right coronary artery (Figure 1). A stent was performed in the proximal Cx swelling with a TIMI III flow rate. The evolution was favorable without complications.

#### DISCUSSION

Anatomical variations of the coronary arteries have been found in 0.64 to 1.55% of patients submitted to a coronary angiography. These authors also affirm that the circumflex branch originating in the right coronary artery is the most common anatomical variations of the coronary artery (1, 2). The first case series of PCI performed on such aberrant vessels was described in 1982 (4). Samarendra et al. (5) affirmed that the circumflex branch of the coronary artery originating in the right side, is the most common "benign" coronary anomaly and is not considered the cause of ischemia or myocardial infarction, which confirms the conclusions of Click et al. (6) when they claim that the most common anomaly involving the coronary artery is the one of the circumflex branch, although such anomalies are not common in adults. It must be considered however, that this condition can be present at birth, being little symptomatic during childhood, and being found incidentally through the coronary arteriography or necropsy. In this present report, the diagnosis of this aberrant coronary artery was made

after undergoing a percutaneous coronary intervention for myocardial infarction.

Although it was not our goal in this work, we believe that the assumption made by some authors that the circumflex branch originating in the right coronary artery must be considered as an anatomical variation and not an anomaly, must be studied more deeply to be validated.

#### CONCLUSION

The coronary artery anomaly origins may cause myocardial ischemia and sudden death. Coronary angiography is the key in the diagnosis of these abnormalities. Difficulties may occur in the diagnostic procedure but recognition and adequate visualization of the anomaly is essential for proper patient management especially in patient undergoing evaluation for percutaneous coronary intervention.



Figure 1. A stenosis of a major thrombotic circumflex which arises directly from the right coronar

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#### **BRIEF REPORT**

# *Pulmonary embolism in deep waters: A rare diagnosis*

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#### INTRODUCTION

Diving accidents include several entities varying in severity. . Decompression accidents (DA) represent 30-60% of diving accidents (1). They may vary from minor accidents (cutaneous and musculoskeletal accidents or simple malaise) to very severe accidents involving the neurological system, the vestibilum and the respiratory system. The spinal cord is the most affected in severe accidents (2). Although it is rare in DA, air pulmonary embolism, should be suspected in the presence of some suggestive diagnostic clues. This diagnosis could be explained by, on one hand, the excessive importance of degassing which exceeded the victim's pulmonary filtering abilities (on account of the abruptness of the accident and of the important depth leading to the formation of real gaseous mantles and, on another hand, by activation of the clotting process. Prolonged and continuous immobilization of the paraplegic patient, in addition to the increased blood viscosity are in the present case some associated factors. In our review of the literature we found only one similar case, but pulmonary embolism occurred on the 6th day after the accident. The mechanism seems, therefore, to be different (2)

#### CASE REPORT

This case in about a 33-year-old professional diver from the north west of Tunisia who dived at a depth of 105 meters using a tri-mixture at 35% of helium. After 18 minutes at this depth, his lower limbs opened and he came back up to the surface. As his lower limbs immediately afterwards felt heavy, the patient was rapidly enclosed in a home-made hyperbaric chamber for 7½ hours but the patient's condition did not improve and he was rushed to hospital.

History taking revealed that the patient had no relevant medi-

cal history. It also revealed that while in the hyperbaric chamber, the patient had a feeling of pressure in the chest and urinary retention.

The physical examination yielded the following findings: GCS 15/15, T=37°c, pulse 100 pm, BP 130/70 mmHg, FR at 22 cpm and SPO2 at 94%. The patient also had a distended bladder. The neurologic examination revealed a flabby paralysis of the lower limbs with a syndrome of funiculus posterior medullar spinalis, thermal and algesis hypoesthesia with a sensitivity at D8, a pyramidal syndrome at the upper limbs associated with a bilateral Hoffman's sign and a plantar reflex on both side laboratory tests showed D-dimeres at 9320 ng/ml and blood gas analysis revealed a hypoxia at 69 mmHg and a hypocapnia at mmHg. The patient received 250 mg of aspirin. He was hydrated and put on broadband normobaric oxygen therapy. On arrival at the Emergency Department, the patient had a 60-minute session of hyperbaric oxygen therapy (Hbo) at 2.2 ATA because he arrived late (more than 12 hours after the accident).

In view of the feeling of pressure in the chest, polypnea, of the tachycardia, the results of blood gas analysis, the normal findings of chest X-ray (fig A) of Well's score (4.5 indicating an intermediate probability and the raised D-dimeres, a chest CT scan was performed. It revealed a sub-segmental antero and postero basal pulmonary embolism at the right lower lobe (FigB). Considering the neurological manifestations which were suggestive of the spinal medulla-involvement, an MRI of the brain and spine was ordered (Fig C). It revealed hypersignal T2 intramedullary ischemic lesions spreading from C3 to C7 with a swollen dorsal medulla

The patient was admitted to the Neurology Department where he was put on aspirin and HBPM. Ten sessions of HBO were also prescribed as a consolidation treatment. Neurologically, the course was unfavourable since the deficits in the lower limbs persisted and were complicated by other problems related to the supine position. The patient was then referred to a rehabilitation centre. He did not go back to work.

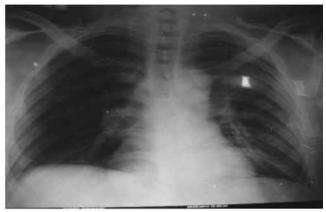


Figure 1. Normal chest X-ray

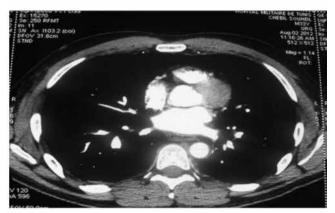


Figure 2. Chest CT scan: sub-segmental antero and postero basal pulmonary embolism at the right lower lobe

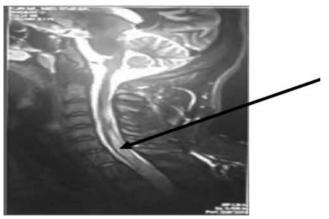


Figure 3. MRI of the brain and spine: hypersignal T2 intramedullary ischemic lesions spreading from C3 to C7 with a swollen dorsal medulla

#### CONCLUSION

During serious diving accidents spinal involvements are usually the most frequent. They are feared very much due to the neurological deficits that may follow (1,2,3). Symptomatic degassing in the intravascular area is much less frequent and should be looked for systematically whenever there are presenting symptoms or signs suggestive of arterial or venous embolism (3,4). Pulmonary air embolism is very rare in DA(2,). At an early stage, HbO therapy permits an important reduction in the size of the air bubbles and thereby in the consequences of their formation. In fact, beyond 12 hours, the expected benefit derived from HbO therapy is much less on account of the transformation of the air emboli into combined emboli, air and fibrinocruoric emboli (2)

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#### **BRIEF REPORT**

# *Gayet-Wernicke's encephalopathy complicating vomiting on the grounds of hyperemesis gravidarum*

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Gayet- Wernicke's encephalopathy is a rare neurological pathology which is due to a thiamine deficiency. It is considered as a neurological emergency and may lead to death if untreated. . It mainly attacks people addicted to alcohol. However, some cases occurring in the context of incoercible gravidal vomiting were published. Its prevalence among the developed countries, which is estimated as ranging between 0.1 and 0.6%, is probably underestimated. In fact, several atopic cases were described. The diagnosis is clinical before the classic triad confusion syndrome. Oculomotor disorders and ataxia. Magnetic resonance and determination of thiamine in the blood are the two diagnostic tests.

