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ORIGINAL ARTICLE

Emergency Room Thoracotomy (ERT): A Retrospective Audit of Results

Barbaro I. Monzon[1*], Maria del Carmen Ortega[2], Jacques Goosen[3], Dietrich Doll[4], Maeyane Stephen Moeng[5]

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Abstract

Background: An Emergency Room Thoracotomy (ERT) is a resource-intensive, high-risk procedure in which rapid decision-making is essential. In a resource-constrained system, identification of the group of patients that could achieve the best outcome will avoid futile use. Incorporating physiological and metabolic parameters at the time of arrival to the emergency department into the management algorithm may assist with better patient selection and could improve outcomes.

Material and Methods: A retrospective review of the results of subjects who underwent Emergency Room Thoracotomy at a Level 1 Academic Trauma Center over a 13-year period (01 January 2005 to 31 December 2017) was conducted. Mechanism of injury, physiological and metabolic parameters, anatomical injuries, Injury Severity Score (ISS), calculated Revised Trauma score (cRTS), volume and type of fluids administered, and mortality were analyzed comparing survivors and non-survivors.

Results: One hundred and ten (n=110) patients underwent ERT during the study period**.** Variables such as the mechanism of injury, physiological and metabolic parameters, type, and volume of fluids administered did not show any statistically significant influence in the final outcome. Penetrating cardiac and chest trauma had better survival (40.6 % and 20 % respectively) compared to those with thoraco-abdominal, abdominal, pelvic, and femoral vessel trauma. Overall survival was 21,8%.

Conclusions: In a resource-constrained environment an Emergency Room Thoracotomy should be performed in patients with a thoracic injury, especially cardiac, to achieve the best possible outcome.

Keywords: Trauma, ERT, Mortality

Original article, no submission or publication in advance or in parallel

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Introduction

The major causes of early trauma deaths are severe traumatic brain injury and irreversible haemorrhagic shock secondary to uncontrolled bleeding [1-4].

Early, aggressive control of haemorrhage, with rational use of blood and goal directed management of coagulation and limited use of crystalloid fluids improves survival [2-11].

The improvements in the emergency medical rescue systems that have occurred in recent years increases access to hospital care, therefore a larger number of otherwise *"fatally"* injured bleeding patients arrive to emergency departments with significant physiological and metabolic deterioration. Efforts to salvage these patients often involve desperate measures to control haemorrhage and restore tissue perfusion.

Opening the chest in the emergency department to relieve cardiac tamponade, suture a lacerated heart, cross-clamp the supra-diaphragmatic thoracic Aorta to reduce the

rate of bleeding in the abdomen and pelvis, control bleeding from the lung and mediastinal great vessels and perform open cardiac massage for traumatic cardiac arrest have been part of the surgical arsenal for many years. [1,12-18]

The current scientific literature clearly supports the use of ERT for injuries in the chest and especially the heart where the best outcomes are obtained [1,13-33]. However, there are ongoing debates about its role in blunt trauma [24-33]. Futile use is a large concern in overloaded under-funded trauma systems and centers [19,20,21,22]. The risk of performing an ERT in blunt trauma victims has to be weighed against the expected benefit for the individual patient in these situations [32,33].

The Resuscitative Endovascular Balloon Occlusion (REBOA) is emerging as an alternative to cross-clamping of the Aorta during ERT. REBOA seems to benefits those patients with abdominal and pelvic bleeding, however, this procedure is not yet widely available and offers no benefit in chest trauma. [35,36]

The caveat of ERT is the high mortality rate, poor neurological outcomes, risk of complications and hazards present during ERT, especially the transmission of infectious diseases to health care personnel, as well as the high costs involved in the management of these very ill patients [1,13-33] These factors have prompted investigators to analyze the outcomes of ERT to identify the patient population with the best results.

The aim of this study was to analyze the clinical characteristic of the subjects that underwent ERT in our hospital and their potential influence in their survival.

We hypothesize that in our resources-constrained health care system an ERT should be directed only to those patients with the best chances of survival and that incorporating physiological and metabolic data to the decision-making algorithm could assist in selecting the patients for the procedure. The experience obtained could be relevant to centres and hospitals that have resource limitations similar to our institution.

Material and Method

The study describes the findings of the results of adult patients who underwent ERT between 1st January 2005 and 31st December 2017, at the Charlotte Maxeke Johannesburg Academic Hospital Trauma Unit. The information was extracted from the Digital Patient Registry of the Unit, clinical notes and theatre registry. Data selected for analysis included: age and gender; mechanism of injury, haemodynamic status (heart rate, respiratory rate, systolic blood pressure-sBP, Glasgow Coma Score (GCS); oesophageal temperature (measured in operating theatre once patient arrived there); coded Revised Trauma Score (cRTS) and Injury Severity Score (ISS); primary anatomical area of injury; arterial blood gas results if obtained, and 24-hour mortality.

The data extracted was analyzed with the Statistical Package for the Social Sciences (SPSS) software, version 21.0 (Mac OS) from IBM Corporation (Armonk, NY, USA) under a temporary license obtained from www.ibm.com/sofware/analytics/spss/

The analysis included all patients whose records were available, further analysis was done between survivor and non-survivor sub-groups. *Student T* test and *Chi squared* (X^2) test were used to establish significance, a value of $p < 0,05$ was considered significant.

The Human Research Ethics Committee of the University of Witwatersrand granted permission for the study (M180501).

Results

One hundred and ten patients underwent ERT during the study period. One-hundred and one were males (92%) and 9 females; the median age was 29 years (Inter Quartile Range - IQR 16-58). Of the total number of patients, 61 sustained stab wounds (55.5 %), 43 sustained gunshot wounds-GSW (39 %) and 6 were blunt trauma victims (5.5 %).

Overall, the physiological parameters were recorded as follows: Heart Rate (HR) 84 beats per minute (IQR 0-154); Systolic Blood Pressure (SBP) 60 mmHg (IQR 0-104); Respiratory Rate (RR) 10 breaths per minute (IQR 0-56) and Glasgow Coma Score 8. (*Table 2)*

Only 55 of the 110 patients had a complete arterial blood gas analysis recorded in the emergency department. The mean pH was 7.16 (IQR 6,5-7,65); Base Excess -15,7 (IQR -3 to -31) and serum Lactate 12.4 mmol/L (IQR 2.4-22) denoting the severe metabolic acidosis that accompanies major trauma.

Majority of the patients were hypothermic during and after the ERT, median Temperature was 35 ^{0} Celsius (IQR

Table 1 Demographics

	All n=110,(%, IQR)	Survivors n=24, (%, IQR)	Non-survivors n=86, (%, IQR)
Male	101	22	79
Female	9	2	7
Median Age	29 (16-58)	28 (17-36)	29,2 (16-58)
Stabs	61 (55.4)	20 (18.1)	41 (37.2)
GSW	43 (39)	4 (3.6)	39 (35.5)
Blunt	6 (5.4)	0	6

IQR: inter quartile range; GSW gunshot wound

Table 2 Comparative Physiological and Metabolic Variables

Variable	**Survivor n=24 (IQR)**	**Non-survivor n=86 (IQR)**
Systolic BP mmHg	57 (0-98)	48 (0-104)
Respiratory Rate	13 (0-45)	11 (0-56)
GCS	8	7
Heart Rate	97 (0-154)	81 (0-154)
Temperature 0C (Oesophageal measured in OR)	35,3 (35-36,5)	35 (32-37)
pH	7.16 (7.34-6.67)	7.16 (7.38-6.50)
Base Deficit	-15.8 (-24 to -6.9)	-16 (-31 to -3)
Serum Lactate	10.3 (2.4-15)	13 (4.7-22)
cRTS	5,6 (0-12)	4,2 (0-11)
ISS	24 (10-29)	27 (16-59)

IQR: inter quartile range; BP: blood pressure; GCS: Glasgow coma score, cRTS: calculated revised trauma score, ISS: injury severity score, OR: operating room

32-37). The oesophageal temperature measurement was obtained in the operating room after the patients were moved there to complete the procedure, as part of the anaesthesia protocol for trauma patients.

Comparing the results, there was only a minor difference in the serum Lactate levels in favor of the survivors (10,3 mmol/L versus 13 mmol/l). However, none of the physiological and metabolic parameters were statistically significant when comparing survivors with non-survivors. *Table 2*

Overall, the mean ISS was 25 (IQR 16-59) and RTS was 4,5 (IQR 0-12) with an overall probability of survival of 50.4 %. The mean ISS of the group of survivors was 24 (IQR 10-29) versus 27 (IQR 16-59) for the non-survivors, not statistically significant results.

Most patients received crystalloids (Ringer Lactate) as part of the initial resuscitation protocol; the mean volume administered to the survivors was 1625 ml (IQR 0-3000 ml) versus 1550 ml (IQR 0 to 4000 ml) for the non-survivors. Nearly 40 % of patients also received a synthetic colloid infusion, the mean volume was 479 ml (IQR 0-3000 ml) for survivors versus 1027 ml (IQR 0 to 9000 ml) for non-survivors. Seventy-three patients (66.3 %) received transfusions during the ERT; survivors received a median of 2,3 units of Packed Red Cells, to a maximum of 10 units during the resuscitation versus 3,2 units for the non-survivors (maximum 13 units)

The survivors received 1 unit of Fresh Frozen Plasma compared to 2 units for non-survivors. The volume and type of fluids used during the ERT did not showed a statistically significant impact in mortality.

ERT were performed for injuries in the thorax (n=65), abdomen (n=17), thoraco-abdominal (n=25) and pelvis and femoral vessels (n=3). Six patients had ERT for blunt trauma. The overall survival of the series was 21,8 % (40.6 % survival for cardiac injuries; 20 % for thoracic injuries and 1.8 % for injuries below the diaphragm). Patients with stab wounds have better survival (32.8 %) that those with GSW (9.3 %) or blunt trauma (0 %).

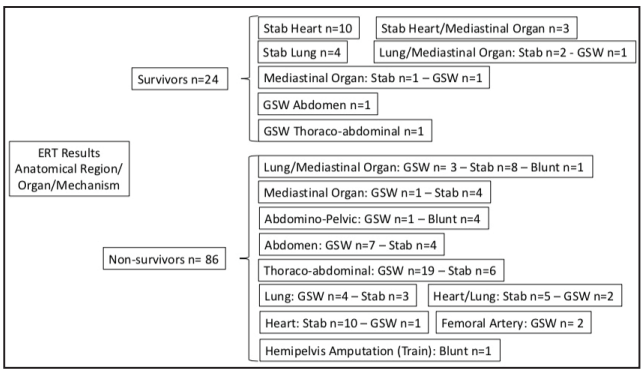
Comparing isolated chest trauma (n=65) to injuries elsewhere in the torso the difference in survival is significant: Thorax alive n= 22 versus other areas alive n=2 ($p = 0.001$) Cardiac injuries were present in 29 % of patients (n=32) resulting in the best outcome: Alive n= 13 (40.6 %) ($p = 0.032$).

Table 3 Comparative Outcome by Injured Region

Anatomical Region	Survivor: n(%)	Non-survivor:n(%)
Chest n=65	22 (20) (p=0.001)	43 (80)
Abdomen n=17	1	16
Thoraco-abdominal n=25	1	24
Pelvic-femoral n=3	0	3
Heart n=32 (29 %)	13 (40.6) (p=0.032)	19 (56.5)

Two patients survived the ERT when performed for injuries elsewhere in the torso, one patient with abdominal GSW and one with thoraco-abdominal GSW. No other patient survived an ERT for injuries outside the chest.

Figure 1 Outcomes Anatomical Region/Organ/Mechanism of Injury



Discussion

Patients arriving to the Trauma Unit at Charlotte Maxeke are transported by ambulance services and occasionally by private vehicles. The level of care in the ambulances varies among services, with some of the ambulances manned by Emergency Medical Technicians and others by basic rescue providers. Unfortunately, communication between pre-hospital rescue personnel and the base hospital is limited, seldom the condition of the patient is known before arrival.

In most South African Trauma Centres an ERT is performed to assist with the resuscitation of patients with cardiac tamponade or exsanguination from penetrating torso trauma. The use of ERT for blunt trauma victims remains controversial due to the accompanying high mortality and limited availability of resources in state funded hospitals.

Most of the international literature of the late 1990's and early 2000's [13-31] discouraged the use of ERT in blunt trauma, however there are recent studies of the use of ERT in blunt trauma with acceptable success. [32, 33]

In our literature review we did not find any reports of the use of metabolic parameters to help selecting the patient for ERT, our hypothesis was that patients with penetrating torso injuries below the diaphragm were presenting with severe metabolic derangement similar to the one exhibited by blunt trauma victims, therefore incurring in high mortality despite ERT. As shown by our results the metabolic derangement was important but not statistically significant between the survivor or non-survivors.

The overall mortality of the series was 78,2 %. The available literature reports mortality above 50% for penetrating torso trauma and near 100% for blunt injuries, however a recent systematic review from Scandinavia showed encouraging results for blunt trauma victims. [13-33]

In 1991, *Ivatury et al* [19] reported an overall survival of 9.8% following ERT (24.5 % Stab vs. 4.7 % GSW vs. Nil in Blunt trauma), they demonstrated that best results are achieved in patients with vital signs on arrival and those with a potential cardiac injury. *Asensio et al* [14] in 1998 reported an overall survival of 16% for patients following ERT for penetrating cardiac injury, in whom, determinants of survival were the presence or absence of sinus rhythm, mechanism of injury (Stab vs. GSW), need for aortic cross-clamping and inability to restore organized rhythm or Blood Pressure after the thoracotomy. In 2004, an analysis of 42 series of patients (7,035 patients including children) found that 11.1% survived penetrating injuries vs. 1.6% blunt, with an overall mortality rate of 92.2 %. [20]

It should be noted that the use of synthetic colloids has been eliminated in our unit and the initial crystalloid use is limited, with early blood product administration according to the current guidelines for the management of bleeding trauma patients [2-11]. It could be of interest to assess the impact of this change in fluid management strategy in the subgroup of patients requiring ERT under these conditions.

The overall survival of the series was 21,8%, further analysis combining mechanism of injury, anatomical zones and mortality revealed statistically significant better survival ($p=0.032$) for penetrating cardiac trauma. Penetrating chest trauma in general (cardiac, lung and mediastinal) had a statistically significant ($p=0.001$) lower mortality than the rest of the combined anatomical areas, irrespective of mechanism. These results correlate well with the available literature [1,13-34]

It is self-explanatory that a patient with a (potential) cardiac injury will benefit from rapid evacuation of the tamponade and control of the cardiac laceration, therefore these patients are the ideal candidates for ERT, as long as there are signs of cardio-respiratory activity (breathing effort, palpable pulse, blood pressure and organized cardiac rhythm) or a witnessed cardiac arrest on arrival to ED. Same rationale applies to the rapid exsanguination or air embolism secondary to penetrating mediastinal and pulmonary trauma.

Barring the obvious limitations of a retrospective review our results suggest that the traditional indications to use ERT could be adjusted, especially in a resources-constrained environment. In patients with blunt injuries and penetrating thoraco-abdominal or abdomino-pelvic trauma, the degree of physiologic and metabolic deterioration and the magnitude of the injuries significantly reduce the possibility of survival. In these situations, the decision to perform an ERT should be individualized. Despite the lack of statistical power of our results, we believe that the severity of injury expressed as physiological and metabolical derangement that can be demonstrated by immediate point of care blood gas analysis (pH, Base Deficit, Lactate) could still play a significant role in predicting negative outcomes in patients undergoing ERT.

Further studies to include these variables in the decision-making process may give us a better answer.

Conclusions:

In a resource constrained environment an Emergency Room Thoracotomy should be performed in patients with a thoracic injury, especially cardiac, to achieve the best possible outcome.

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ORIGINAL ARTICLE

Salvage Total Hip Replacement after Failed Internal Fixation of Trochanteric Fracture Femur

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Abstract

Background: Total hip replacement (THR) is one treatment option for failed hip fracture fixation. It is considered as a salvage procedure for older patients, patients with poor bone stock, avascular necrosis of the femoral head, associated with damaged acetabular articular cartilage.

Patients and Methods: Total hip replacement was done for forty patients with failed internal fixation of trochanteric femoral fractures, 28 males and 12 females completed the follow up and six patients were lost. The procedure was carried out through a lateral exposure in all cases. Harris hip score (HHS) was used for clinical evaluation preoperatively, postoperatively. Radiographic evaluation comprising anteroposterior radiographic views of the pelvis and femur and a lateral view of the femur were performed at follow-up visits.

Results: The mean time of follow up was 48 months (range from 36-72 months). The mean Harris hip score was improved from a mean of 24 points preoperative to 88 points at final follow up. Pain relief and gait correction were noted at the final follow up. Twenty-eight patients (70%) could freely walk outdoors using a cane or elbow crutch; eight patients (20 %) had a limited walking ability using two axillary crutches, and four patients (10 %) were able to walk indoors only.

Conclusion: Total hip arthroplasty is a good salvage procedure after failed internal fixation of trochanteric femoral fractures. Individual selection of the implant depends upon the age of patient, level of activity, the bone stock of proximal femur, and the condition of the acetabulum. To maintain stability, reattachment of the greater trochanter should be done. To avoid intraoperative fractures of osteoporotic bone, dislocation of the hip should be very careful.

Key words: total hip, replacement, trochanteric fracture, failure of fixation.

Introduction

Stable trochanteric femoral fractures can be treated by internal fixation methods with union rates as high as 100% when optimal implant and good reduction have been achieved. Failure rates have been reported in literature due to comminution, osteoporosis and suboptimal fixation [1]. Functional disability and pain are the end result of failed fixation of trochanteric femoral fractures. Failure rates may be due to failure of the device (3% - 12%); device penetration in (2% and 12%), nonunion (2-5%) and malunion with Varus deformity in (5- 11%). Certain unstable fracture patterns have been reported to have failure rates as high as 56% [2-6]. Revision of internal fixation for non-united trochanteric fractures of the femur has been reported to have good results in younger patients with good bone stock [6-10].

Total hip replacement (THR) is one treatment option for failed hip fracture fixation. It is considered as a salvage procedure for older patients, patients with poor bone stock, avascular necrosis of the femoral head, associated with damaged acetabular articular cartilage [7]. The cause of symptoms and the reason for failure include infection, malunion, nonunion, femoral head osteonecrosis, and progressive degenerative arthritis due to internal fixation failure. There are many technical difficulties during conversion hip arthroplasty such as extraction of implants, bone deformity, bone loss, poor bone quality and associated trochanteric nonunion [11- 13].

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The aim of this work was to evaluate the early results of total hip arthroplasty in a group of patients with failed internal fixation of trochanteric femoral fractures including the clinical and radiological results.

Patients and methods

From January 2009 to December 2017, forty patients with failed internal fixation of trochanteric femoral fractures were treated by total hip replacement as a salvage procedure. The study started by 46 patients but only forty patients were available at the end of follow up. The mean age of the patients was 50 years (range: 42–66 years) and the sex distribution was 28 males and 12 females (Table 1). The type of fracture was intertrochanteric in 30 patients and subtrochanteric in 10 patients. The failed implants used in primary fractures treatment were: Dynamic hip screw in (DHS: 31 cases), proximal femoral nail in (PFN: 6 cases), dynamic condylar screw in (DCS: 3 cases). The mean time from primary fixation to the salvage arthroplasty was 28 months (range, 12 to 34 months).

Table 1: All patients data preoperative

Mean Age (range)	50 (42-66)years
Sex	Male: 28
	Female: 12
Side affected	Right: 15
	Left: 25
Implant in first operation	*DHS: 31
	**PFN:6
	***DCS: 3
Mean duration between first operation and salvage	28(12-34) months
Type of prosthesis (fixation method)	Cement less: 32
	Cemented: 4
	Hybrid: 4
Stem used	Standard stem: 32
	Long stem: 8

(dynamic hip screw) **(proximal femoral nail) *(dynamic condylar screw)*

Intraoperative cultures were positive in 8 patients and no growth of organisms in thirty-two patients. Two stages procedure was used in 8 infected cases (Figure 1), and one stage revision was done in 32 cases (Figure 2).The inclusion criteria of patients included in this study were either one or a combination of nonunion, loss of fixation, avascular necrosis of the femoral head, screw penetration of the acetabulum, chondrolysis or hip incongruity.

Bipolar prosthesis was used in patients with implant failure but normal acetabulum, and those cases were excluded, also cases with active infection not done until debridement and cure of infection at least nine months after skin closure without sinuses then second stage was done for them after laboratory investigations to ensure no microbial activity.

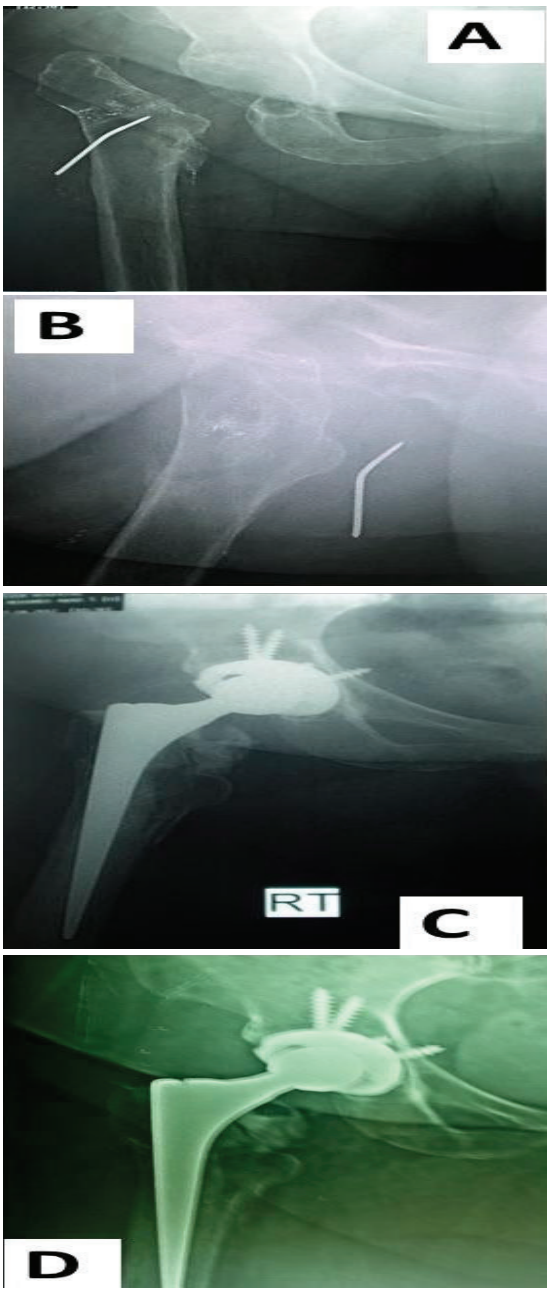


Figure 1: Female patient 54 years old (Case No. 22): A&B) preoperative x-ray 1 year after debridement and implant extraction due to infection; C) postoperative x-ray with hybrid THR (cementless cup and cemented stem); D) 3 years postoperative x-ray.

The implant type used was Hybrid prosthesis in 4 hips (Cementless cup and cemented stem), cementless prosthesis was used in 32 hips, and cemented prosthesis in 4 hips. A 28 mm metal head was used in 30 cases, 32mm metal head in 10 cases (Fig 3).

Harris hip score (HHS) [15] was used for clinical evaluation preoperatively, postoperatively and at last follow up The score has a maximum of 100 points (best possible

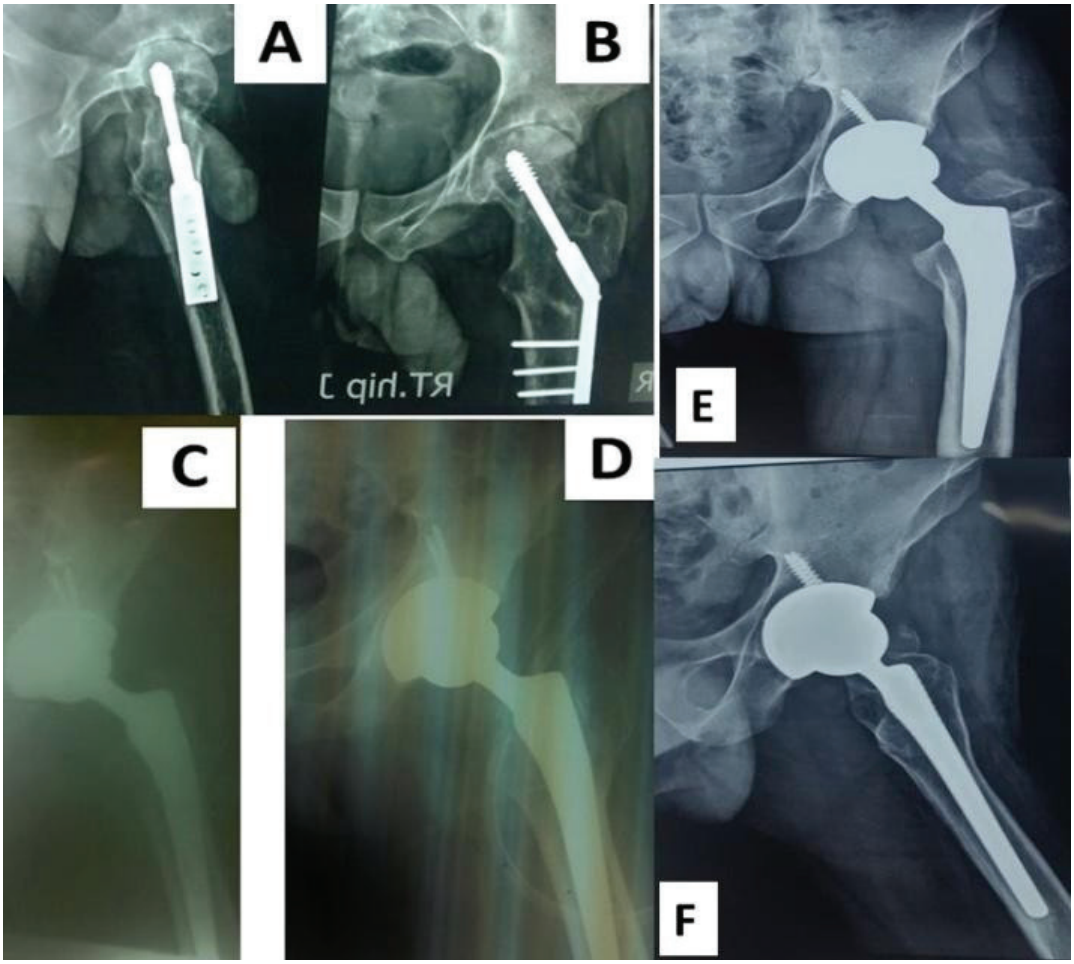


Figure 2:

Male patient 65 years old (Case No. 9):

A&B) preoperative x-ray with hip posttraumatic degeneration,

C&D) postoperative x-ray (cementless THR);

E &F) 4 years postoperative.

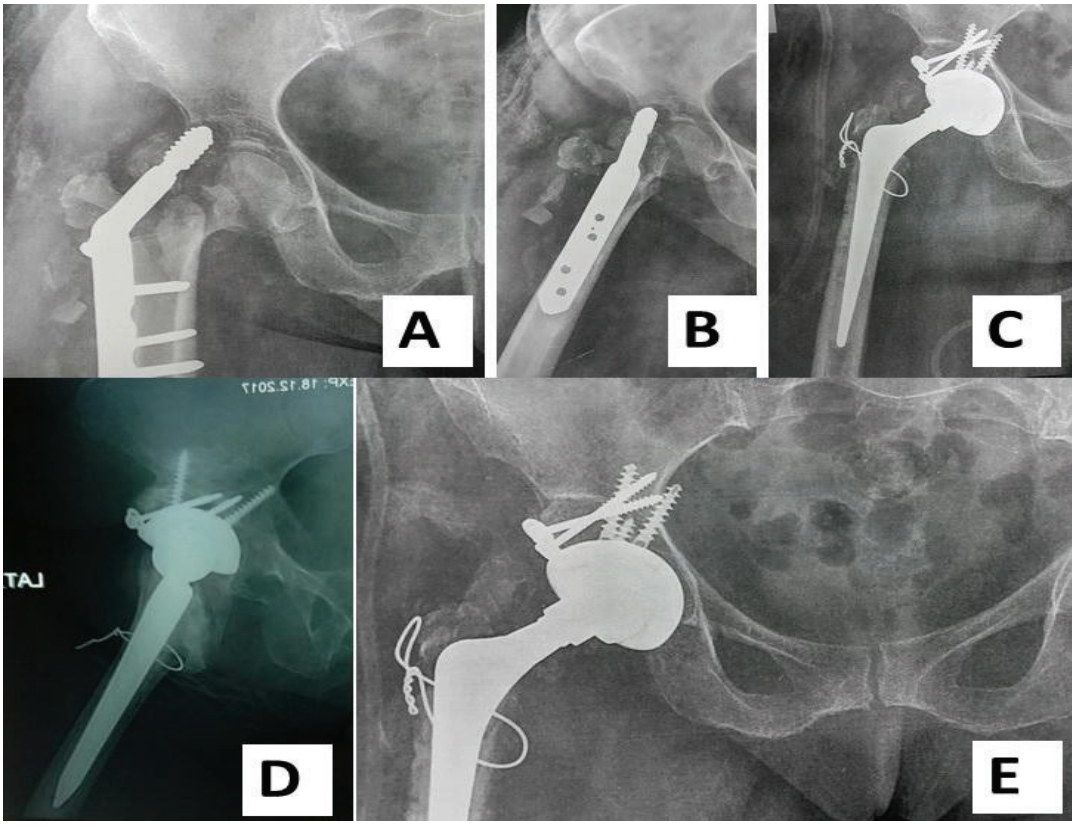


Figure 3: Female patient 62 years old (Case No. 11):

A&B) preoperative x-ray with screw penetration and acetabular erosion and segmental defect;

C&D) postoperative x-ray with hybrid THR (cementless cup and cemented stem) with acetabular reconstruction with bone graft from the head remnant.

outcome) covering pain (1item,0–44points), function (7items,0-47points), absence of deformity(1item,4points), and range of motion (2items, 5points). The score of (90-100 points) HHS is excellent, good (80-90), fair (70-80), and poor (below 70 points) [16]. Limb length measurement, preoperative clinical examination and, hematological investigations as complete blood count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were done for all patients regarding occult infections.

Radiographic evaluation comprising AP radiographic views of the pelvis and proximal femur with lateral view of the femur were performed at follow-up visits. Engh et al [17] criteria were used for femoral stems evaluation. Radiolucency in bone-prosthesis interface was recorded and evaluated according to Gruen et al [18] zonal system. De Lee and Charnley [19] criteria for acetabular evaluation. Acetabular inclination was measured using the interteardrop line as a reference point. Acetabular inclination was considered accepted when between 35° and 55°. Cementless cup loosening was defined as implant migration, a complete radiolucent line at the implant bone interface, or fixation screws breakage [20]. Heterotopic ossification according to Brooker et al [21] system, and classes III and IV were considered clinically important.

Operative procedure

Spinal anesthesia in all operations were used. Hardinage approach in lateral position was performed in all cases. The skin incision included the previous scar in 10 patients and new incision not related to previous scar in 30 patients. To avoid intraoperative femoral shaft fracture, the hip was dislocated before removing the implant in 14 cases. In those 14 cases, the hip was quite stiff and the bone was of poor quality. The implant was removed before dislocation in 10 cases, and in situ neck osteotomy was performed in 8 cases, and the implants were extracted in a previous sitting in 8 infected cases. The greater trochanter nonunion was found in twelve patients and stainless-steel wire was used for reattachment after insertion of the stem in 6 of them (Fig 3), and ac bond for other 6.

In eight patients malunion of greater trochanter was found (five with valgus and three with varus deformity). Five patients had screw cut out, and one of this cases had acetabular defect due to lag screw cut through which was reconstructed using bone graft during the operation (Fig 3). Hardinage of the femoral canal was found in most cases due to new bone formation, deformity of proximal femur and fibrosis. Flexible reaming on a guide wire to ream the canal was used for femoral preparation. Patients with intramedullary nails had great difficulty in canal reaming due to the old entry and bone sclerosing. Image intensifier was prepared routinely in all cases. Stem selection for patients depended upon available bone quality and stability of trial on table. In four patients, intraoperative fracture extension or new fracture occurred, in four cases calcar replacement stem was used, and augmentation plate fixation in two cases when the fracture was distal to the stem end. Closure of the wound over suction drains which kept in situ for 2 days. Prophylaxis for deep vein thrombosis (DVT) using medical and mechanical methods was done for all patients. Clexane 40 units subcutaneous were used 24 hours preoperative and from 2nd day through 3weeks postoperative in all patients. Patients stay in hospital ranged from 6 to15 days. After removal of stitches by 2 weeks regular monthly visits for six months, and every six months up to the end of follow up.

