LETTERS TO THE EDITOR

On the role of tranexamic acid in emergency department patients with trauma

Acerca del papel del ácido tranexámico en pacientes con traumatismo en urgencias y emergencias

To the editor:

We have read with great interest the systematic review conducted by Morales et al.[1] on the use of tranexamic acid (TXA) in the emergency department (ED) of patients with severe trauma (ST). Despite its positive results, there are still some questions to clarify, optimize and establish a future perspective on the use of TXA in these patients that we would like to comment on.

In this review and meta-analysis, the conclusion is that the use of TXA before 3 hours after trauma reduces mortality by 11% (OR 0.89 (95% CI 0.83-0.96); P = 0.004), with an excellent degree of statistical homogeneity among the studies (I2 = 0%). Despite this, caution should be exercised in the interpretation of results, since the CRASH-2 study was the trial with the greatest weight, including 97.6% of patients analyzed. On the other hand, the review included studies of two very different populations, both in physiopathology and clinical management, such as traumatic brain injury (TBI) and hemorrhagic shock. We must remember that the I2 index measures statistical heterogenicity, but not the clinical or methodological heterogeneity of the studies, so it is necessary to interpret them with caution. Furthermore, in the analysis of the subgroup with TBI, the benefit did not reach statistical significance, something that has been objectified in a recent review and meta-analysis[2].

On the other hand, despite the fact that no increase in thrombotic events was observed in this review among patients who were administered TXA (OR 1.05, 95% CI 0.36-3.05, P = 0.93), with a high degree of statistical heterogenicity (I2 = 66%) and an overall sensitivity of 1.05 (CI95% 0.36-3.05), the controversy continues and iatrogeny cannot be ruled out[3]. It should not be forgotten that the tendency ought to be towards individualization of treatments and not towards "coffee for all". In the case of hemorrhagic shock in ST, different phenotypes of coagulation and fibrinolytic status have been described in these patients[4]. This is why in those where there is no hyperfibrinolytic state, or even where a hypofibrinolytic state is expressed, the administration of TXA could be harmful. Therefore, knowing the status of the fibrinolytic pathway before administration, ideally by viscolastic methods, which are rapid and reliable, would be a matter of choice.

Finally, there is wide scope for improvement in the percentage of patients who are prescribed TXA in the context of ST but do not receive it for a variety of reasons. Therefore, the application of predictive models for patients at high risk of mortality from bleeding of traumatic origin could be helpful in optimizing the prescription of TXA in these patients[5].

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Authors' reply

Respuesta de los autores

To the editor:

In response to the letter to the editor of Viejo-Moreno et al., firstly we would like to express our appreciation for the interest shown in our systematic review and meta-analysis[1] on the use of tranexamic acid (TXA) in the severe trauma patient in the emergency department. The results[1] conclude that there is a reduction in mortality in patients who were administered TXA with a good degree of statistical homogeneity. The CRASH-22 study was the most significant in this review. In the guidelines[3-6] currently being used in this regard, the administration of TXA in patients with severe trauma is recommended, based exclusively on the CRASH-22 study and the MATTERs study developed in a military environment during the war in Afghanistan[7].

Our systematic review and meta-analysis[1] includes 4 studies with differing populations in terms of clinical homogeneity; specifically the CRASH-22 study assumed considerable variability in admitting any patient with signs of hypovolaemia, including patients with traumatic brain injury (TBI) and hypovolaemic shock[2]. Furthermore, it shows a significant risk of selection bias as it is based on the principle of uncertainty of the physicians participating in the CRASH-22 study, as we detected when we did the review[1].

On the other hand, the CRASH-3[8] study is currently underway and recruitment ended in January 2019, so it is expected that results on the administration of TXA in patients with TBI will be presented soon. A systematic review published by

Weng et al.[9] showed positive results on the administration of TXA in patients with TBI.

In turn, other authors, such as Sprigg et al.[10], have analyzed in the TICH-2 study the effect of the administration of TXA in patients with spontaneous intracranial hemorrhage, whose physiopathology could be assimilated to that of TBI. They conclude that the administration of TXA is beneficial in those treated patients.

As stated by Viejo-Moreno et al., the ideal and current trend is the customization of medicine. However, according to several authors[2,7] the benefit of TXA administration has been observed when it is administered in the first 3 hours after the traumatic event[2,7]. This circumstance implies initiating therapy in the pre-hospital setting where analytical methods to determine the state of coagulation are not available, which would be ideal.