We present the case of a 25-year-old patient without amedical history and who is pregnant at 27 weeks of amenorrhoea. The patient consulted the Emergency Department for diplopia, ataxia and vertigo that had started in the 4th month of pregnancy.

The patient was hospitalized in the first trimester of pregnancy for incoercible vomiting requiring prolonged rehydration with serum glucose. She subsequently presented diplopia, ataxia, multi directional nystagmus, temporary disorientation and a deficit of the epicritic sensitivity of the two lower limbs. She was then hospitalized in the Neurology Department where the exploration was completed and treatment with parenteral vitamin B1 supplementation was introduced.

**Conclusion :** Gayet Wernicke's encephalopathy should be referred to all neurological manifestations in a pregnant patient with hyperemesis gravidarum in order to avoid irreversible after effects. This observation recalls the danger of infusions of serum glucose alone in situations of undernutrition.

#### INTRODUCTION

Gayet-Wernicke's encephalopathy is an acute neurological complication secondary to thiamine deficiency (vitamin B1). It is frequently encountered in heavy drinkers, but can sometimes be found in other circumstances. We report a case of Gayet-Wernicke's encephalopathy complicating incoercible vomiting on hyperemesis gravidarum.

#### A CLINICAL CASE

Mrs. Amina B. is a 25-year-old female at 27 weeks of pregnancy consulting in the eEmergency Department for deep asthenia and the inability to walk and stand up. She is a patient with no specific pathological history, G2P1, hospitalized during the first trimester of pregnancy in the Gynecology Department for severe vomiting with severe ionic disorders and outgoing under iron one month ago.

The clinical examination shows an emaciation of more than 10 kg since the beginning of pregnancy with a mucous skin pallor, a slight confusion, horizontal nystagmus and fluctuating diplopia, with cerebellar ataxia and net dysmetry as well as hypotonia of leg muscles with falling feet and steppage without sensory deficit. Biology showed hypoglycemia (Gly 4.1 mmol / L), iron deficiency anemia (Hb 9.6 g / dl VGM 88.3 FL TCMH 29.9 pg) and transaminases 2 times the normal. The rest was normal.

The diagnosis of Gayet's and Wernicke's encephalopathy was then mentioned, a parenteral supplementation with thiamine in charge dose (1g) and then in daily intake (500mg) was immediately introduced. Confirmed by a low dosage of vitamin B1 at 64nmol / l (N: 76nmol-185nmol) therapeutic management and exploration were completed in the Neurology Department with a normalized MRI and an electromyogram showing ssensitivo-motor distal abnormalities.

The young woman led her pregnancy to term and gave birth to a healthy child and the evolution under thiamine at the dose of 300mg per os per day was favorable with a gradual regression of ataxia and a complete disappearance of other disorders.

Gayet-Wernicke's encephalopathy is an acute neuropsychiatric complication due to vitamin B1 deficiency (thiamine). It was first described in 1881 by Carl Wernicke.

It is a rare disease. The autopsy prevalence estimated at 0.8-2.8% is much higher than that observed with clinical manifestations (0.04 - 0.13%) [1]. vitamin B1 is present in the diet. Daily requirements are in the order of 1.4 mg / day and are increased by a high-calorie or high-carbohydrate diet.

Absorption is performed at the duodenum level and the passage of the blood-brain barrier is active and mostly passive as a function of the concentration gradient. Its active biological form is thiamine pyrophosphate, which is an essential coenzyme of several biochemical reactions in the brain [1]. Thiamine deficiency leads to cerebral damage, lesions of varying severity, ranging from hemorrhagic sufferings to destruction of neurons.

Gayet-Wernicke's encephalopathy is more commonly observed in chronic alcoholism, but more generally in a context of severe malnutrition. For example, pregnancy vomiting, prolonged parenteral nutrition, hunger strike, gastrointestinal tumors, cancers and chemotherapy [2], digestive surgery, pyloric stenosis, chronic renal failure

at the final stage and anorexia nervosa. Concerning our patient, incoercible vomiting lasted 2 months, denutrition and secondary ionic disorders led to hospitalization in gynecological service where a sugary diet without vitamin supplementation was prescribed which rapidly increased the risk of the onset of the disease, encephalopathy. This rapid decompensation is due to the sudden consumption of the last bodily reserves of thiamine during the supply of sweet solutes alone.

Thiamine deficiency results in brain damage in 2 to 3 weeks [4], the time required to deplete B1 stocks in the body being 18 days. The onset of clinical signs is on average of 4 weeks. In our patient's case, a month elapsed between leaving hospital and consultation in emergencies, but her neurological signs (vertigo and asthenia) had begun long before and the patient put them on the account of pregnancy.

The diagnosis is clinical but the triad associating ophthalmoplegia, mental confusion and ataxia, present in our patient, is found only in 10% of cases [5]. In 19% of patients, none of these was found [6. A non-specific confusional state is most often encountered with other clinical signs such as cognitive disorders, somnolence, stuporous state or coma, which can be found in 80% of patients. Differential diagnosis in some cases may be difficult with acute alcohol poisoning or withdrawal syndrome. The same is true in the post-operative period when complications may mask the picture or precipitate it.

Metastasis or a brain tumor, ischemic stroke or haemorrhagic stroke can also simulate the picture. For some authors, diagnosis is very likely when two of the following four conditions are present: malnutrition, oculomotor disorders, cerebellar disorders, impairment of mental state or even moderate memory impairment7].In the presence

of a suspicion of Gayet-Wernicke encephalopathy, MRI is the reference examination [8]. Its sensitivity and specificity are respectively 53% and 93% [9]. It shows hypersignals in T2, FLAIR and diffusion, typical of their localization and symmetrical character around the aqueduct of Sylvius, the third ventricle and especially at the level of the mamillary tubercles [8]. Normal imaging does not eliminate the diagnosis.

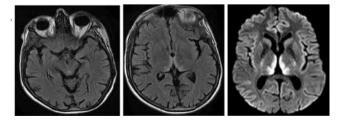


Figure 1. Cerebral MRI showing bithalamic and peri aqueducal hypersignal in FLAIR sequences (A and B) which persist in Diffusion sequences with an elevated ADC (C).

thy can be confirmed by the determination of the blood concentration of thiamine or its phosphate derivatives (monophosphate or diphosphate). Normal levels range from 60 to 220 nmol / l in adults.

In the case of our patient, vomiting decreased significantly after leaving the Gynecology Department, so the minimal intake of thiamine through the patient's poor diet could explain normal imaging and the thiamine level at 64 nmol / l. Gayet-Wernicke's encephalopathy is a medical emergency. Treatment should be started early as soon as the diagnosis is suspected and should not be delayed by vitamin B dosage.

There is no consensus on the amount of thiamine to be delivered, the duration of treatment and the number of doses administered per day.

However, the European Federation of Neurological Societies recommends that thiamine be administered 200 mg three times daily, preferably intravenously before glucose is administered and normal diet is resumed [9]. Treatment should be continued for some patients until vomiting is stopped and normal diet is resumed [11], and for others until the end of pregnancy [2, 8]. Our patient received 500 mg / day of vitamin B1 injectable for seven days with a good progression and an oral relay providing 500 mg of thiamine per day.

The prognosis of Gayet-Wernicke's encephalopathy is extremely variable. It is favorable when the disease is diagnosed early with an adequate treatment and a marked improvement in symptoms, as observed in the case of our patient.

Only 16% of inadequately treated patients recover completely. Mortality rate is 17-20%.

#### CONCLUSION

Gayet-Wernicke's encephalopathy is a rare disease. Faced with a risk situation, the triad ophthalmoplegia, mental confusion and ataxia is evocative. The MRI is the reference examination and the vitamin dosage will be done if necessary and possible. Early treatment allows for a favorable outcome and avoids complications and death.