Results

The mean time of follow up was 48 months (range from 36 -72 months). The operative time ranged from 140 to 225 minutes (Average 165), with a mean blood loss of 1200 ml (range from 800 to 2200 ml). The minimum follow up period was 3 years. Forty patients only were available at the end of follow up as six patients were lost during follow up. The mean preoperative Harris hip score (HHS) was 24 points with poor score in all patients, and improved significantly to a mean of 88 points (range: 75-96 points) at the latest follow up. At the end of follow up, sixteen patients had excellent results (40 %); fourteen with good results (35%), eight hips (20 %) with fair results and two hips (5 %) had poor results. When comparing the mean HHS in cases with cemented stem (10 stems) and cases with cementless stem (30) there was no significant difference (Table 2).

Pain relief and gait correction were documented at the final follow up. Limb shortening was detected in ten patients (25 %) and ranged from 15 to 30 mm (average 22 mm). Preoperatively, ten patients (25 %) had moderate pain with using two crutches for ambulation; twenty-one patients (52.5 %) had severe pain and were unable to walk, and nine (22.5%) had limited walking ability using a walker. Postoperatively, no pain or residual mild pain which did not interfered with daily activities was found

Table 2: Clinical results and complications.

Harris hip score	Mean score (points)		Postoperative score (number of patients %)				
	Preoperative	Postoperative	Excellent	Good	Fair	Poor	
	24 points	88 points	16 (40%)	14(35%)	8(20%)	2(5%)	
Complications	Postoperative dislocation	Heterotopic ossification		Infection		Revision	D V T
	2 patients	Grade II(3patients)	Grade III(1patient)	Superficial (3cases)	Deep (1case)	(1 case)	3 cases

in 20 patients (50%), trochanteric pain in six (15 %), and anterior thigh pain in 12 patients (30 %). In two patients (5 %) moderate to severe pain was found. Postoperative DVT proven by Doppler examination was found in three patients and were treated medically. All patients were able to walk with different walking ability. Thirty patients (75 %) could freely walk outdoors using a cane or elbow crutch; six patients (15 %) had a limited walking ability using two axillary crutches, and four patients (10%) were able to walk indoors only.

Radiologically, follow up x-rays AP, Lateral views of hip joint with AP view of pelvis were done for all patients every month for 6 months, and every 6 months later tell the final follow up. Postoperative dislocations occurred in two patients (5%) and closed reduction was done in the two cases (Fig 4). Heterotopic ossification was seen in four (10 %) of the patients and it was Brooker grade II in three, and grade III in one patientbut this ossification did not lead to ankylosis (Figure 5). The acetabular inclination was within the accepted range 35-55 degrees in 36 hips (90 %), with four cups (10 %) were vertically oriented, and no cup was horizontally oriented. The femoral stem was in neutral position in 32 stems (80 %), 5 stems (were in 12.5 %) in varus, and 3 stems (7.5 %) were in valgus position.

According to Engh's criteria [17], 26 of 32cementless stems were stable and had bony in growth with no significant subsidence, 5 were stable fibrous, and one stems was loose and infected. This patient had revision at 24 months postoperative with long stem cementless modular prosthesis (Figure 6). Radiolucency of 1 mm of cementless acetabular component was seen in 2 zones in six hips (15%), (zones 1 & 2 in 4 hips, and zones 2 & 3 in 2 hips) and these lucencies



Figure 5: X-ray showing hypertrophic ossification grade III (Case No.32).

were not progressive. Two cemented stems with probable loosening at 4 and 6 years, but clinically the patient had minimal discomfort and no revision needed for these two cases. According to Gruen zones criteria [18] for femoral stem, four stems had radiolucent line of 3mm in 2 zones but stems were stable. At the final follow up, all cemented acetabular cups except two were stable. In one patient, the radiolucent line around the cemented cup in 2 zones with cup orientation changed from 45 degrees postoperative to 60 degrees at final follow up, but the patients did not agree revision. Superficial infection was found in three cases treated conservatively by repeated dressings and I V antibiotics. Septic loosening found in one case had two stage revision.

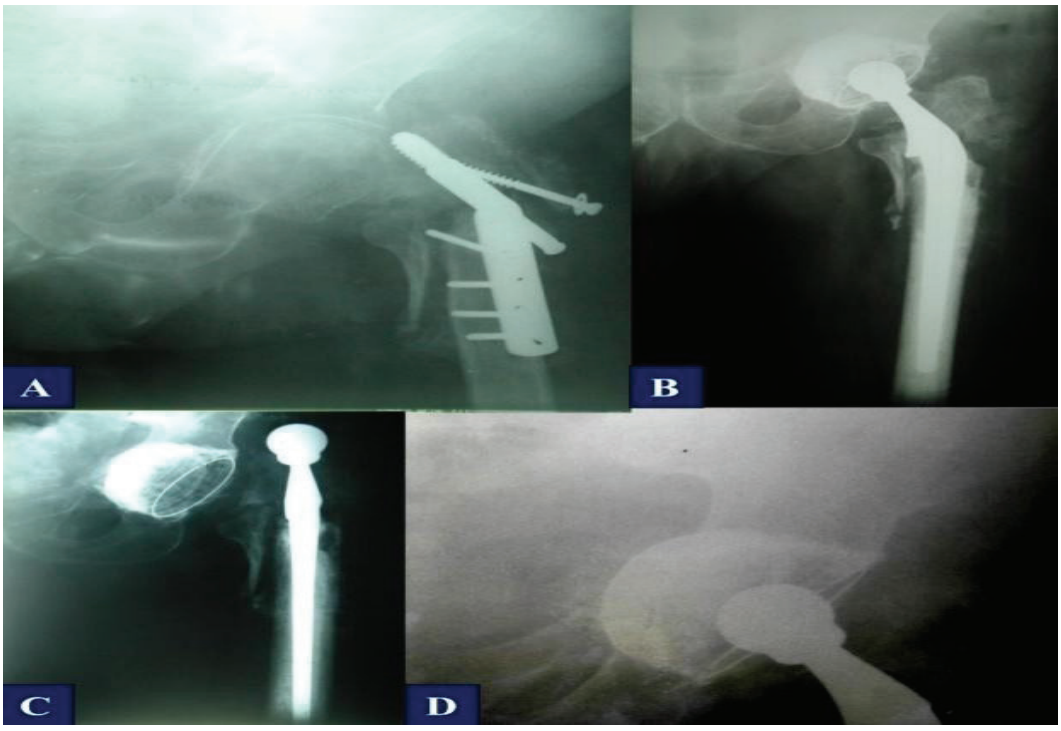


Figure 4: Male patient 68 years old (Case No. 18): A) preoperative x-ray with implant failure; B) postoperative x-ray with cemented THR; C) postoperative dislocation 3 weeks postoperative; D) x-ray after closed reduction

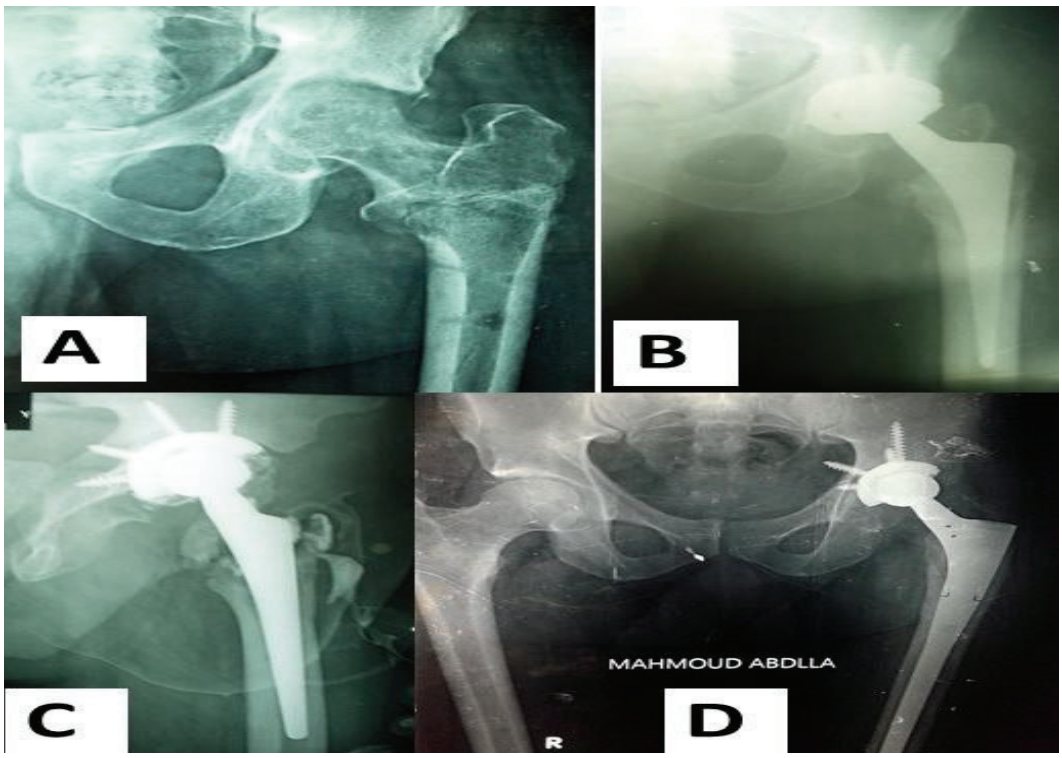


Figure 6:
Male patient 44 years old (Case No. 32):
A) x-ray after DCS extraction with nonunion and avascular necrosis of femoral head;
B) postoperative x-ray with cementless THR;
C) x-ray 1.5 years postoperative with septic loosening;
D) x-ray after revision with long stem calcar replacement.

Discussion

Failed internal fixation of trochanteric fractures of the femur can cause significant pain and functional disability affecting the patient's daily activities. Hip replacement options were used to manage these patients either hemi arthroplasty or total hip replacement. The type of prosthesis can be affected by the patient age, type of implant failure and the bone stock remained after removal of the implant. The method of fixation either cemented or cementless can be determined intraoperative after removal of implants [1, 3, 5, and 22].

Multiple technical difficulties present in these cases as the holes after removal of hardware, malunion and deformity of proximal femur with loss of landmarks, loss of bone stock, regional osteopenia, and soft tissue fibrosis with muscle weakness. Difficulties in canal reaming due to fibrosis, old entry of cephalon medullary nail, new bone formation were found in this series, so the beginning of reaming using flexible reamer over a guide wire under image intensifier was used and in eight cases there were no proximal femoral bone for implant stability, so long cementless stem was used in these cases. In cases with trochanteric nonunion reattachment and stainless-steel wire fixation was used in 12 cases [22]. Calcar replacement, fully coated stems were used in four patients in this study due to loss of proximal femoral bone with no support to the standard implant.

Thakur et al. [23] reported on 15 patients with failed intertrochanteric fractures using hip arthroplasty using a modular distally fixing stem total hip replacement. Harris hip score was improved from 35.9 preoperative to 83 postoperative. They had two patients (13.3%) walking without aid, 10 (66.7%) using a cane and 3 (20%) using a walker for ambulation. They had no patients with dislocation, DVT in one patient (6.67%), and heterotopic ossification in seven patients; 5 patients Brooker's grade (1) and 2 patients grade (2). They used constrained liner in two patients due to questionable stability of the hip intraoperative.

In the study of *Haidukewych and Berry* [4], there were sixty patients of failed internal fixation treated with hip arthroplasty, 32 total hip replacements and 28 hemiarthroplasties. They reported 39 (89%) of survived 44 patients had mild or no pain after a mean follow up period of 65 months. There were 91% of their patients able to walk; and 59% using arm support.

Zhang et al. [24] evaluated the results of arthroplasty in 19 cases with 14 cemented 3 cement less, and 2 hybrid hip replacement after failed internal fixation of intertrochanteric fractures and they reported 47% incidence of complications with 31% intraoperative fracture and 16% postoperative dislocation. Clinically, the mean Harris hip score after follow up of 2 years was 79.8.

The decision using total hip replacement in this work was due to acetabular damage either due to screw penetration, chondrolysis, or present osteoarthritis. The selection of cemented or uncemented stem was according to bone stock remained and stability of stem in press fit during reaming. Long stem was used when trochanteric area was comminuted and prosthesis not contained in proximal calcar part.

In this work, good results may be due to the relative young age of patients and the selection of the suitable technique for the right patient. The survival rate in6 years were 95% as two patients required revision. Dislocation rate was 5% in this series, closed reduction was done in both

cases. The Harris hip score improved from 24 preoperative to 88 postoperative with no or mild residual pain in 18 patients (45%), trochanteric pain in six (15 %), and anterior thigh pain in 14 patients (35 %). In two patients (5%) sever pain was found, in one patient septic loosening and revision was done at 24 months postoperative (Figure 6), the other one had aseptic loosening but refused revision.

Conclusion

Total hip arthroplasty is a good salvage procedure after failed internal fixation of trochanteric femoral fractures. Individual selection of the implant depends upon the age of patient, level of activity, the bone stock of proximal femur, and the condition of the acetabulum. To maintain stability, reattachment of the greater trochanter should be done. To avoid intraoperative fractures of osteoporotic bone, dislocation of the hip should be very careful.

COI Statement: This paper has not been submitted in parallel. It has not been presented fully or partially at a meeting or podium or congress. It has not been published nor submitted for consideration beforehand.

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ORIGINAL ARTICLE

Demographic Profile of Hand Injuries in North India: A Tertiary Care Hospital Experience.

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Abstract

Introduction: Hand injuries are the most complex injuries when compared to other bodily injuries. A better understanding of the biological, behavioral, and socioeconomic risk factors that are associated with hand injuries is therefore needed. This data can help identify individuals at risk and define preventive measures to help reduce the incidence.

Material and Methods: We present a study of 350 consecutive patients of hand injury treated between 2017- 2018. The demographic profile of the patient along with the type & cause of the injury sustained, hand dominance, type of procedure, and requirement of hospital administration was extracted from hospital records.

Results: 159 (45.5%) of the patients were in the age group of fewer than 20 years. Out of the 350 patients, 288 (82%) were male. 302 (86%) patients were right-handed. The most common mode of injury was machine injury in 205 (59%) patients. 181 (52%) patients had crush injury, 107 (31%) had the sharp cut injury, and 32 (9%) had blast injury. 94 (27%) patients needed hospital admission for management. 119 (34%) patients had the injury to the thumb, 89 (25%) had injury to the middle finger. Primary suturing was done in 116 (33%) patients, tendon and nerve repair in 209 (60%), and 177 (51%) patients respectively.

Conclusions: The study describes the demography and etiology of the cases of hand injury. The study has a limitation of having absence of assessment of functional outcome. There is a necessity of hand trauma registry to quantify the burden of hand injuries and formulate a prevention strategy at the national level.

Keywords: demography, hand injury, tendon injury, neurovascular injury,

Introduction:

The hand has an intricate design and is a very peculiar work of anatomy. Any injury to the structures of the hand results in the person becoming handicapped. To minimise this risk, even the smallest hand injuries require good medical evaluation and care. Injuries of the hand need fast and accurate initial evaluation, which allows for medical treatment to be started quickly so that the complications can be reduced.

Hand injuries are the most complex injuries when compared to other bodily injuries [1].A better understanding of the biological, behavioral, and socio-economic risk factors that are associated with hand injuries is therefore needed. This data can help identify individuals at risk and define preventive measures to help reduce the incidence [2, 3].

In today's societies many daily activities require highly skilled hand work. Hand injuries thus cause major problems for individuals. Hand injuries that require acute medical attention usually deserve special attention as these injuries place a large burden on the healthcare system. There is however limited epidemiological information on hand injuries.

Most studies present in Indian literature are limited to a few centres. The study describes the demography and etiology of the cases of hand injury. It is important to establish targeted strategies for the prevention of hand injuries, thus more information on the occurrence and characteristics of hand injuries is required at a national level through various centres.

Original article, no submission or publication in advance or in parallel

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Material & Methods:

We present a study of 350 patients of hand injury treated over a period of 2 year. Review of data of patients treated for acute hand injuries in the department was done. Demographic profile of the patient along with other data like the type & cause of injury sustained, hand dominance, injured hand, type of procedure was extracted from hospital database. Consent was taken. Departmental Review Board Clearance was done.

This is a Retrospective observational study conducted in a tertiary care hospital in north India from June 2017 to May 2019. All patients satisfying the inclusion criteria were included in the study.

Inclusion Criteria:

a) Hand injuries distal to the wrist.

Exclusion Criteria:

a) Patients with hand injury due to burns.

b) Patients with previous chronic upper limb disease like carpal tunnel syndrome, neuropathy etc.

c) Hand injuries at wrist or proximally.

Results:

Of the 350 patients' 294 (84%) of the patients were below 40 years of age. 159 patients were within 20 years of age. 135 patients were between 20-40 years of age and remaining 56 patients were more than 40 years old (figure 1). Thus showing a huge number of young adults falling victim to injuries.

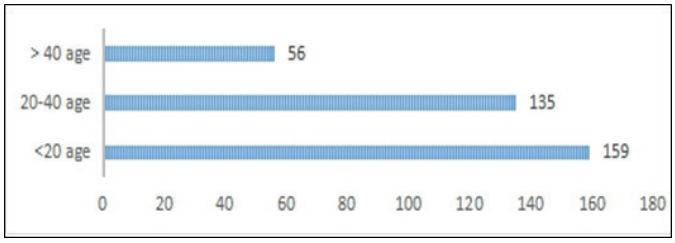


Figure 1: Age Distribution

Of the 350 cases, 288 (82%) patients were male, while 62 (18%) were female (figure 2).



Figure 2: Sex Distribution

302 (86%) of the 350 patients injured were right hand dominant (figure 3).

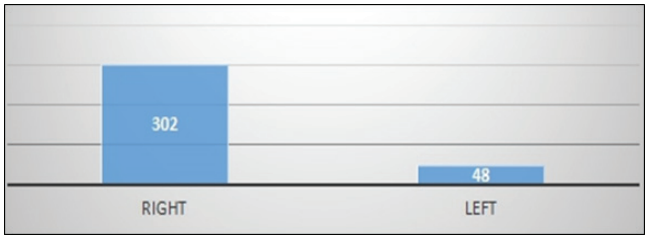


Figure 3: Dominant Hand

217 (62%) of these 350 patients had suffered injury to the right hand (figure 4).

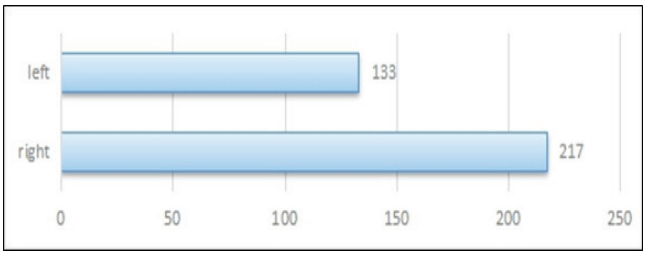


Figure 4: Injured Hand

256 (73%) of the patients did not require admissions and were treated as outpatients while rest 94 (27%) required admission for their injuries (figure 5).

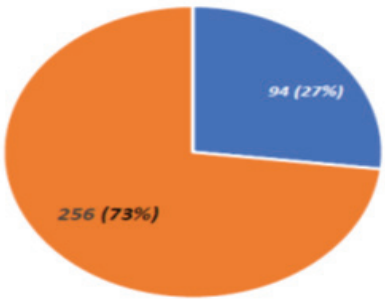


Figure 5: Hospital Admission

The most common mode of injury was machine injury (WMI) in 205 (59%) patients followed by road traffic accidents (RTA) in 111(32%), blast or firearm injury (B/FAI) in 32 (9%) and in human and animal bites (H/AB) in 2 patients (figure 6).

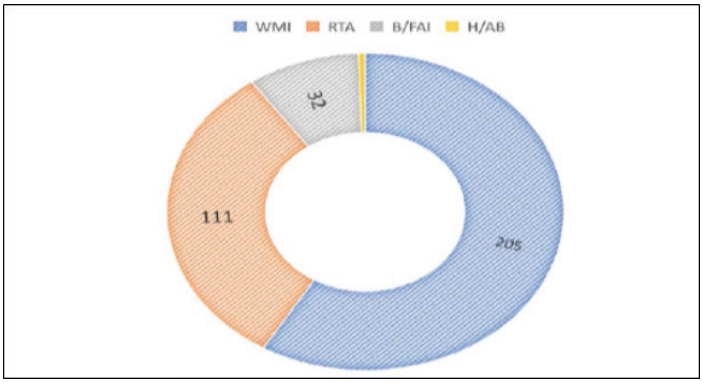


Figure 6: Mode of Injury

Crush injuries(CI) formed majority of the type of injuries seen in 181 (52%) patients followed by sharp cuts (SC) in 107 (31%), blast injuries (BI) in 32 (9%), avulsion (Av) and degloving (Deg) in 15 patients each (figure 7).

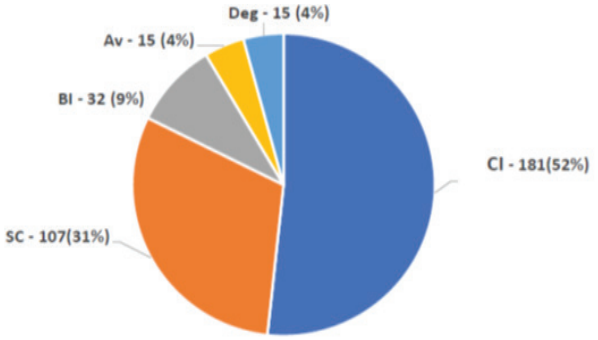


Figure 7: Type of Injury

The most common finger injured was thumb seen in 119 (34%) followed by middle (89), index (76). ring and little fingers were involved in 52 and 14 cases respectively (figure 8).

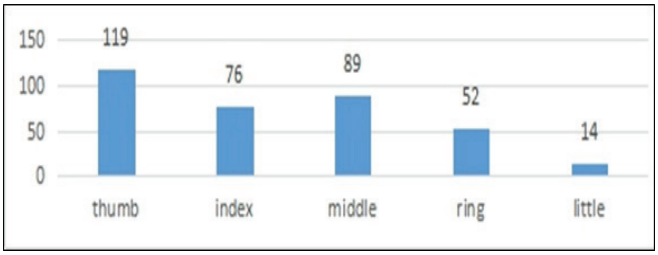


Figure 8: Finger Injured

Most of the injuries and multiple digit injuries and Primary suturing was done in 116 (33%) patients, the skin grafting in 42 (12%), flap coverage in 96 (27%) patients. 209 (60%) patients required tendon repair and 177 (51%) required nerve repair. Fracture fixation was done in 112 (32%) patient. Successful revascularisation was done in 65 (19%) patients. 118 (34%) patients were managed with stump closure (figure 9).

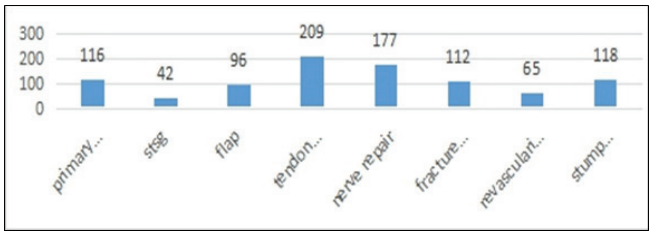


Figure 9: Treatment Given

Discussion

Epidemiological studies are necessary to determine the requirements of any population to improve the quality of life and health of the citizens of any country.

The epidemiology of hand injuries can provide information about how people are injured, mode and type of injuries and susceptible groups. Hand injuries are considered to be the most frequent body injuries [4], the treatment of which is of long duration and cause social and economic problems.

Trauma to the hand usually presents with multiple soft tissue and bony injuries which are often unrelated. It is important to approach the injured hand with a logical and systematic diagnostic plan which allows the surgeon to recognize the location and severity of the injury and deliver comprehensive primary treatment accordingly. Understanding the mechanism of trauma and the injury patterns will help in guiding surgical reconstruction, rehabilitation, and prevention of hand injuries [5].

It has always been challenging to assess and treat crushed hand. These are combined injuries that can lead to sub optimal functional recovery based on the severity of the tissue trauma [6]. Spontaneous and aggressive initial management afford the best chance to optimize results. The basis of primary care is the identification of the pathoanatomy, assessment of the magnitude of the injury, and focused treatment in the context of the complete injury.

The spectrum of hand injuries can range from mild lacerations of fingers to multiple finger amputations and mutilated hand [7]. The medical expenses, loss of time and wages increase dramatically for severe type of injuries. In addition to this, there is tremendous physical and emotional pain.

Hand injuries are one of the common causes of presentation in emergency departments. Patients who require plastic surgical unit care [8] for specialist surgery can be easily identified by a careful history examination and plain X-rays. Criteria for transfer to plastic surgery unit include injury to nerves, tendons or joints, skin loss or complex fractures, injuries requiring skin grafting or reconstruction, and burn injuries [9].

In our study, of 350 cases, 288 (82%) patients were male and 62 (18%) were female. This finding is consistent with most of the other studies that have been conducted. Packer and Shaheen [10] found out that most of the fracture cases in their study were found to be male patients between the age group of 10 to 40 years. Gupta et al [11] in their study, found an expected male dominance in economically viable individuals of 21 to 30 years, which formed 50% of the patients of which 22.9% were labourers and students each.

In this study, we found that among the total 350 patients, 159 were in the age group of <20 years. Trybus et al [12] found the average age to be 37.0 years (±15) in their study.32 patients were children with blast injuries. Other patients were mostly unsupervised children with chara cutting injuries. The chara cutting injuries in children was more as the machine are available at homes and children are usually unsupervised. Packer and Shaheen [10]. found that hand fractures in their study were most commonly found in the age group of 10 to 40 years.

302 (86%) patients' sustained injuries were right dominant hand. This was similar to the findings of another

study. Gupta et al [11] also found in their study that the majority of hand injuries were sustained in the dominant hand. 217 (62%) of these 350 patients had suffered injury to the right hand and 133 (38%) had injuries to their left hand.

Hung et al [13]documented that in their study, crush injuries occurred in 37.8% of the patients. Bazroy et al also conducted a study in Pondicherry, India in a glass bottle manufacturing plant. They found that the commonest types of injuries were cuts and lacerations (50.1%). In this study we found that 181 (52%) of the total hand injuries were crush injuries which was also the dominant mode of injury in both genders followed by sharp cuts in 107 (31%) and blast in 32 (9%) patients. Chara cutting hand injuries formed bulk of the cases. The pattern of injury was different compared to injuries presenting to emergency services in the west [14].

In our study, out of the total cases of 350, 94 (27%) patients were admitted, 256 (73%) did not require admission to the hospital and were treated on an out-patient basis or they left against medical advice. Larsen et al [15] found in their study that only a small proportion of the victims were admitted into hospital. They went on to state that most of the injuries in their study were due to leisure activities and the severe injuries were due to occupational accidents.

The most common finger injured was thumb seen in 119 (34%) followed by middle (89) as compared to index finger seen in the study by Gupta et al. [11] Banhiam Carey Kharrngi, Darpanarayan Hazra et al [16] also found index finger to be the most commonly involved finger.

Primary suturing was done in 116 (33%) patients, skin grafting in 42 (12%), flap coverage in 96 (27%) patients. 209 (60%) patients required tendon repair and 177 (51%) required nerve repair. Fracture fixation was done in 112 (32%) patient. Successful revascularisation was done in 65 (19%) patients. 118 (34%) patients were managed with stump closure. Bharghav desai et al [17] showed that out of the 129 patients that needed operative intervention; 27(20.93%) required amputation whereas rest 102(79.07) required some orthopaedic intervention.

It is noted that the psychological impact of a visible injury is significantly higher than non-visible disability. Plastic surgeons have a huge role in reducing the patient's psychological stress by correcting and improving the appearance of the injured hand wherever possible. However, this parameter was not included in our study.

Improvement in health and safety practices and legislation's have reduced the incidence of mangling hand injuries in developed countries, however in developing countries, such recommendations are often flaunted.

The pattern of hand injuries in the developed world differs from the pattern of hand injuries in the developing world. In developed countries, leisure activities and sports are the leading cause of hand injuries. In developing countries like India, the leading cause of hand injuries is by far occupational injuries.

Most significant limitation of this study was the lack of proper and adequate follow up of the study subjects. These studies require meticulous documentation. There may be a need for multicentric data with formation of unique code system for simple documentation similar to the ICD system for hand injuries.

Hand injuries are seen to occur in high numbers in the young population causing significant morbidity. Thus a need for preventive strategies is required to minimize it. There should an early response to such injuries with the aim to restore maximum hand function and sensation. To minimize these consequences, emphasis should be put on the workplace, which could reduce the incidence of hand injury by targeting some of its preventable causes. Better training of surgeons in hand care to offload the burden on central institutions [18].

Furthermore, improving access to specialist hand surgery care could help to promptly and appropriately treat those injuries that cannot be prevented.

Hence in conclusion, hand injuries are important because of their consequences, such as permanent disability and their high treatment costs. This study points out many important risk factors, modes and types of injuries and grade of injury. The inclusion of medical records from hospital data into national database will help in the prevention of these injuries, and help in development of diagnosis, treatment and rehabilitation.

Conclusions:

The study describes the demography and etiology of the cases of hand injury. The study has a limitation of having absence of assessment of functional outcome. There is a necessity of hand trauma registry to quantify the burden of hand injuries and formulate a prevention strategy at the national level.

COI Statement: This paper has not been submitted in parallel. It has not been presented fully or partially at a meeting or podium or congress. It has not been published nor submitted for consideration beforehand.

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ORIGINAL ARTICLE

The Benefits of early Extubation in OR and ICU after Cardiac Surgery

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Abstract

Objective: Operating room (OR) extubation after adult cardiac surgery with cardiopulmonary bypass CPB is rare. We examined the outcome, factors and benefits of OR extubation.

Methods: We operated 60 patients in German Hospital Tirana, from January 2019 to September 2020, who had undergone CABG cardiac operations: 52 patients, mitral valve repair 5 patients, aortic stenosis 1patient, Bentall procedure 1 patient, left atrial myxoma 1 patient. The patients age was from 46-82 years old, there were 24 female patients and 36 male patients, 24 diabetic patients, 36 non-diabetic patients, in all cases we did not apply epidural anesthesia.

Anesthesia was used with low doses of fentanyl. in combination with propofol, sevoflurane. In all cases neostigmine was used for decurarisation.

The quality and depth of anesthesia was assessed with obvious signs such as tachycardia, hypertension, sweating. Endogenous stress was also assessed by monitoring glycemia during the intervention.

As extubation criteria were assessed the patient's consciousness, respiratory mechanics, hemodynamic stability, diuresis, bleeding from drains.

Results: 16 patients were extubated in the OR and 44 patients were extubated 15-20 minutes after the intervention in ICU. There was no reintubation. 2 patients were transferred immediately from OR to the repart. 35 patients were transferred to the ward 3-4 hours after extubation. 23 patients were transferred to the ward the next morning. Patients left the hospital after 5-7 days.

Conclusions: Extubation in the OR in the early postoperative period has now become a routine in all specialized clinics. The time spent in the ICU is very low and the day spent in the ward was 5-7 days. The benefit is in the best and fastest activation of patients in the early postoperative period as well as in reduced intervention costs.

Keywords*:* OR extubation, Early extubation, Cardiac surgery, Benefits

Abbreviations: Operating Room - OR; Cardiopulmonary Bypass – CPB; Coronary Artery Bypass Graft – CABG; Intensive Care Unit - ICU. The Society of Thoracic Surgeons – STS; Adult Cardiac Surgery Database – ACSD; Aortic Valve Replacement – AVR: Hematocrit – Hct; Calafiore - intermittent warm BCP; Crystalloid Cardioplegia - CCP; Blood Cardioplegia – BCP; Mitral Valve Replacement – MVR.

Introduction

Early extubation of Coronary Artery Bypass Graft (CABG) patients has been shown to reduce costs as well as intensive care unit and hospital lengths of stay [1.2]. It has been a focus of several studies to improve outcomes in the care of CABG patients. According to an analysis from the Society of Thoracic Surgeons Adult Cardiac Surgery Database (STS ACSD) there is a significant variation in post-operative ventilation times in CABG patients providing an opportunity for quality improvement across many institutions [3]. Most studies have focused on CABG patients and few include the impact of early extubation protocols on patients undergoing valve or combined valve and CABG procedures. Prolonged ventilation, defined in the STS ACSD as intubation longer

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than 24 h, is now one of five morbidity measures utilized in composite scores for evaluating performance of isolated CABG, isolated aortic valve replacement (AVR), AVR plus CABG, and mitral or mitral plus CABG procedures [4.5]. In this report we outline our early extubation protocol and have found that it can be effectively adopted for patients having valve and combined CABG and valve procedures as well as isolated CABG procedures.

Methods and Results

We applied the early extubation of patients undergoing cardiac surgery at German Hospital Tirana and the postoperative results were satisfactory.