In conclusion, the authors would like to indicate that we agree with the controversy that this topic generates and that we consider that the possibilities of improvement are great with regard to the management of bleeding in the patient with severe trauma, and specifically with regard to the administration of TXA.

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Another perspective on the management of multiple intentional-injury victims in the future: the Victory I Consensus

Consenso Victoria I: otra perspectiva cara al futuro de los incidentes con múltiples víctimas intencionados

To the editor:

The publication of the Victoria Consensus I[1] and its approach to a systematic approach to multiple intentional victimization incidents is most welcomed. Defining a tactical survival scheme allows for the clarification of areas, the consideration of actions and the inclusion of the approach according to the prevention phases, and denotes a novel approach compared to other survival chains.

However, the coincidence with the Ibero-Protocol[2] creates two parallel approaches to intervention and operational duplication when the unity of criteria is needed to address these incidents.

Although we highlight the suggestion of a centralized registry of injuries for emergency services and hospital centers, we suggest that these incidents be considered as priority epidemiological events and that they be followed up by the National Center of Epidemiology and the Coordination Center for Health Alerts and Emergencies of the Ministry of Health.

The introduction of quaternary prevention as a limitation of damage by medical activity or by any first responder is missed, although it should not pose a problem since the very nature of the incident limits the possibility of action. In any case, the separation of functions within tertiary prevention would appear to be essential. Including within primary prevention everything that involves training of the population and first responders, such as bleeding control, coping with active shooters or other actions, is an effort that should continue to be pursued by the administrations responsible in this area. Lenworth et al.[3] defend the use of the capacity of first responders in basic life support techniques. Schwartz et al.[4] established a training programme based on competence frameworks to develop skills in these situations.

The necessary equipment in the sectorized areas is noteworthy. In times of crisis where several agencies are involved, multiplying police, military or health teams implies an over-strengthening of personnel, means and assistance and tactical training. We consider that a simplification is necessary in view of the publication of the Victoria II consensus.

Clinically we agree with the level of care complexity according to danger, but we believe that aspects such as airway management, administration of antidotes, antibiotics and analgesics should be assessed taking into account the time required, the necessary staff and qualification.

The mention to NBCR incidents (nuclear, biological, chemical and reactive) appears to be in need of further study and deserves a more intense analysis because of their characteristics and the social alarm they produce.

The importance of coordination centres in decision-making is established, although they are not conside-

red vulnerable elements requiring protection as centres for receiving information and mobilizing resources. It is not clear how the analysis of the threat in the civil environment or the integration into the operation of the regulatory centre should be carried out. The introduction of initial response into computer systems, the participation of small coordination centres in incidents that exceed their capacities, and the active and passive security already mentioned are some of the challenges that these management units must face. Intervention in epidemiological intelligence, in its dual aspect of indicator-based and event-based surveillance, is essential[5] for the collection, analysis of information and formulation of operational plans by these centres or, preferably, by specific health intelligence units.

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Author's reply

Respuesta de los autores

To the editor:

In connection with the letter of Rodríguez Aguado et al. regarding our work previously published in EMERGENCIAS[1], we would like to make a series of considerations. The "Protocolo Ibero"[2] has not been published in any journal indexed in the Journal Citation Reports (JCR). References can only be found in web pages without indicated methodology, so a comparison with our work cannot be made at the same level of production or scientific evidence.

Our manuscript already mentions the development of registers. It was considered that, since the competences of health care are transferred to the autonomous communities, the registers should be carried out by the competent bodies of these public entities, thus always maintaining the principle of respect for the transferred competences. Quadrennial prevention is not defined, since it is a concept developed in the different procedures of the emergency medical systems (EMS), within the quality criteria understood as patient safety.

This paper already contemplates the separation of functions at the tertiary level (*"In tertiary action, the official designation and accreditation of reference centres for traumatology according to levels (I, II, III and IV) is fundamental, as is the implementation of the codes or processes of care for polytraumatic patients in the EMS"*)[1], *as well as what is referred to as primary prevention ("...is defined as that which should be aimed at training the population and professionals from various fields in bleeding control programmes, as well as knowing what attitudes should be taken in the face of a situation with an active shooter or terrorist attack. This is the origin of the concept of "chain of survival in incidents with multiple intentional victims", given the involvement and interrelation of all the agents intervening in this context, from the population, first responders and specialized teams, to the hospital"*)[1].