#### **BRIEF REPORT**

# *Threatening Intra-alveolar haemorrhage revealing lungworts metastases of a malignant melanoma*

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#### INTRODUCTION

The intra-alveolar-haemorrhage(IAH) corresponds to a clinicopathoglogical syndrome characterized by intraalveolar accumulation of red blood cells that originates from the interstitial capillaries. The etiologies are multiple. Neoplastic IAH is rare and its mechanism remains hypothetical.

#### **CASE REPORT**

We report the observation of a 24-year-old woman with a history of a malignant melanoma of the scalp at the age of 13 treated by surgery and chemotherapy hospitalized for hemoptysis of big abundance associated with a severe anemia. The thoracic imaging showed a parenchymatous condensation of the right upper lobe with multiple nodular infiltrates of bases. The bronchiolo-alveolar lavage confirmed the IAH and the patient was put under general corticotherapy with a clinical, biological improvement and a partial and fast cleaning of the radiological infiltrates. The lung biopsy realized showed a histological and immunohistochemical aspect of a metastasis of melanoma with spindle cells. We retained the neoplastic etiology to this IAH. The evolution was unfavourable and the patient died after a hemoptysis of big abundance after one year of follow-up.

#### CONCLUSION

Our observation may correspond to the first reported case of alveolar haemorrhage caused by lung metastases of a melanoma of the scalp. The initial favourable evolution after corticotherapy is in favour of the immunological origin in this IAH.

KEYWORDS : Hemoptysis, Malignant melanoma, metastasis lungwort, neoplastic intra-alveolar haemorrhage

#### INTRODUCTION

The intra-alveolar hemorrhage (IAH) corresponds to is a clinicopathoglogic syndrome characterized by intra-alveolar accumulation of red blood cells that originates from the interstitial capillaries. Its etiologies are multiple. IAH is associated with a number of clinical entities and several histopathologic subtypes. Three groups are distinguished according to the mechanism involved: IAH of immune origin (such as Systemic lupus erythematosis (SLE), Antiglomerular basement membrane antibody

disease (Goodpasture's) and ANCA-associated granulomatous vasculitis...), IAH of non-immune origin (such as mitral stenosis) and IAH without apparent cause classified as idiopathic. [1] We report a case of IAH of rare cause. It is about a neoplastic IAH in a young woman with pulmonary metastases of a malignant melanoma of the scalp. Through this personal observation, the authors propose to discuss the mechanisms involved in IAH of neoplastic origin.

#### **OBSERVATION**

A 24 years old woman, housewife, was hospitalized in the Pulmonary Department in November 2009 for haemoptysis of medium abundance with anemia.

She has as main medical history a melanoma of the scalp diagnosed at the age of 13 treated by surgery and chemotherapy with frequent relapses requiring repeated treatment. Clinical examination at admission found a patient in good hemodynamic state (TAS = 140 mmHg, TAD = 90 mmHg, accelerated pulse at 95 b / min). The plumonary examination revealed a respiratory rate at 19 c / min and crackling rales at the right pulmonary field. The rest of the clinical examination was without abnormalities apart from the scars of bilateral cervical lymph node dissection. Biologic examination showed, microcytic normochromic anemia at 9.4 g / dl, correct renal function. Arterial gases was in favor of hyperventilation respiratory alkalosis (PH: 7.59, PaCO2: 21 mmHg, PaO2: 92 mmHg, HCO3: 20 mmol / l, SatO2: 96%).

The chest x-ray (Figure 1) showed an alveolar infiltrate of the right upper lobe associated with multiple nodular lesions occupying the right pulmonary and left basal regions.

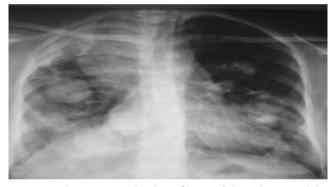
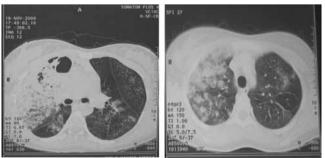


Figure 1. Chest X-Ray : alveolar infiltrate of the right upper lobe associated with multiple nodular lesions occupying the right pulmonary and left basal regions.

Thoracic Chest Tomography (CT) (Figures 2-3) showed parenchymal condensation in the ventral segment of the right upper lobe with multiple nodular lesions with confluent contours.



Figures 2-3. Thoracic Chest Tomography (CT) : showed parenchymal condensation in the ventral segment of the right upper lobe with multiple nodular lesions with confluent contours.

The patient was initially treated with hemostatic treatment and an immediate evolution has been marked by the worsening after 2 days and the haemoptysis became of great abundance causing a deglobulinization of 3.5 g / dl (the hemoglobin decreased from 9.4 g / dl to 5.8 g / dl) with clinical signs of bad tolerance of anemia with signs of acute respiratory failure. The patient was then transferred to the intensive care unit where she was transfused with reinforcement of the hemostatic treatment.

Bronchial fibroscopy visualized a diffuse bleeding of the whole bronchial tree more marked in the ventral segmental of the upper right lobe, an aspect evoking an intra-alveolar haemorrhage. Bronchoalveolar lavage (BAL) in serial lavages was hemorrhagic with a macrophage predominance formed by 100% of siderophages in the cytological study. In the presence of this IAH and taking into account the patient's life-threatening risk, treatment with intraveinous bolus of corticosteroids (Methylprednisolone 500mg per day for 3 consecutive days) was initiated with oral corticosteroids at 1 mg / kg / day. The evolution was rapidly favorable with drying up of the bleeding and complete cleaning of the alveolar and nodular lesions as well on the chest X-ray and thoracic CT in a few days (Figures 4-5)

After stabilization of the patient's clinical state, an etiological investigation was initiated, the immunological assessment (antinuclear antibody, ANCA, rheumatoid factor) was normal, 24 hour proteinuria was negative, bronchial bacteriological and parasitological examinations and tumor markers (ACE, CA 15- 3, CA 125, KHCG, CA 19-9) were normal. After a negative etiological investigation and especially the reappearance of nodular lesions on the CT scan at 6 months of corticosteroid treatment, a pulmonary biopsy was performed which revealed a histological and immunohistochemical aspect compatible with a pulmonary metastasis of achromic melanoma fusiform cells with multifocal positivity with HMB-45, melan A is negative. (Figure 4)

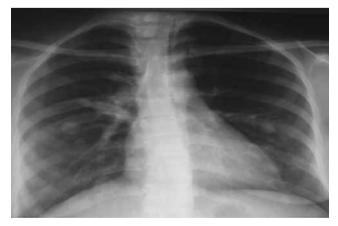


Figure 4. Chest X-Ray : improvement and radiological cleaning of alveolar and nodular lesions under general corticosteroid therapy

The patient was therefore diagnosed with a neoplastic HIA revealing pulmonary metastases of a melanoma of the scalp. Second line chemotherapy was indicated but formally refused by the patient. Corticosteroids were maintained at a maintenance dose of 20mg per day of Prednisone. The patient died following haemoptysis after one year of follow-up.

#### DISCUSSION

Intra-alveolar haemorrhage(IAH) is associated with multiple immunological and non-immunological etiologies. The neoplastic origin is a very rare cause. It has been described in the literature as reported cases, butthe mechanism involved is not well defined. [2] The neoplastic IAH has been associated with certain types of cancer including pulmonary Kaposi sarcoma. Table I presents the various cases published in the literature

### Table 1. The different cases of neoplasia associated with an IAH as reported in the literature

Type of neoplasia	Number of cases reported	References
Pulmonary Kaposi's sarcoma	22	[3-4]
epithelioid	3	[5-6-7]
haemangioendothelioma		
angiosarcoma	4	[8-9-10-11]
myeloma	1	[12]
choriocarcinoma	1	[13]
Neoplastic vascularitis	1	[14]
ovarian angiosarcoma	1	[15]

The IAH revealed the underlying neoplasia in most cases reported. [5-15] To our knowledge, our observation represents the first described case of HIA revealing pulmonary metastases of a malignant melanoma.