We operated 60 patients from January 2019 to September 2020, who had undergone CABG cardiac operations 52 patients, mitral valve repair 5 patients, aortic stenosis 1patient, Bentall procedure 1 patient, left atrial myxoma 1 patient.

The patients age was from 46 - 82 years old, there were 24 female patients and 36 male patients, 24 diabetic patients, 36 non-diabetic patients, in all cases we did not apply epidural anesthesia. All patient data are summarized in the table below.

We used anesthesia with low doses of fentanyl 5-6 mcg / kg / total fractionated in induction of anesthesia, sternotomy and at the time of insertion into the pump. 2.5 mg Midazolam, 120-180 mg Propofol and 8 mg Pancuronium were used to induce anesthesia.

Maintenance anesthesia was done with Propofol 0.5 mg / min in combination with sevoflurane.

The quality and depth of anesthesia was assessed with obvious signs such as tachycardia, hypertension, sweating. All patients who underwent surgery did not have tachycardia, hypertension and sweating during the anesthesia. During intervention was performed hypnosis, analgesia and satisfactory relaxation. Endogenous stress was also assessed by measuring glycemia during the intervention. Glycemic values in non-diabetic patients ranged from 90-115 mg / dl, while glycemic values in diabetic patients ranged from 150-170 mg / dl.

Calafiore blood cardioplegia was used in all patients in normothermia in most cases. In 3 patients was used moderate hypothermia 34-35 ° C throughout the intervention. We took care in the administration of the amount of fluid intake, 1500 ml in prime and 500 ml during the intervention used by the surgeon.

During CBP the value of hematocrit (Hct) was kept above 25% and good perfusion flows of 2.4 l / min / m2 were maintained.

Urine flow during the intervention was maintained above 200 ml / h using 10 mg Lasix in most cases.

In some cases, positive inotropes (adrenaline, dopamine, dobutamine, noradrenaline) were used for CBP cleavage in minimal doses, mainly in patients with EF <40%.

As extubation criteria were assessed the patient's consciousness, respiratory mechanics, hemodynamic stability, diuresis, bleeding from drains. In all cases neostigmine was used for decurarisation, 10 mg Morphine and 1000 mg Analgin with electrical syringe were used for antidolorific therapy. In some cases, paracetamol 1000 mg iv and non-steroidal anti-inflammatory drugs were used.

16 patients were extubated in the OR and 44 patients were extubated 15-20 minutes after the intervention in ICU. There was no reintubation. 2 patients were transferred immediately from OR to the repart. 35 patients were transferred to the ward 3-4 hours after extubation. 23 patients were transferred to the ward the next morning. Patients left the hospital after 5-7 days.

Discussion

Early extubation following cardiac surgery is not a novel concept. It was described as early as 1974 by Midell and colleagues in 100 consecutive patients undergoing AVR, MVR, and combined AVR and MVR. Ninety of their patients were able to be extubated in the operating room or within two hours of arrival in the ICU, challenging the standard practice of the time. Morphine was avoided during induction or during the procedure and was used sparingly in the postoperative period. Patients were awakened at the end

60 Patients	N: Patients	Weight/kg	Sex/M	Sex/F	Age	Diabetic/patients	Non- diabetic/patients	Operation time/min	CBP time/min	Aortic clamping time/min	N: Cardioplegia	Prime/ml	Diuresis during CBP/ml	Lasix/mg	Drugs after CBP	Nitro-glycerine after CBP	OR Extubation	ICU 15-20/min extubation
CABG	52	83	31	21	58	23	29	125	52	33	1.2	1500	500	10	15	48	11	41
Aortic stenosis	1	75	1	0	82	0	1	122	42	29	1	1200	300	0	0	1	1	0
Bentall operation	1	78	1	0	48	0	1	140	80	70	2	1500	400	10	0	1	1	0
Mitral valve repair	5	80	3	2	52	1	4	117	45	32	1.2	1500	300	0	1	3	2	3
Left atrial myxoma	1	72	0	1	53	0	1	102	35	26	1	1500	200	0	0	0	1	0

of the procedure, given what today would be considered a "spontaneous breathing trial", and extubated with satisfactory clinical assessment and arterial blood gases. In the early days of cardiac surgery, the routine use of mechanical ventilation was considered a mainstay in the treatment of respiratory failure following extracorporeal circulation. As many of the causes of post perfusion respiratory failure were eliminated, the need for prolonged ventilator support also decreased. Yet it was still standard practice to sedate and ventilate cardiac surgical patients overnight to minimize myocardial oxygen demand and resulting ischemia [6]. In 1977, *Prakash and colleagues* demonstrated that 123 of 142 adult cardiac surgical patients were able to be extubated in the operating room or within three h of admission to the recovery room [7]. This included patients who had isolated valve replacements and coronary artery bypass procedures. Only five of the 123 patients were re-intubated. They also utilized a spontaneous breathing trial and established criteria for continued mechanical ventilation. If adequate ventilation was maintained with a stable end title CO_2 of less than 5.5% and other hemodynamic criteria were met their patients were extubated. The most common indication for continued mechanical ventilation was low mixed venous oxygen saturation and an elevated left atrial pressure of greater than 20 torr. A controlled randomized trial comparing early extubation within 2 h–4 h to late extubation 18 h–21 h following coronary artery bypass surgery was published in the Anesthesia literature in 1980 [8]. This study demonstrated significantly less cardiopulmonary morbidity in patients who were extubated early. Supporting early extubation of patients following coronary artery bypass surgery was the well described evidence of the pulmonary and cardiac physiologic benefits on hemodynamic, and ventricular performance [9.10]. Another prospective, randomized, controlled trial by *Cheng et al*." evaluated the outcomes and safety of early extubation after coronary artery bypass grafting [2]. Modifying fentanyl dosing during surgery enabled them to safely extubate 85% of their patients assigned to the early extubation group. They demonstrated an improvement in postextubation intrapulmonary shunt fraction and a reduction in ICU and hospital length of stay in these patients. Weaning the cardiac surgeon and the care team from the obligatory overnight use of mechanical ventilation has taken more time. *The STS ACSD* was utilized to study 274,231 patients who underwent elective isolated CABG from 1,008 centers to assess postoperative ventilation time in 2009 and 2010 [3]. In this multi-institutional study of uncomplicated patients who were ventilated for less than 24 h, there was substantial variation in ventilator time across centers. Ventilation times were 1.8 times higher in centers above the 90th percentile compared to those below the 10th percentile and that difference was not accounted for by patient characteristics after adjusting for case mix. This study was published in 2013 and was a clarion call for a quality improvement initiative to strive for the shortest possible ventilation times for all patients. The institution of an effective rapid wean program for cardiac surgical patients is a multi-disciplinary team effort that includes cardiac surgeons, anaesthesiologists, physician assistants, intensive care unit (ICU) nurses, and respiratory therapists. When we evaluated our traditional weaning process, we recognized that one of the impediments to rapid weaning was the need for an individual order for each step of the process. We eliminated that by establishing a protocol with a single order set to initiate the Cardiothoracic Care Unit Rapid Wean Protocol on arrival from the operating room. We also recognized the importance of consistent application of objective criteria for determining the readiness to wean and extubate as outlined in Appendix 1. A Cochrane review and meta-analysis of weaning protocols in critically ill patients has concluded that weaning protocols decrease total duration of ventilation, weaning duration, and length of stay in the intensive care unit [11]. However, these weaning protocols were not specific for cardiac surgery. A standardized protocol for decreasing postoperative mechanical ventilation for cardiac surgical patients is the framework that drives the process. These criteria provide a framework for our care team to proceed independently and proactively with weaning and extubation. The intensive care nurses as well as the respiratory therapists become the drivers of the process [12]. We recognize a major weakness of this manuscript lies in its retrospective and non-randomized design. In addition, we did not attempt propensity matching of the patients. Our goal was to implement a rapid wean protocol for all of our cardiac surgical patients and measure how well we achieved that process as a quality improvement initiative. We did not measure outcome variables in our assessment of this process improvement project but plan to do so. Other studies have demonstrated improved clinical outcomes as well as improved utilization of health care resources can result from early extubation of cardiac surgical patients [1.2]. We embarked on this quality improvement initiative and have demonstrated that a rapid wean protocol can be safely implemented for patients undergoing coronary artery bypass surgery, isolated valve surgery, and combined CABG and AVR procedures. It requires a multidisciplinary team effort with modification of the anesthetic management, adjustments in postoperative pain management, and protocol driven weaning parameters. Most importantly it requires a team effort to insure effective implementation.

Conclusions:

Extubation of patients in the operating room and in the early postoperative period has now become routine in all specialized clinics. The time spent in the ICU is very low and the length of stay in the ward is 5-7 days. The benefit is the avoidance of complications that occur from postoperative respiratory assistance, better and faster activation of patients in the early postoperative period as well as in the reduced costs of the intervention.

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ORIGINAL ARTICLE

Relation between Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio and Cerebral Infarct Volume in patients with Ischemic Stroke

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Abstract

Objectives: The activation of inflammatory processes in ischemic stroke might be important for the pathophysiological processes of ischemic stroke. The correlation between the Neutrophil to Lymphocyte Ratio (NLR), Platelet to Lymphocyte Ratio (PLR), and stroke volume is increasingly being recognized as a prognostic biomarker for patient outcome after an ischemic stroke incidence. This retrospective study aimed at determining if there is existed a correlation between the NLR, PLR, and stroke volume in patients presenting with ischemic stroke at the emergency department. The results will aid emergency doctors to gain an understanding of how to rapidly identify the most high-risk patients based on the NLR and taPLR obtained from routine blood tests permitting rapidly therapeutic interventions and better long-term survival outcomes for patients with ischemic strokes.

Methods: A retrospective study was performed between May 2016-2019. Patients 18 years and older of both genders presented to the emergency department with symptoms of ischemic stroke with a time of onset of symptoms within the last 24 hours of whom complete blood count (CBC) tests were conducted and ischemic stroke was confirmed by Diffusion-weighted Magnetic Resonance Imaging (DWI-MRI) were enrolled. NLR and PLR were calculated from CBC tests and ischemic stroke volume was measured in mm^3 using Manual Segmentation Process.

Results: A total of 489 patients were enrolled in this study of which 266 (54.5%) were male and 223 (45.6%) were female. Was observed a statistically significant correlation between the ischemic stroke volume and NLR while no significant correlation was observed between stroke volume and PLR.

Conclusion: There is a significant weak positive relationship between NLR and ischemic stroke volume. NLR is significantly correlated with cerebral ischemic stroke volume and thus can be utilized as a guide by emergency doctors in the emergency department to predict the severity and the outcome of patients diagnosed with ischemic stroke.

Keywords: ischemic stroke, Neutrophil, Lymphocyte, Platelet, Emergency

Introduction

Strokes are one of the most common causes for mortality and the third leading cause of morbidity worldwide. Among all strokes, ischemic stroke accounts for approximately 80% to 85% of mortality in patients, and is characterized by the disruption of cerebral blood flow [1]. It has been suggested that inflammatory response is implicated in all stages of ischemic stroke. Thrombolytic therapy is the treatment of choice for ischemic stroke. However, risks associated with this form of therapy is intracranial bleeding and as such, only a limited number of patients will benefit from thrombolytic therapy [2]. To this effect, it is of utmost important to determine risk-stratification biomarkers that can be utilized for the prognostic significance after an acute ischemic stroke event. The most commonly utilized markers for patient outcome after an episode of ischemic stroke are the stroke volume and the National Institute of Health Stroke Scale (NIHSS) [3]. Atherosclerosis has been established to occur due to inflammatory processes and several inflammatory biomarkers have been identified that can be utilized to predict patient outcome after the occurrence of an ischemic stroke [4]. Elevated NLR has been associated

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with an adverse outcome after a cardiovascular event or surgery as well as an acute kidney injury and remote diffusion weighted image lesions in acute intracranial haemorrhage [5]. Increased NLR levels have additionally been observed post-operationally in diabetes patients after metabolic surgery and studies conducted by Luo et al. (2020) demonstrated that NLR can serve as a prognostic marker in acute minor stroke or transient ischemic attack with elevated levels of NLR being correlated with short term unfavourable functional outcome in patients diagnosed with transient ischemic stroke [6]. Studies conducted by Fang et al. (2017) demonstrated that elevated NLR is of prognostic significance and can predict the survival outcome of patients that have been diagnosed with non-atrial fibrillation caused by an ischemic stroke [4]. A meta-analysis conducted by Song et al. (2019) demonstrated that higher NLR levels were correlated with an increased risk of ischemic stroke and an unfavourable outcome and increased mortality 3 months after the ischemic event [7]. To this effect this study will aim at determining the correlation between NLR, PLR and stroke volume in patients that presented at the emergency department with an ischemic stroke event.

Materials, method, patient enrolment and data collection:

This retrospective observational study was carried out in the Emergency Department of a tertiary care teaching hospital between May 2016-2019. Patients 18 years and older of both genders diagnosed with ischemic stroke were retrospectively identified based on their medical records. Patients presented to the emergency department with symptoms of ischemic stroke with time of onset of symptoms within the last 24 hours of whom complete blood count (CBC) tests were conducted and ischemic stroke was confirmed by Diffusion weighted magnetic resonance imaging (DWI-MRI) were enrolled. Patients with haematological malignancies, patients with systemic infections or sepsis, patients on steroid therapy and patients receiving chemotherapy or radiotherapy for malignancies were excluded from this study. After excluding 84 patients for the reasons already mentioned a total number of 489 patients were enrolled in this study with 266 males and 223 females. The parameters that has been studied are the Neutrophils to Lymphocyte Ratio (NLR), Platelet to Lymphocyte Ratio (PLR), ischemic stroke volume measured by (mm^3), the anatomical location of the stroke (anterior vs posterior circulation stroke) and the gender of the patient. The patient's parameters were revised from hospital medical electronic records. DWI MRI's were revised from INFINITT PACS 7.0 software. The stroke volume was analysed by Manual Segmentation Process using ITK- SNAP 3.8.0 software and this has been done by a well-trained radiologist. SPSS Statistics 23.0 package program was used for statistical analysis. This study was approved in 10.07.2019 by the local ethics committee (Ethics Committee Ruling number (2019/514/157/1).

Results

1. ***Determination of a correlation between ischemic stroke volume, NLR and PLR:***

A total of 489 patients were enrolled in this study of which 266 (54.5%) were male and 223 (45.6%) were female. Anterior circulation stroke was identified in 318 (65%) of the study participants while a posterior circulation stroke was identified in 171 (35%) of the participants with both males and females in each group. A mean stroke volume of 569.28±777.29 was recorded in all 489 patients with a minimum of 0.001 and a maximum of 2249.0. A mean NLR (minimum=0.67 and maximum=24.67) of 4.12 ±3.42 and a mean PLR (minimum =0.01 and maximum =1098.57) 163.12 ±94.41 was recorded for all patients as well. A summary of the results is shown in (Table 1). Kendall's Tau b correlation analysis was performed to reveal the presence of the relationship between stroke volume and NLR and PLR variables due to the abnormal distribution of all variables. Kendall's Tau B correlation analysis revealed a negative weak relationship between stroke volume and NLR variables ($r=-0.106$, $p<0.05$). This relationship between stroke volume and NLR is statistically significant. The correlation coefficient between stroke volume and PLR variables was found to be $r = – 0.055$ and this relationship was not statistically significant ($p> 0.05$) (Table 2).

Basic Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Stroke volume	489	0.001	2249.0	569.2883	777.29
NLR	489	0.67	24.67	4.12	3.42
PLR	489	0.01	1098.57	163.239	94.41

Table 1: The mean of the Stroke volume, NLR and PLR as a function of the minimum and maximum values in 489 patients.

		NLR	PLR
Stroke volume	Kendall's Taub Correlation Coefficient	-.106*	-.055
	P value (2-way)	.002	.100
	N	489	489

Table 2: Kendall's Tau b correlation analysis to determine the relationship between stroke volume, NLR and PLR variables (denoted statistical significance at levels $p < 0.05$)*

2- Correlation between stroke volume, NLR and PLR as a function of the anterior and posterior circulation.

A measure of the stroke volume in terms of the anterior and posterior circulation demonstrated that a mean stroke volume of 395±722.22 for the anterior circulation was calculated for 318 patients while for 171 patients, the mean stroke volume for posterior circulation was estimated at 892.099±774.94519 (total = 569.28±777.29468). The NLR in function of anterior circulation was 4.0063 ± 3.17691

while the mean posterior circulation was recorded as 4.3531± 3.84544 with a total of 4.1276± 3.42563 for all 489 patients being recorded. In terms of the PLR, a mean anterior circulation of 163.302± 96.26 was calculated for 318 patients while a mean posterior circulation of 163.1223±91.14 was recorded for 171 patients (total =163.29±94.41). Results shown in (Table 3).

Circulation Type		Stroke volume mm^3	NLR	PLR
Anterior Circulation	Mean	395.7013	4.0063	163.3023
	N	318	318	318
	Std. Deviation	722.22478	3.17691	96.26835
Posterior Circulation	Mean	892.0994	4.3531	163.1223
	N	171	171	171
	Std. Deviation	774.94519	3.84544	91.14514
Total	Mean	569.2883	4.1276	163.2394
	N	489	489	489
	Std. Deviation	777.29468	3.42563	94.41467

Table 3: The mean stroke volume, NLR and PLR as a function of the anterior and posterior circulation.

a- ***Correlation between stroke volume of the anterior circulation, NLR and PLR.***

The relationship between stroke volume of anterior circulation, NLR and PLR was calculated and analyzed by calculating Kendall's Tau b correlation coefficients due to the persistence and abnormal distribution of the variables. The correlation coefficient between the posterior circulation stroke volume and NLR was estimated to be r=-0.101 demonstrating a weak correlation between both variables which was statistically significant ($p<0.05$). Kendall's Tau b correlation coefficient indicating the direction and level of relationship between the anterior circulation stroke volume and PLR was found to be r=-0.032. The relationship between the anterior circulation stroke volume and PLR was not statistically significant ($p> 0.05$) (Table 4)

		NLR	PLR
Anterior Circulation Stroke volume	Kendall's Taub Correlation Coefficient	-.101*	.032
	P value (2-way)	.020	.457
	N	317	317

*Table 4: Kendall's Tau b correlation coefficient between anterior circulation stroke volume and NLR and PLR. A * denoted statistical significance with ($p<0.05$)*

b- ***Correlation between stroke volume of the posterior circulation, NLR and PLR***

The relationship between stroke volume of posterior circulation, NLR and PLR was calculated and analyzed by calculating Kendall's Tau b correlation coefficients due to the persistence and abnormal distribution of the variables. The correlation coefficient between the posterior circulation stroke volume and NLR was estimated to be r=-0.147. As such existed a weak, negative correlation between the posterior circulation stroke volume and NLR and this was statistically significant ($p<0.05$). The correlation coefficient between the posterior circulation stroke volume and PLR was found to be r= -0.087 and it was not statistically significant ($p>0.05$) (Table 5).

		NLR	PLR
Posterior Circulation Stroke volume	Kendall's Taub Correlation Coefficient	-.147*	-.087
	P value (2-way)	.006	.105
	N	174	174

*Table 5: Kendall's Tau b correlation coefficient between posterior circulation stroke volume and NLR and PLR. A * denoted statistical significance with ($p<0.05$)*

Discussion

In this retrospective study of patients presenting with ischemic stroke symptoms at the emergency department, we demonstrated that there is a significantly negative correlation between stroke volume and NLR. It was observed a statistically significant correlation between the stroke volume (in anterior and posterior stroke circulation) and NLR. The correlation coefficient of Kendall's Tau b, which shows the relationship between the anterior and posterior circulation stroke volume and NLR, denoted a significantly weak level of correlation which is significant. As NLR increases, stroke volume decreases or the reverse holds true wherein the, stroke volume increases while NLR decreases. On the other hand, it was observed that the relationship between the stroke volume (in anterior and posterior circulation stroke) and PLR was not statistically significant. Increased NLR has been reported to be correlated to poor patient outcome and a significant predictor of short-term mortality in patients presenting with an ischemic stroke episode [8-12]. Several studies have established the function of the inflammatory system in the different stages of acute ischemic stroke. During an ischemic episode, the release of proinflammatory cytokines and the recruitment of immune cells at ischemic sites might be responsible for secondary brain lesions [13]. Neutrophils are the primary immune cells that are most often recruited to brain lesions. These neutrophils exacerbate brain injuries due to their secretion of proteolytic enzymes such as acid phosphatase or reactive oxygen species (ROS) [14]. The relationship between increased NLR and patient mortality might be due to the fact that the NLR might be elevated due to the activation of an inflammatory response to an ischemic stroke episode or it can act as a predictor for the extent and severity of neurological damage due to the presence of necrotic tissue. The early stratification of patients diagnosed with ischemic stroke is essential for the determination of the best course of treatment for patients leading to improved patient outcome. NLR is an efficient biomarker in terms of stroke volume and

can be utilized to predict patient outcome after an ischemic episode. A higher NLR might be indicative of the severity of an ischemic episode thus highlighted the importance of this biomarker for risk stratification. We thus suggest that NLR might be utilized to identify and stratify high-risk ischemic stroke patients that are in need of endovascular interventions.

Limitation:

There existed several limitations in this study of which was the lack of information on the long-term survival of the patients included in this study. Secondly, despite the fact that patients with active infections and other underlying conditions such as patients with hematological malignancies, patients with sepsis and patients on steroids were excluded from the study, many other diseases that might activate inflammatory processes might have not been considered. Studies with long-term follow-up are thus needed to establish the prognostic significance of NLR in patients diagnosed with ischemic stroke.

Conclusion:

In conclusion NLR is significantly correlated with stroke volume and thus might be utilized as a guide in deciding the therapeutic interventions that are required to treat the patient.

COI Statement: This paper has not been submitted in parallel. It has not been presented fully or partially at a meeting or podium or congress. It has not been published nor submitted for consideration beforehand.

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ORIGINAL ARTICLE

Emergency Medical Care and Management of Sports Injuries on the Football Court

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Abstract

Introduction; Sports medicine is a clinical subspecialty that deals with the examination, monitoring, diagnosis, treatment, and prevention of injuries that occur during sports events, training and physical activities in pre-hospital settings. Managing dramatic situations with minor and multiple injuries is a challenge that requires a quick approach to a dramatic event in managing minor and multiple injuries on the football field and in other sports in support of SHME at pre-hospital and hospital level.

Purpose of the paper. Providing emergency medical care at all basic stages of managing minor and multiple injuries on the football field and in other sports in order to implement BLS, ACLS, BTLS, PTLS, ATLS care measures reducing morbidity, disability, and mortality.

Material and methods. The research is of retrospective, descriptive, qualitative type. The material was taken from the archive of the Emergency Clinic of UCCK for the period January-December 2019. Only the sick or injured in sports matches were taken in the research; Age, gender, type of illness and injury and type of medical care, equipment available, and training and education.

Result. Sports injuries are very costly, and according to the pathology with diseases were 15 cases or 21.4 %, injuries were 55 cases or 78/6 %. Injured by age. The largest number of injured with injuries in the field of football sports the most affected age was the age of 21-25 years with 28 cases or 40.00%, over 25 years were 27 cases or 38.58% and with a smaller number were aged 15-20 years15 cases or 21.42%.

Discussion and conclusions. A very important factor in sports injuries is the provision of optimal medical care for footballers and other sports in head, neck, spine, chest, abdomen, and pelvis and limb injuries and with a joint communication with the cooperation of health care professionals in the selection of priority cases. Education of medical staff, nurses, paramedics with courses, use of medical equipment, BLS, ACLS, BTLS, PTLS, ATLS as well as standard procedures for providing and transporting medical care to the hospital.

Key word. Illness, injury sports, health care, collision football, medical care, EMS.

Introduction

Key Points: Advancing and empowering EMS through emergency medical care law, sports law and possible national intervention strategy is a very important and priority modality to identify intervention needs for the prevention of sports injuries. Research on the mandatory organization of change, education, training and education to prepare and train health care professionals as well as EMS and after training to be able to provide care and emergency assistance at the right time and moment and this approach can provide new research opportunities aimed at preventing injury and disability and morbidity in sports. Our research was sensitizing to create the awareness of sports clubs should always have a medical team during sports events by invoking the law on medical care, the Law on Sports and the national strategy for injury management in sports. From the research, our evidence has been used extensively in sports injury prevention studies, and to evaluate, modify policy interventions in order to function better.

Sports medicine is a clinical subspecialty undertaken in providing emergency medical care to improve their performance of athletes, in recovering from injuries and to prevent further injuries occurring during sporting events, training and physical activities. Emergency sports medicine

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in mass gatherings provides emergency medical care in minor and mass incidents, sympathizers grouped more than 1000 fans in a football match as well as in other sports. The first priority of any dramatic scene where people's lives are threatened,

EMS are obliged to do the assessment of the scene or the scene to be is safe to enter and can continue assessment, triage and treatment according to priorities.

Multiple disaster management which mainly as its factors of origin of disaster are directly related to the behavior of sympathizers in sports fields. *(F-MARC Football Medicine Manual 2nd Edition)*.

Acute and life-threatening illnesses, injuries and poisonings and require attention to initially stabilize the victims before reaching the SHME. Managing dramatic situations with multiple victims is a challenge that requires ongoing study in theoretical, practical and experiential terms in order to provide clues to an event or disaster. EMS should be present at a dramatic event, but of course unlikely to control the situation but should be prepared and provided in advance, EMS in managing multiple victims in football as well as in other sports when the need arises. *(Sports Emergency Care: A Team Approach, Second Edition)*

Managing dramatic situations with multiple and minor casualties in sports fields requires the provision of human resources, EMS medical staff, other support services in the management of minor disasters, and sympathizers**.** *(Lenjani Emergency sports medicine 2018)*.

Factors influencing the management of mass incidents at such sporting events are: Availability, failure to separate sympathizers, failure of match organizers to adhere to guidelines, presence of shutters around the field, EMS access to the field, non-categorization inadequate "risk level" during the match, inadequate access system, insufficient EMS, insufficient barriers, inadequate functioning of the Operations Center, inadequate access system, insufficient trained personnel, inadequate match locations large, the use of tear gas, pre-sale of tickets, matches with large crowds and unreserved seats. *(F-MARC Football Medicine Manual 2nd Edition)*.

The escalation of minor and major risk, based on risk classification is usually based on: mass gathering, the nature of the expected crowd, rivalry of sympathizers, the timing of the football match, the forecast of weather conditions are prerequisites for the occurrence of diseases or injuries can be expected. *(F-MARC Football Medicine Manual 2nd Edition)*.

Moderate risk escalation expected crowds of more than*;* 50% of stadium capacity, sports match time day, week, night, meteorological conditions, hot, cold, snow and humidity, nature of sports match, importance, resentment, known rivalry, expected chaos, alcohol present wet conditions / expected rain, sale of regular or black tickets, seats, reserved seats are prerequisites that can generate obvious and very serious problems. *(F-MARC Football Medicine Manual 2nd Edition)*.

Also other factors that may increase the risk are*;* Insufficient food and drink for spectators, lack of additional capacity, lack of inadequate EMS, lack of emergency exits, lack of adequate signage for basic services in the stadium, provision and intentional use of pyrotechnic devices or tear gas are prerequisites to control the crowd .The number of people seeking integrated EMS during mass gatherings depends on the venue and the legislation of that country and may vary depending on the mass present from 1,000 to 25,000 people or more. *(Lenjani Emergency sports medicine 2018)*.

EMS are obliged within the security perimeter of the stadium and provide medical care including in all areas within the safety zone, scheduled match, lack of previous information, lack of space for action or dysfunctional, lack of adequate communication in the stadium, insufficient education and training of administrators and security staff, insufficient food and drink for spectators.

Mandatory requirements for the football match (obligations from UEFA). The host club is responsible for providing; EMS staff (emergency medicine specialist), at least one stretch for the medical team to arrive at the stadium / hall and until evacuation of the injured player. *(Sports Emergency Care: A Team Approach, Second Edition)*

EMS components to the mass gathered at the scene requires; adequately educated and trained staff, support staff, physician with appropriate equipment and supported by infrastructure, logistics and mobilization of the integrated system of EMS**.** *(Robb Rehberg Sports Emergency Care (A Team Approach) 3rd Edition)*

Medical monitoring and diagnostic equipment which are necessary for the management of diseases and injuries in sports fields which are mandatory and mandatory standards by the home of UEFA and FIFA.

Airway, neck and spinal cord management equipment*;* manual aspirator, respirators, respirator, lubricant, rigid cervical neck support set. *(Lenjani Emergency sports medicine 2018)*.

Respiratory management equipment*;* stethoscope, pulse oximeter, oxygen, trauma masks, tubes, pocket masks. mask with bag and valve, separating device for bronchodilators, portable oxygen cylinders. *(F-MARC Football Medicine Manual 2nd Edition)*.

Circulation management equipment; infusion equipment for IV, external automatic defibrillator (AED), equipment for measuring blood pressure with cuffs of suitable sizes, glucometer / test strip**.** *(F-MARC Football Medicine Manual 2nd Edition)*.

Other (small) equipment; tourniquets, adhesive fixing materials, adhesive fixing materials, light for pupil examinations, IV cannulas of different sizes, solid scissors, disinfectants, disposable gloves, sharp tool boxes, goggles. *(F-MARC Football Medicine Manual 2nd Edition)*.

Emergency medicine bag*;* adrenaline 1: 10,000 injection, antihistamines, hydrocortisone, benzodiazepines,

cardiac life-saving drugs, epinephrin or Anapen® (adrenaline autoinjector), bronchodilators, glycerol trinitrate spray, glucose tablets / gel, emergency diabetic drugs and antiemetic *(F-MARC Football Medicine Manual 2nd Edition).*

Major (mandatory) equipment*;* spinal trauma carrier, vacuum spoon or mattress stretcher and sufficient fixation equipment, complete set of splints, spinal trauma carrier, vacuum spoon or mattress stretcher and sufficient fixation equipment and complete set of splints. *(F-MARC Football Medicine Manual 2nd Edition).*

Recommended: The following items should be available; cricothyrotomy set with disposable scalpel equipment for intubation, anti-hypertensive drugs, basket stretcher or stove, external pacing defibrillator and capnography for CO2 monitoring**.** *(Lenjani Emergency sports medicine 2018).*

Emergency medical care Injuries ABC... and per non-trauma CAB. Victim assessment and primary examination 1 minute. CPR and stabilization 5 minutes, Immobilization and transport to hospital 4 minutes. Manage the airways. Control sprains and immobilize head and neck spine and transport. Treatment of sports injuries as follows; Bubbles - impact broken bone break, ice, ligament, elevation. In open and closed fractures and in DRABC ligament injuries and after the stabilization of the vital signs of the injured, emergency transport with medical care to the hospital. In DRABC sprains and after stabilization of vital signs of the injured, emergency transport with medical care to the hospital. *(Lenjani First aid – AED 2019). (Lenjani Emergency sports medicine 2018).*

In a football stadium is an environment where a large number of people gather, to watch • sports matches, medical emergencies often occur on football fields as well as on sports fields and this component must be managed quickly, effectively and efficiently by EMS. Must be adequate and appropriate medical professionals, cooperative and available to provide necessary medical care. All medical professionals must have education, training and education in a football event *(Czarny JM, et al. J Med Ethics 2010; 36: 203-206. Doi: 10.1136 / jme.2009.033621.)*

Purpose of the research:

Providing emergency medical care, prevention, treatment, is necessary to ensure full recovery in the prevention of other injuries in all the basic stages of managing minor and multiple injuries in football and other sports. BLS, ACLS, BTLS, PTLS, ATLS reducing morbidity, disability and mortality. EMS helps prevent, treat, and speed recovery, reduce pain, and promote movement of all injured muscles, restoring normal function, and preventing any recurrent damage or discomfort to the affected tissue. The purpose is also to coordinate medical actions with experienced multidisciplinary medical teams that include surgeons / emergency physicians, orthopedists, cardiologists, nurses.

Material and Methods:

2.1 Participants

The research material was taken from the archive of the Emergency Clinic of UCCK. The research is of retrospective, descriptive, qualitative type, for the period January-December 2019. Only injuries in the field of football sports were taken into research. In the research were taken 70 cases only sick or injured in sports matches; age, gender, type of illness and injury, medical care, available equipment and education. The average age of males was 18-30 years, while according to gender 58 cases for males and 12 cases for females.

2.2. Variables

Age and gender were chosen as variables to obtain data on sports injuries. simple demographics for subjects. Types of Injuries was used as a variable to obtain data based on time seasons time series and injuries were categorized into echoes, neck, spinal cord injuries to head and neck, chest, abdomen, upper and lower limbs and pelvis, as a variable for the study were the type of system level injuries.

2.3. Statistical analysis

Data were analyzed using the IBM SPSS program. Simple descriptive statistics, tables, diagrams, which were used to explain injury patterns between systems.