We must however point out that what you call "over-exertion" is nothing more than a firm commitment to quality care and to providing the best assistance in complex places. An example of this is the figure we have determined as the Tactical Rescue Team (ETR in Spanish), which already exists in the Guardia Civil's Rapid Action Group (GAR) known as the Tactical Response and Rescue Team (ETRR) or the Medical Support Team for Tactical Environments (EMAET) which is also present in the form of Special Preventive Device for Anti-Social Acts (DEPAS) of SAMUR-PC or ORCA teams in the EMS of Catalonia. Of the Advanced Tactical Medical Teams (EMTA) we also have an example in the different army units with the ability to deploy medical personnel in stabilisation cells when faced with a requirement such as a level 5 anti-terrorist alert. We also highlight the efforts in health training that are already being made in what we call Assault Teams (AT), as is the case of the Special Operations Group (GEO) of the National Police, or in which we call First Response and Security Teams (EPRS), such as the citizen security units of the National Police Force, Civil Guard, Local Police, etc.

All recommendations related to techniques or use of drugs are already classified according to the participant and therefore according to safety zones and care phases, being supported by international guidelines that are referenced in the paper. The publication requirements make it impossible to develop the subject of radiological, nuclear, biological and chemical (RNBQE) risks adequately and with the quality that we wanted, so we understand that it is a subject to be developed in our own article and not as part of it.

Regarding the coordinating centres, our article already contemplates the criterion of contingency plans (*"The coordinating centre must be capable, with the information it has, of sizing up the response of the system, always bearing in mind that new foci may appear and, therefore, it must prepare and foresee the new response, and contingency plans must be established"*)[1]. The threat analysis must be performed by law enforcement professionals, so this point is not part of the competence of an article on emergency medicine that aims to es-

tablish health recommendations. The management of computer resources is something specific to each emergency service, so it must also be left out of our recommendations. Epidemiological surveillance is also referred to in our document (*"...establishment of a register of injuries in incidents with multiple victims (unique for EMS and hospitals)"*)[1].

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On the usefulness of brain natriuretic peptide as a prognostic biomarker in patients with influenza syndrome

Reflexiones sobre la utilidad de NT-proBNP como biomarcador pronóstico en pacientes con síndrome gripal

To the editor:

We have read with great interest the article by Valero Cifuentes et al.[1] We find the conclusion they reach very interesting: to consider NT-proBNP as a prognostic marker in patients admitted with influenza symptoms.

From the data provided we conclude that immunofluorescent rapid tests (IRT) are performed in all patients, and polymerase chain reaction (PCR-RT) techniques are used in patients with positive immunofluorescence. IDSA guidelines recommend molecular tests to confirm the diagnosis in patients admitted with suspected influenza virus infection (IVI)[2]. A broad meta-analysis establishes that IRT has high specificity but moderate sensitivity for detecting IVI[3]. Given that PCR-RT brings us closer to the aetiological certainty, we would have liked to know this data in patients with negative IRT.

We think it is only appropriate to include age and heart failure in the multivariate analysis, but we miss having forced some variable related to renal function, since renal clearance is the main way to eliminate NT-proBNP. We conjecture that patients with chronic renal disease are not included because they do not score significantly in the univariate analysis.

The authors conclude that the presence of pneumonia is independently associated with poor prognosis in the subgroup of patients with influenza syndrome and negative influenza test, but not in those who are positive. One could instinctively think otherwise. Perhaps in a homogeneous sample (all patients with confirmed IVI) the final results could be analogous.

Our group prospectively studied 287 patients with pneumonia and determination of NT-proBNP. An etiological diagnosis was obtained in 43 patients, 5 of which had IVI confirmed by IRT and PCR-RT[4] (Table 1): 80% for influenza A (H3N2) and 20% for B (Table 1). The majority of IVIs are uncomplicated infections of the upper respiratory tract. In the subgroup of patients with influenza and parenchymal lung infection, a worse prognosis could be expected, due to the development of primary viral pneumonia or synergistic influenza-bacterial superinfection-coinfection that produces higher mortality[5]. However, our results are in line with those of the authors. Although our patients do not coincide in gender or subtype of influenza virus with the study by Valero Cifuentes et al., none of the 2 patients died with positive influenza, pneumonia and poor prognosis according to their criteria. The cut-off point for NT-proBNP reached by the authors detected one of our two patients with poor prognosis criteria (939 pg/ml).

Given that IVI has up to 5 times greater risk of triggering acute cardiovascular disease (acute coronary syndrome, heart failure, cardiac arrhythmias or myocarditis) especially in the first three days of infection, it is plausible to think that as a cardiovascular stressor it increases the stress on the wall of the myocardium, which is the stimulus for the expression of the BNP gene.