Two hypotheses are possible to explain the mechanisms of this IAH in our patient,

- Either the presence of vascular tumor emboli that would result in tumor invasion and pulmonary vascular destruction. However, data from the anatomopathological examination of the pulmonary biopsy exclude this hypothesis since they have shown the presence of fusocellular tumor proliferation with high mitotic activity in the absence of endovascular neoplastic emboli.
- Or it must be the existence of a neoplastic autoimmune phenomenon linked to the melanocytic tumor cells. This hypothesis is more plausible since the initial

development under general corticosteroid therapy was rapidly favorable.

Many observations suggest that human malignant melanoma expresses antigens that can induce a beneficial immunological reaction which has opened a new therapeutic pathway to immunotherapy in malignant melanoma. [16] The favorable progression under corticosteroid therapy was also observed in a case reported by Rajdev et col

about a primary hemangiosarcoma of the metastatic heart associated with intra-alveolar hemorrhage and presumed of the immunological mechanism. [17]

This hypothesis was also advanced in some cases of myelodysplastic syndromes where there is a satellite vasculitis of the haematological process. [18]



Figure 5. Thoracic Chest Tomography (CT) : on the same level of parenchymal cut as in figure 2, there is a regression in size of the excavated parenchymal condensation of the ventral segment of the right upper lobe after general corticosteroid therapy.

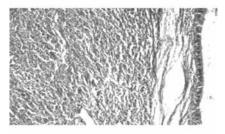


Figure 6. Histological section :tumor proliferation of the fusocellular type with high cell density well circumscribed in the unencapsulated periphery.

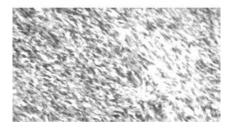


Figure 7. Histological section : the immune-histochemical study shows a multifocal positivity with HMB-45.

#### CONCLUSION

Our observation corresponds to the first reported case of IAH due to pulmonary metastases of a melanoma of the scalp. The susceptibility of human malignant melanoma to express antigens that can induce an immune reaction and the initial rapid favorable evolution to corticosteroid therapy in our patient argue in favor of the immunological origin of this neoplastic IAH.

#### **CONFLICT OF INTEREST**

The authors stated that they have no potential conflicts of interest in relation to the theme of the article.

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#### **BRIEF REPORT**

# *Acute headache revealing Fahr's syndrome in Emergency Department*

R. Hamed, K. Saïdi, D. Chtourou, B. Bouhajja

Department of Emergency Medicine, Charles Nicolle teaching Hospital. Tunis. Tunisia.

Fahr's syndrome is a rare entity encountered in emergency medicine and characterized by a large clinical spectrum. It can be idiopathic ,known as Fahr's disease and related to an autosomic genetic dominant transmission, or secondary to multiple causes.

KEY WORDS : Fahr's syndrome ; neurological rare disease ; symmetric basal calcinosis ; hypocalcemia

#### CASE REPORT

A 40-year-old woman presented to the Emergency Department with a complaint of 7-day persistent headache and dizziness history. On medical history, there was no prior similar episodes, no recent medication use or trauma. On clinical examination, the patient was awake, afebrile, with normal vital signs and neurological exam. The electrocardiogram showed a prolonged QTc with regular sinusal activity. A calcemia of 1,1mmol/l was noticed on laboratory examination. The patient's cranial computerized tomography image is shown on figure 1.

#### DIAGNOSIS

Fahr's syndrome secondary to hypocalcemia.



Figure 1. Non contrast cranial computerized tomography shows bilateral symmetric calcinosis

Bilateral striopallidodentate calcinosis (BSPDC) is a rare condition characterized by massive symmetrical calcifications involving mainly the basal ganglia with subsequent neuronal loss (1). This entity has been described in the elderly but also known as Fahr's disease related to a chromosomic autosomic dominant mutation. These intracranial symmetric calcifications have also been described with other secondary conditions such as metabolic disorders (hypocalcemia), infectious or inflammatory situations, encephalitis or poisoning (2). Clinical presentation is heterogeneous: patients can be asymptomatic or present with a large panel of neuropsychiatric clinical findings (3).

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Manual Cardiopulmonary Resuscitation Versus CPR Including a Mechanical Chest Compression Device in Out-of-Hospital Cardiac Arrest : A Comprehensive Meta-analysis From Randomized and Observational Studies.

Judith L. Bonnes, MD; Marc A. Brouwer, MD, PhD; Eliano P. Navarese MD, and all. Ann Emerg Med. 2016;-:1-12

#### PROBLEMATIC

Mechanical chest compression devices have been developed to facilitate continuous delivery of highquality cardiopulmonary resuscitation (CPR). Despite promising hemodynamic data, evidence on clinical outcomes remains inconclusive.

#### **STUDY OBJECTIVE**

The aim of this study is to compare the effect of mechanical CPR versus manual CPR on clinical outcomes after out-of-hospital cardiac arrest.

#### **METHODS**

A systematic search that includes all eligible studies (randomized controlled trials and non-randomized studies) that compared a cardiopulmonary resuscitation strategy including an automatic mechanical chest compression device with a manual CPR strategy only. Outcome variables were survival to hospital admission, survival to discharge, and favorable neurologic outcome.

#### RESULTS

Twenty studies were included in the meta-analysis, of which 5 had a randomized design. The studies involved a total of 21,363 patients, of whom 9,391 were allocated to the mechanical arm and 11,972 to the manual arm.

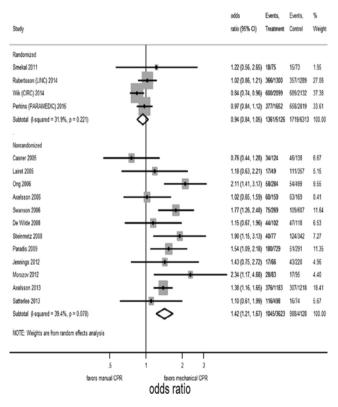


Figure 1. Individual study and pooled estimates for survival to hopital admision for patients who received mechanical versus manual CPR.

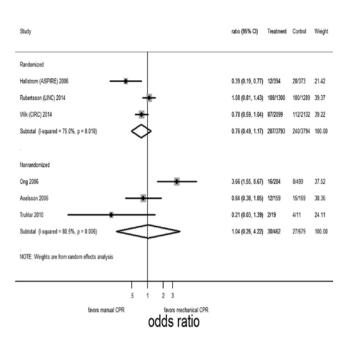


Figure 2. Individual study and pooled estimates for favorable neurologic for patients who mechanical manual CPR.

#### LIMITATIONS

This meta-analysis is based on the results of both randomized and nonrandomized studies. The actual adherence to the endorsed protocols was not studied because these data were not scored or reported in the majority of studies.

# Passive Leg Raising (Prp) For Predicting Fluid Responsiveness: A Systematic Review And Meta-Analysis.

*Xavier Monnet, Paul Marik, Jean-Louis Teboul.* Intensive Care Med (2016) 42:1935–1947

#### PROBLEMATIC

In patients with acute circulatory failure, predicting whether volume expansion will actually induce a significant increase in CO has become a common practice, is recommended by International guidelines.

#### **STUDY OBJECTIVE**

Evaluate the changes in cardiac output (CO) and pulsed arterial pressure (PP) induced by passive leg elevation (PRP) as predictors of fluid response in adults.