Results:

The research material was taken from the archive of the Emergency Clinic of UCCK only from sports injuries on the football field. The research is of retrospective, descriptive, qualitative type, for the period January-December 2019. *(Table 1.)*

Table 1. Pathology according to diseases and injuries.

Pathology	No. (%)
Diseases	15 (21.4)
Injuries	55 (78.6)
Total	70 ((100)

Table 2. Number of sick and injured by gender.

Age	No. (%)
15-20 year	15 (21.2)
21-25 years old	28 (40.0)
Over 26 years old	27 (38.8)
Total	70 (100)

Graph 1. Number of sick or injured in sports matches by age.

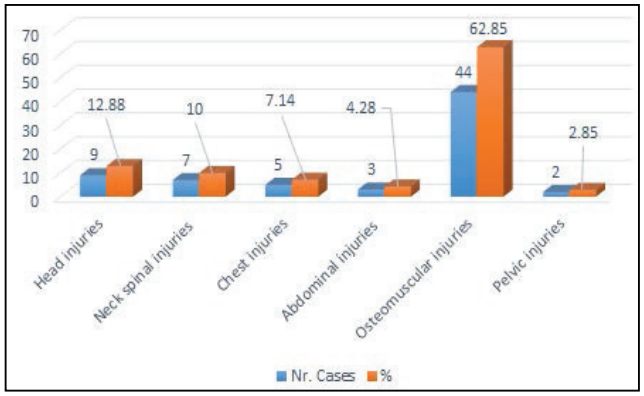


Table 3. Most common diseases.

Illness	i No. (%)
Convulsive seizures	4/26.6
Heart attack	3/20.0
Brain attack	1/6.6
Hypoglycemia	4/26.6
Cardiac arrest	1/6.6
Asthma	1/6.6
Total	15/

Table 4. Number of educated and trained medical staff managing sports clubs.

Compulsory courses	No. (%)
BLS	24
ACLS	4
BTLS	/
ATL	/
PHTLS	/
Total	28

Table 5. Equipment ambulance EMS.

Equipment Ambulance EMS	
Ambulance BLS	75/78.9
Ambulance ACLS	5/5.2
Ambulance no-equipment	15/15.9
Total	95/100

Table 6. EMS Transport private and EMS.

EMS Transport	No. (%)
Privat	15 (21.4)
EMS	55 (78.6)
Total	70/100

Discussion and Conclusion:

The results of our study showed that problems appear in different steps during the management of diseases and injuries in sports fields in the absence of mobile teams, capacities, human resources, medical equipment, triage areas and their system. Lack of coordination of actions was the main cause, delays in the management of the sick and injured on sports fields.

Injured by age the largest number of injured with injuries in the field of football sports the most affected age was the age of 21-25 years with 28 cases or 40.00%, over 25 years were 27 cases or 38.58% and with a smaller number were aged 15-20 years15 cases or 21.42%.

Injured according to pathology with osteo-muscular injuries were 44 cases or 62.8%, with head injuries were 9 cases or 12.8%, with neck and spinal injuries were 7 cases or 10.0%, with chest injuries were 5 cases 7.1%, with abdominal injuries were 3 cases or 4.2% and with pelvic injuries were 2 cases or 2.8%.

The most common diseases according to frequency with Convulsive seizures 4 cases or 26.6% with heart attack 3 cases or 20.0%, brain attack1 cases or 6.6%, hypoglycemia 4 cases or 26.6%, cardiac arrest 1 case or 6.6% and with asthma 1 case or 6.6%. These cases were among the sympathizers. All these cases were hospitalized after admission, monitoring, diagnostic observation and treatment were placed in the appropriate clinics according to the nature of the disease.

All cases were transported by private cars without care and medical transport, because EMS were insufficient. EMS ambulances with BLS medical equipment were 75 ambulances or 78.9% with ACLS 5 ambulances or 5.2% and EMS ambulances not equipped with medical equipment were 15 ambulances or 15.9%. It is required that EMS should be modernized respecting the standards of medical care transport based on the law of medical care as in education, education and training with basic courses for outpatient service, but this component is not developed, so we must review the current laws that regulate EMS. Medical treatment at the scene was low-key because the medical teams did not have any medical training and most of them were uneducated, educated and trained with compulsory courses and the triage system was deficient in assessing the condition of the patients. and the injured.

As for the national medical team, they have been trained by the UEFA Medical Committee, but among them are not professional medical teams and in their composition is a pediatric surgeon and two physiotherapists, but bypassed the emergency doctor, orthopedic, anesthesiologist, cardiologist, nurses who have been eliminated, not respecting the recommendations of UEFA and FIFA. This issue should be regulated by the National Football Federation of Kosovo.

A very important factor in sports injuries is the provision of optimal medical care for footballers and in other sports in head, neck, spine, chest, abdomen, pelvis and limb injuries as well as joint communication in collaboration

with health care professionals in selection of priority cases. (F-MARC Football Medicine Manual 2nd Edition). National Sports Federations of Kosovo based on the rules written by UEFA, FIFA national sports teams must manage doctors' professional multidisciplinary medical teams such as emergency physicians, anesthesiologists, sports doctors, traumatologists, cardiologists, nurses, educated physiotherapists, trained and certified with the required courses BLS-D, PHTLS, ACLS, ATLS, T-triage.

Education of medical staff, nurses, paramedics with courses, use of medical equipment, BLS, ACLS, BTLS, PTLS, ATLS as well as standard procedures for providing and transporting medical care to the hospital. The Sports Law of the Republic of Kosovo, No. 2003/24 - XIV, must be supplemented and amended to meet the recommendations of FIFA and UEFA for emergency medical care in sports, including Article 60 of this Law on Health Protection and the use of stimulant substances and methods in sports.

The results of this research work suggest that the National Federation of Kosovo should oblige sports clubs to provide EMS during training and during the organization of sports games, to prevent treatment and wanting to achieve an optimal recovery. The establishment of the national center and the national strategy is immediate is a valuable reflection of the scope of our research in the prevention of sports injuries.

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ORIGINAL ARTICLE

Management of COVID-19 Patient in Cardiac Surgery with Cardiopulmonary Bypass

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Abstract

Introduction: The diagnosis of COVID-19 is quite challenging due to the inconsistent correlation between laboratory findings, radiological imaging, and the clinical picture and contact history of the patient. The patients who underwent cardiac surgery with cardiopulmonary bypass (CPB) face double risk because CBP triggers an intense inflammatory response and the leading cause of mortality in COVID-19 patients is "cytokine storm". In our institution 15 confirmed cases operated on with open-heart surgery. 9 cases isolated CABG, 4 cases valvular combined with CABG, and 1 valvular disease.

Materials and method: All patients undergoing elective or urgent cardiac surgery at "Mother Theresa" 's Hospital from 11 March to 30 November 2020 were included in this study. Patients diagnosed with COVID-19 infection via positive throat swab taken due to clinical suspicion postoperatively were reviewed. Patients characteristics, type of intervention, date of COVID-19 diagnosis.

Results: 9 patients (72%) normal recovery, no respiratory failure, only 3-5 days of fever (max 39,4). 3 of them a moderate respiratory failure. 3 patients with severe respiratory failure. Only 3 deaths (26,6%).

Recommendation: It's important to a preoperative screening for COVID-19 patients. The outcome of cardiac surgical patients who contracted COVID-19 infection perioperatively is extremely poor. Aggressive respiratory assistance (early intubation), high doses of corticosteroids, and anticoagulation, better results.

Key words. COVID-19. Cardiac surgery. Impact, Cytokine storm

Introduction:

First confirmed case of coronary virus SARS-CoV -2 in Albania was identified in 8 march 2020. After first death case in eleven march, Albanian government, like in any part of the world. took a restrictive measure, to reduce the number of the contaminated people. Another important measure, in order to eliminate the possibility of infection of health personnel, and to focus attention on solving unknown problems from this new disease, was the cessation of elective operations. In this way vacancies could be provided in intensive care, so important for patients with COVID-19. These statistics show that the greatest possibility for contamination of health personnel in in ICU and in ward, where there is direct contact with infected patients**.**

Impact of postponing cardiac surgery.

Postponing heart surgery will increase the risks of morbidity and mortality of the patients in the waiting list. A PubMed search of original, observational studies reporting complications while awaiting CABG or percutaneous coronary intervention (PCI) revealed that mortality, non-fatal myocardial infarction, and urgent revascularization are higher in patients with severe angina and left ventricular dysfunction [1]. The type of surgery should also be considered to determine the level of priority for the planned cardiac interventions. A prospective cohort analysis of death rates while waiting for cardiac surgery revealed that patients waiting for valve surgery have a higher risk of mortality than patients waiting for isolated CABG [2]. Postponing elective surgery has an important effect in early postoperative mortality in our center. During three months (March- June), morbidity and postoperative complication were increased, using intra-aortic balloon pump (IABP), and continuous

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renal replacement therapy (CRRT). The mortality was tripled compared with the same time of the last year.

Risk for health care workers.

To perform a cardiosurgical intervention necessitates a considerable number of medical staff, starting from cardiac surgeons, anesthetists with their assistants, nurse, and perfusion physician. This level of traffic is a risk factor for surgical site infection and human errors [3]. To reduce the spread of the virus and the contamination of the health personnel and the patient admitted for intervention a series of measures had been taken, starting use of PPE mask, hand sanitizer, apneic intubation suggested by *Peng and Hota* during induction of anesthesia, and closed respiratory circuits, with special incorporated filter [4] A retrospective multicenter clinical study comprising 37 patients (5 confirmed and 32 suspected COVID-19) scheduled for emergency procedures, including cardiac procedures, showed that strict adherence to the guidelines of infection control could effectively decrease cross-infection in the operating room [5]. Despite these restrictive measures, 90 % of works in ICU, 60% in ward and only 10 % of nursing staff in operating room, were infected with this virus

Materials and methods.

All patients undergoing elective or urgent cardiac surgery at "Mother Theresa" 's Hospital from 11 March to 30 November 2020 were included in this study. Patients diagnosed with COVID-19 infection via positive throat swab taken due to clinical suspicion postoperatively were reviewed. Patients characteristics, type of intervention, date of COVID-19 diagnosis.

Results.

During the study period in our institution were performed 556 operation. 15 of them resulted positive of covid-19 in postoperative period. Mean age was 57,6 (49-72) years. Only three of them were female. Three operation were performed in urgent situation and 13 were hospitalized days before. Patients demographic data are presented in table 1.

Nine (n=9) procedures were coronary artery bypass graft (CABG). Aortic valve replacement (n=1), mitral valve replacement (n=1). Bivalvular replacement (n=1), and 2 cases of combined surgery (CABG +Valvular replacement). Preoperative hospital stay was 6.2±5 day, and time of diagnosis was 6,9±4 day postoperatively. 14 patients had a pyrexia immediately after surgery and 11 radiology changes. 12 patients developed a satisfactory postoperative course, Mortality was 26,6%.

Discussion.

COVID-19 is a very serios respiratory disease, and in a patient with comorbidities leads to severe respiratory failure, and in death due to multi organ failure (MOF). COVID-19 infection following cardiac surgery is associated

Table 1 Patients characteristics diagnosed of COVID-19

Patient	M/ F	Age	E/U	Operation	Bypass/Min	Preoperative Day
1	F	72	E	MVR + CABG REDU	95	10
2	M	56	E	CABG	77	8
3	M	62	E	CABG	56	5
4	M	58	E	CABG	63	7
5	M	52	E	CABG	68	5
6	M	53	E	MVR+AVR	125	6
7	M	66	E	CABG	83	10
8	M	49	E	CABG	74	7
9	M	55	E	AVR	70	9
10	M	73	E	MVR + CABG	144	8
11	M	72	E	AVR + CABG	133	3
12	M	57	U	CABG	84	2
13	F	71	U	CABG	37	1
14	M	59	U	MVR	84	2
15	M	79	E	CABG	105	10

Table 2 - Clinical features on the day of COVID-19 diagnosis

Patient	Day of COVID diagnosis	Outcome	Pyrexia	Raised WCC	Raised CRP	Radiology changes
1	3	Died	39.2	No	Yes	Yes
2	8	Home	38.5	Yes	Yes	No
3	5	Home	38.5	No	Yes	No
4	5	Home	39,1	yes	Yes	yes
5	5	Home	38,5	yes	Yes	yes
6	6	Died	39,2	No	Yes	yes
7	10	Home	38,5	Yes	Yes	yes
8	7	Died	38,4	Yes	Yes	yes
9	9	Home	37,8	No	Yes	no
10	8	Home, died	39.5	No	Yes	yes
11	3	Home	36.7	No	Yes	Yes
12	4	Home	38.1	No	Yes	Yes
13	7	Home	36.5	No	No	Yes
14	14	Home	38.6	No	No	No
15	10	Home	?	Yes	Yes	Yes

COVID-19: coronavirus 2019; CRP: c-reactive protein; WCC: white cell count.

with very poor outcomes and in our series of 15 patients, a mortality of 26.6%, but this mortality is not real, because the firs patient diagnosed postoperatively with COVID-19, after aggressive assistance in Cardiac surgery ICU (8 days in mechanical ventilation, CRRT) was transferred in infective disease hospital, died after 3 days. The second patient died, after acute postoperative tamponade, and the third died after he was discharged from hospital. In a similar study of nine patient the mortality was much higher 44% [6].

Why is so high the mortality in cardiac patients? Is the use of extracorporeal circulation?

Cardiac surgery involves a unique concern in contrast to other elective surgeries, which is the use of cardiopulmonary bypass (CPB). The exposure of blood to the non-endothelial surfaces during CPB triggers an inflammatory response by activation of coagulation pathways, complement system, and increasing the level of tumor necrosis factor a (TNF-a) and interleukin 10 (IL-10) [7]. There is evidence attributed the cause of ARDS in COVID-19 to cytokine storm syndrome, especially that high levels of proinflammatory cytokines (TNF-a and IL-10) were measured in patients with COVID- 19 and this has also been correlated with the severity of the disease [8] It is unclear as regards the contribution of cardiopulmonary bypass, postoperative ventilation and obvious cardiac comorbidities to the outcomes in these patients.

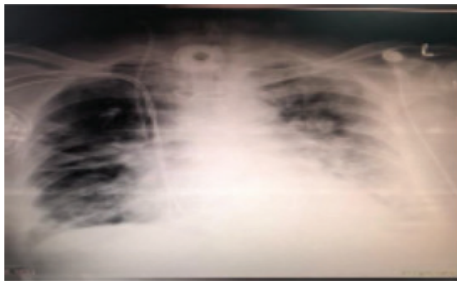
All, our patients have been in contact with a virus, before or during hospital stay before surgery. However, the clinical manifestations only appeared in the postoperative period. There was no established COVID -19 screening protocol preoperatively and postoperatively during the period in which these patients were operated on. Gradually we become informed from COVID hospitals for high morbidity and mortality of this disease, and our experience also increased. We have instituted local protocols aimed at thorough screening of all patients before and on arrival in our unit to ensure that we do not admit or operate on anyone with the virus and isolating patients with unknown COVID-19 status To illustrate our work, we are presenting a special case of postoperative COVID-19.

Case; A woman 72 years old, was scheduled for elective operation. She was suffering for mitral regurgitation and aortic stenosis, pulmonary hypertension (55 mmHg), low ejection fraction FE-35%, diabetes mellitus with insulin, and impaired renal function. Three years before it was implanted a permanent pacemaker DDD-R, after she came to hospital in cardiogenic shock. After preoperative preparation the patient was send in operation room. Operation consisted in both replacement of aortic and mitral valve with biologic prothesis. Cross clamp time 92 min and by pass time 120 min. Weaning from cardiopulmonary bypass with support of inotropic drugs. Postoperative period in firs 3 days went relatively well, in fifth days shorten of breath and reduction of oxygen saturation (O2Sat) to 85%. Diuretic therapy doesn't improve the situation, so after the thorax CT scan (fig 1), COVID-19 was suspected. PCR-test resulted also positive. Her daughter resulted positive, in the USA, after leaving Albania days before her mother.

Figure 1 Evolution of radiologic images of COVID-19 in acute phase.



Before Operation



7 days after Operation



Chest CT-scanner 10 days after Operation

Situation became much worse, and mechanical ventilation after intubation was started. The patient was ventilated with Acute lung Injury set up of the ventilator with low tidal volume and high PEEP (max 8 mmHg). Antibiotic therapy, initially with Piperacillin + Tazobactam, and amikacin, because klebsiella pneumonia was explored in sputum. Heparin iv was started and a PTT was maintained at value 70-90 sec. High doses of methylprednisolone (500 mg in first two days and half dose in 2 other consecutive days. In fifth day, under protective measures, percutaneous tracheostomy was performed. Piperacillin was changed with imipenem, and metronidazole was started too. Gradually laboratory data came towards improvement. (Tab.3)

Table 3 Evolution of laboratory data.

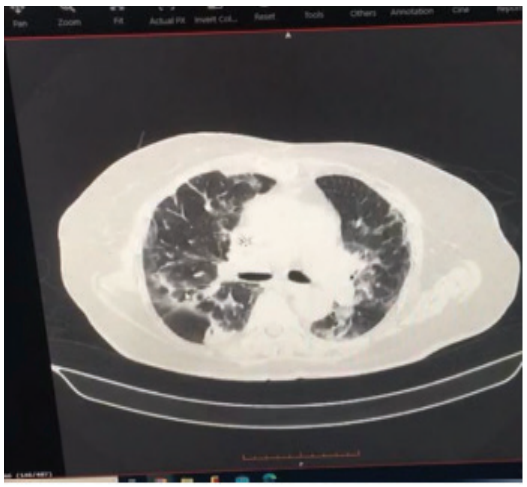
Lab value	9.10.2020	11.10.2020	21.10.2020	25.10.2020	29.10.2020	2.11.2020	6.11.2020
Leukocytes	9.41	16.684.7	3.92	11.95	7.57	4.75	8.09
Lymphocytes	12.7	4.7	6.9	2.4	4.8	6.9	7.1
D-dimer			2834	8703	9566	5796	4043
Fibrinogen			420	403.7	472	395	
Ferritinemia			1100		1089	939	846
CRP	4,99	169.44	96.82	63.5	38.58	25.69	78.21

Respiratory parameters began to improve day by day and PaO2/FiO2 <200. Twenty days after operation, the patient was in spontaneous respiration, with a little support of oxygen. Despite non correlation between radiologic imaging (Fig 2) and blood oxygen improvement, health situation became better. Tracheostomy was removed and thirty-five days after operation the patients was discharge from hospital in stable condition.

Figure 2 Evolution of radiologic images of COVID-19.



15 days



30 days

Conclusion

Treating a COVID-19 patient after cardiac surgery is very challenging. After postoperative COVID-19 diagnosis, should be prepared for worst scenario. Should be implanted rigorous protocols aimed at maintaining a COVID-19 protective environment to minimize additional lifethreatening complications related to this virus infection. In case of infection, aggressive, respiratory assistance, high doses of corticosteroids, anticoagulation better results.

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REVIEW ARTICLES

Management of Frailty and its Challenges in Geriatric Patients on General Abdominal Anesthesia

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Abstract

Introduction: In that material, we are doing to informed for frailty, how we can measure it, surgical outcome and its management from the anesthesiologist. Frailty is a condition of decreased physiological reserves that often increases with increasing age and decided in adverse outcomes.

Frailty in elderly surgical patients may be varied from 25,5 -56.1% and is a strong predictor for surgical outcomes.

The anesthetist needs to predict how a geriatric patient will tolerate the stress of surgery and to do what is necessary to protect and save elderly lives.

In Albania, there are almost 439 000 elderly people in 2021 and suspect to 626 000 in 2051. According to the WHO, 1 in 25 persons performed surgery, so the number of geriatric patients that done surgery will be very high.

According to deficits' in function, mobility, cognition, chronic diseases, and geriatric syndromes we can use the clinical frailty scale, the Edmonton Frailty Scale, or frailty index for calculation of frailty.

We need frailty patients to evaluated preoperative risk-classification, intra-operative care, management of general anesthesia, early immobilization as well as treatment of postoperative delirium because frailty increased intra-operative morbidity, increased postoperative complications especially delirium, extends hospitalization, non – home discharge, and mortality.

Anesthesiologists would be always aware to prepare the geriatric patients for surgery, to maintain the intra-operative functional reserve of frailty patients, to manage perfect anesthesia, to realized early mobilization, and discharge back home.

Conclusion: Many geriatric patients have multi-organ problems. Frailty is a practical, unifying concept in the care of these older people that directs attention away from organ-specific diagnoses towards a more holistic viewpoint of the patient and their medical medicament. All geriatric patients need to screen for frailty.

Keywords: Clinical frailty scale, delirium, frailty syndrome, frailty index, general anesthesia.

Introduction

People over 65 years of age have been regarded as elderly and this is still used as a social definition.

Aging is not equal disease, disability or punishment. Aging is a biological process, the progressive physiological changes in an organism that lead to aging or decline in biological functions and the body's ability to adapt to metabolic stress. [1] Getting old is like climbing a mountain; you get a little out of breath, but the view is much better! this phrase of Ingrid Bergman looked very realistic for the elderly people.

In the Albania there are currently 439 thousand people over 65 years of age. In 1979, there were 76.5 thousand people aged 65. Further increases in the number of seniors are projected at 2051, this number is expected to increase to 641 thousand, reaching 667 thousand in 2060.

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The growing number of older people is a direct result of the increased life expectancy, which has been observed over previous decades and that is thought to continue in the coming decades. Actually, is over 77.4 years old for men and over 80.5 years old for women [2]. It follows that there will be ever increasing number of elderly patients presenting for surgery.

Currently, According to World Health Organization the number of surgical operations is estimated to be 250 million a year, or 1 operation each 25 people. In Albania, about 50 000 surgical interventions are realized every year [3] and over 15% of the population are geriatric patients so the demands for surgical interventions increase. The aging a patient is on presentation for surgery, the greater is their risk of morbidity and mortality. Strategies to realize anesthesia and intensive care for reduced and improve outcomes in aging surgical patients will be the theme of this review. Comprehensive geriatric assessment (CGA) is a multidisciplinary diagnostic process that assesses the medical, functional, psychological, and social abilities to ultimately assess the status of weakness and geriatric syndromes. A consequence of age-related decline is the clinical condition of frailty. Frailty assessment and CGA can be applied in risk stratifications such as mortality or morbidity [4]. Frailty is a condition of decreased physiological and/or cognitive reserves that often increases with increasing age to external stressors [5]. However, frailty is a dynamic and not an irreversible process. Frailty in elderly surgical patients may be varied from 25,5 -56.1% and is a strong predictor for surgical outcomes in most clinical situations [6].

Many tools or criteria have been introduced to define frailty in recent years, and the definition of frailty has gradually converged into several consensuses [4-6]. Frailty is a proinflammatory state mediated by disorder and decline across multiple physiological systems. Identification of geriatric patients who are frail or at risk of becoming frail with appropriate subsequent evaluation and intervention constitutes a foundation stone of geriatric medicine [7]. A number of other definitions have also been described in the literature, including FRAIL (Fatigue, Resistance, Ambulation, Illnesses, Loss of weight) (International Academy of Nutrition and Aging) [8]. According to the cardiovascular health study that enroll 5317 geriatric patients, the prevalence of frailty was 6.9% with frailty increasing with age and female sex [9]. An important role according to a large literature for definition of frailty played potential etiologic factors as: aging (increasing with age), genetic& metabolic factor, lifestyle& environment stressor and acute or chronic diseases. It´s suggested several important multisystem path physiologic processes in the pathogenesis of the frailty syndrome, including chronic inflammation and immune activation, and those in musculoskeletal and endocrine systems.

Chronic inflammation is likely a key underlying mechanism that contributes to frailty directly and indirectly through other intermediate path physiologic processes [7].

Although no one operational definition or simple assessment tool has been agreed, a consensus has been suggested that frailty 1) is a clinical syndrome, 2) indicates increased vulnerability to stressors, leading to functional impairment and adverse health outcomes, 3) might be reversible or increased by interventions, and 4) is useful in surgery word [10].

The two main models of frailty are the phenotype model 3 and the cumulative deficit model, which forms the basis of the Canadian Study of Health and Aging (CSHA) frailty index [6,13]. The phenotypic definition of frailty as a geriatric syndrome was proposed by Fried et al as a large-cohort study of over 5,300 community-dwelling older men and women in the US. [6,9,10].

The phenotype of frailty was defined by the presence of three from the following five clinical features: unintentional weight loss (Self-reported weight loss of more than 4·5 kg or recorded weight loss of ≥5% per year), weakness (Grip strength), self-reported exhaustion (3–4 days per week or most of the time), slow walking speed and low physical activity level [6,9-11]. This phenotype was shown to be predictive for falls, hospitalizations, disability and death [9]. Others authors as *Mitnitski et al* [12], define frailty as summery of deficits (symptoms, signs, functional impairment and laboratory abnormalities) and use it to appreciate the individual's level of illness. This model regards successful aging as an efficient damage control process. Failure to do so will lead to accumulation of deficits and to increased biological age (relative to the individual's chronological age).

Study [13], was a 5-year prospective study (n=10263) designed to investigate the epidemiology and burdens of dementia in aging people in Canada (mean age 82 years). Deficits accumulation depended from function, mobility, cognition, chronic diseases and geriatric syndromes .92 baseline variables of symptoms (low mood), signs (tremor), and abnormal laboratory values, disease states, and disabilities (collectively referred to as deficits), were used to define frailty [12]. The frailty index was a summary of the presence or absence of each variable as a proportion of the total and is calculated as the number of deficits the patient has, divided by the number of deficits considered (e.g., 20 deficits present, of a possible 92 gives a frailty index of 20/92=0·22). Thus, frailty is defined as the cumulative effect of individual deficits "the more individuals have wrong with them, the more likely they are to be frail" [14]. *Velanovich and al* modified frailty index score 0-11 points, the presence of each variable was scored as1 point. This may be applicable for the national databases and clinical practice. (Table 1) [16].

This is a mathematical model for frailty because it implies that the frailty index has properties that fully support the idea of reduced homoeostatic reserve. According to Canadian study of health and aging [13,14,15]

Rockwood defined the Clinical Frailty Scale using the terminology of *Streiner and Norman*. Based in a theoretical model of fitness and frailty and the importance of function (which we reported in earlier investigations) [13] our

Functional Status	Score 0	Score 1
History of diabetes mellitus		
History of congestive heart diseases		
History of hypertension requiring medicaments		
History of either transient ischemic attack or cerebrovascular accident		
Functional Status 2 not independent		
History of myocardial infarction		
History of either peripheral vascular diseases or rest pain		
History of cerebrovascular accident with neurological deficit		
History of chronic obstructive pulmonary diseases or pneumonia		
History of percutaneous coronary intervention, prior cardiac surgery or angina		
History of impaired sensorium		

Table 1 modified frailty index score

Clinical Frailty Scale (Table 2) ranges from 1 (robust health) to 7 (complete functional dependence on others).

In order to assess frailty in the elderly, *Rolfson et al*. tested a brief and user-friendly screening interview in both the inpatient and outpatient settings. The "Edmonton Frail Scale" was a valid measure of frailty compared to the clinical impression of geriatric specialists after their more comprehensive assessment. Frailty status that can be assessed using the Edmonton Frailty Scale consists of nine domains examined are: cognition, functional performance, general health status, functional independence, social support, pharmacological condition, nutritional aspect, mental condition and continence and eleven items, each scoring 0 points (frailty absent or normal health), 1 point (minor errors or mild/moderate impairment), or 2 points (important errors or severely impaired). Total Scoring is: 0-17 point [17]. In the table below we can see the association among Edmonton Frailty Scale with multi-dimensional geriatric conditions assessed with specific screening tools (Table 3) [18].

A limitation of this study has been the lack of information considering social support and incontinence due to practical consideration for this number of patients. No appropriate scales with defined scores are known. In addition, data

Clinical Frailty Scale	
1 - Very fit	The people who are active,robust, energetic & motivated; they tend to exercise regularly and are among the fittest for their age
2- Well	Without active disease, but less fit than people in category 1
3- Wellwith treated co morbid disease	Disease symptoms are well controlled compared with those in category 4
4 -Apparently vulnerable	Although not dependent on others for daily helps, these people commonly complain of being "slowed up" or have disease symptoms
5 -Mildly frail	With limited dependence on others for instrumental activities of daily living (finances, transportation, heavy house work)
6- Moderately frail	Help is needed with both instrumental and non-instrumental activities of daily living
7- Severely frail	Completely dependent on others for activities of daily living, or terminally ill.

Table 2 Clinical Frailty Scale

Edmonton Frail Scale area	**Evaluation tools**	**β**	**CI 95%**	***p*- value**
Cognition	Mini Mental State Examination	−0.988	−0.149; −0.048	$p<0.001$
General health status	Number of diseases	0.108	−0.001; 0.217	0.052
Functional independence	Activities daily living (ADL)	−0.512	−0.674; −0.351	$p<0.001$
	Activities daily living (IADL)	−0.338	−0.491; −0.184	$p<0.001$
Social Support	No recorded			
Use of medication	Number of drugs	0.110	0.022; 0.199	$p<0.05$
Nutrition	Mini Nutritional Assessment	−0.413	−0.487; −0.338	$p<0.001$
Mood	Geriatric Depression scale	−0.314	−0.332; −0.296;	p<0.001
Continence	No recorded			
Funcional Performance	Handgrip	−0.114	−0.173; −0.055	$p<0.001$
	Barthel Index	−0.037	−0.049; −0.024	$p<0.001$

Table 3 Edmonton Frailty Scale

were collected only by the administration of the test in the interview with the patient. Functional performance or time up and go test, measured by a walking test in which measure the time (0-10s, 10-20s,>20s), it takes for the patient to get up from a chair, walk about 3 m away and return to sit, were instead represented in the statistical test of Handgrip since this was most easily detectable in immobile patients [18]. As frailty is called as a vulnerable state associated with high risk for increased morbidity and mortality when exposed to a stressor, the frailty syndrome is considered a useful clinical tool for risk stratification in elderly population. Evidence supporting this notion demonstrated that frailty predicts increased falls, hospitalization, dependence, and mortality [7]. The surgery for the frailty syndrome should aim to prevent, delay, reverse, or reduce the severity of frailty, and also prevent or reduce adverse health outcomes in those whose frailty is not reversible. Effective interventional strategies likely B.R.A.I.N (Benefits, Risk, Alternative, Intuition and Nothing) have large benefits for elderly individuals, their families, and the whole society. A decision not to operate should be made at consultant level, ideally together with other members of the interdisciplinary team and with input from the family. Where possible, the patient should be involved in any discussion. An appropriate decision not to undertake major surgery should be viewed as a positive one. However, there may still be the necessity for palliative surgery to improve the quality of life. Anesthesia should not be withheld in these instances, providing the anesthetist feels that the patient has been suitably prepared. All stages of decision-making should be documented [19]. Frail elderly people receiving inpatient comprehensive geriatric assessment on specialist elderly care wards are more likely to return home, are less likely to have cognitive or functional decline, and have lower in-hospital mortality rates than do those who are admitted to a general therapy ward [6]. Complex interventions based on comprehensive geriatric assessment delivered to elderly people in the community can increase the likelihood of continuing to live at home, mainly through a reduced need for care-home admission.

To discuss postoperative outcomes, we can divide the recovery phase of surgery into three distinctive phases [20]. 1- Early phase (first 24 h to 7 days)—the early phase is influenced mostly by pain, nausea, peri-operative medications, and delirium. 2- Intermediate phase (28 days to 60 days)—this phase is influenced mostly by pain, anxiety and depression, physical impairment, and cognitive dysfunction. 3- Late postoperative phase (6 weeks to 3 months)—problem suffered in the early and intermediate phase can persist into this phase. After preoperative care that is obligatory to achieve a good outcome, we are going to emphasize intra-operative care of frail patients or early phase. No specific intra-operative strategy exists to impact outcomes for people with frailty.

Anesthetic techniques that are appropriate for adults may be unsafe when used to anesthetize elderly patients. There should be guidelines to ensure that an anesthetist experienced in the care of the elderly is responsible for these cases. It is recommended that the choice of anesthesia (technique/ drugs/ dosage) be individualized based on the characteristics of the patient and the type of intervention, to reduce the incidence of postoperative delirium and facilitate recovery [24].