New studies will be required to consolidate the prognostic efficacy of NT-proBNP in the IVI, since according to these data the ROC curves suggest limited prognostic utility (68%) and, even in univariate analysis, the lower limit of the OR confidence interval is shown as a protective rather than a risk factor.

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Table 1. Characteristics of patients with pneumonia and influenza virus infection established by immunochromatographic analysis for the qualitative detection of influenza nucleoprotein antigens using nasooropharyngeal swab samples. and subsequently molecular biological diagnosis by genome amplification techniques using polymerase chain reaction methods

Case	Sex	Age	HF	IHD	CKD	A	DA	ICU	Death	NT-proBNP	SCR	CRP	PCT
1	H	46	No	No	No	No	–	No	No	19	0.92	5.20	0.11
2	H	41	No	No	No	No	–	No	No	45	1.08	5.04	0.10
3	H	36	No	No	No	No	–	No	No	64	1.12	3.10	0.30
4	M	89	No	No	No	Sí	10	No	No	939	0.66	16.60	0.12
5	H	22	No	No	No	Yes	6	Yes	No	32	0.92	14.70	0.50

IHD: ischemic heart disease; SCR: serum creatinine (mg/dl); DA: days of admission; CKD: chronic kidney disease; M: male; A: admission; HF: heart failure; F: female; NT-proBNP: N-terminal fragment of brain natriuretic peptide (pg/ml); CRP: C-reactive protein (mg/dl); PCT: procalcitonin (ng/ml); ICU: intensive care unit.

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Brugada syndrome, Brugada phenocopy, or simply arrythmia induced by cocaine intoxication?

¿Síndrome de Brugada, fenocopia de Brugada o solo intoxicación arritmogénica?

To the editor:

Brugada syndrome is a hereditary disease associated with the occurrence of ventricular fibrillation (VF) and sudden death in patients without structural heart disease. The diagnosis is based on the detection of a distinctive electrocardiographic pattern with ST segment elevation ≥ 2 mm and negative T wave in the right precordial ECG leads. These leads are observed spontaneously or during the performance of an inductive test with sodium channel blockers[1]. It is a channelopathy caused by mutation of the cardiac sodium channel that leads to a loss of function of the channel. Other non-genetic factors may trigger a similar ECG; and the ED should initially rule out diseases or drugs that may simulate the electrocardiographic pattern of Brugada.

We report the clinical case of a 26-year-old woman with a history of cocaine, heroin and cannabis use. She had no family history of sudden death and was not taking any drug treatment. She had a cardiorespiratory arrest due to VF in public. After defibrillation, two minutes of advanced cardiopulmonary resuscitation and orotracheal intubation, the patient regained spontaneous circulation and the ECG showed a sinus rhythm.

The ECG on admission to the intensive care unit (ICU) (Figure 1A) showed a right branch block with ST segment elevation and a T wave inversion in the V1-V2 leads, suggestive of a Brugada pattern (type I). The blood test showed a normal ionogram. Urine tox screen was positive for cocaine. Head CT scan showed no abnormalities. The patient could have been extubated early in the ICU. After extubation, the patient confirmed oral intake of 3 g of cocaine. After 72 hours, the patient presented an ECG without a Brugada pattern (Figure 1B). The patient requested voluntary discharge from the hospital where she was initially treated and referred to our centre, which completed the study.

Structural heart disease was ruled out at our center with echocardiography and MRI. The flecainide test was negative. Cessation of drug use at discharge was strongly recommended, given the high risk of new arrhythmic episodes.

We report a case of suspected Brugada syndrome in a patient with sudden death from VF recovered in association with a suggestive ECG type I pattern. However, the ECGs - including the ECG with V1-V2 in the second intercostal space -, once the intoxication was resolved and the flecainide test was performed, were normal.

There are several situations in which an ECG can be found to simulate the Brugada pattern. The differential diagnosis that should be made includes: Brugada phenocopy, Brugada-like electrocardiographic pattern and acquired form of Brugada syndrome[2] (Table 1).

Patients with Brugada phenocopy have an underlying condition which causes the electrocardiographic pattern, and once this resolves, the ECG is normalised. Examples are: pulmonary thromboembolism, right ventricular ischemia, mechanical compression of the right ventricular outflow tract and metabolic alterations[1,3].