#### METHODS

a systematic review of all studies evaluating the ability of the PLR test to predict a significant increase in CO, cardiac index, stroke volume compared to that induced by a subsequent fluid infusion.

#### RESULTS

21 studies were included in the meta-analysis (991 adult patients, 995fluid challenges) that reported the ability of the PLR to predict fluid responsiveness.

Receiver operating characteristics curve for the prediction of fluid responsiveness by the effects of passive leg raising on cardiac output or surrogates.

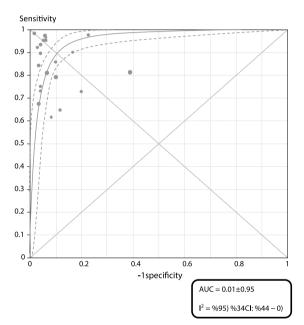


Figure 1. Receiver operating characteristics curve for the prediction of fluid responsiveness by the effects of passive leg raising on cardiac output or surrogates.

#### LIMITATIONS

The heterogeneity of the included studies represents a limitation of the meta-analysis. A further limitation of this study is that the included studies were mainly conducted in the ICU, the sample size was generally small and that several different methods of measuring of CO were used.

Additional limitations include the fact that studies not reporting sensitivity/specificity were not included, non-full-text studies, studies not in English, and unpublished studies.

Finally, two of the authors (X.M. and J.L.T.) were the authors of a large number of the studies included in the meta-analysis.

# *The Use of Very Low Concentrations of High-sensitivity Troponin T to Rule Out Acute Myocardial Infarction Using a Single Blood Test*

*Richard Body, Christian Mueller, Evangelos Giannitsis, Michael Christ, Jorge Ordonez-Llanos et all* ACADEMIC EMERGENCY MEDICINE 2016;23:1004–1013.

#### PROBLEMATIC

Serial troponin dosing remains necessary before the diagnosis of AMI can safely be excluded. This causes anxious waiting for patients, contributes to the growing problem of overcrowding in the emergency, and entails a financial cost.

#### STUDY OBJECTIVE

Determine whether hs-cTnT concentrations measured at the time of arrival in the ED can safely exclude AMI using cutoffs below the 99th percentile, when used either alone or in combination with ECG findings.

#### METHODS

A prospective diagnostic cohort study including patients with suspected cardiac chest pain within 6 hours of peak symptoms. The primary outcome, prevalent AMI, was adjudicated based on sensitive troponin I levels. Major adverse cardiac events (MACE) including AMI, death, or rehospitalization for acute coronary syndrome with coronary revascularization were determined after 30 days.

#### **RESULTS** :

Tabke 1. Diagnostic Accuracy of Early Puie-out StrategyEvaluated fo the Dianosis of AMI.

Strategy to Exclude AMI	Number (%) of Patients With AMI Excluded	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR (95% CI)
Initial hs-cTnT < 3 ng/L (LoB)	419 (32.7)	98.6 (95.9–99.7)	38.9 (36.0-41.9)	24.3 (21.5-27.3)	99.3 (97.9–99.9)	1.61 (1.53–1.70)	0.04 (0.01-0.11)
nitial hs-cTnT < 5 ng/L (LoD)	560 (43.7)	98.1 (95.3–99.5)	52.0 (49.0-55.0)	29.0 (25.7-32.4)	99.3 (98.2–99.8)	2.04 (1.92-2.18)	0.04 (0.01-0.10)
nitial hs-cTnT < 14 ng/L (99th percentile)	895 (69.8)	88.7 (83.7–92.7)	81.5 (79.0-83.8)	48.8 (43.8-54.0)	97.3 (96.0-98.3)	4.79 (4.19-5.48)	0.14 (0.09-0.20
Initial hs-cTnT < 3ng/L (LoB) and no ECG ischemia*	350 (27.3)	99.5 (97.4–100.0)	32.7 (29.8–35.6)	22.8 (20.1-25.6)	99.7 (98.4–100.0)	1.48 (1.42-1.54)	0.01
nitial hs-cTnT < 5 ng/L (LoD) and no ECG ischemia*	471 (36.7)	99.1 (96.7–99.9)	43.9 (40.9-46.9)	26.0 (23.0-29.2)	99.6 (98.5-100.0)	1.76	0.02
Initial hs-cTnT < 14 ng/L (99th percentile) and no ECG ischemia*	694 (54.1)	94.8 (91.0–97.4)	63.9 (60.9–66.8)	34.4 (30.5–38.4)	98.4 (97.2–99.2)	2.63 (2.41–2.86)	0.08

#### LIMITATIONS

The study is observational in nature.

# Amiodarone or lidocaine for cardiac arrest: A systematic review and meta-analysis

*F. Sanfilippo a, C. Corredor b, C. Santonocito a, G. Panarello a, A. Arcadipane a, G. Ristagno* c,d, T. Pellis d,e Resuscitation 107 (2016) 31–37

#### PROBLEMATIC

Guidelines for treatment of out-of-hospital cardiac arrest (OOH-CA) with shockable rhythm recommend amiodarone, while lidocaine may be used if amiodarone is not available. Recent underpowered evidence suggests that amiodarone, lidocaine or placebo are equivalent with respect to survival at hospital discharge.

#### **STUDY OBJECTIVE**

Evaluate the efficacy of amiodarone versus lidocaine versus placebo.

#### **METHODS**

A systematic review and meta-analysis including studies published in PubMed and EMBASE databases from inception until May 15th, 2016. (7 studies). The primary outcomes were survival at hospital admission and discharge in out-of-hospital cardiac arrest OOH-CA

#### RESULTS

A total of seven findings were included in the metanalysis (three RCTs, 4 non-RCTs).

	AMIODA	RONE	PLACE	BO		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
KUDENCHUK et al, 1999	18	246	17	258	10.2%	1.12 [0.56, 2.22]	<u>+</u>
KUDENCHUK et al, 2016	182	967	175	1055	89.8%	1.17 [0.93, 1.47]	
Total (95% CI)		1213		1313	100.0%	1.16 [0.93, 1.44]	•
Total events	200		192				
Helerogeneity: Chi <sup>2</sup> = 0.01,			= 0%			0.01	0.1 1 10 100
Test for overall effect: Z = 1	.35 (P = 0.1	8)					Favours PLACEBO Favours AMIODARONE
	LIDOC	AINE	PLACE	EBO		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
HARRISON et al. 1991	7	62	1	54	0.5%	6.75 [0.80, 56.70]	
HERLITZ et al. 1997	14	185	8	105	5.4%		
KUDENCHUK et al. 2016	233	985	222	1056			
Robertonon et al, 2010	200	500		1000	04.075	1.10 [0.04, 1.40]	
Total (95% CI)		1232		1215	100.0%	1.19 [0.97, 1.45]	•
Total events	254		231				ľ
Heterogeneity: Chi <sup>2</sup> = 2.74		0.25				⊢	
Test for overall effect: Z =			21 75			0.0	
l est for overall enect: Z =	1.05 (P = 0	.10)					Favours PLACEBO Favours LIDOCAINE
	AMIODAI	RONE	LIDOC/	AINE		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
DORIAN et al, 2002	9	180	5	167	2.7%	1.71 [0.56, 5.20]	±
KUDENCHUK et al, 2016	237	970	233	985	97.3%	1.04 [0.85, 1.28]	
							T
Total (95% CI)		1150		1152	100.0%	1.05 [0.87, 1.30]	•
Total events	246		238				
Helerogeneity: Chi <sup>2</sup> = 0.72,			= 0%			0.01	0,1 1 10 100
Test for overall effect: Z = 0	.58 (P = 0.5	6)				0.01	Favours LIDOCAINE Favours AMIODARONE

#### LIMITATIONS

The studies included are largely different in several aspects. These studies, in fact, reported pooled data from patients who presented differences in the setting of collapse, rate of witnessed events and bystander-initiated CPR, resuscitative protocols

Employed, that varied based on concurrent guidelines, with different shock protocols and time to drug administration.