Abdominal elective surgery is difficult, but early recognition can help anesthetists to identify the need to minimize fasting time, to use personalized medicine also to reduce drugs that may precipitate acute delirium (benzodiazepines, opioids, anticholinergics, and deep anesthesia , use minimal alveolar concentration, propofol is suitable for older patients because of the rapid recovery time, and favorable adverse event profile) to think about the postoperative destination of the patient, and required flawless anesthetic technique preferring MAC (Minimal Alveolar Concentration), pay attention to hemodynamic status, lung protective ventilation, normothermia and hydration (blood transfusion) during the perioperative period[21]. Age-related changes in the cardiovascular and autonomic nervous systems reduce cardiac responsiveness to stress [24]. Intraoperative hypotension is a common side effect of general anesthesia and might lead to inadequate organ perfusion especially cerebral and myocardial. It is unclear to what extent hypotension during noncardiac surgery is associated with un-favorable outcomes. They present an overview of 42 articles on reported associations between various absolute and relative intraoperative hypotension definitions and their associations with postoperative adverse outcomes after noncardiac surgery. Elevated risks of end-organ injury were reported for prolonged exposure (≥10 min) to mean arterial pressures < 80 mm Hg and for shorter durations < 70 mm Hg. Reported risks increase with increased durations for mean arterial pressures < 65-60 mm Hg or for any exposure <55-50 mm Hg [22]. So according to guidelines in elderly anesthesia of SFAR 2019 for general anesthesia to geriatric patients will be directed hemodynamic therapy for treated intraoperative hypotension without delay. Our goal will be maintained of mean arterial pressure within 20% of the preoperative reference value and using MAC, for halogenic anesthesia to avoid hypotension and postoperative delirium. But when we used general anesthesia, we ought to realize lung protective ventilation strategies intraoperative for minimized postoperative pulmonary complications. The ventilator should initially be set to a tidal volume of 6-8 ml kg^{-1} predicted body weight and PEEP (Positive End-Expiratory Pressure) 5 cm H_2O. PEEP should be individualized thereafter. When recruitment maneuvers are performed, the lowest effective pressure and shortest effective time or the fewest number of breaths should be used. [23,24].

In the elderly, overhydration, especially in the presence of borderline or overt renal failure, can cause acute cardiac failure and pulmonary oedema. Dehydration, which can be difficult to assess in the elderly, may precipitate further renal impairment so the anesthetist must be very carefully [19]. The literature recommends adequate monitoring to maintain

a "near-zero" fluid balance [24]. Anemia and transfusion are associated with increased morbidity and mortality in surgical patients. PBM (Patient Blood Management) is a multimodal, multidisciplinary, strategy aimed at minimizing the use of blood products and improving patients' outcomes, they recommend transfusion in geriatric patients follows a restrictive transfusion strategy (red blood cell transfusion threshold: Hb < 8 g/dl) and red blood cell transfusion when symptoms of intraoperative hypoxia and/or lactic acidosis and hemorrhage are present, regardless of the severity of anemia. The standard treatment for severe perioperative anemia is transfusion of allogenic red blood cells [24]. Maintenance of body temperature pre-, intra-, and postoperatively is essential. Elderly patients may be unable to increase their metabolic rate to counteract heat loss. Shivering may increase oxygen demand above respiratory capacity. Conservation of heat by the use of active warm air systems, by warming intravenous fluids and by operating, where possible, in a warm ambient environment all help to maintain body temperature and aid recovery [19,24]. Active warming techniques to keep temp ≈ 36.2˚C should be continued in recovery. Full resources for the provision of this type of care must be enabled by management.

In postoperative period we need to used general strategies for optimizing postoperative recovery [24]. ERAS protocols aimed at reducing postoperative morbidity cover the whole perioperative period [25] Optimal postoperative pain control and use of nonopioid analgesia, absence of a nasogastric tube and prevent PONV (post-operative nausea and vomiting); early mobilization, oral nutrition, and removal of the urinary catheter, early resumption of feeding, early mobilization and walking or using physiotherapy [24,25]. Importantly, reduction in surgical stress through ERAS appears to be particularly effective in reducing complications and supporting recovery in older and frail patients and especially post-operator delirium [24]. They recommended that prevention, recognition and treatment of postoperative delirium (POD) must be an objective of the multidisciplinary team. They emphasized that patients at risk for POD be monitored with validated diagnostic tools such as the CAM or 4AT, starting when they wake from anesthesia and continuing for 5 days thereafter. POD happened 1 in every 8 patients aged > 65years. It is also important to recognize the potential role of family and caregivers in supporting the patient. Flexibility of visiting hours, and the use of investigative tools to determine the patient's needs and preferences, should be encouraged. Cognitive changes after anesthesia also include postoperative neurocognitive disorders. Specific risk factors for such disorders should be evaluated in susceptible patients [24].

Conclusions

Many elderly people have multiorgan problems. Frailty is a multidimensional syndrome and an independent factor in the care of elderly patients that directs attention away from organ-specific diagnoses towards a more holistic viewpoint of the patient and their predicament. It is a state of vulnerability to poor resolution of homoeostasis after a stressor event and is strongly associated with adverse outcomes. This means that anesthesiologists need to be familiar with frailty, its assessment, manifestations, and strategies for optimization. Distinction of frail elderly people from those who are not frail should therefore be an essential part of preoperative assessment that might result in an invasive procedure or potentially harmful medication. It allows anesthetist to calculate benefits and risks, and for patients to make properly informed choices. Failure to detect frailty potentially exposes patients to interventions from which they might not benefit and indeed could be harmed. The most evidence-based process to detect and grade frailty for severity is comprehensive geriatric assessment. However, this assessment is a resource-intensive process, including the important issue of clinical sensibility so all geriatric patients ought to screen for frailty. This aim might be achieved by development and further validation of currently available frailty-specific multidimensional questionnaires, but the usefulness of existing clinical data sets, especially in primary care. Such a simple method would help to gain a deeper insight into the complex mechanisms of frailty and aid the development and evaluation of interventions to improve outcomes. It would also have considerable clinical medical ward because it would be the basis for a shift in the care of frail elderly people towards a more appropriate goal-directed care in which individually framed clinical outcomes. Overall, 30%–50% of older patients presenting for major surgery will be living with frailty, which results in a more than 2-fold increase in risk of morbidity, mortality, and development of new patient-reported disability. The Clinical Frailty Scale appears to be the most feasible frailty instrument for use before surgery; however, evidence suggests that predictive accuracy does not differ significantly between frailty instruments such as the Fried Phenotype, Edmonton Frail Scale, and Frailty Index. With the aging patient need to integrate the expertise of surgeons, anesthetists, geriatricians, and other specialists and health care professionals. These roles might vary according to the phase and setting of care and the patient's condition.

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REVIEW ARTICLES

Efficacy and Safety of AZD1222, BNT162b2 and mRNA-1273 vaccines against SARS-CoV-2

Ilir Alimehmeti*

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Abstract

SARS-CoV-2, the beta coronavirus causing COVID-19, was isolated and categorizes as a novel one on January 7th, 2020 in China.[1] To date, official reports depict that SARS-CoV-2 has already infected 88.828.387 persons and caused 1.926.625 deaths worldwide.[2] On January 12th, 2020, China officials made public its genetic sequence, thus paving the way towards the research and development of diagnostic tests and vaccines.

With regard to vaccination, e large number of clinical trials were designed and are currently undergoing, of which 189 are listed in ClinicalTrials.gov. [3] However, up to date, only three vaccines have published their respective phase III clinical trial results in peer-reviewed medical journals. [4-6]

Vaccines are needed to reduce the morbidity and mortality associated with Covid-19, and multiple vaccine platforms as AZD1222 (AstraZeneca) [4], BNT162b2 (Pfizer/BioNTech) [5] and mRNA-1273 (Moderna) have been involved in the rapid development of vaccine candidates.

Methodology: In this review, PubMed, Embase, Web of Science, Scopus, medRxiv, and bioRxiv were systematically scrutinized for peer-reviewed and preprint articles on phase III clinical trials of vaccines against SARS-CoV-2. In total, only three peer-reviewed papers fulfilling the search criteria were identified.

Conclusions: All vaccine candidates should publish in peer-reviewed journals their efficacy and safety well before requesting approval to the national or international authorities…

Keywords: COVID-19, SARS-CoV-2, vaccination, review, clinical trials

Introduction:

SARS-CoV-2, the beta coronavirus causing COVID-19, was isolated and categorizes as a novel one on January 7th, 2020 in China.[1]

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With regard to vaccination, e large number of clinical trials were designed and are currently undergoing, of which 189 are listed in ClinicalTrials.gov. [3] However, up to date only three vaccines have published their respective phase III clinical trials results in peer-reviewed medical journals. [4-6]

The above-mentioned vaccines AZD1222 (Astra-Zeneca) [4], BNT162b2 (Pfizer/BioNTech) [5] and mRNA-1273 Moderna [6] have already been approved from the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and national boards in different countries. [7-11] Recently a minimal vaccination wave has begun in Albania too, but such a vaccination program has been covered only by media sources, while to date it is short of an official report from the national health authorities. [12]

Nevertheless, the vaccines' development effort itself was characterized by a mediatic coverage that had the upper on scientific peer-reviewed publications worldwide, thus bypassing critical review of the published data, which is inherent of mediatic sources where not all the vital data are published, in contrast to the the scientific medical journals routine.

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Therefore, the aim of this paper is to critically assess efficacy and safety of the anti-SARS-CoV-2 vaccines published phase III clinical trials data.

Methodology:

In this review, PubMed, Embase, Web of Science, Scopus, medRxiv and bioRxiv were systematically scrutinized for peer-reviewed and preprint articles on phase III clinical trials of vaccines against SARS-CoV2.

In total, only three peer-reviewed papers fulfilling the search criteria were identified. Chronologically, by publication order, these articles presented results from phase III trials of the following vaccines: AZD1222 (AstraZeneca) [4], BNT162b2 (Pfizer/BioNTech) [5] and mRNA- 1273 (Moderna) [6], which were all published closely to each-other, respectively on December 08th, 2020, December 10th, 2020 and December 30th, 2020. [4-6]

In this order, each publication was rigorously qualitatively reviewed to gather insights on: sample selection, inclusion and exclusion criteria, clinical trial methodology, reported safety and efficacy, and, last but not the least, external validity of the findings.

Results:

AZD1222 vaccine (AstraZeneca) [4]

The AZD1222 vaccine has been developed at the Oxford University and is compounded by a chimpanzee-derived replication-deficient adenoviral vector (ChAdOx1), which contains the gene for the SARS-CoV-2 structural surface glycoprotein antigen, also known as the spike protein. The clinical trial consists of a randomized controlled trial divided in three different arms that took place in the United Kingdom, Brazil and South Africa, which present major and unexplainable methodological differences.

Blinding:

The British and Brazilian groups underwent a single blind trial, while the South African trial was double blinded. Thus, in the first two arms, researchers had clear knowledge of who was being vaccinated and who was not, foretelling the hypothetical opportunity of subtle differential alterations of both registering and reporting processes, while the South African arm follows a rigorous and superior double-blind study design.

Control group:

Again, both the British and Brazilian arms do not inject placebo (saline solution) but have interestingly chosen to inject meningococcal vaccine in the control group. Yet aging the South African arm follows the robust design of employing placebo in the control group. It is worth mentioning that using another vaccine in the control group confounds the side effects findings of the at-study vaccine candidate, as most of these side effects would be similar to the side effects exerted by any vaccine employed as a control. Such shadowing would not be possible if placebo were employed.

Most interestingly, in the final publication, authors have reported only data from the British and Brazilian arms, dodging data from the South African arm, condoning their choice because of the lack of enough cases accrual during the study period.

Inclusion and exclusion criteria:

In the inclusion criteria is directly observable by how far the studied population differs from the general population, especially from the population at high risk for severe COVID-19.

Age:

The study population comprises no one aged beneath 18 years old, while 88% are 18-55 years old, 8% are 56-70 years old and only 4% are aged over 70 years old. Hence, from design this study lacks the statistical power to detect efficacy and safety in the underrepresented old age groups. Moreover, excluding old age groups is an old trick of vaccine clinical trials, as, physiologically, old aged persons gradually lose the ability to create or retain the vaccine-induced immunity memory, and such an exclusion would result in an expectable overestimation of the immune response to the vaccine.

Body mass index:

The study population presents an almost ideal body mass index averaging around 25 kg/m^2, whilst obesity is a known risk for severe COVID-19.

Chronic diseases:

Given the relatively young and healthy study population, also chronic diseases present a low prevalence, respectively: respiratory diseases 12%, cardiovascular diseases 11%, and diabetes only 2%. These low figures may undermine the external validity and generalizability of the efficacy and safety findings in the particularly at-risk individuals with several chronic diseases.

Special populations:

It is not clearly reported if persons with autoimmune diseases and pregnant or breastfeeding women have been included or excluded from the clinical trial.

Total study population:

In total, 11.636 have been studied, characterizing such a trial as a relatively small one, which is able to spot common and most uncommon side effects, but is not powered enough to identify rare side effects at an order lower than 1 out of 10.000 cases.

Follow-up:

The mean follow-up time was 2.4 months from the day of receiving the second vaccine dose. Again, such a period

might be sufficient for identifying common and rapid side effects, por cannot inform on rarer side effects or longer than three months appearing ones.

Primary outcome:

The main primary outcome was a positive RT-PCR result after complaining at least one symptom of COVID-19. Such an outcome is a soft and problematic one, more so if considered the relatively young and health study population, as such a population is not categorized as vulnerable. Hard outcomes worth considering would have been severe COVID-19, hospitalization, and mortality.

Efficacy:

In the follow-up period, symptomatic COVID-19 was diagnosed in 0.5% of the vaccinated persons and in 1.7% of the nonvaccinated controls. Such figures can be computed as a highly significant absolute risk reduction of 70%. Nevertheless, such a reduction is generalizable only to young and healthy population. In older age groups it can only be speculated that the effect would be expected to be lower.

Importantly, no vaccinated individual was hospitalized, while there were 10 hospitalizations in the control arm. In long term such a number would be expected to surge in favour of the vaccine arm. The hospitalization outcome is far more impressive than the absolute risk reduction of positive RT- PCRs in such a young and healthy population and, although it lacks statistical significance, is a powerful positive signal of efficacy.

Safety:

Serious events were observed in 0.7% of the vaccinated persons and 0.8% of the control persons. But, taking into account that the control arm has been injected with the meningococcal vaccine and not placebo, it is deductible that AZD1222 causes no more serious events than the meningococcal vaccine does. Not the less, the real AZD1222 absolute risk of side effects cannot be assessed unless tested against placebo.

A total of 79 different serious events developed after vaccination, with the vast majority not being connected to the vaccine itself. The only alarming event was the identification of two cases of transverse myelitis that developed a few weeks after receiving both doses of the vaccine. As transverse myelitis is a rare disease with an incidence of 1 to 8 cases per million,[16] the incidence of 2 cases in only 6.000 vaccinated persons raised legitimate concern. One of the cases had multiple sclerosis, a known risk factor for transverse myelitis, but the other case had no risk factor at all. As the trial is underpowered to detect for rare side effects, pharmacovigilance data are vital to early detect incident cases during and after the vaccination campaigns.

Summary:

AZD1222 vaccine present an efficacy of around 70% generalizable to relatively young and healthy populations, but the trial also provides important harm signals that warrant further and larger studies. Such a vaccine might be recommendable to high-risk population, where benefit outweighs risks, but this is not the case for low-risk populations. Moreover, until further clarity is made on inclusion criteria, persons with autoimmune diseases, allergies, pregnant and breastfeeding women may be advised to stand by.

BNT162b2 (Pfizer/BioNTech) [5]

BNT162b2 is a lipidic nanoparticle with a nucleoside-level modified RNA, coding the whole sequence of the spike antigen of SARS-CoV-2, modified by two proline mutations blocking it into prefusion conformation. [13-15]

Blinding and control:

The phase III clinical trial employed a randomized, double-blind, placebo-controlled study design, a far more robust study design compared to the above-mentioned AZD1222.

Inclusion and exclusion criteria:

Inclusion age was 16 years old and older. However, less than 5% were aged over 75 years old. Chronic diseases were included only when they were deemed as stable. All persons under immunosuppressive therapy, with former allergy to vaccines, with autoimmune diseases, and pregnant or breastfeeding women were excluded. As a result, findings are not generalizable to these populations.

Again, as volunteers are fundamentally healthy and relatively young, the efficacy and safety results might be overestimated and not generalizable to elderly with chronic diseases, which is of particular interest given the fact that the mean number of chronic diseases in fatal cases of COVID-19 is 3.6. [17]

A positive figure is that prevalence of obesity was 35%, thus conferring external validity to the findings for the obese population, as it is a known risk factor for severe COVID-19.

Total study population:

In total, 43.548 persons were enrolled in the clinical trial ensuring high statistical power to find rare side effects with an estimated incidence of 1 out of 10.000 persons, but not lower.

Primary outcome:

Once more, the primary outcome was a positive RT-PCR finding after the possible manifestation of COVID-19 symptoms, a soft outcome compared to the most interesting hard outcome as severe COVID-19, hospitalizations, and mortality.

Efficacy:

COVID-19 was diagnosed in 0.05% of the vaccinated

persons and 0.9% of the placebo-controlled persons, thus an absolute risk reduction of nearly 95% can be calculated, a figure that is both an impressive and highly significant one.

An additional positive figure is that such efficacy seems to hold also in the over 75 years old age group, where five cases developed in the control arm, but none developed in the vaccinated group. Albeit no statistical significance could be computed due to the small sample, the signal remains positive.

Regarding severe COVID-19, only one vaccinated person and nine nonvaccinated persons developed it during the follow-up period. Absolute risk reduction is nearly 89% but, again due to the small study sample, the statistical significance cannot be achieved.

Safety:

A total of 240 severe events were registered in the vaccination arm, while 139 happened in the control arm, resulting in a 73% increase. However, researchers did not report a detailed list of severe events encountered, adopting instead an *en bloc* report. Following vaccination in the United Kingdom, at least two persons had an anaphylactic shock after receiving the vaccine, [18] thus highlighting the necessity to report every single type of severe events clearly.

Serious events were reported in 0.6% of the vaccinated and 0.5 of the control persons, with no significant difference but, again, with no clear listing of the event type.

Summary:

BNT162b2 vaccine showed a 95% absolute risk reduction of symptomatic COVID-19 in a relatively young and healthy sample and an 89% nonsignificant absolute risk reduction of severe COVID-19. Taking into account that 98.8% of the did not suffer any severe event, such a vaccine could be considered also in older adults and in high-risk persons, in whom the benefit/harm ratio is in favour of the vaccine employment. However, continuous observations are warranted to assess, care and report cases of anaphylaxis, if any. Up to date children aged under 16 years old, persons with allergies, autoimmune diseases, immune suppression, and pregnant or breastfeeding women should not use this vaccine until it is thoroughly tested.

mRNA-1273 (Moderna): [6]

mRNA-1273 vaccine shares the same technology as BNT162b2 does, but presents a small difference given that the second dose is distanced 28 days from the first one, compared to BNT162b2 that needs only a 21-day long period. Given the similarity in technology and action mechanisms, it follows that similar results were expectable.

Blinding and Control:

This phase III clinical trial employer a robust randomized, double-blind, place-controlled study design.

Inclusion and exclusion criteria:

Ages over 18 years old were included in the study, yet again only 5% were aged over 75 years old. Participants had to be healthy or in a stable chronic condition. Exclusion criteria were presence of allergies, immune suppression, and pregnancy or breastfeeding. The main body mass index was 29 kg/m^2, which resembles the source population.

Chronic diseases presented a low-to-medium prevalence: 5% had chronic pulmonary diseases, 5% had cardiovascular diseases, 7% were obese and 10 had diabetes.

Total study population:

In total, 30.420 participants were enrolled, an intermediate sample size with comparison made to the above-mentioned clinical trials.

Primary outcome:

Once more the primary outcome was a positive RT-PCR after developing at least two symptoms similar to COVID-19. Similarly, to the other trials, the primary outcome was a soft one and not severe COVID-19, hospitalization or mortality.

Efficacy:

Symptomatic COVID-19 was diagnosed in 0.07% of the vaccinated and 1.3% of the nonvaccinated persons, eliciting a highly significant absolute risk reduction of 94%. In the age group over 65 years old, an absolute risk reduction of 86% was observed, thus deducting that such a vaccine has a high efficacy also in this age groups, admitting that there are no data for ages over 80 years old.

Most interesting, severe COVID-19 developed in 30 persons of the control arm and in not a single one from the vaccinated arm.

Safety:

In both vaccinated and nonvaccinated arms 1.0% of the participants presented serious events. Though the difference is not significant, a ratio of 1 out 100 is not ideal. Nevertheless, dissimilarly from the BNT162b2 study group, the mRNA-1273 researchers reported a thorough list of all severe and serious events. After scrutinizing the list, no serious event could be considered as a vaccine liability, diversely from the cases of transverse myelitis in the AZD1222 clinical trial. Moreover, none of such serious events present any significant difference between the vaccine arm and the control arm.

Summary:

Taken together, data from the mRNA-1273 clinical trial provide solid basis of efficacy and safety. Nonetheless, there are no data on specific groups, including children and adolescents under 18 years old, elderly over 80 years old, people with a suppressed immune system, allergies, and pregnant or breastfeeding women. Whilst the high risk for severe COVID-19 in age groups over 80 years old may warrant their vaccination, such a notion does not hold in the other above-mentioned categories.

Discussion:

In summary of this systematic qualitative literature review of the efficacy and safety of the vaccines against SARS-CoV-2, published data could be found only on the following three vaccines: AZD1222, [4] BNT162b2 [5] and mRNA-1273[6].

After scrutinizing the methodology of each clinical trial, followed by the critical review of the results reported on their efficacy and safety, the highest safety profile appears to be provided by the mRNA-1273 (Moderna) vaccine, closely followed by the BNT162b2 (Pfizer/BioNTech) vaccine, whereas in the clinical trial of AZD1222 (AstraZeneca) important signals of alarming side effects could be found. However, all studies are powered enough to find side effects ranging from common to uncommon but are unsuited to identify rare side effects. Such a fact should be carefully considered given the very high absolute number of people that have to be vaccinated in each country in order to achieve herd immunity. Pharmacovigilance and transparent reporting of serious events in each country are highly warranted.

Regarding efficacy, mRNA-1273 (Moderna) and BNT162b2 (Pfizer/BioNTech) exhibit almost identical efficacities but that can be generalizable only to relatively younger and healthier populations. While BNT162b2 (Pfizer/BioNTech) has supporting nonsignificant data up to 70 years old, mRNA-1273 (Moderna) extends such a claim also to age groups up to 80 years old. Nevertheless, given the high risk for severe COVID-19, also older age groups can be eligible to vaccination with the above-mentioned vaccines, but further studies are needed to exactly assess efficacy and safety in these age groups. On the other hand, AZD1222 (AstraZeneca) present a lower efficacy profile, only 70%, and at the same time presents the same issues of external validity, thus being inferior to both other RNA-based vaccines.

Additionally, the AZD1222 (AstraZeneca) clinical trial presents different very important biases in its methodology, including a single blind design and employment of a meningococcal vaccine instead of placebo in the control arm.

Collectively, all three studies not including a representative number of elders present an overestimation of the efficacy and safety of their products that presents no external validity and, most probably, including older ages would have slightly diluted their quite optimistic findings. ***In conclusion;*** larger studies are warranted including not only older ages but also paediatric ones.

In lack of these data, vaccination should be avoided in children and adolescents under the age of the respective trial inclusion criteria, whilst efficacy and safety of the vaccination of persons over 70 years old must be actively assessed during the national vaccination campaigns. Last but not least, further vaccine candidates should publish in peer-reviewed journals their efficacy and safety well before requesting approval to the national or international authorities.

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REVIEW ARTICLES

An Overview of Treatment of Crush Syndrome

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Abstract

Natural mass disasters directly or indirectly affect huge populations, who need basic infrastructural help and assistance to survive. However, despite the potentially negative impact on survival chances, the authorities often dismiss these health care issues.

This impact is of great importance, especially in the emerging world, where the casualty rates are much higher because of inappropriate building materials and lack of appropriate construction standards. Thus, massive destruction can occur with earthquakes of even moderately low magnitude.

The first description of the crush syndrome appeared in the modern medical literature after the Messina earthquake in 1909. Since crush syndrome is quite rare in daily practice, mistakes are frequent in treating these cases.

This review summarizes the etiopathogenesis of traumatic rhabdomyolysis and crush syndrome based acute kidney injury. The clinical and laboratory features, prophylaxis, and treatment of crush cases are described as well.

The importance of early and dynamic fluid resuscitation is indicated for the prophylaxis of acute kidney injury. Treatment of both acute and chronic kidney diseases (CKDs) is especially problematic after disasters because they almost always require complex technology and equipment, whereas specific drugs may be difficult to obtain to treat chronic kidney patients.

Although crush syndrome is a major cause of mortality in the rescued victims of massive earthquakes, the number of deaths due to crush syndrome (or fatalities of renal disaster) can be decreased by appropriate management.

Keywords: crush syndrome, acute kidney injury, traumatic rhabdomyolysis

Introduction

Disasters are unexpected catastrophes causing massive material damage and suffering; residents of the involved area may become homeless, be wounded, or die. Although some disasters are human-made, in general, most of them are natural geological or meteorological events.

There are many natural catastrophes like Kashmir, Iran, Haiti, Marmara, Japan earthquakes, which have affected densely populated and/or geographically extensive areas directly or indirectly, where necessary infrastructural help is needed and support to survive. According to the detailed statistics, during the Marmara-Turkey 1999 earthquake, nearly 16 000 000 people were somehow affected by the disaster [1, 2].

This figure includes displaced populations, those who lost their jobs due to economic collapse and deprivation, and those who lost properties [3] where >130 000 buildings collapsed entirely, making 600 000 people homeless. There were reported 51 deaths and up to 750 people injured, and 12,181 people were reported to be living in temporary accommodation during the earthquake of 26 November 2019 in Albania. This impact is of great importance, especially in the emerging world, where the casualty rates are much higher because of inappropriate building materials and lack of appropriate construction standards. Thus, massive destruction can occur with earthquakes of even moderately low magnitude.

Clinical crush syndrome is presented frequently in traumatic injury in disasters, where rhabdomyolysis is one of the leading causes of acute renal failure (ARF). The first description of the crush syndrome appeared in the modern medical literature after the Messina earthquake in 1909 [2].

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Trauma-related crush syndrome was first identified as a single/broad pathophysiologic entity in 1941. During the bombing of London, Bywaters and Beall described the clinical picture in four crush cases. Three of them were oliguric, and all produced dark brownish urine. All four patients died; histopathological examination of the kidneys revealed pigmented casts, polymorphonuclear invasion, and acute tubular necrosis (ATN). The true incidence of acute kidney injury in rhabdomyolysis is not easy to establish depending on various definitions and clinical scenarios. The incidence of acute kidney injury due to rhabdomyolysis was higher among persons who had undergone trauma [4]. The term 'acute kidney injury' (AKI) was substituted as a pathophysiological better option to the earlier definition of acute renal failure, and this term was suggested to be used for disaster crush casualties. AKI with impact on clinical outcome is accepted to be present in case of an abrupt (within 48 h) reduction in kidney function defined either as an absolute 1.5-fold increase in serum creatinine or by 0.5 mg/dl or a decrease in glomerular filtration rate by 50%, and/or a reduction in urine output to below 0.5 ml/kg/h for 46 h [5]. This notion means that even small changes in kidney function may profoundly alter the outcome.

Physiopathology of AKI:

The histopathologic lesion in crash-related AKI is ATN, in which hypovolemic (ischemic) and nephrotoxic factors play a role. Crushed patients frequently develop hypovolemic shock in the first few hours after extrication from under the rubble. Hypovolemia etiologies are numerous, including lack of oral fluid intake, hemorrhage from associated injuries, and profound third spacing. By releasing the external pressure, intravascular fluids flow into the intracellular compartments, and the injured area begins to sequester large volumes of fluids (compartment syndrome).

Limbs can hold up to 12 L of fluid in their large compartments. Besides, the distributive shock also can develop from the release of inflammatory mediators caused by reperfusion injury. Hypovolemia then can lead to further ischemia and cell death. Acidemia often accompanies these metabolic derangements, in large part owing to ongoing hypoperfusion. AKI often is prerenal at first, with later evolution into ATN if hypovolemia is not appropriately treated [6, 7].

Muscle trauma, although the primary injury that happens, does not always lead to rhabdomyolysis, not all rhabdomyolysis leads to ARF, and not all ARF related to the crush syndrome is attributable to rhabdomyolysis [6].

Rhabdomyolysis refers to the disintegration of striated muscle release of muscular cell constituents into the extracellular fluid and the circulation [8]. Trauma and muscle compression are believed to cause rhabdomyolysis through direct injury to the muscle, resulting in disruption of the sarcolemma and direct leakage of cell contents driving to an unregulated increase in intracellular calcium. Sarcoplasmic calcium is strictly regulated by a series of pumps, channels, and exchangers that maintain low calcium levels when the muscle is at rest and enables the increase needed for actin-myosin binding and muscle contraction.

Depletion of ATP impairs the role of these pumps, resulting in a persistent increase in sarcoplasmic calcium that leads to persistent contraction and energy depletion and the activation of calcium-dependent neutral proteases and phospholipases; the result is the eventual destruction of myofibrillar, cytoskeletal, and membrane proteins, followed by lysosomal digestion of fiber contents. Ultimately, the myofibrillar network breaks down, disintegrating the myocyte [4-6]. Myoglobin is one of the critical compounds being extensively released in circulation after trauma, and myoglobinuria is the central element in the development of rhabdomyolysis-induced ARF. Myoglobin, an 18,800-Dalton oxygen carrier, is like hemoglobin but contains only one heme moiety.

Usually, only small amounts of myoglobin reach the urine because it is mainly bound to plasma globulins. When massive amounts of myoglobin are released, the binding capacity of the plasma protein is exceeded. Myoglobin is then filtered by the glomeruli and reaches the tubules, where it may cause obstruction and renal dysfunction [2, 8]. The obstruction happens when myoglobin precipitate in combination with the Tamm-Horsfall protein, forming tubular casts, especially in the presence of acid pH. This process is promoted by volume depletion, resulting in concentrated urine. Acute kidney injury associated with myoglobinuria is a common complication of both traumatic and non-traumatic rhabdomyolysis [8], and it may be life-threatening. It may manifest from a subclinical rise of creatine kinase (CK) to a medical emergency comprising interstitial and muscle cell edema, intravascular volume contraction, and pigment-induced acute renal failure (ARF).

In patients with rhabdomyolysis generated by trauma, further injury occurs from ischemia-reperfusion and inflammation by neutrophils that infiltrate injured muscle. Reperfusion injury during crush syndrome causes muscle ischemia due to tissue pressure that exceeds capillary perfusion pressure. The reperfusion, which happens when the compression is relieved (ischemia-reperfusion injury), represents rhabdomyolysis's fundamental pathophysiologic mechanism. When compression is removed, amongst others, leukocytes migrate into the injured tissue, where they are activated and release free radicals and other injurious compounds. Superoxide, the anion form of oxygen (O_2-), and hydrogen peroxide (H_2O_2) react to form the hydroxyl radical, which, in a large enough concentration, damages cellular molecules and causes lipid peroxidation [9, 10]. Lipid peroxidation leads to cell membrane destruction and cell lysis [11]. This damage leads to a further increase in fluid, calcium, and sodium absorption into the damaged cells.

Alternative causes of ARF in patients with crush injury are sepsis and drug nephrotoxicity [8].

Diagnostic:

Myoglobin's measurement in plasma or urine is unreliable for diagnostic purposes because myoglobin is metabolized in the liver quickly and in an unpredictable fashion. On the other hand, the enzyme creatine kinase (CK) is ubiquitously present in striated muscle (CKMM) and is the more stable marker to assess muscle damage's presence and intensity than is myoglobin.

Phosphorus and potassium are elevated while calcium is reduced. Massive lysis of muscle cells substantially increases potassium in circulation. Renal insufficiency and acidosis increase the potassium levels further on. Hyperkalemia is a life-threatening condition; its pathogenesis is multifactorial (with causes such as massive tissue destruction, acidosis, lysis of transfused red blood cells, or decreased urinary potassium excretion caused by renal failure) and needs immediate treatment due to potassium cardiotoxicity. Hyperkalemia is the most critical laboratory abnormality. In the presence of hyperkalemia, hypocalcemia may lead to severe cardiac arrhythmias. Portable electrocardiography machines may be useful to detect life-threatening hyperkalemia in disaster fields. Further on the course of the disease hypercalcemia is present.

Phosphorus is released by damaged muscle resulting in hyperphosphatemia. Renal insufficiency is also a cause of hyperphosphatemia, which causes deposition of calcium-phosphate complexes in tissues and suppresses 1a-hydroxylase, the enzyme responsible for producing the active vitamin D, contributing further to hypocalcemia. The diuresis should be carefully monitored, and renal biomarkers showed to be followed [2, 4-6].

Management of Crush syndrome acute renal failure

The main principle in the management of Crush syndrome to prevent AKI is administering fluids to prevent hypovolemia and hypoperfusion. Inadequate Alternatively delayed fluid administration increases the risk of AKI. Although considered crucial, the treatment and the amounts of fluids should be individualized, taking into account the time into the rubble, length of extrication procedure, volume status, and diuresis, characteristics of the patients (age, BMI, etc.), and environmental conditions.