Secondly, the Brugada-like electrocardiographic patterns must be assessed with ST segment alterations that can be interpreted as a type I Brugada pattern. They are usually associated with additional abnormalities in other ECG leads. Most correspond to cases of ST elevation se-

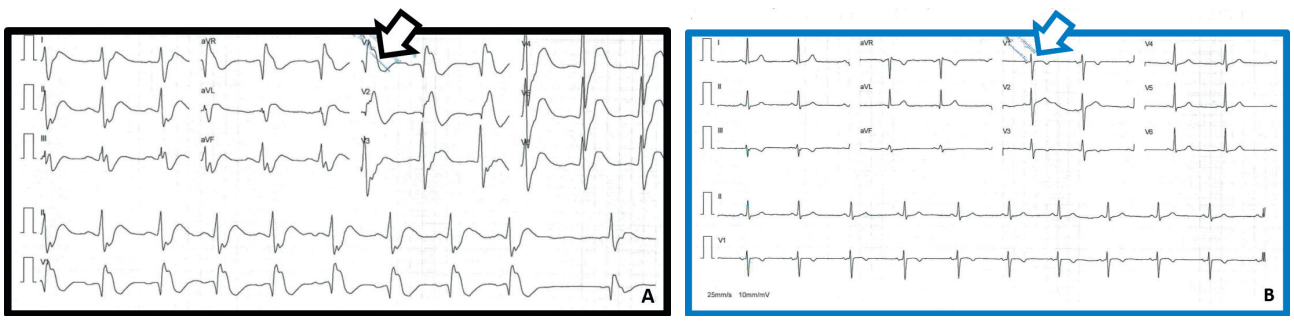

Figure 1. Electrocardiogram on admission (A) and at 72 hours (1B). Black arrow indicates Brugada pattern (type I); blue arrow indicates ECG normalization in precordials.

condary to anterior descending artery ischemia[1].

However, the exposed case corresponds to an acquired form of Brugada syndrome in the context of intoxication. This term is reserved for cases in which the ECG pattern is induced by a drug that modulates transmembrane ionic currents: sodium channel blocking antiarrhythmics -such as ajmaline or flecainide-, propofol, tricyclic antidepressants, fluoxetine, lithium, trifluoperazine, antihistamines and cocaine.

The findings that support the fact that we are dealing with an acquired form of Brugada are: the patient was intoxicated by cocaine, normalization of the ECG once the intoxication was resolved, absence of family history of sudden death and negative provocation test. Since everything in this patient was produced by the intoxication and the flecainide test was negative, no genetic study was performed.

A small dose of cocaine has been described to trigger VF, while a high dose may lead to asystole[5]. However, this has not been demonstrated and we can find in the literature cases of ventricular arrhythmia after consumption of a high dose of cocaine[6], as in our case. References in the literature to cases where a Brugada-pattern ECG is presented after cocaine use are scarce[7]; but most of the cases described of cardiac arrest associated with Brugada-pattern ECG and cocaine use occurred after oral intake of the drug. After oral intake, plasma concentration increases slowly and peaks at 45 minutes. But after nasal administration, the plasma concentration is substantial even during the first minute, showing two peaks (10 and 45 minutes)[8]. Oral administration may be more toxic because of its slow absorption and the later subjective feeling of well-being, which may lead to an increase in the amount of drug consumed.

In summary, before establishing the diagnosis of Brugada syndrome of genetic origin, the differential diagnosis described above should be considered during initial ED management. In the ED it is important to rule out diseases or drugs that may simulate the electrocardiographic pattern, as these conditions are reversible or potentially treatable. Genetic studies are not necessary in cases where the ECG pattern is secondary to poisoning with a subsequent negative provocation test.

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Intercostal pseudohernia following blunt chest trauma

Pseudohernia intercostal tras un traumatismo torácico cerrado

To the editor:

Rib fractures are the most com-

Table 1. Differential diagnosis that should be performed

	Brugada Phenocopy	Brugada-like ECG pattern	Acquired form of Brugada
Definition	Underlying condition that causes the electrocardiographic pattern. Once this condition resolves, the ECG is normalised. A term that should not be used4 in cases where the ECG pattern is caused by a sodium channel blocker.	Most correspond to cases of ST elevation secondary to ischemia of the anterior descending artery.	This term is reserved for cases where the ECG pattern is induced by a drug that modulates transmembrane ionic currents.
Treatment	Treatment is specific to the underlying disease/condition.	Treatment of ischemia: in case of ST elevation in V1-V2 due to suspected ischemia, a coronary angiography should be performed.	Removing the drug and avoiding sodium channel blockers and drugs related to the acquired form of Brugada.
Examples	Pulmonary thromboembolism, right ventricular ischemia, mechanical compression of the right ventricular outflow tract and metabolic disorders.	Acute coronary syndrome with ischemia/infarction in the anterior descending artery region.	Sodium channel blockers (such as ajmaline, flecainide, procainamide), propofol, tricyclic antidepressants, fluoxetine, lithium, trifluoperazine, antihistamines, and cocaine

mon injury after closed chest trauma, with an incidence of 7-40%, although they may sometimes go undiagnosed. Denervation of the intercostal muscles by nerve injury after a rib fracture may condition the appearance of a pseudoherniation in the chest wall, although this is very rare. Here is the case of a patient with a history of chest trauma, treated in the emergency department after the sudden appearance of a non-symptomatic lump in the costal wall, who was diagnosed with intercostal pseudoherniation of post-traumatic origin.

A 70-year-old man with no personal history of interest, who arrived at the emergency department with a lump in the inferolateral region of the right chest wall, which appeared suddenly after an access of coughing and progressive growth in the last week. The patient reported that 4 months ago he had suffered a chest trauma after a fall at home, hitting the right costal region and the pelvis, although without visiting the emergency department. On examination there was a marked thoracic asymmetry, highlighting a large lump in the lower right costal region below the eighth costal arch, which increased with Valsalva manoeuvres, without other accompanying findings (Figure 1A). Computed tomography (CT) showed a posterior fracture of the eighth costal arch, unknown until then and already consolidated, with widening of the next intercostal space and elongation of the musculature without evidence of disruption, which protruded without any abdominal viscera (Figure 1B and C). It was diagnosed as a post-traumatic pseudoherniation of the intercostal muscles, due to probable denervation secondary to the rib fracture.

Pseudohernias are delimited muscular protrusions resembling a hernia, in the absence of an associated muscular or aponeurotic defect[1]. Their prevalence is very low. They develop most frequently in the abdomen and are secondary to neuropathy (of infectious origin, as in the case of herpes zoster, or in spinal cord injuries) or after nerve disruption (post-traumatic or iatrogenic, following surgical incisions in the abdominal flanks, such as lumbotomy)[2]. This very rare phenomenon has also been evidenced in the intercostal muscles of the chest wall, after various situations leading to muscle laxity and weakness[3], and triggering chronic or intense coughing[4]. Costal fracture associated with coughing episodes has been described in the literature, conditioning the subsequent appearance of intercostal pseudoherniation. The particularity of our case lies in the association between thoracic trauma and sequelae, which has never been described before. We consider that the intercostal muscle bulge had its origin in a possible nerve injury from the post-traumatic rib fracture, which went unnoticed. In view of these findings, the anamnesis should always include the traumatic history, and in this case diagnostic confirmation was achieved by CT scan. Surgical treatment should be limited to symptomatic cases (with herniation of abdominal viscera, which caused the symptoms), and in most cases conservative management should be chosen, including treatment of pain, weight loss, use of a brace and physical therapy[3,5].

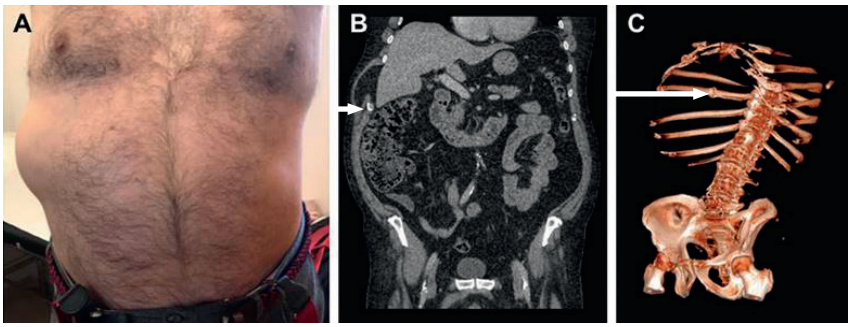

Figure 1. A) Tumor in the right lateral costal region B) Coronal section of the computed tomography (CT): an intercostal pseudohernia (arrow) without abdominal visceral content is evident, due to the proximity of the right hepatic lobe. C) Three-dimensional reconstruction (CT): the callus of the posterior fracture of the eighth costal arch and separation of the eighth and ninth ribs (arrow).

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