## Delivering safe and effective analgesia for management of renal colic in the emergency department: a double-blind, multigroup, randomised controlled trial.

Sameer A Pathan, Biswadev Mitra, Lahn D Straney, Muhammad Shuaib Afzal, Shahzad Anjum, Dharmesh Shukla

Kostantinos Morley, et all. Lancet 2016; 387: 1999-2007

#### PROBLEMATIC

The excruciating pain of patients with renal colic requires effective analgesia to be administered in the shortest possible time. Trials comparing intramuscular non-steroidal anti-inflammatory drugs with intravenous opioids or paracetamol have been inconclusive.

#### STUDY OBJECTIVE

The aim of the study is to develop definitive evidence regarding the choice of initial analgesia and the route of administration in patients with renal colic in the emergency department.

#### **METHODS**

A double-blind, randomised controlled trial with three treatment groups : diclofenac (75 mg/3 mL intramuscular), morphine (0.1 mg/ kg intravenous), or paracetamol (1 g/100 mL intravenous)

#### **INCLUSION CRITERIA**

Patients aged 18 years or older and younger than 65 years who presented with renal colic of intensity on a Numerical pain Rating Scale (NRS 0 to 10)21 of 4 or more The primary outcome was the proportion of participants achieving at least a 50% reduction in initial pain score at 30 min after analgesia,

#### RESULTS

### Table 1. Primary and secondary outcomes in the intention-to-treast population

	Dic <b>l</b> ofenac	(n=547)	Paracetam (n=548)	o	Morphine (n=549)	p va <b>l</b> ue
Median pain scores						
NRS0-	10–7) 8)		10–7) 8)		1689-0	(10–7) 8
NRS30-	5–2) 3)		5-2) 3)		0049.0	(5-2) 4
NRS60-	2-0) 0)		3–0) 1)		0001.0	(4-0) 1
NRS90-	1-0) 0)		20) 0)		0001.0	(2-0) 0
Time to NRS score ≤2 (min)	0008-0	(90-3	0) 60	(90–30	) 60	(60–30) 60
Primary outcome						
Reduction in initial pain by ≥%50, at 30 min	041.0	(%61) 3	35	(%66) 36	4	(%68) 371
OR (%95 CI); p value	73·1–05 0187·0	1) 35-1);	62·1–99 0629·0	·0) 26·1);	1	-
Secondary outcomes						
NRS30-	3.2) 3.3)		4.2) 3.3)		0049-0	(6-2) 8-3
Reduction by NRS score $\geq$ 3, at 30 min	%82) 448)		190-0	(%78) 42	9	(%82) 448
Rescue analgesia required	%12) 6	3)	%20) 111)		0001.0>	(%23) 126
Persistent pain at 60 min (NRS >2)	%24) 131)		%30) 162)		0001.0>	(%38) 207
Acute adverse events	%1)7)		%1)7)		012.0	(%3) 19

Data are median (IQR), n (%), or mean (SD). The number with the NRS score indicates the time the NRS score was measured at—eg, NRS30- is the NRS score measured at 30 min. NRS=Numerical pain Rating Scale.

#### LIMITATIONS

This study has some limitations, including enrolment of patients from a single centre who were mostly young and healthy. The dose of morphine was chosen as 0.1 mg/kg on the basis of participant weight. A higher dose might have been more effective, but the dose chosen is the recommended single initial dose for adult participants in severe pain, and higher doses might be associated with higher rates of adverse events.

# *The Effects of Low-Dose Ketamine on Acute Pain in an Emergency Setting: A Systematic Review and Meta-Analysis*

*Eun Nam Lee, Jae Hoon Lee* PLOS ONE 2016.

#### PROBLEMATIC

Currently ketamine is not used often as an analgesic in the emergency department (ED). Nonetheless, it can increase the efficiency of opioids and decrease their side effects.

#### STUDY OBJECTIVE

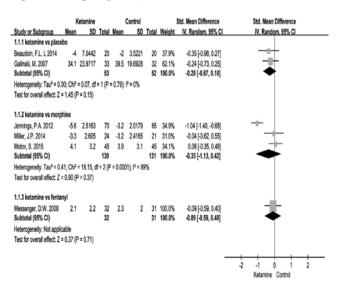
The purpose of this study was to evaluate whether low-dose ketamine in the ED provides better analgesia with fewer adverse effects.

#### **METHODS**

A systematic review and meta-analysis : 6 studies fulfill the inclusion criteria form the basis of this review. The primary outcome measure was the acute pain score 30 minutes after the injection of ketamine, placebo, or opioids. The secondary outcome measures were the cumulative frequencies of all the adverse events described in the studies

#### RESULTS

#### Figure 1. Subgroup Analysis of Pain Reduction



	Ketamir		Contro			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H. Fixed, 95% Cl
1.2.1 gastrointestinal							
Beaudoin, F.L. L 2014	4	40	1	20	5.6%	2.00 [0.24, 16.74]	
Galinski, M. 2007	8	33	4	32	17.1%	1.94 [0.65, 5.81]	
Jennings, P.A. 2012	4	70	6	65	26.1%	0.62 [0.18, 2.10]	
Miller, J.P. 2014	4	24	3	21	13.4%	1.17 [0.29, 4.63]	
Motov, S. 2015	8	45	9	45	37.8%	0.89 [0.38, 2.10]	
Subtotal (95% CI)		212		183	100.0%	1.10 [0.65, 1.84]	<b>—</b>
Total events	28		23				
Heterogeneity: Chi <sup>2</sup> = 2.4 Test for overall effect: Z				6			
1.2.2 neurological							
Beaudoin, F.L. L 2014	9	40	2	20	13.1%	2.25 [0.54, 9.45]	
Galinski, M. 2007	8	33	0	32	2.5%	16.50 [0.99, 274.52]	
Jennings, P.A. 2012	4	70	1	65	5.1%	3.71 [0.43, 32.37]	
Miller, J.P. 2014	2	24	2	21	10.5%	0.88 [0.13, 5.68]	
Motov, S. 2015	24	45	14	45	68.8%	1.71 [1.03, 2.86]	
Subtotal (95% CI)		212		183	100.0%	2.17 [1.37, 3.42]	◆
Total events	47		19				
Heterogeneity: Chi <sup>2</sup> = 3.9	95. df = 4 ()	P = 0.4	41):   <sup>2</sup> = 09	6			
Test for overall effect: Z				•			
1.2.3 psychological							
Beaudoin, F.L. L 2014	5	40	0	20	17.7%	5.63 [0.33, 97.10]	
Galinski, M. 2007	10	33	1	32	27.2%	9.70 [1.32, 71.46]	
Jennings, P.A. 2012	12	70	0	65	13.9%	23.24 [1.40, 384.76]	
Miller, J.P. 2014	7	24	0	21	14.3%	13.20 [0.80, 218.11]	
Motov, S. 2015	19	45	1	45	26.8%	19.00 [2.66, 135.97]	
Subtotal (95% CI)		212		183	100.0%	13.86 [4.85, 39.58]	-
Total events	53		2				
Heterogeneity: Chi <sup>2</sup> = 0.7	74, df = 4 (l	P = 0.9	95); l <sup>2</sup> = 09	6			
Test for overall effect: Z	= 4.91 (P <	0.000	001)				
1.2.4 major cardiopulm	onary						
Beaudoin, F.L. L 2014	0	40	2	20	41.4%	0.10 [0.01, 2.04]	· · · · · · · · · · · · · · · · · · ·
Galinski, M. 2007	0	33	1	32	19.1%	0.32 [0.01, 7.66]	
Jennings, P.A. 2012	0	70	1	65	19.5%	0.31 [0.01, 7.47]	
Miller, J.P. 2014	0	24	1	21	20.0%	0.29 [0.01, 6.84]	
Subtotal (95% CI)		167		138	100.0%	0.22 [0.05, 1.01]	
Total events	0		5				
Heterogeneity: Chi <sup>2</sup> = 0.3 Test for overall effect: Z				6			
1.2.5 minor cardiologic							_
Beaudoin, F.L. L 2014	3	40	0	20	56.1%	3.59 [0.19, 66.22]	
Jennings, P.A. 2012	4	70	0	65	43.9%	8.37 [0.46, 152.42]	
Subtotal (95% CI)		110		85	100.0%	5.69 [0.75, 42.84]	
Total events	7		0				
Heterogeneity: Chi <sup>2</sup> = 0.1	16, df = 1 (l	P = 0.6	69);   <sup>2</sup> = 09	6			
Test for overall effect: Z							
							0.01 0.1 1 10 1
							Control Ketamine