Isotonic saline is the first and the best option for volume replacement because it helps to prevent AKI and carries a low risk for complications. Besides, sodium bicarbonate solutions added to half-isotonic saline could prevent tubular deposition of myoglobin and uric acid, correct metabolic acidosis reduces hyperkalemia but is not always available in chaotic circumstances [5]. Not all fluids are safe in crush syndrome; solutions containing even small amounts of potassium (e.g., Ringer lactate) should be avoided because fatal hyperkalemia may occur at any moment, even in the absence of renal failure [12].

There is some controversy about mannitol's administration to disaster crash victims, and it should not be administered to all crush patients. Mannitol has diuretic, antioxidant, and vasodilatory properties; prevents renal tubular cast deposition; expands extracellular volume; and reduces intercompartmental pressure, muscle edema, and pain. It is important to be underlined that mannitol may replace or extend the time for a surgical fasciotomy [13]. On the other hand, mannitol requires very close monitoring, which is very difficult in disasters because it may cause congestive heart failure and nephrotoxicity [14], and it requires close monitoring, which is often impossible after massive disasters. The decision to administer mannitol should be individualized, response to a test dose should first be assessed, with continuation only in a positive urinary response.

Loop diuretics are not recommended to be used routinely in the treatment of AKI. However, these agents may be useful in managing volume overload and theoretically could limit renal injury by enhancing tubular fluid flow, flushing out obstructive debris, converting oliguric AKI into non-oliguric AKI, reducing active tubular sodium reabsorption [15]. Decreasing renal oxygen consumption is evidence that they are not beneficial in this case and increase the risk of mortality. They could acidify the urine and increase the risk of cast formation and worsen hypocalcemia by inducing calciuria [16].

In crushed patients, shifting of calcium into the muscles, together with another risk factors like hyperphosphatemia, suppressed calcitriol synthesis, resistance to parathyroid hormone, and kidney failure, may expose them to hypocalcemia [17], which increase the risk for clinical symptoms that associate it like tetany, seizures, and cardiotoxicity [2, 18]. A question may arise if hypocalcemia should be treated? After the first period of hypocalcemia, crush cases are essential to note that hypocalcemia, present during the crush syndrome, should not be treated unless patients are symptomatic hypocalcemia is symptomatic.

Hypercalcemia is frequent in crush victims, especially during recovery, because of the mobilization of the previously precipitated calcium salts from the muscles, the return of sensitivity to parathyroid hormone, and recovery of vitamin D synthesis [19]. During hypercalcemia, which is more common in crush patients who previously received calcium salts, tissular calcium precipitation may trigger cell damage and subsequent complications [4, 20, 21]. Hence, to avoid this, hypocalcemia should be treated only in case of symptoms.

Fasciotomy can effectively decrease the pressure and prevent distal ischemia, irreversible neurologic damage and soft tissue, renal failure, and bone infection [22]. However, fasciotomy takes the risk of infections [23] linked with open wounds, enhancing sepsis, amputation, chronic nerve dysfunction, hemodynamic instability, and death [5].

Fasciotomy is indicated when distal pulses are absent; it needs debridement of necrotic muscle and when the

intercompartmental pressures are higher than 30–40 mmHg [24].

Clinical symptoms like refractory hypercalcemia, hyperkalemia, metabolic acidosis, or refractory oligoanuria need the use of renal replacement therapy. The two alternatives to RRT, conventional hemodialysis, or continuous renal replacement therapy (CRRT), could be used. Conventional hemodialysis does not eliminate myoglobin because of its high molecular weight. However, some authors refer that high-flux dialyzers can make a difference in myoglobinuric AKI. However, hemodialysis resolves the effects of renal dysfunction such as uremia and fluid overload, and electrolyte abnormalities. Plasma exchanges with plasmapheresis have also produced good results in cases of rhabdomyolysis [2, 4, 21, 26]. When it is not possible for hemodialysis modality, peritoneal dialysis can be used, although we can have a slower potassium clearance [26].

The increased mortality in AKI is linked with infectious, pulmonary, cardiovascular, hematologic, gastrointestinal, neurologic, and psychiatric complications. It is unclear which victims will develop a full-blown crush syndrome, although the risk increases with trauma severity. Monitoring all clinical signs, such as brownish urine, oliguria, weight gain, edema, carefully makes able to early hospitalized high-risk patients [2, 21, 27] and reducing this risk.

Conclusion

Medical and logistic principles in disaster victims may differ from those of routine practice, so we need to be aware of this. The published "Recommendations for the Management of Crush Victims in Mass Disasters" by ERBP may effectively guide the health care system to manage disaster victims with renal problems correctly and improve patients' outcomes.

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CASE REPORTS

Incarcerated Amyand's Hernia with Destructive Appendicitis Complicated with Myocardial Infarction. A Case Report and Review of the Literature

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Abstract

Amyand hernia is a rare presentation in inguinal hernias (less than 1% of cases with inguinal hernias) which is evidenced when in herniated masses the presence of inflamed appendix is ascertained or not. It was named after a French surgeon, Claudius Amyand (1660-1740), who performed the first successful appendectomy in 1735, where he found an acute appendicitis in a herniated mass. Most cases are diagnosed intraoperatively, as an accurate preoperative diagnosis rarely becomes evident.

Management is individual depending on the stage of inflammation of the appendix, the presence of abdominal sepsis and concomitant factors. The decision should be based on factors such as the patient's age, the size and anatomopathological shape of the appendix, and in the case of an inflamed appendix, standard appendectomy and retinal herniorrhage should be the gold standard of treatment.

Amyand hernia is usually misinterpreted as a common incarcerata hernia. Symptoms that mimic appendicitis may appear. Treatment consists of a combination of appendectomy and hernia repair. The inflammatory status of the appendix determines the type of hernia repair and the surgical technique. Occasional appendectomy in the case of a normal appendix is not recommended.

Amyand hernia is a rare type of inguinal hernia in which the appendix is located in the hernia sac. We present a case of a recurrent incarcerated Amyand's hernia with complicated appendicitis. The 78 old polymorbide patient with right-sided incarcerated recurrent hernia was emergently operated on and appendectomy and non-mesh hernioplasty performed, on the 3rd postoperative day for a heart attack he was placed cardio stimulator with uneventful outcome. Fifteen months follow up did not show complications or complaints.

Keywords: Amyand's hernia, complicated appendicitis, hernia incarceration, local peritonitis

Introduction

Amyand hernia is a rare type of inguinal hernia in which the appendix is located in the hernia sac. Claudius Amyand first in 1735 described a case of successful appendectomy in an 11-year-old boy for a perforated appendix with an intestinal fistula in right-sided inguinal hernia [1,2]. Since 1953 in abdominal surgery the term "hernia Amyand" was introduced in honor of the French surgeon, Claudius Amyand (1660-1740), [3]. The disease is extremely rare, varies from 0.13 to 1% of all inguinal hernia cases, occurs mainly in males and is almost exclusively on the right side [4,5,6]. Many authors believe that the true incidence of the disease is lower than classically described [7,8].Children and adults suffer more often due to weaker intestinal fixation and demonstrate increased mobility[3,9] Losanoff J. and Basson M. first described a clinical classification with four types in Amyand hernia [10].

The clinical picture of the disease is nonspecific and in almost in all cases the diagnosis is intraoperative. CT, MRI, and inguinal ultrasound can improve preoperative identification of Amyand hernia [6,11]. In the case of incarcerated right inguinal hernia and lack of pathological data for air-fluid levels on abdominal radiography, some authors consider this as a possible indirect sign of the presence of a trapped "Amyand hernia" [12].Different clinical variants are described according to the location of the appendix in the hernia sac: only the tip of the appendix located in the sac, the entire appendix located in the sac and appendicular, the body and tip located in the abdominal cavity**.** A conducted large-scale systematic search in the medical database found a total of 161 patients with Amyand hernia, and the following types of appendix: normal - 73

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(45.4%), uncomplicated - 62 (38.5%) and perforated - 26 (16.1%) [13].

Issues of importance are time of incarceration to operation and the extent of peritonitis. In all cases of hernia incarceration and appendicitis – both appendectomy and herniotoimy should be performed.

Case presentation

We present a case of a recurrent incarcerated Amyand hernia with complicated appendicitis. The patient T.G.U. at the age of 78 with hospital ID № 35263 was admitted urgently in the University Hospital "St. George "- Plovdiv, First Clinic of Surgery on June 11, 2015, with clinical data for right-sided incarcerated recurrent hernia.

The present history was of a painful swelling in the right inguinal area with one day duration. Local pain grew stronger, accompanied with nausea, vomiting and febrility. The patient did have complaints for this hernia more than five years. He underwent surgery three years ago for it and had recurrence at the end of the first year.

On admission, the patient's condition was unsatisfactory. Pulse rate was 70 bpm, BP - 100/60 mmHg. Tongue was dry.

The local physical examination revealed an old scar from the previous operation in the right inguinal area and a fixed, painful on palpation swelling of 5/7 cm. The invagination digital test was negative. The abdomen was respiratory active, at the chest level, painful in the right inguinal area, without the presence of peritoneal irritation, Blumberg (-) neg., Slightly increased peristalsis was present.

Previous disease history included two brain strokes, a myocardial infarction, AH III, CIHD, RCD, HF II, Triple branch coronary disease, AV block III, mitral valve regurgitation, cerebrovascular disease.

Laboratory tests showed leukocytosis (Wbc) - 14.7 x10 ^ 9 / l, mild anemia - Rbc-4.21 x10 ^ 12 / l, Hb-125.0 g / l, Hct-0.384 l / l. Biochemical tests and coagulogram – n.a.d/ no abnormalities detected/. Abdominal radiography - lack of free gas or air-fluid intestinal levels.

The pre-operative diagnosis, based on clinical and laboratory data was considered as "Recurrent incarcerated inguinal hernia". After a short preoperative preparation, the patient underwent emergency surgery with spinal anesthesia. Oblique (indirect) incarcerated hernia right inguinal hernia was found. After dissection, the hernial sac was opened, from which was evacuated 30 ml dark bloody odorless exudate. A microbiological sample was taken. Gangrenous, incarcerated in the upper third appendicitis was found, with partially incarcerated and fused omentum, with local peritonitis/purulent deposits/, without perforation. Debridement and adhesiolysis was done, revealing and appendix of 10x1.5 cm, covered with purulent deposits. The caecum was presented and the base of the appendix ligated with a single suture and a transfix one of the mesoappendix. Typical appendectomy was performed, covering the stump with purse-string and Z-shaped suture. No effusion was detected intraperitoneally. Local lavage and Halstead hernia repair was done without mesh because of the advanced local tissue infection. Thus the patient underwent Herniotomy, Debridement, Adhesiolysis, Appendectomy, Lavage and Halstead inguinal hernia repair.

On the third postoperative day, the patient suddenly complained from severe retrosternal pain, shortness of breath and collapse. He was consulted with an internist and cardiologist and with acute coronary syndrome was transferred to the Invasive Cardiology Clinic, where a temporary pacemaker (EKS) was placed. SCAG (selective coronary angiography) was conducted, followed by balloon PTCA of RCAp. After the invasive procedure, the patient was strictly monitored, hemodynamically stable and with a marked reduction in subjective complaints. The next day, the temporary one was removed and PEX VVI was implanted. The patient was in satisfactory condition, without complaints and rehabilitated to self-care. After the invasive procedure he was discharged on the third day in good general condition.

The consultation with a surgeon registered primary wound healing, followed by suture removal and discharge. The histological result/B№12068-69/ showed phlegmonous appendicitis with periappendicitis. Microbiological testing/№5613/ of peritoneal culture was (-) negative and no pathogenic microorganisms were isolated.

The two recent post-dischsrge surgical examinations did not register any complaints.. The patient was followed for 15 months, with no abdominal complaints and no evidence of hernial recurrence.

Specific in this clinical case is that the hernial incarceration and the appendicitis are the subject of emergency abdominal surgery. The incarcerated inguinal hernia was diagnosed preoperatively, and destructive appendicitis was diagnosed intraoperatively., The patient underwent surgery for appendicitis and local peritonitis with a traditional parainguinal incision. In case of widespread peritonitis with exudate, herniolaparotomy or rarely lower midline laparotomy is advocated. Laparoscopic inguinohernioplasty can be done safely, using TEP or TAPP [14,15]. In case of an unchanged appendix in the hernial sac, there is no standardized operative approach, as the treatment depends on the personal choice of the surgeon [16,17].

Conclusion:

Complicated appendicitis in Amyand's incarcerated hernia is very rare clinical complication in the field of herniology. Due to difficult verification of complicated appendicitis in the incarcerated inguinal hernia by physical examination, image investigations can help the preoperative diagnosis.

Surgery depends on the elapsed time of the incarceration, the destructive changes in the appendix, the prevalence of peritonitis changes and patient general condition.

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CASE REPORTS

Out of Hospital Cardiac Arrest: A Case Report

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Abstract

Introduction: Sudden OHCA (Out of hospital cardiac arrest) is the third leading cause of death in industrialized nations. With more than 60% of cardiovascular deaths resulting from cardiac arrest, it remains the leading cause of death worldwide. Heart rhythms associated with cardiac arrest are divided into two groups: shockable rhythms (ventricular fibrillation/pulseless ventricular tachycardia (VF/pVT) and non-shockable rhythms (asystole and pulseless electrical activity (PEA)). VF is the most commonly identified arrhythmia in cardiac arrest patients. Urgent medical treatment includes cardiopulmonary resuscitation and early defibrillation.

Material and Methods: Materials for this case report are data collected from the medical records of the Emergency Medical Center of Sarajevo protocol of patients.

Case report: Our case report is presented with 59 years old man who had OHCA in his apartment. The initial rhythm was VF, and cardiopulmonary resuscitation was provided due to the Advanced life support guidelines to shockable rhythms. It was delivered 3 DC Shock-s (200J, 300J, 360 J) with the biphasic defibrillator, it was administered 1mg Adrenalin and performed endotracheal intubation. After the third DC shock, we got the return of spontaneous circulation ROSC. The patient was transferred to the University hospital, were he was stabile, and PCI of the LAD was performed as per the standard protocol. Echocardiography performed in the CCU revealed hypokinesia of RV, with preserved systolic function. On hospital day 7 he had a full neurological recovery. He was conscious, oriented, with normal breathing, blood pressure 125/79mmHg, sPO2 99, ECG: sinus rhythm, fr 87/min, without pathological signs. Echocardiography revealed the reduced systolic function of the left ventricle, with mitral regurgitation MR+2.

Discussion: Out-of-hospital cardiac arrest (OHCA) is a major health problem in Europe and in the United States. The numbers of patients who have OHCA annually in these two parts of the world have traditionally been reported to be 275,000 and 420,000 respectively. The success of resuscitation depends on many factors: well-organized health care, organization of outpatient emergency services, but primarily when it comes to OHCA, education of the population on Basic life support, and early Cardiopulmonary resuscitation and use of AED (automated external defibrillator).

Keywords: Out-of hospital, cardiac arrest, Ventricular fibrillation, Cardiopulmonary resuscitation, ALS, BLS.

Introduction

Sudden OHCA (Out of hospital cardiac arrest) is the third leading cause of death in industrialized nations. In Europe, more than 350,000 patients are affected every year. And 100.000 could be saved if lay resuscitation – giving chest-compressions immediately and before the arrival of the emergency medical services (EMS) – was improved all over Europe.[1, 12]

In 2017 the American Heart Association (AHA) updated estimated the total annual burden of Out of Hospital Cardiac Arrest (OHCA) at 356,500. At least 23% of OHCA treated by Emergency Medical Service (EMS) have VF/VT as the initial rhythm.[2]

With more than 60% of cardiovascular deaths resulting from cardiac arrest, it remains the leading cause of death worldwide. [3] Cardiopulmonary resuscitation (CPR) can

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be defined as a set of measures and procedures performed in a patient who has experienced cardiac and/or respiratory arrest with the aim of restoring cardiac function and respiration. Successful resuscitation is considered to be the return of temporarily lost vital functions, primarily cardiac ROSC(return of spontaneous circulation).[4]

Heart rhythms associated with cardiac arrest are divided into two groups: shockable rhythms (ventricular fibrillation/pulseless ventricular tachycardia (VF/pVT) and non-shockable rhythms (asystole and pulseless electrical activity (PEA). The principal difference in the treatment of these two groups of arrhythmias is the need for attempted defibrillation in those patients with VF/pVT. Other interventions, including high-quality chest compressions with minimal interruptions, airway management, and ventilation, venous access, administration of adrenaline, and the identification and correction of reversible causes, are common to both groups. [5]

VF is the most commonly identified arrhythmia in cardiac arrest patients. The first monitored rhythm is ventricular fibrillation/pulseless ventricular tachycardia in approximately 20%, both for in-hospital and out-of-hospital cardiac arrests.[6] The incidence of VF/pVT may be decreasing and can vary according to bystander CPR rates. Ventricular fibrillation/pulseless ventricular tachycardia will also occur at some stage during resuscitation in about 25% of cardiac arrests with an initial documented rhythm of asystole or PEA.[7] VF usually ends in death within minutes unless prompt corrective measures are instituted. [1, 2] Urgent medical treatment includes cardiopulmonary resuscitation and early defibrillation.

Protocols for cardiopulmonary resuscitation are the 2015 guidelines of the European Resuscitation Council (ERC) and the American Heart Association (AHA). Starting a survival chain is invaluable and increases the chances of successful resuscitation, with minimal deficits.

Ventricular fibrillation/ pulseless ventricular tachycardia as the initial rhythm has a better prognosis. Electrical defibrillation provides the single most important therapy for the treatment of these patients.[8]

Material and Methods:

For this case report are medical history from the resuscitation protocol of the Emergency Medical Center of Canton Sarajevo. The aim is to present a case of successful resuscitation in prehospital conditions, by the Emergency Medical Center of Canton Sarajevo, after ventricular fibrillation as *initial rhythm.*

Case report; Dispatch center of Emergency Medical Center of Canton Sarajevo received a call from a woman stating that her husband had fallen ill and that he had fainted. A team consisting of an emergency medicine doctor and two emergency medical technicians is sent from the central checkpoint. The team arrives at their home address in just under 5 minutes. There they find a 59-year-old man lying on the floor unconscious.

The patient is approached, and after checking the vital parameters, it is concluded that he is without consciousness, with no palpable carotid pulse, no spontaneous respirations, and wide non-reactive pupils. A postoperative scar is visible on the chest after heart surgery. Measures of Advanced life support, cardiopulmonary resuscitation, compression, and ventilation in a ratio of 30: 2 are approached, the airway is opened and the oropharyngeal tube is placed, and the patient is ventilated with a BMV with a maximum flow of 100% O2 15L / min.

After placing ECG electrodes to the patient, the VF is read on the monitor as the initial rhythm (Figure 2), and immediately delivered DC Shock 200 J with pedals from the mobile Lifepack 15 defibrillator, and continued with CPR, with ventilation. An intravenous route is opened in a cubital fossa with an 18G diameter cannula, and a 500 ml NaCl 0.9% infusion solution is added. After 2 minutes of a 30: 2 CPR cycle, the pulse is checked, also the rhythm on the monitor. The VF persists, and a second DC Shock 300J is delivered (Figure 3). Resuscitation measures are continued, Adrenaline 1mg is administered in a ratio of 1: 10000. The patient is intubated with tube number 7.5. After 2 minutes of CPR, the pulse and rhythm are checked.

The monitor is still VF, and 3 DC Shock 360 J is

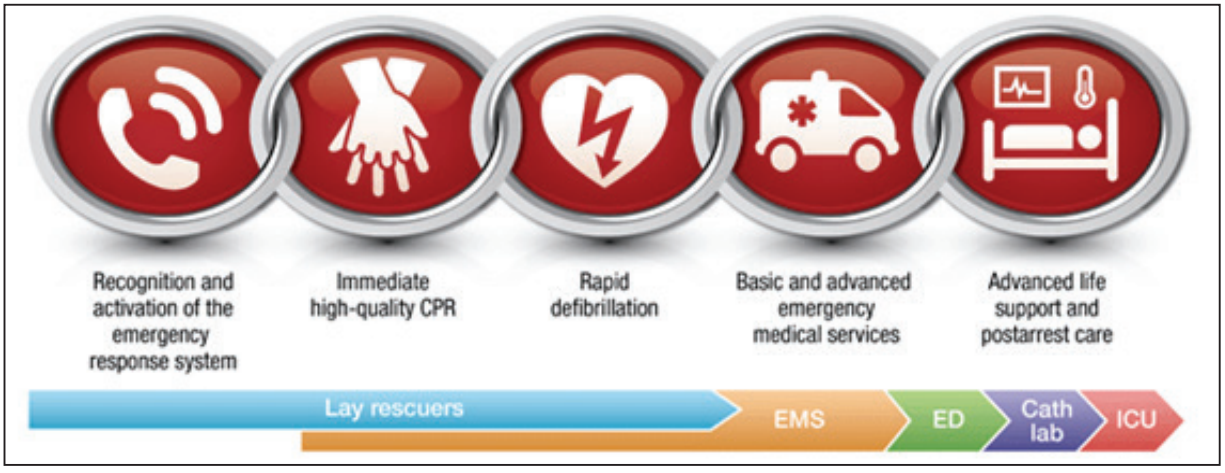


Figure 1: Chain of survival

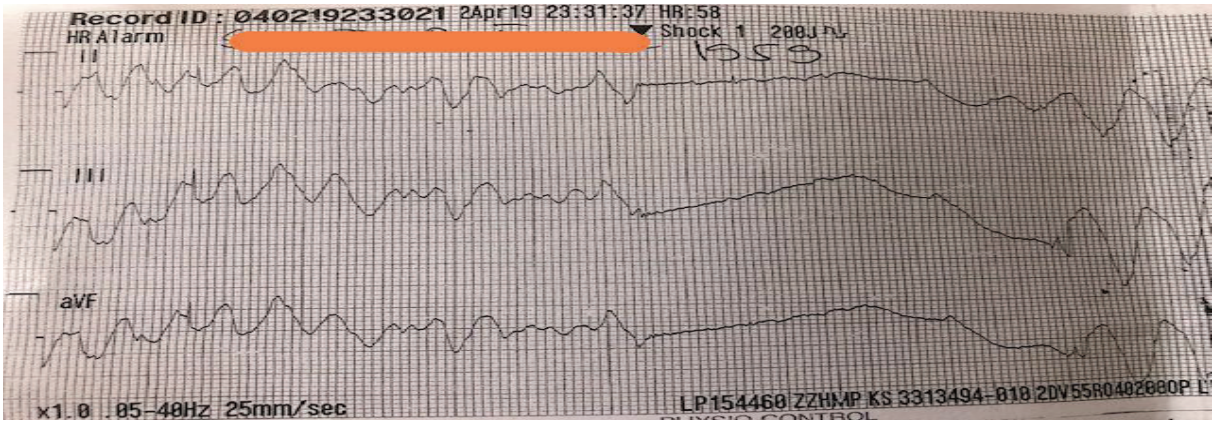


Figure 2: ECG -Initial rhythm VF,first DC Shock

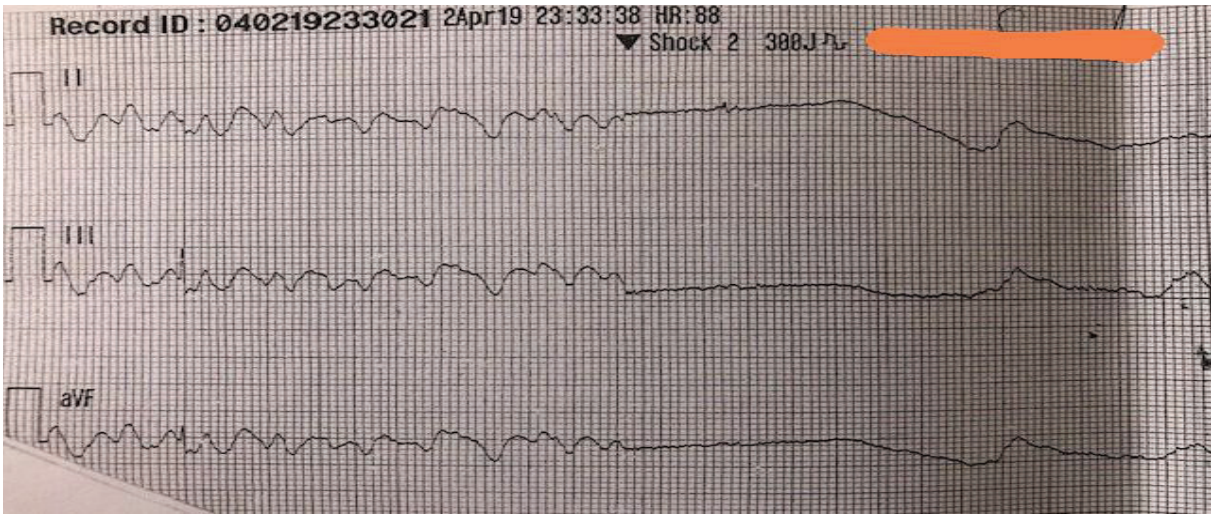


Figure 3: ECG after second DC Shock

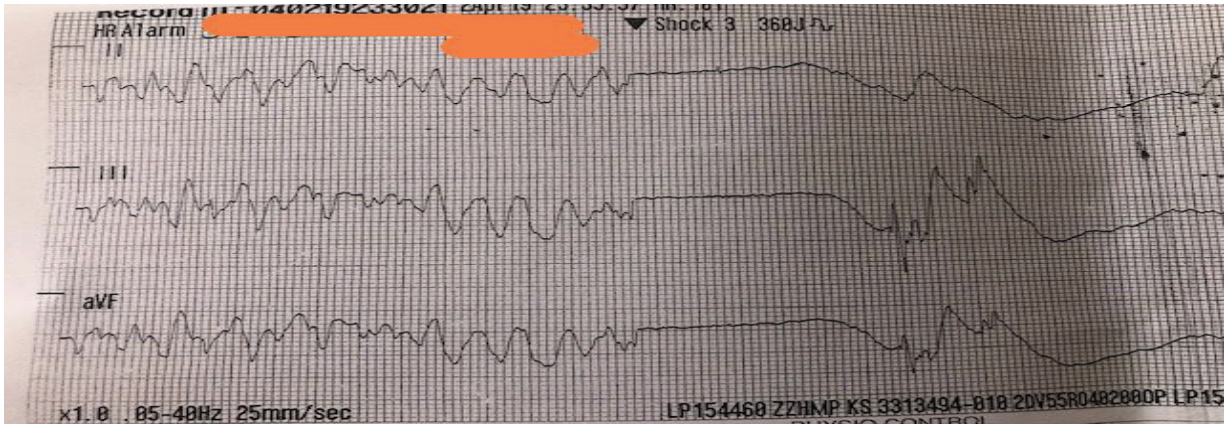


Figure 4:ECG after third DC Shock

delivered (Figure 4). A change occurs. A pulse is palpated over the a.Carotis, sinus rhythm fr 150 / min on the monitor (Figure 5), peripheral pulse present, patients have about 8 spontaneous respirations. The patient is transferred with monitoring of vital parameters to the emergency aid circuit, where he connects to Medumat, an assisted breathing option. Objectively the patient remains unconscious, central and peripheral pulse present, blood pressure 110/70 mmHg, saturation with sPO2 90, pupils react to light, about 10 respirations per minute, glucose 7.8 mmol/L. On a 12-lead ECG sinus rhythm, fr 94 / min, with ST depression present in V2-V6 (Figure 6).

We learn from the family that he had heart surgery a month ago and that Bypass surgery was performed. Longtime cardiopathy. We transfer the patient to the University Clinical Center. The patient already starts

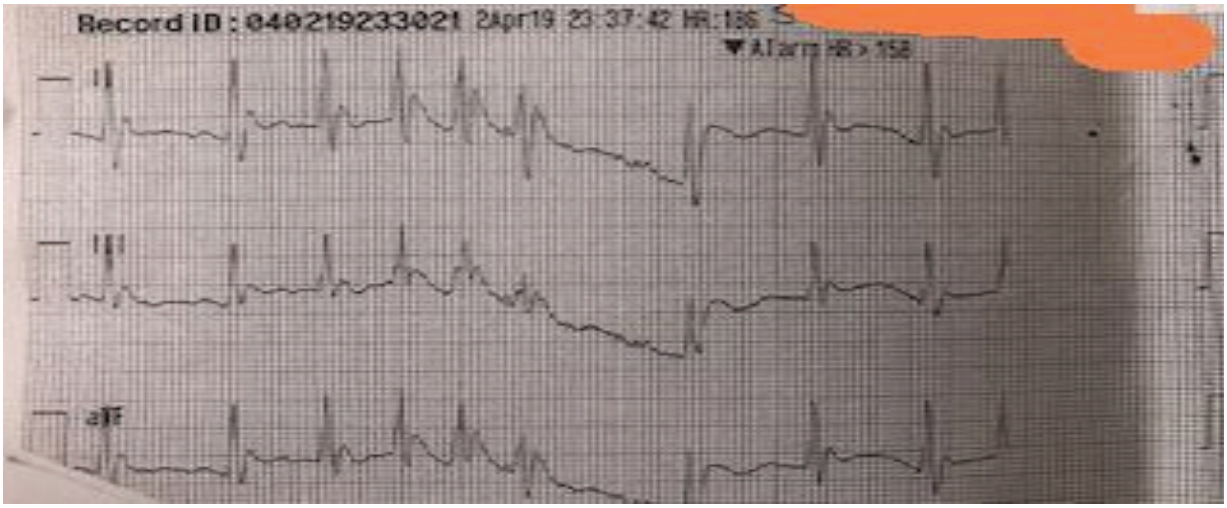


Figure 5:ECG after ROSC

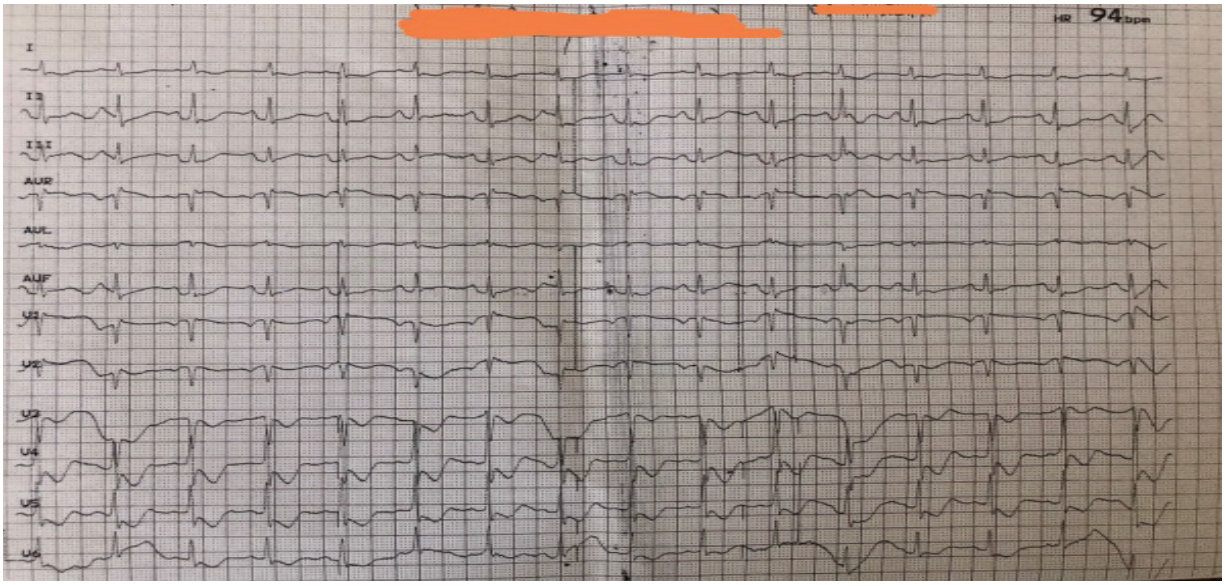


Figure 6: 12-lead ECG after ROSC

moaning, moves his arms, and tries to eject the endotracheal tube. The on-duty cardiologist and anesthesiologist place him in the cardiovascular care unit CCU and start preparations for the PCI procedure. PCI of the LAD was performed as per the standard protocol. Echocardiography performed in the CCU revealed hypokinesia of RV, with preserved systolic function. On hospital day 7 he had a full neurological recovery. He was conscious, oriented, with normal breathing, blood pressure 125/79mmHg, sPO2 99, ECG: sinus rhythm, fr 87/min, without pathological signs. Echocardiography revealed the reduced systolic function of the left ventricle, with mitral regurgitation MR+2.