#### LIMITATIONS

Heterogeneity among the studies was significant.

# Patients without ST elevation after return of spontaneous circulation may benefit from emergent percutaneous intervention: A systematic review and meta-analysis

MichaelG.Millin, AngelaC. Comer, Jose V. Nable, Peter V. Johstet al. Resuscitation September 2016

#### PROBLEMATIC

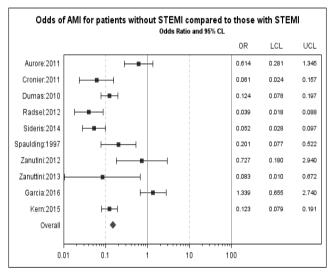
The American Heart Association recommends that post-arrest patients with evidence of ST elevation myocardial infarction (STEMI) on electrocardiogram (ECG) be emergently taken to the catheterization lab for percutaneous coronary intervention (PCI). However, recommendations regarding the utility of emergent PCI for patients without ST elevation are less specific. Study objective: This review examined the literature on the utility of PCI in post-arrest patients without ST elevation compared to patients with STEMI.

#### **METHODS**

A systematic review of the English language literature was performed for all years to March 1, 2015. Primary end point: presence of an expandable lesion.

#### RESULTS

6 studies are included in this study.



#### LIMITATIONS : Heterogeneity among the studies

Therapeutic hypothermia after cardiac arrest: A systematic review/meta-analysis exploring the impact of expanded criteria and targeted temperature.

Aldo L.Schenone Resuscitation, 2016.

#### PROBLEMATIC

Therapeutic hypothermia (TH) is mainly indicated in patients with post-cardiac arrest who have a shockable initial rhythm. However, the benefit of this therapy has not been demonstrated in any type of cardiac arrest.

#### **STUDY OBJECTIVE**

The purpose of this study was to assess the performance of TH after OHCA on hospital mortality and good neurological outcome at hospital discharge.

#### METHODS

A meta-analysis including 11 studies (3RTCs and 8 cohort studies).

#### RESULTS

		A.	Hospi	tal Mor	tality	
	San	pik	Con	irei.		
Author(a) and Year	Morselity	Alive	Mortality	Alka		Odda Ratio (RN), O
General 1997	10	12	17	5		0.25 (0.07 , 0.90
Renard 2002	22	21	22	11		0.50 [ 0.20 , 1.20
HACA 2002	51	86	-	-		0.5010.37,0.96
Laurent 2005	12	10	14	5		0.45 [0.11 , 1.51
Oddo 2006 Shock arm	19	24	x	u	<b>⊢</b> ∎-∔	0.52   0.22 , 1.22
Odde 2006 Non shock arm	10	2	10		+ + +	0.50   0.04 , 6.44
Gailland 2007	14	10	20	13	⊢∎∔	0.44 [0.17 . 1.17
Derwall 2009		29	14	u.	·	0.20   0.12 , 0.96
Fermina 2009	15	30	15		<u> </u>	20.00120.00
Don 2009 Shock arm	ज	44	57	36	H	0.52   0.39 , 0.97
Don 2009 Non Shock arm	86	æ	155	ж	. <b>⊢</b> ∎∔-	0.86 [0.49 , 1.51
Patrow: 2011	20	25	30	7		0.1010.07.051
Walkers 2011	16	19	18		r+-	0.55   0.10 , 1.66
Random effect model Test for he erogeneity f	(92 - 4.06	,96%C	1 (0.0, 52.)	550.	+ TH began TH w	051   0.40 , 0.64 19796

	Sar	npie	Col	low				
Author(in) and Year	Neuro	Non/Neuro	Neuro	NonNeuro				Odda Radio (99% Ci
Dornard 1997	н	н	3	10				6.33   1.45 , 27 73
Bernard 2002	21	72	9	25				2.65 [ 1.01 , 6.90
HA.GA 2002	64	73	41	ar .			HEH	2.07 [ 1.26 , 3.45
Oddo 2006 Shock arm	10	24	н	32		3		23010.80, 573
Bollard 2007	22		w	19				2.86   1.04 , 7.85
Downali 2006	21	16	14	u		-		1.50[0.61 , 4.17
Females 2009	25	24	5	21				430 [ 1.42, 13.47
Don 2009 Shock arm	28	50	14	79				2.90   1.44 , 6.19
Don 2009 Non Shock arm	14	100	π	174		F		1.39 [0.63 , 2.80
Petrovic 2011	25	19	7	20			<b>→</b>	5.95 (2.12, 15.15
Walters 2011	8	20	3	20		,		3.45 ( 0.82 , 14.53
Random effect model Test for helerogeneity f	· (96) = 0.0.	95%CI (0	.0-69.B4	0			+	248[1.91, 2.22
					THE	ectes 1	THibe per	
					0.05 0	125 1	00 400	

Figure 1. Impact of expanded usr of TH after OHCA on mortality and neurological outcome at hospital discharge (A) Results of 11 studies (3 RCTs and 8 cohort studies) on the impact of expanded use of TH after OHCA on hospital mortality. Summary OR=0.51

#### LIMITATIONS

The addition of observational cohort studies leads to potential for a higher risk of bias. The study enrollment was restricted to only those studies reporting achieved temperatures during cooling, which might have led to selection bias.

## Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Adnan I. Qureshi. N Engl J Med 2016.

#### PROBLEMATIC

Limited data are available to guide the choice of a target for the systolic blood-pressure level when treating acute hypertensive response in patients with intracerebral hemorrhage.

#### **STUDY OBJECTIVE**

The aim of this study is to determine the effectiveness of rapidly lowering the level of systolic blood pressure during cerebral hemorrhage in patients in a window of earlier time after onset of symptoms.

#### **METHODS**

A randomized, multicenter, twogroup, open-label trial to determine the relative efficacy of intensive versus standard antihypertensive treatment that was initiated within 4.5 hours after symptom onset and continued for the next 24 hours in patients with spontaneous supratentorial intracerebral hemorrhage. Inclusion criteria: participants with intracerebral hemorrhage (volume, <60 cm3) and a Glasgow Coma Scale (GCS) score of 5 or more (on a scale from 3 to 15, with lower scores indicating worse condition). The primary outcome was death or disability (modified Rankin scale score of 4 to 6, on a scale ranging from 0 [no symptoms] to 6 [death]) at 3 months after randomization, as ascertained by an investigator who was unaware of the treatment assignments.

#### RESULTS

Among 1000 participants with a mean (±SD) systolic blood pressure of 200.6±27.0 mm Hg at baseline, 500 were assigned to intensive treatment and 500 to standard treatment.

#### Table 1. Primary, Secondary, and Safety Outcomes, According to Treatment Group.\*

Outcome	Intensive Treatment (N =500)		Unadjusted Ana	lysis	Adjusted Analysi	st
			Relative Risk or Beta Estimate (%95 CI)	P Value	Relative Risk or Beta Estimate (%95 CI)	P Value
Primary outcome: death or disability — no./total no. (%)‡	38.7) 481/186)	37.7) 480/181)	0.83) 1.02 to 1.25)	0.84	0.85) 1.04 to 1.27)	0.72
Hematoma expansion — no./total no. (%)§	18.9) 450/85)	24.4) 426/104)	0.59) 0.78 to 1.04)	0.09	0.58) 0.78 to 1.03)	0.08
Neurologic deterioration within 24 hr — no. (%)¶	11.0) 55)	8.0) 40)	0.92) 1.38 to 2.07)	0.13	0.92) 1.39 to 2.09)	0.11
Freatment-related serious adverse event within 72 hr — no. (%)	1.6) 8)	1.2) 6)	0.46) 1.33 to 3.84)	0.59	0.47) 1.37 to 3.95)	0.56
Any serious adverse event within 3 mo — no. (%)	25.6) 128)	20.0) 100)	0.99) 1.28 to 1.66)	0.06	1.00) 1.30 to 1.69)	0.05
Hypotension within 72 hr — no. (%)	1.2) 6)	0.6) 3)	0.50) 2.00 to 8.00)	0.33	0.49) 1.96 to 7.87)	0.34
Death — no. (%)	6.6) 33)	6.8) 34)	0.60) 0.97 to 1.57)	0.90	0.61) 0.99 to 1.60)	0.97
EQ5-D utility index score**++			0.05-) 0.01- to 0.02)	0.47	0.05-) 0.02- to 0.02)	0.29
Median	0.7	0.7				
Range	0.1-to 1.0	0 to 1.0				
EQ5-D visual-analogue scale score**‡‡			5.28-) 1.14- to 2.99)	0.59	5.25-) 1.32- to 2.60)	0.51
Median	62.5	70				
Range	0 to 100	0 to 100				

<sup>1</sup> The relative misk or beta estimate with %35 confidence intervals for the modified Bankin scale score, hematoma expansion, European Quality of Life-5 Dimensions (EQ5-D) utility index score, and EQ5-D visual-analogue scale score wave based on analyses inclusive of missing data imputed by the multiple-imputation method. The analysis was adjusted for age, basedine Glasgow Coms Scale (SCS) score, and the presence or absence of intraventicular hem onthinge at baseline. The modified family using radius relative score scores ranging form 0 (nosymptoms) to 6 (death). The primary outcome was defined as a score of 4 to 6.

sa sare of 4 o 6. Heurologic deteriorisms defined as increase of %30 or none in the heuration advance from baceline to 4 heuron. Heurologic deteriorisms defined as decrease from baceline of 2 or more points on the GCS score or an increase from baceline to 4 heuron. Heurologic deteriorisms defined as decrease from baceline of 2 or more points on the GCS score or an increase from baceline to 4 heuron. Heurologic deteriorisms defined as decrease from baceline of 2 or more points on the GCS score or an increase from baseline to 4 heuron. Heurologic deteriorisms device metal was subtained for at least 8 hours. Firstament-addated resolutions or heuron was easiened by the heurological Since and the two-back and the resolution and the metal data. Heurologic deteriorisms device metal was easiened by the heurological Heurologic deteriorisms device metal was easiened by the heurological Heurologic deteriorisms device metal was easiened by the heurological Heurologic deteriorisms device metal was easiened by the heurological Heurological deteriorisms device metal data was and expension of heurological data was and expension. Data were missing for 14 heurological data was and expension. Data were missing for 144 patients in the intensive-treatment group and for 2 in standard-treatment group.

#### LIMITATIONS

Primary treatment failure was seen in 12 % of the participants within 2 hour and in 15% of the participants within 24h after randomization.

Immediate total-body CT scanning versus conventional imaging and selective CT scanning in patients with severe trauma (REACT-2): a randomised controlled trial

The Lancet 2016

#### PROBLEMATIC

Published work suggests a survival benefit for patients with trauma who undergo total-body CT scanning during the initial trauma assessment; however, level 1 evidence is absent.

#### **STUDY OBJECTIVE**

To aim of study is to examine the eff ect of immediate totalbody CT scanning as part of the primary assessment of patients with severe trauma on in-hospital mortality, and compared it with that of the standard work-up of conventional imaging supplemented with selective CT scanning.

#### **METHODS**

An international, multicentre, randomised controlled trial. Patients aged 18 years or older with trauma with compromised vital parameters, clinical suspicion of life-threatening injuries, or severe injury were randomly assigned (1:1) by ALEA randomisation to immediate total-body CT scanning or to a standard work-up with conventional imaging supplemented with selective CT scanning. The primary endpoint was inhospital mortality

#### RESULTS

1403 patients were randomly assigned: 702 to total-body CT scanning and 701 to standard work-up. 203 patients were excluded after random allocation.

Mortality	Total-body CT vs standard work-up	Total-body CT n (%)	Standard work-uj n (%)	P		Odds ratio (95% CI)	p valu
All patients	541 vs 542	86 (16%)	85(16%)	-	⊢	1-02 (0-73-1-41)	0-92
Patients with polytrauma	362 vs 331	81 (22%)	82 (25%)	-+	-	088 (062-1-24)	046
Patients with traumatic brain injury	178 vs 151	68 (38%)	66 (44%)	-+	-	080(051-1-24)	0-31
			01	<u>ا</u>	$\rightarrow$	n 00	
			1	Favours otal-body CT	Favours standard work-up		

Radiation exposure (mSv)‡					
In the trauma resuscitation room					
All patients, ITT	520	20.9 (20.6-20.9)	531	20-6 (9-9-22-1)	<0.00011
Patients with polytrauma	346	209 (201-209)	323	20-6 (17-6-22-7)	0-271
Patients with TBI	172	209 (200-209)	146	20-6 (10-5-22-4)	0-0401
Total during hospital stay					
All patients, ITT	520	210 (20-9-25-2)	531	20-6 (11-8-27-6)	<0.00011
Patients with polytrauma	346	22-3 (20.7-26-5)	323	22-5 (200-33-1)	0-771
Patients with TBI	172	22-7 (20-6-26-4)	146	21-4 (15-1-29-1)	0-0681
Hospital outcomes					
Hospital costs (€)	479	24967 (95% Cl 21880-28752)	488	26995 (95% Cl 23326-30908)	044
Complications	541	129 (24%)	540	124 (23%)	0-73*
Blood transfusions in hospital§	540	147(27N)	542	150 (28%)	0.91*
Duration of stay¶					
Days in intensive care unit	286	3(1-8)	295	3 (1-8)	0-831
Ventilation days	286	2 (1-5)	295	1 (1-6)	0-781
Readmission within 6 months[]	395	67 (17%)	412	44 (11%)	0-01*
Serious adverse events (safety endpoint)**	541	3(1%)	542	1(<1%)	0-3711

#### LIMITATIONS

46% of patients in the standard work-up group underwent sequential segmental CT scans of all body regions, comprising a total-body CT scan in the end. This high percentage might introduce bias in the interpretation. The number of totalbody CT scans in the standard work-up group might have been higher than in daily practice because trauma team members became more experienced during the course of the trial. A common limitation in trauma care is the unmasked randomisation procedure.

Note	