Discussion

Out-of-hospital cardiac arrest (OHCA) is a major health problem in Europe and in the United States. The numbers of patients who have OHCA annually in these two parts of the world have traditionally been reported to be 275,000 and 420,000 respectively.9 10 The success of resuscitation depends on many factors: well-organized health care, organization of outpatient emergency services, but primarily when it comes to OHCA, education of the population on Basic life support, and early Cardiopulmonary resuscitation and use of AED (automated external defibrillator). According to the American Heart Association's 2014 data, nearly 45 percent of out-of-hospital cardiac arrest victims survived when bystander CPR was administered. The majority of Out of Hospital Cardiac Arrests (OHCA) occurs in public settings (18.8 percent), mostly homes/residences (69.5%) and nursing homes (11.7%).11 Early CPR measures and early defibrillation are invaluable. To increase the number of effective cardiopulmonary resuscitation we need a CPR national and regional register, educated and well-equipped ambulance stationed AEDs. In some European countries, there are applications, with which we can see

the network of AEDs in individual cities, where they are located. Educating the public about BLS (Basic life support) with the use of AEDs is crucial. The high success rate of resuscitation itself depends on the early CPR usually started by bystanders. Good organization of the emergency medical service, equipment, and education greatly contribute to a better outcome. The importance of the speed of arrival, which depends on the organization of the service itself, the dispatch center, and the deployment of teams in the city, is of great importance. Standardized equipment in all vehicles, and educated staff with the implementation of advanced life support measures.

Conclusion

Our case report showed successful resuscitation of OHCA in the patient's apartment. In this case, the ALS guidelines were applied. CPR was started immediately, after the detection of VF, defibrillation was delivered, and good ventilation and intubation of the patient ensured oxygenation. The speed of the team's arrival at the address, early CPR measures, early defibrillation, and airway management greatly contributed to the success of resuscitation. Transport to the University Hospital with monitoring of vital parameters and post-resuscitation treatment enabled the patient to be discharged without any neurological sequelae in good psycho-physical conditions.

COI Statement: This paper has not been submitted in parallel. It has not been presented fully or partially at a meeting or podium or congress. It has not been published nor submitted for consideration beforehand.

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CASE REPORTS

A case report of Xanthogranulomatous Cholecystitis – A Rare Entity

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Abstract

Xanthogranulomatous cholecystitis is a benign, uncommon type of chronic cholecystitis manifested by focal or diffuse severe inflammatory process of the gallbladder (GB). It is inflammatory disease of the gallbladder characterized by the infiltrations of plasma cells, lipid-laden histiocytes, and the fibroblasts proliferation in GB wall. Gallstones are present in all patients, and like most symptomatic gallbladder diseases, there is a female predominance. It is an active inflammatory process which could leads to significant morbidity. The term Xanthogranulomatous cholecystitis was initially proposed by Goodman and Ishak in 1981. The pathogenesis of XGC is the rupture of Rokitansky-Aschoff sinuses and extravasation of bile into the muscular layer. The rupture of the serosa results in adhesion to the adjacent liver, duodenum, and transverse colon. Macroscopically, it appears like yellowish masses in the wall of the GB. Radiologically it is an important mimic of gallbladder carcinoma.

Key words: Xanthogranulomatous cholecystitis, gallbladder MRI, GB carcinoma, Chronic cholecystitis.

Case presentation

Our case is a 69-year-old male with recurrent attacks of upper abdominal pain for more than 10 yrs. There is also history of weight loss of 9 kg over 2 months, loss of appetite, decreased activity and generalized weakness. No history of jaundice or fever. On examination there is suspected mass in the RUQ which is tender on palpation. Patient did US abdomen in private clinic that showed GB wall thickening.

Investigations.
IMAGING: MRI Abdomen and MRCP:



Figure 1 Shows distended GB with thickened wall and high signals intramural pockets.

Original article, no submission or publication in advance or in parallel

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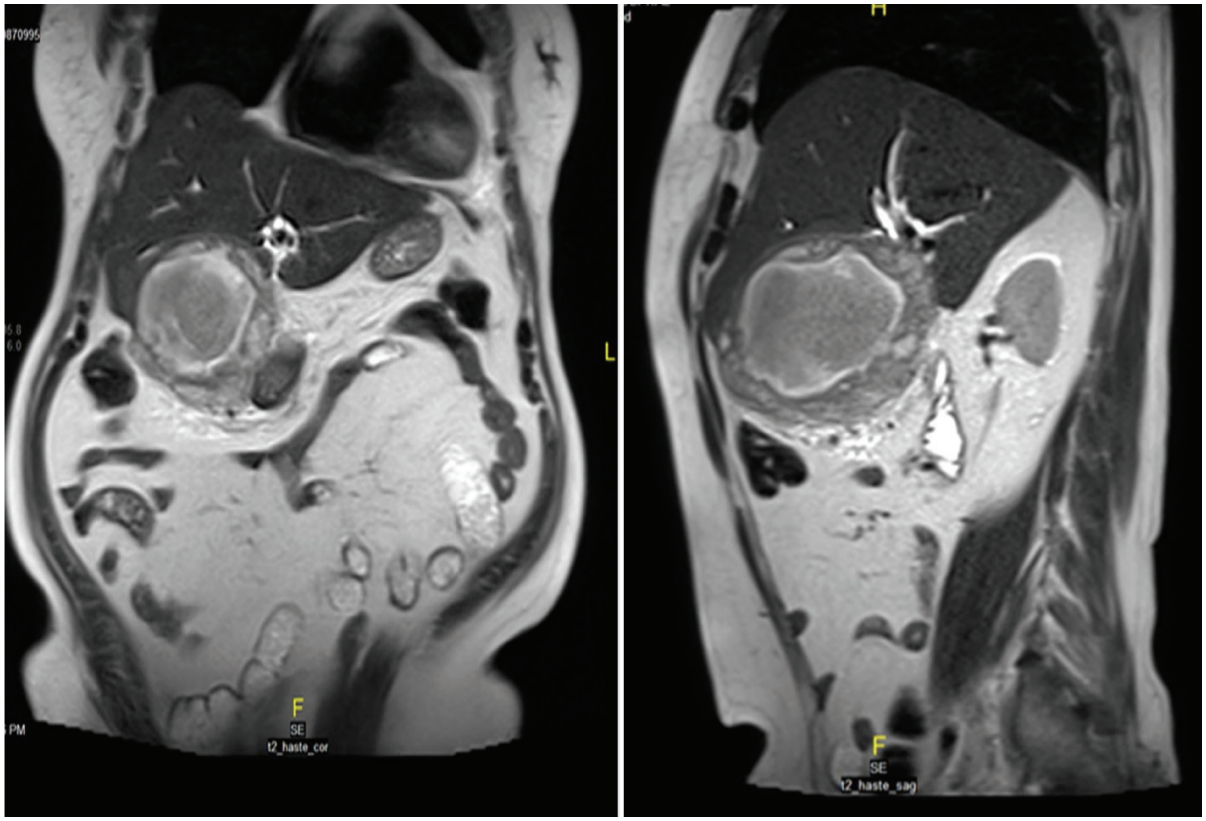


Figure 2 T2 WI Coronal and Sagittal, re-demonstration of distended, thick G.B wall with high signal intramural pockets. Blurring of interface between GB and liver. Pericholecystic edema and fat stranding. Mild intrahepatic biliary radicles dilatation.

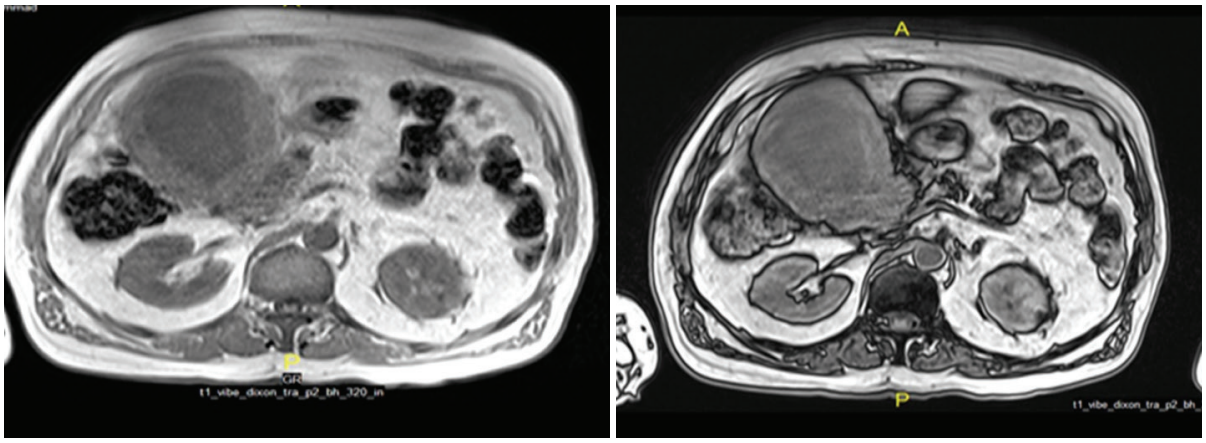


Figure 3 IN and OUT phase revealed absence of fat contents.

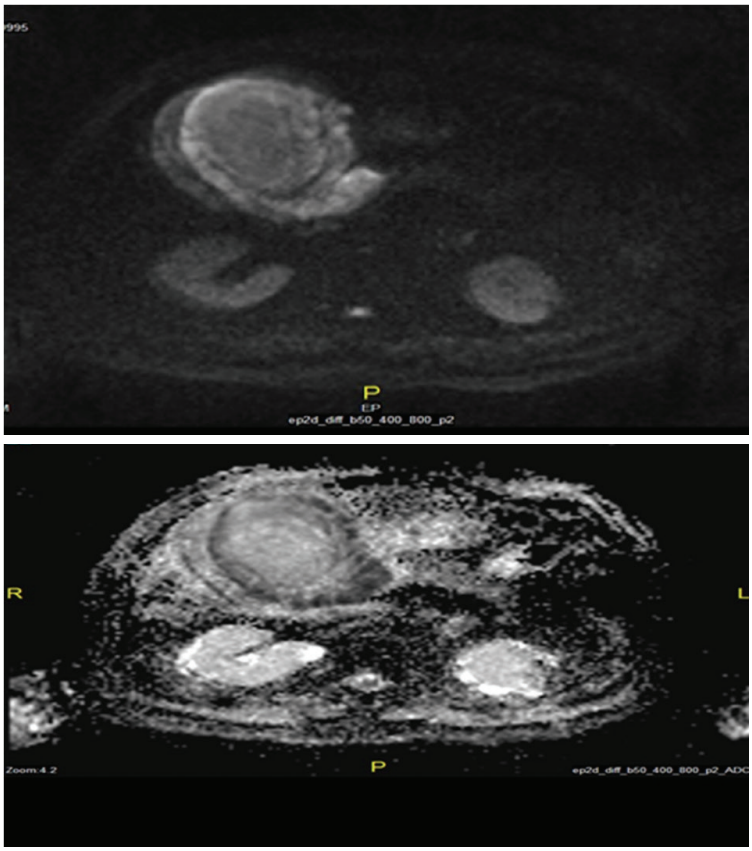


Figure 4 DWI and ADC revealed restricted diffusion of the pockets (abscesses) without restriction of septae between it.

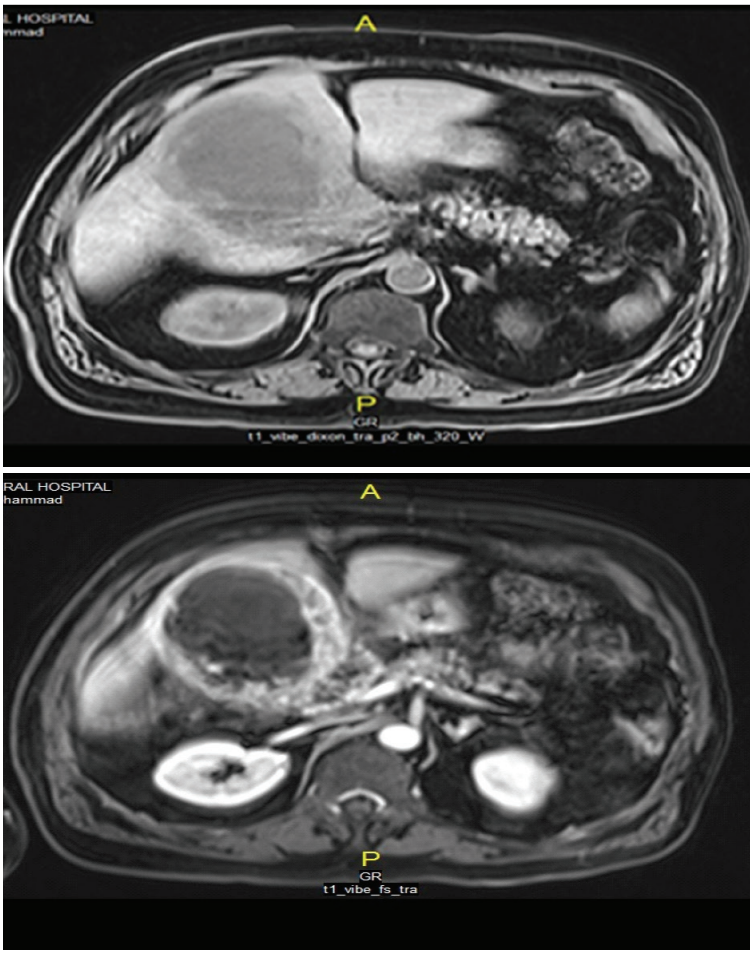


Figure 5 Pre and Post contrast revealed enhancement of the gall bladder wall without washout. The pockets are not enhanced.

LABS: Laboratory investigations were normal except elevated liver function tests (LFTs) that showed aspartate aminotransferase 54 UI/L, alanine aminotransferase 39 UI/L, total bilirubin 45.7 umol/L, direct bilirubin 17.4umol/L.

Differential diagnosis

Primary GB carcinoma was the main concerning differential.

Acute or chronic cholecystitis and acute cholangitis.

Treatment

Laparoscopic cholecystectomy was converted to an open cholecystectomy with liver resection due to extensive adhesions.

Outcome

Surgical pathology revealed

-Acute suppurative and hemorrhagic cholecystitis on top of Xanthogranulomatous cholecystitis.

-Benign hepatic tissue is identified, shows steatosis.

-Negative for dysplasia or malignancy.

Discussion

This patient presented with intermittent RUQ pain with tender palpable mass. However, there was no jaundice or fever. Only 20% of patients with Xanthogranulomatous cholecystitis (XGC) manifested with obstructive jaundice which is not a frequent presentation [1]. XGC is an uncommon variant of chronic cholecystitis characterized by xanthogranulomatous inflammatory changes of the GB. Intramural accumulation of lipid-laden macrophages, acute and chronic inflammatory cells is the main features [1]. XGC could be severe and spill over to the adjacent organs as liver, bowel and stomach resulting in dense adhesions, perforation, abscesses, fistulous communication with adjacent bowel. XGC is an uncommon, focal, or diffuse destructive inflammatory process of the GB. This issue was first described in 1970 by Christen and Ishak as fibroxanthogranulomatous inflammation [2]. Recently, these terms, as ceroid granuloma, ceroid-like histiocytic granuloma of the GB [3] and biliary granulomatous cholecystitis [4], have been abandoned in favor of XGC, a descriptive term first used by McCoy et al [5]. McCoy et al [6] in 1976 though it was first described in 1970 by Christensen et al [7]. Christensen et al [7] and Amazon et al [8] had observed a pseudo tumoral expression of chronic cholecystitis which was specified by the xanthoma-like foam cells, scarring and contained ceroid (wax-like) nodules in an inflamed GB wall. XGC is manifested by irregular GB wall thickening with formation of yellowish nodules which composed of lipid-laden macrophages, inflammatory cells, and fibroblasts. The pathogenesis is chronic inflammation and gallstones are present in most of the patients. XGC could mimic GB cancer or results in complications such as perforation, abscess, and fistula.

In 78–98% of XGC cases, gallstones are noted [11], obesity and/or diabetes mellitus are common [10]. The pathogenesis of XGC could suggested that the extravasation of bile into the GB wall, either from ruptured Rokitansky-Aschoff sinuses or focal mucosal ulceration [3,9]. Gallstones obstruction and intraluminal bile stasis also involved [12].

Patients can present with features of acute cholecystitis (22%), chronic cholecystitis (88%), pain (95%), obstructive jaundice (22%), cholangitis (2%) and palpable mass (5%) [13]. On examination, a palpable mass or positive Murphy's sign could be localized. However, these clinical features are not specific for XGC and often no clinical difference between XGC and GB carcinoma [14].

Complications in about 32% of cases including perforation, abscess formation, fistulous tracts to the duodenum or skin, and extension of the inflammation to the liver, colon, or surrounding soft tissues [15]. Yu et al [16] stated that elevation of tumor biomarkers could happened in XGC which added further confusion in differentiating XGC with GB carcinoma.

XGC is connected with GB carcinoma in 8.5% - 30.5% of cases [17].

Possibility of coexisting infection has also been proposed. Howard et al [21] have stated that intraoperative cultures of the bile and GB was positive for Escherichia coli, Klebsiella, Enterococcus and, less frequently, Pseudomonas, Serratia and Staphylococcus aureus.

Parra et al [22] observed that the wall thickening was hyperechoic in comparison to the liver in 100% of patients examined by ultrasound. The presence of hypoechoic nodules or bands in the thickened GB wall could be seen. The sonographic hypoechoic nodules were reported in 15% and 73% cases by Parra et al [22] and Kim et al [23] respectively. Hypoechoic band was reported in 19% of cases [22,24]. Hypoechoic bands could be result from generalized involvement of the mucosa [22]. Complications as perforation, abscess and hepatic infiltration could be assessed on ultrasound [22,23].

CT findings of patients presenting with acute symptoms and patients presenting with chronic symptoms are usually not much different [25]. CT findings including diffuse or focal wall thickening, luminal surface enhancement (LSE) with continuous mucosal lines or mucosal lines with focal breach and intramural hypoattenuating nodules in the thickened walls. Cholelithiasis and choledocholithiasis are often found.

GB thickened wall from 4.0 mm to 18.5 mm and is usually diffuse [25]. Diffuse GB wall thickening has been seen in 88.9% and 87.8% of patients by Goshima et al [26] and Zhao et al [25] respectively. Focal thickening is less common in XGC, and is more with GB carcinoma. Diffuse thickening is usually symmetrical but diffuse asymmetrical thickening has also been found in 22.2% cases [25,26].

The intramural nodules (85.7% and 61.1%) by Zhao et al [25] and Goshima et al [26] respectively) are either xanthogranulomas or abscesses. A large area of the thickened GB wall by intramural nodules is highly associated with XGC [27]. XGC is more often revealed on imaging than abscesses as the abscess results in more complications [19].

A continuous mucosal lining is more seen with XGC (66.7% of cases) in comparison with disrupted mucosal line (33.3%) [26]. XGC is abnormalities of GB wall and hence mucosal surface is intact or only focally denuded. On the other hand, GB carcinoma arises from the GB epithelium and induces mucosal disruption in most of the cases. Mucosal disruption was observed in 82.2% cases of GB carcinoma. Mucosal disruption in XGC is only seen with diffuse thickening of the GB wall and patients with disrupted mucosal lining are more prone to have complications [25].

The infiltration of adjacent structure scan manifest as pericholecystic fat strandings, blurring of interface between liver and GB, early enhancement of liver (or transient hepatic attenuation difference), infiltration of bowel (duodenum/colon), infiltration of stomach and invasion of abdominal wall. While pericholecystic fat stranding and blurring of interface between liver and GB are common, the other findings are less appreciated.

Hepatic infiltration appears as an early parenchymal enhancement in 40% of cases [25]. Other complications are GB perforation, abscesses or fistulations. Inflammation of the biliary tree (xanthogranulomatous choledochitis) could be seen [29]. However, lack of dilated intrahepatic biliary is more seen in XGC and it could differentiate it from GB carcinoma.

Lymphadenopathy (> 10 mm short axis diameter) has been mentioned by different studies. Zhao et al [25] stated an incidence of 10.2%, Goshima et al [26] stated an incidence of 90%. However, both studies stated that regional lymphadenopathy could be useful in differentiation from GB carcinoma. 41% patients with GB cancer showed homogeneous enhancement of enlarged lymph nodes in comparison to 100% of XGC [26].

MRI, In-phase and out of-phase chemical shift imaging demonstrating fat within the thickened gallbladder wall in XGC [20]. Zhao et al [25] subjected intramural nodules to chemical shift imaging. 77.7% of XGC nodules displayed reduction of signal intensity on opposed -phase images. This variability of the intramural nodule on MRI could be due to the presence of different contents as foamy histiocytes, lymphocytes, plasma cells, polymorphonuclear leucocytes, fibrosis, giant cells, micro abscess and necrosis within these nodules [26].

Areas of iso- to mildly high signal on T2 WI, displaying mild enhancement in early phase and intense enhancement in delayed phase, consistent with areas of excessive of xanthogranulomas [28]. Areas with very high signal intensity on T2 WI without enhancement matched with necrosis and/or abscesses [28].

Enhanced areas in the liver bed in early phase on CT and MR images could by associated with XGC which consistent with accumulation of inflammatory cells and extensive fibrosis [28].

A study by Binit Sureka, et al, 2017, stated that the majority of cases (73.3%) showed discontinuous mucosa. 75% were found with thickened wall 3–10 mm and 0% normal wall thickness (p=0.03). Diffuse thickened wall in 76.7%, focal thickening in 10% and polypoidal thickened wall in 6.7% cases. Intramural nodules with discontinuous mucosal lining in 87.5%.

The study concluded that, discontinuous mucosal lining is evident in XGC. Diffuse thickened wall, intramural nodules, continuous or discontinuous mucosa and Gall stones could suggest XGC rather than GB cancer [30].

Kang et al [43] have showed the value of diffusion-weighted magnetic resonance imaging (DWI) in differentiating XGC from GB wall-thickening type of cancer. DWI restriction was founded in GB cancer (68%) and in XGC (7%). Also, the mean ADC value of XGC was higher than GB cancer wall-thickening type with statistical significance (1.637 × 10-3 mm2/s vs 1.076 × 10-3 mm2/s respectively, P = 0.005) [31]. The study concluded that DWI in addition to routine MRI improves differentiation between XGC and wall-thickening of gallbladder cancer.

It was concluded that coexisting of diffuse gallbladder wall thickening, low-attenuated intramural nodules, continuous mucosal line, mucosal enhancement and gallbladder stone highly suggest XGC. XGC commonly infiltrating the liver and surrounding fat. Chemical-shift MRI helps classifying intramural nodules in the gallbladder wall.

Abbreviations; US – Ultrasound; RUQ - Right Upper Quadrant; GB – Gallbladder: MRI - Magnetic Resonance Imaging; MRCP - Magnetic Resonance Cholangiopancreatography; LFTs - Liver Function Tests; LABS- Laboratory; RUQ - Right Upper Quadrant; XGC - Xanthogranulomatous Cholecystitis;

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CASE REPORTS

Acute Erythroleukemia in a Trauma Patient. A Case Report

Eriselda Taulla*

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Abstract

Introduction: Acute erythroid leukemia (AEL) is a rare type of acute myeloblastic leukemia. Acute erythroid leukemia is characterized by a predominant erythroid proliferation, there are 2 subtypes: erythroleukemia (erythroid/myeloid leukemia) and pure erythroid leukemia…

Myelodysplastic syndromes (MDS) are a group of biologically and clinically heterogeneous clonal disorders characterized by ineffective hematopoiesis and peripheral cytopenia due to high apoptosis

The purpose to presenting this case is how to differentiate an acute erythroleukemia (AEL) from myelodysplastic syndrome (MDS).

Case report. A 74 year old man came to emergency room after he falling down from the stairs and then was hospitalized with a two weeks history of severe weakness, anorexia, weight loss. He suffered of diabetes mellitus type II insulin dependent, and HTA. The physical examination showed cutaneous and conjunctival pallor, large ecchymosis in the low extremities and hepatosplenomegaly. CBC showed: pancytopenia and macrocytosis, neutrophils 60%, normoblasts 4:100 and reticulocyte count 3%.

Conclusions*:* The diagnosis was Acute Erythroid Leukemia. The % of myeloblasts in bone marrow was > 20% of non-erythroid cells. Erythroleukemia characterizes from hepatomegaly this is found and in our case. Differential diagnosis is based mainly in bone marrow aspiration, immunophenotyping (flow cytometry)

Keywords: acute erythroleukemia, myelodysplastic syndrome, erythroblast

Introduction:

Acute erythroid leukemia (AEL) is a rare type of acute myeloblastic leukemia. Acute erythroid leukemia is characterized by a predominant erythroid proliferation, and in the current World Health Organization (WHO) classification scheme there are 2 subtypes: erythroleukemia (erythroid/myeloid leukemia) and pure erythroid leukemia. Morphologic findings are most important for establishing the diagnosis. The erythroleukemia subtype, which is most common, is defined as the presence of 50% or more erythroid precursors and 20% or more blasts in the nonerythroid component. The pure erythroid leukemia subtype is composed of 80% or more immature erythroblasts. It accounts for less than 5% of cases of acute myeloblastic leukemia. Usually occurs in patients 50 years of age or older. It is characterized by a prominent component of erythroblast.

The term leukemia is used for the first time in 1847 from Virchow. In 1857 Friedreich recognized acutae and chronic types. Di Guliemo described acute erythroleukemia in 1917.

Erythroleukemia is subtype of acute myeloblastic leukemia LAM6 according to French-American-British (FAB) classification.

As all hematologic malignancies the etiology for AEL and MDS is unclear but some risk factors are: prior chemotherapy (particularly alkylating agents and epipodophyllotoxins), ionizing radiation, benzene exposure, constitutional chromosomal abnormalities and smoking.

Case Report:

A 74-year-old man came to emergency room after he falling down from the stairs and then was hospitalized with a two

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weeks history of severe weakness, anorexia, weight loss. He suffered of diabetes mellitus type II insulin dependent, and HTA. The physical examination showed cutaneous and conjunctival pallor, large ecchymosis in the low extremities and hepatosplenomegaly.

CBC showed: pancytopenia and macrocytosis, neutrophils 60%, normoblasts 4:100 and reticulocyte count 3%. Serum B12-1225pg/ml and folates -21ng/ml. DTC negative, ITC negative, LDH 1660 U/L, total bilirubin 1,1 mg/dl, total proteins 5,6 g/dl, glucose 388 mg/dl, and other parameters within the normal range. The bone marrow aspiration revealed: myeloblasts 6%, promyelocytes 1%, myelocytes 6%, metamyelocytes 6%, bands 5%, neutrophils 4%, proerythroblasts 4%, basophilic normoblasts 4%, polychromatophilic normoblasts 4%, promegaloblasts 7%, basophilic megaloblasts 10%, polychromatophilic megaloblasts 36%, orthochromatic megaloblasts 7%. The rate myeloid/erythroid = 1/3, showing the predomination of the erythroid line which constitute 65% of all cells. The proportion of proerythroblasts and basophilic erythroblasts was 38% of all erythroblastic cells. The proportion of megaloblastic forms was 80% of all erythroblasts. PAS staining of bone marrow smears showed typical cytoplasmatic positivity of pathologic erythroblasts: granular in more immature cells and diffuse in more mature ones, confirming the diagnosis of erythroleukemia.

We treat him with Cytarabine 100mg/m² every 12h day1-7. The patient had an extremely aggressive clinical deterioration and he died ten days after admission.

Discussion:

Acute erythroid leukemia (AEL) is a rare type of acute myeloblastic leukemia. AML 6 according to FAB classification. There are 2 subtypes: erythroleukemia (erythroid/myeloid leukemia) and pure erythroid leukemia. Morphologic findings are most important for establishing the diagnosis. The erythroleukemia subtype, which is most common, is defined as the presence of 50% or more erythroid precursors and 20% or more blasts in the nonerythroid component. The pure erythroid leukemia subtype is composed of 80% or more immature erythroblasts. It accounts for less than 5% of cases of acute myeloblastic leukemia. Usually occurs in patients 50 years of age or older but it can occur in children too (the incidence is rare). It is characterized by a prominent component of erythroblast. Erythroleukemia often come after Myelodysplasia, but it can also develop de novo. The prognosis of erythroleukemia is poor. The median survival is 3 months. Acute erythroleukemia should be distinguished from Myelodysplasia, refractory anemia with excess blasts, reactive erythroid hyperplasia following therapy administration with erythropoietin, megaloblastic anemia, acute myeloblastic megakaryocytic leukemia (LAM 7), lymphoma and Acute lymphoblastic leukemia.

Immunophenotyping on bone marrow aspirate shows glycophorin A, CD36+, CD71+. Erythroleukemia characterizes from hepatomegaly this is found and in our case. Myelodysplastic syndromes (MDS) are a group of biologically and clinically heterogeneous clonal disorders characterized by ineffective hematopoiesis and peripheral cytopenia due to high apoptosis and by variable tendency to evolve to bone marrow failure or acute myeloblastic leukemia. Commonly manifesting with macrocytosis and cytopenia due to impaired blood cell production.

Conclusions:

The diagnosis was Acute Erythroid Leukemia. The % of myeloblasts in bone marrow was >20% of non-erythroid cells. Erythroleukemia often come after Myelodysplasia, but it can also develop de novo. Immunophenotyping on bone marrow aspirate shows glycophorin A, CD36+, CD71+, CD 45+, CD 117+-, CD33+-, CD13+- but HLA-DR is negative and CD34-.

Erythroleukemia characterizes from hepatomegaly this is found and in our case. Differential diagnosis is based mainly in bone marrow aspiration, immunophenotyping (flow cytometry)

The prognosis of erythroleukemia is poor. The median survival is 3 months. The treatment is with chemotherapy cytarabines (ara C)

The regimen for induction therapy is the "7 + 3" regimen: Cytarabine at 100 mg/m2/d intravenously (IV) by continuous infusion on days 1-7 plus an anthracycline (idarubicin 12 mg/m2 or commonly used daunorubicin 45-60 mg/m2) or anthracene Dione (mitoxantrone 12 mg/ m2) (IV) push on days 1-3. [14, 15]

The regimen for consolidation therapy includes 2 options. The high-dose ara-C (HiDAC) regimen includes cytarabine at 3 g/m2 IV q12h on days 1, 3, and 5 for 4 cycles. [16] The "5+2" regimen includes cytarabine at 100 mg/m2/d IV continuously infused on days 1-5 plus daunorubicin at 45 mg/m2 IV on days 1 and 2 for a total of 2 cycles. [17]

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Acknowledgement:

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CASE REPORTS

Treatment of COVID-19 Complications at Home Conditions

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Abstract

This paper reports the clinical characteristics, diagnosis, and treatment of myself after being infected with Covid-19. After comprehensive treatment including nasal cannula oxygen therapy, antiviral and anti-infection therapies, liquid volume management, glucocorticoids, analgesia and sedation, blood tests control, anticoagulation, and thrombus prevention, and electrolyte balance maintenance, after 24 days finally my health situation was good. The purpose of this case report is to provide a reference for the clinical diagnosis and treatment of myself, in-home condition in this critical situation.

Keywords: COVID-19, clinical characteristics, clinical diagnosis, treatment, Favipiravir, Methylprednisolone

Introduction

In COVID-19 deep airway and alveolar destruction occurs due to inflammatory reaction resulting into severe pneumonia. In COVID-19, lung injury is not only due to viral damage to the tissues, but it is also due to the immune response that leads to activation of inflammatory cells and release of cytokines. In COVID-19, acute respiratory distress syndrome ARDS is produced due to mucinous or cellular fibro myxoid exudates, desquamation of pneumocytes and alveolar damage and hyaline membrane development. Within 5-7 days the disease becomes more aggressive due to pneumonia and respiratory failure. It is important to start the prompt and strong treatment for suppression of inflammatory response and cytokine storm.

Infection with COVID-19 can be classified into three stages of increasing severity [1]

Stage I: The early infection or viral response phase during which symptoms of upper respiratory tract infection dominate.

Stage II: The pulmonary phase when the patients develop full-blown pneumonia with all its associated symptoms.

Stage III: The hyper inflammation phase when patients develop acute respiratory distress syndrome (ARDS), sepsis, and kidney and other organ failures. (Fig.1) [2]

Case Report

Patient (myself) 45-years old, weight: 82 kg, Sex: Male, Blood group: A +, without concomitant diseases except dyslipidaemia. Cured 5 years ago for hypertension with Ramipril 2.5 mg x 1 / day. Hypertension subsequently dominated by physical activity and diet. Currently without medical therapy.

Infected with Co-Vid 19 at the end of October 2020. The first symptoms appeared on 31.10.2020 with fever up to 37.5 ° C, conjunctivitis, general weakness, sweating, back muscle pain.

On the third day the PCR test was performed which resulted positive for CO-VID-19.

On the same day I started the therapy with: Aspirin 100 mg / d, Enoxaparin 4000 UI x 2 (s/c) and antiviral therapy with Favipiravir: the first day 1600 mg x 2 and for 5 other days 600 mg x 2. Max temp 37.8 ° C. On the 5th day I also did a lung CT (Fig 2.)

On day 5 I had pain localized in the right zygomatic area and I suspected recurrence of right maxillary sinusitis. After we saw in CT- scanner the pulmonary opacities described above and with the suspicion of right maxillary sinusitis recurrence, I decided to start Dexamethasone 4 mg x 2 times a day and antibiotic therapy Ceftriaxone 1 g x 2 a

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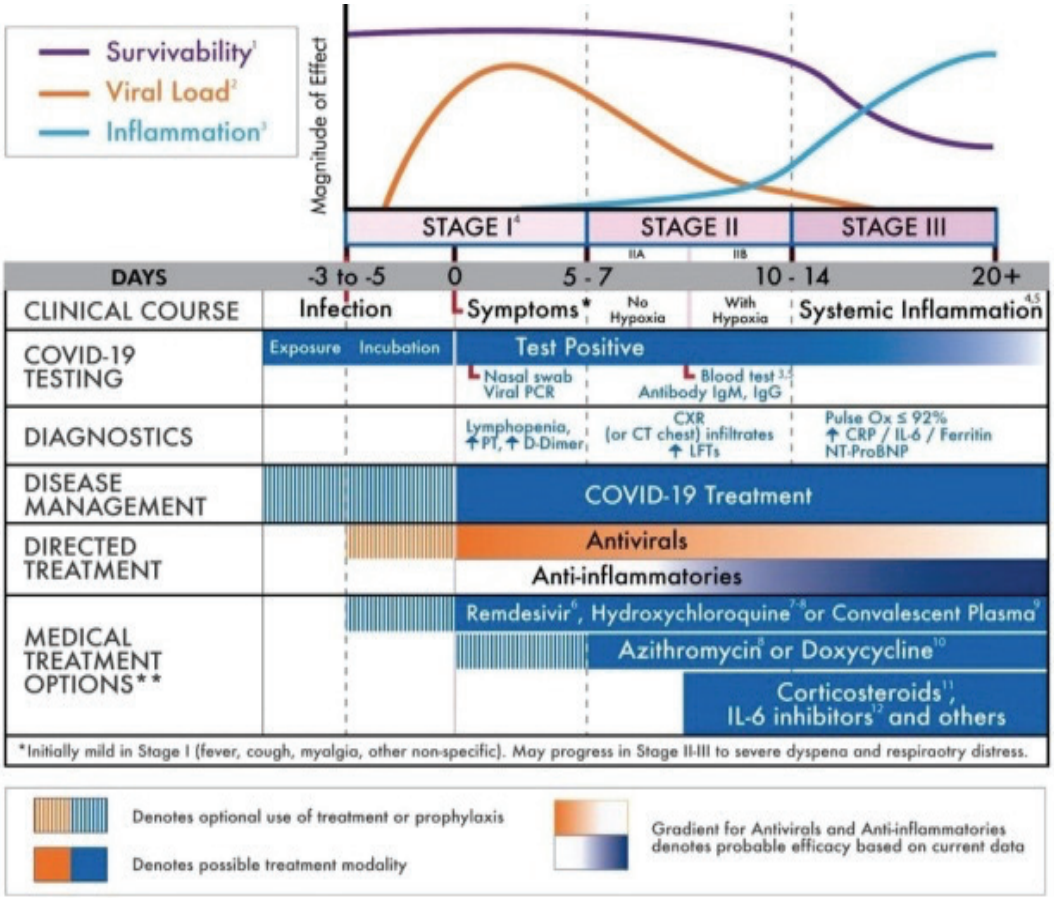


Figure.1 COVID-19 Clinical Stages and Management Strategy [2] (Reference 1-12)

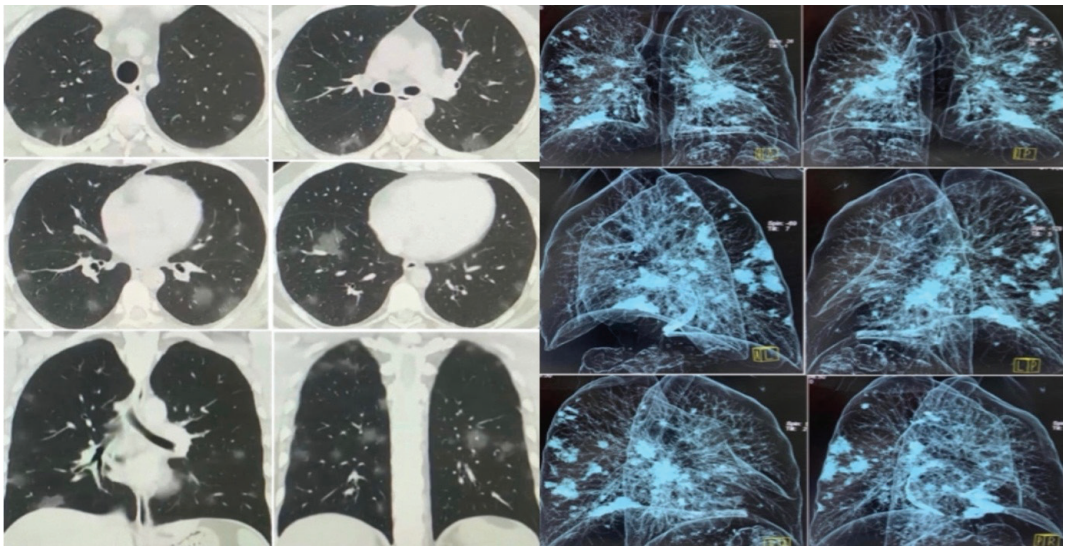


Figure 2. CT scanner 5th day, ground glass opacities with peripheral and bilateral distribution are observed, with the presence of dilated vessels inside the opacities

Pulmonary lobes	Involvment in %	Points
Right upperlobe	5-25%	2
Right middle lobe	5-25%	2
Right lower lobe	25-50%	3
Left upper lobe	5-25%	2
Left lower lobe	25-50%	3
CTSS (total)	**12 from 25 (moderated)48%**	

day + Levofloxacin 500 mg x 1/ day.

Day 7-8 max temp 37.2. I was relieved from the pain and discomfort from sinusitis.

Day 8 the situation started to get worse.

The temperature reached 38.5° C with shivering, O_2 saturation 92%, I noted a slight feeling of dyspnoea, HR started to increase up to 110 b / min.

Thinking that the situation from Covid19 was getting worse or maybe the fear of the beginning of a bacterial pneumonia, in consultation with my colleagues, I decided to start Methylprednisolone and Tazocine.

On day 9 another CT was realized (Fig.3).

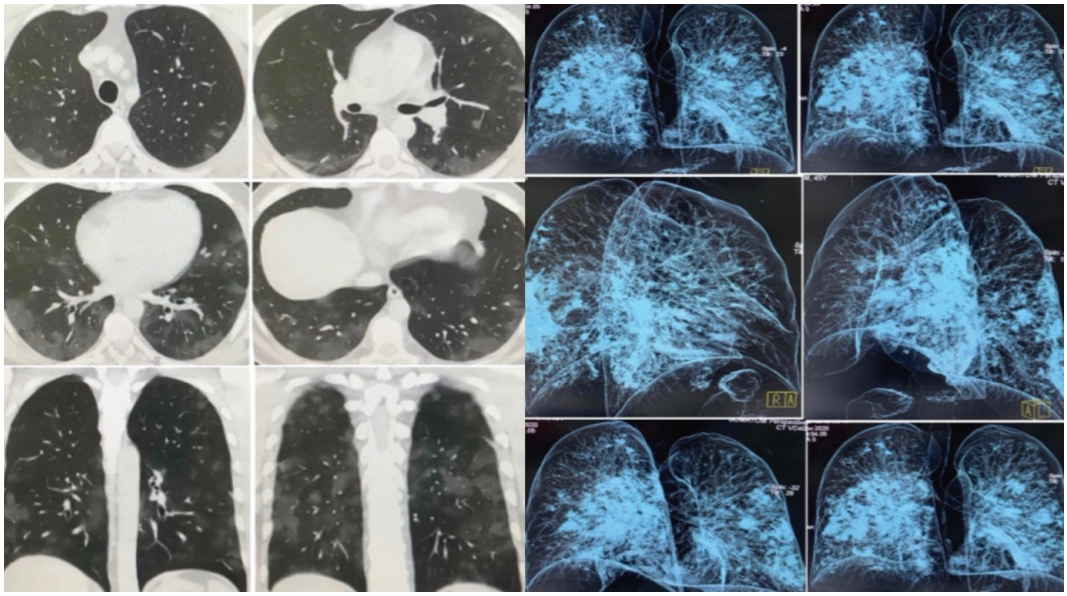
for Covid19 were at the highest levels. On day 12 the situation began to improve, Sat O_2 93%. The temperature started to drop to 37-37.5 °C. HR ~ 110-125 /min at minimum efficiencies, especially during and after shower.

After the 16th day, the temperature was always below 37 ° C. What worried me was the tachycardia after small physical efforts.

To rule out any possible cardiac problems I did an echocardiography, where we did not detect any cardiac problem. Cardiac function was normal.

But dyspnoea during stair rising and at minimal efforts was present.

Figure 3. CT scanner 9th day, there is a reduction in the density of opacities, with the spread of the affected area but without the appearance of new focuses, with a tendency for confluence (crazy-paving). A small focus of alveolar consolidation at the right pulmonary base is suspected.



Pulmonary lobes	Involvmentin %	Points
Right upper lobe	25-50%	2
Right middle lobe	5-25%	2
Right lower lobe	25-50%	3
Left upper lobe	25-50%	3
Left lower lobe	25-50%	3
CTSS (total)	**14 from25 (moderated)56%**	

Blood tests were repeated with alteration of erythro-sedimentation, neutrophils, and PCR was seen as in the table below. PCT procalcitonin resulted 1.9 ng/ml, a questionable result.

I decided that Levofloxacin should also be taken I/V.

During 9th-11th day, the condition continued to be the same, temp: 38.5°C; Sat O_2 90-91%; on the 10th day it was necessary to use 2-3 l of nasal O_2 and stay upside down in bed.

During these days I also did pulmonary gymnastics, balloon bloating and ball aspiration, to prevent alveolar atelectasis.

On the 11th day, I repeat the blood tests again. Markers

On the 17-th day, I did the PCR Covid19 test again, and the result was negative, I repeated the blood tests that were improving, I repeated the PCT, which resulted 0.13 ng / ml.

After the 18th day, as an anticoagulant, I started Xarelto (Rivaroxaban) 15 mg replacing Enoxaparin and Aspirin.

The clinical situation, laboratory data and complete treatment for both weeks will be summarized in the table below. (Tab 1)

57 days after the beginning of Covid-19, I made a control MRI of the lungs where you can observe some fibrotic bands in the posterior segments of the inferior lobes of both lungs. (Fig.4)

	Clinical outcomes			Blood results									Medical treatments					
Days	Temperature	Sat O2 %	HR/min in effort	WBC 10^3/µl	Neutrophils %	Lymphocytes %	PCR mg/l	Fibrinogen mg/dl	Ferritinemia ng/ml	D-Dimer ng/ml	RBC Sedimentation	Favipiravir i mg	Dexamethasone mg	Medrol mg	Ceftriaxone 2g/d iv	Tazocinl 4.5g *3/d iv	Levofloxacin 500mg/d iv	Clindamycin 600mg/ po
1	37.5	98	105															
2	37.6	97	104															
3	37.8	98	102	4.78	75	15	11.2	368	380	100	3	3200						
4	37.3	98	101									1200						
5	37.8	96	110									1200	8		+		+	
6	37.4	96	108									1200	8		+		+	
7	37.5	95	110	7.73	84.8	9.1	26.3					1200	8		+		+	
8	38.5	92	118										8	125	+	+	+	
9	38.7	92	121	13.60	90	4.3	84							250		+	+	
10	38.5	91	120											250		+	+	
11	37.4	93	122	15.33	90.1	3.6	126		1500	435	56			250		+	+	
12	37.5	93	124											125		+	+	
13	37.2	95	128											125		+		
14	36.8	96	125											80		+		
15	37.4	96	123											80				+
16	37.2	97	125											40				+
17	36.8	98	125	14.46	79	13	32	461	1147	777	25			8				+
18	36.4	98	120											8				+
19	36.5	98	117											8				+
20	36.6	98	115											4				
21	36.4	98	112											4				
22	36.3	98	115				5,6		936	225				4				
23	36.2	98	114											4				
24	36.3	98	112											4				

Table 1- Clinical outcomes

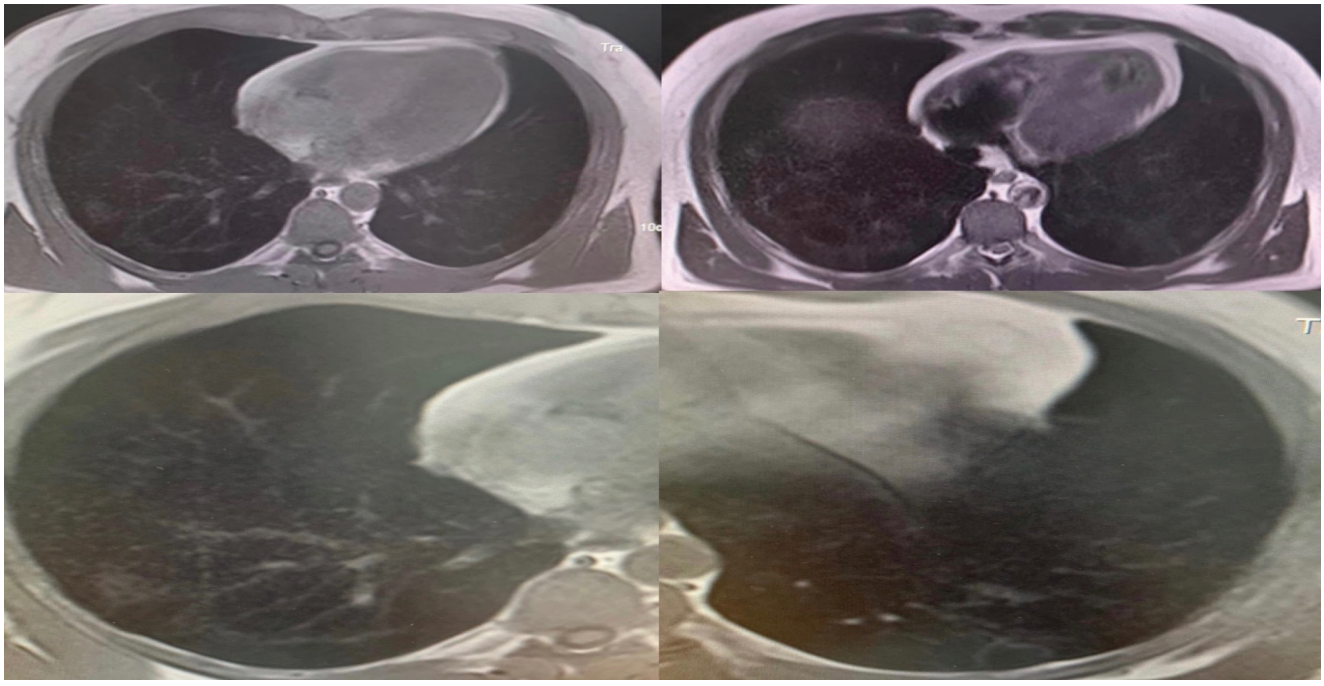


Figure 4. Control MRI after 57 days

Discussion

There is much discussion about the use of antivirals in patients infected with the corona virus. Favipiravir *(T-705; 6-fluoro-3-hydroxy-2-pyrazinecarboxamide)* is an anti-viral agent that selectively and potently inhibits the ribonucleic acid (RNA)-dependent RNA polymerase of RNA viruses [3]. In Japan, it is approved for use with novel influenza virus and is thought to be an effective drug for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronavirus disease 2019 (Covid-19) presents a complex pathology including inflammation, endothelial damage, thrombus formation, and acute respiratory failure [4, 5, 6].

This syndrome requires complex treatment to reduce viral genome amounts, anti-inflammatory drugs, and anticoagulation.

The decision to start Favipiravir was based on the use of Favipiravir in some infected colleagues a few months ago, with moderate pulmonary involvement. These patients did well, had no aggravation of the pulmonary situation and were treated at home, although they had moderate forms of pulmonary involvement.

There are many studies that support the use of Favipiravir for the first 10 days.

One of the studies is by a Japanese team, authored by Hitoshi Yamamura *(Posted 25 Jun, 2020)* Effect of Favipiravir and an anti-inflammatory strategy for Covid-19.

This study has aimed to evaluate the effect of cocktail (Favipiravir, steroid and heparin) therapy for severe Covid-19.

The treatment protocol of this study was as follows: oral Favipiravir (3600 mg on day 1, 1600 mg from day 2 to day 14), methylprednisolone (1000 mg for 3 days), and low molecular weight (2000 IU every 12 h) or unfractionated heparin (10,000–12,000 IU/day).

We decided to use methylprednisolone based on our experience with two patients who underwent heart surgery with valvular problems and CABG which were infected with coronavirus. Starting methylprednisolone at a dose of 250 mg /d significantly improved the pulmonary radiological repertoire and significantly affected the good performance of these two patients by extubation after 7 days.

The results are seen even in many studies but the most prominent with the authors: Maryam Edalatifard, Maryam Akhtari published in the European Respiratory Journal on: Intravenous methylprednisolone pulse as a treatment for hospitalized severe Covid-19 patients: results from a randomized controlled clinical trial

In this study, we assessed the intravenous methylprednisolone effect on the treatment of patients with severe Covid-19 patients. Clinical data showed that methylprednisolone administration at the beginning of the early pulmonary phase of illness improved remarkably pulmonary involvement, oxygen saturation, dyspnoea, HR, RR, temperature and inflammatory markers such as CRP and IL-6 serum level in patients, suggesting that methylprednisolone could be an efficient therapeutic agent for hospitalized severe Covid-19 patients at pulmonary phase [7].

Methylprednisolone administration was begun on the 8th day, when the Favipiravir administration stopped.

Conclusion

It should be noted that the situation I passed through was very difficult, viral pneumonia and bacterial overgrowth were important and the pulmonary situation could worsen. I think that aggressive treatment with the antiviral (Favipiravir) methylprednisolone, strong I/V antibiotics, and pulmonary gymnastics prevented this situation from getting worse.

COI Statement: This paper has not been submitted in parallel. It has not been presented fully or partially at a meeting or podium or congress. It has not been published nor submitted for consideration beforehand.

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CASE REPORTS

Ulcerative colitis: the role of elective and emergency surgery

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Abstract

Inflammatory bowel disease (IBD) is a group of auto-inflammatory conditions characterized by chronic, remitting, and relapsing inflammation of the alimentary tract. It is comprised of two phenotypically different entities: Crohn's disease, and ulcerative colitis (UC). The aim of this article is to explore the role of the general surgeon regarding the treatment of patients suffering from UC while presenting a case of a 55-year-old woman with low-differentiated colon adenocarcinoma associated with ulcerative colitis. Patients with UC have a high-risk of developing colorectal cancer. While medical treatment is commonly the initial approach to UC, surgery constitutes a major contributor in dealing with UC.

Case report. A 55-year-old female with hypertension and iron deficiency anemia presented to our emergency department with fever, diarrhea, and epigastric pain for 24 hours which was not associated with heartburn, vomiting, melena, or hematemesis. On examination, the patient's temperature was 39°C, heart rate was 104 beats per minute, blood pressure was 108/65 and the respiratory rate was 20 breaths per minute. Her abdomen was soft, without distension, and with no evidence of palpable mass...

Keywords: ulcerative colitis, colorectal cancer, colorectal surgery

Introduction:

Inflammatory bowel disease (IBD) is a group of auto-inflammatory conditions characterised by chronic, remitting and relapsing inflammation of the alimentary tract [1]. It is comprised of two phenotypically different entities: Crohn's disease -which is capable of affecting the entire length of the digestive tract, causing focal, segmental and transmural inflammation- and ulcerative colitis (UC) -which causes superficial, diffuse inflammation, extending in a continuous manner from the rectum to the proximal colonic segments [2]. More specifically, Ulcerative Colitis is a chronic disease that involves the colonic mucosa and causes inflammation and ulcers [3-4]. The frequency of UC is increasing among the population per year, but the most worrying fact is that universal findings indicate that patients with UC have a high-risk for developing Colorectal Cancer (CRC) [5]. UC-related CRC represents 1-2% of all cancers and it is considered a serious complication of UC resulting in 10-15% of all deaths of patients with IBD. However, it should be noted that some recent studies estimate a much lower UC-related CRC frequency (approximately 1/500-1/1600 patients annually) [5]. Except for the duration of UC, other risk factors are primary sclerosing cholangitis (PSC), a long-term disease that affects the bile ducts, family history, smoking, severity of inflammation, and medical therapy used [4-5]. The mechanism behind the initiation and the development of cancer is widely studied and it mainly focuses on inflammation. More specifically, chronic inflammation and repeated stimulation of epithelial cells for proliferation is considered as an excellent environment for tumor formation and results in low-grade dysplasia which can easily be transformed into high-grade dysplasia [3, 6]. Inflammation also leads to reactive oxygen species (ROS) production, which cause cellular damage and can affect processes like DNA synthesis and repair [3]. Moreover, IBD is associated with abnormal intestinal mucosal barrier function, permitting bacterial invasion, thus bacterial microbiome is involved in the pathogenesis, as well as inflammatory cytokines [3, 6]. Regarding the molecular

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mechanism, several signaling pathways and particularly their regulation by miRNAs is involved [4, 7]. UC-CRC can be highly aggressive and leads to metastases, therefore, patients with UC need to proceed with regular screenings for cancer [3]. Surveillance colonoscopy is proposed to be conducted regularly, usually annually, since the diagnosis of UC. During a colonoscopy, the doctor uses a long and flexible tool to examine the colon and detect dysplasia. If any alterations are observed, a biopsy can also follow. The treatment of CRC that is usually used is the total colectomy which involves removing the entire colon. In some cases, however, a polypectomy, polyps' removal from the inside of the colon, or a proctocolectomy, removal of both colon and rectum, can be applied. This option is mainly dependent on the type of malignancy, its distribution, and the characteristics of dysplasia [4]. It should also be noted that in presence of an IBD disease, like ulcerative colitis, chemoprevention which includes the use of an anti-inflammatory therapy can decrease the risk for cancer development. Among the agents that can be used are 5-aminosalicylic acid (5-ASA), ursodeoxycholic acid (UDCA), mesalazine, and sulfasalazine. All these agents are safe, inexpensive and they inhibit inflammation pathways, that as we have already seen, play an important role in pathogenesis and malignant transformation of cells [4-5].

While medical treatment is commonly the initial approach to UC, surgery constitutes a major contributor in dealing with UC [8]. The aim of this article is to explore the role of the general surgeon regarding the treatment of patients suffering from UC, while presenting a case of a 55-year-old woman with low-differentiated colon adenocarcinoma associated with ulcerative colitis.

Case Presentation:

A 55-year-old female with hypertension and iron deficiency anemia presented to our emergency department with fever, diarrhea and epigastric pain for 24 hours which was not associated with heartburn, vomiting, melena or hematemesis. On examination, the patient's temperature was 39^{o}C, heart rate was 104 beats per minute, blood pressure was 108/65 and respiratory rate was 20 breaths per minute. Her abdomen was soft, without distension and with no evidence of palpable mass. Rectal examination was performed and was negative for blood. Her routine blood tests revealed hemoglobin of 9.1 g/dL, 16890 leukocytes and 112000 platelets. Liver and renal function test, serum amylase and lipase were normal, while serum level of butyrylcholinesterase was low [9]. Chest and abdominal radiography showed no abnormalities. A further computed tomography (CT) scan of the abdomen was performed and revealed an approximately 7-cm tumor in the sigmoid colon. There was no evidence of free air, abscess formation or metastases. The patient was hospitalized for 3 days in the surgical clinic and underwent exploratory laparotomy the 3th day of her hospitalization, as symptoms of pain and fever were persistent. In the operating room following general anesthesia, midline incision was performed. The small and large bowel was inspected from the ligament of Treitz till the rectum. During the running of the large bowel a visible mass was recognized in the sigmoid colon as well as inflammation of the inner lining of the ascending, transverse, and descending colon (Figure 1). Subtotal colectomy with temporary end ileostomy was performed. The patient did not have any postoperative complication and she was mobilized 12 hours postoperatively. She was started on oral diet on postoperative day three and was discharged on postoperative day six. Her final histopathology report was suggestive of low-differentiated adenocarcinoma associated with ulcerative colitis.

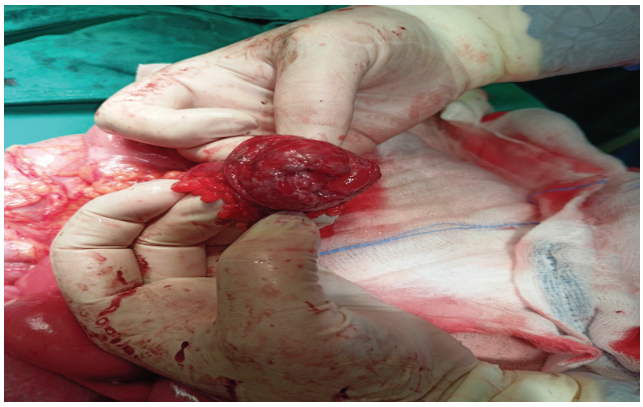


Figure1. Inflammation of the inner lining of the descending colon

Discussion:

Ulcerative Colitis and Elective Surgery

As a principle, surgical intervention, encompassing the dissection of the colon and the rectum, is curative for ulcerative colitis [10]. Patients suffering from this condition have an overall 25-35 % chance of undergoing surgery during their lifetime [11]. Surgical intervention in UC can provide treatment options in elective as well as emergent situations.

Chronic continuous ulcerative colitis refractory to immunosuppressive treatment, high grade dysplasia and malignant transformation constitute indications for elective surgery [12]. Colectomy offers a number of benefits to patients with severe refractory UC that is unresponsive or only partially responsive to medications as it entails complete removal of the colon, thus abolishing its associated risks (toxic megacolon, hemorrhage, dysplasia, carcinoma) as well as avoiding potent medications and their potential side effects [13]. Regarding the incidence of colorectal cancer in UC, it is approximately 4/1000 per person per year with an average prevalence of 3.5% [14]. The risk for colorectal cancer increases as time progresses and is 2%, 8% and 18% after 10, 20 and 30 years of disease [15]. Moreover, 45-50% of patients diagnosed with high grade dysplasia or non-adenoma dysplasia associated lesion or mass (DALM) have developed colorectal cancer at the time of colectomy [16]. These data

clearly demonstrate the importance of surgery when dealing with ulcerative colitis in non-emergency settings.

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the procedure of choice [17]. It consists of the complete removal of the colon from the cecum down to the dentate line and the consequent restoration of the continuity of the gastrointestinal tract with the creation of an ileal reservoir, most commonly in the form of a J-pouch [12, 18]. The advantages of this technique include markedly decreased risk of UC-associated neoplasia as the entirety of the target organ is excised, reduced to no need of immunosuppressive medication while it also offers patients an unchanged body image with no stoma and a preserved anal route of defecation safeguarding the patients' quality of life [17, 19-21].

Ulcerative Colitis and Emergency Surgery

The indications for emergent surgery include perforation, uncontrolled haemorrhage, fulminant disease, and toxic megacolon [22].

Fulminant colitis and toxic megacolon represent acute exacerbations of UC associated with high morbidity [23]. Their overall incidence in UC is approximately 10% [15, 24]. The clinical presentation of both of these clinical entities includes acute onset of bloody diarrhoea, anorexia, abdominal tenderness, and colicky pain [25]. In order for a patient to be considered as toxic at least two of the following must be present: fever greater than 38.6°C, tachycardia, leucocytosis greater than 10.500/L and hypoalbuminemia (<3.0 g/100 mL), however the distinguishing feature of toxic megacolon is a total or segmental non-obstructive dilatation of the colon (>5.5 cm) [24-26]. Subtotal colectomy with temporary end ileostomy is considered to be the operation of choice, as the preservation of the rectum safeguards the possibility of restoring the continuity of the intestinal tract with an ileal-pouch rectal anastomosis [23]. The initial treatment should be medical, support with fluids, electrolytes, albumin and blood transfusion are necessary for the adequate resuscitation of the patient, whereas steroids and immunomodulators such as cyclosporin and infliximab are recruited in order to control the inflammatory response. Postoperative pain control can be achieved by administration of paracetamol and parecoxib in order to avoid side effects of opioid analgesics [27-28]. Surgery is reserved for patients not responding to medical treatment, though early surgical intervention is entailed with decreased morbidity and mortality [23, 29].

Up to 3% of ulcerative colitis patients, mainly those with pan-colonic disease and in the setting of an acute flare, may develop acute severe lower gastrointestinal bleeding – usually attributed to diffuse mucosal ulceration [30]. Although it is an uncommon complication, it accounts for approximately 10% of all urgent colectomies for ulcerative colitis [31]. The presence of an endoscopically treatable lesion is uncommon, and surgery is required in less than half of cases during the initial hospitalization. Indication for surgery is considered either a massive initial bleeding with hemodynamic instability and need for catecholamines or if a patient requires more than 4 red blood cell concentrates per 24 h [12]. Recurrent hemorrhage is not rare, and for these cases surgery may be the most appropriate treatment [32].

Free perforation is a rare occurrence complicating ulcerative colitis in approximately 2% of cases. Perforation typically takes place in the setting of toxic megacolon but also may occur as a result of surveillance colonoscopy. Diagnosis of perforation in this setting may be delayed if the patient is on high-dose steroids or other immunosuppressants. In these settings, the appropriate management involves urgent resuscitation, administration of broad-spectrum antibiotics, and emergent surgical intervention [33].

In emergent situations the recommended operation is colectomy and ileostomy, leaving the rectum intact, since reconstruction is not an option in the acute setting [34-35]. A total proctocolectomy should be avoided because it is associated with greater postoperative morbidity and mortality due to increased operative time, risk of blood loss, pelvic sepsis, pelvic nerve damage, and small bowel obstruction greater postoperative morbidity and mortality due to increased operative time, risk of blood loss, pelvic sepsis, pelvic nerve damage, and small bowel obstruction [33]. A three-stage procedure is conducted in patients with a considerably reduced general health condition, or in patients depending on high doses of steroid therapy as avoidance of proctectomy and ileal pouch formation avoids pelvic sepsis and higher risk of pouch failure [35]. The first step includes subtotal colectomy and terminal ileostomy with Hartmann stump formation. Secondly, after stabilization of the patient, a proctectomy with IPAA and protective ileostomy is performed. The loop ileostomy is then taken down in the third step finally restoring the continuity of the gastrointestinal tract [12, 15]. Some of these surgical operations can also be performed laparoscopically having the advantages of laparoscopic procedures, such as lower hospital stays and earlier return to activities [36-38].

Conclusion:

To summarize, the treatment of inflammatory bowel disease necessitates a multidisciplinary approach by a team of specialized gastroenterologists and general surgeons. It is apparent that the contribution of both specialties is catalytic in both elective and emergency situations, in order to safeguard both the safety and the quality of life of the patient.

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Disclosure: The authors declared no conflict of interest. No funding was received for this study.

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AJTES

Albanian Journal of Trauma and Emergency Surgery

EDITORIAL POLICY

Scope and Mission

Albanian Journal of Trauma and Emergency Surgery (AJTES) that comes out two times a year, peer-reviewed and open-access international journal. The journal is the official scientific publication of the is the official publication of the Albanian Society for Trauma and Emergency Surgery (ASTES) Tirana, Albania. The language of the journal is English.

AJTES was founded in 2017 for the first time and publishes scientific articles that aims to promote interest, knowledge, and quality of care in emergency and trauma surgery. Its mission is to open an interdisciplinary forum that allows for the scientific exchange between basic and clinical science related to pathophysiology, diagnostics, and treatment of traumatized patients. The journal covers all aspects of clinical management, operative treatment, and related research of traumatic injuries and health care research, conducted in all fields of medicine and health care, as well as interesting case reports and clinical images, invited reviews, invited medical education papers, editorials, opinions and viewpoints, comments and letters to the Editor. The structure of each edition of the publication comprises section categories determined by the Editor and reflects the views of the Editorial Board.

AJTES encourages academicians, researchers and specialists of different medical and health care fields from all over the world to publish their valuable research in all branches of medicine and health care.

The journal's aim is to publish original articles with high scientific and ethical quality.

The Editorial Board of the *AJTES* and the Publisher adhere to the principles of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the US National Library of Medicine (NLM), the World Medical Association (WMA), the US Office of Research Integrity (ORI), the European Association of Science Editors (EASE), and the International Society of Managing and Technical Editors (ISMTE).

AJTES permits and encourages authors to post items approved for publication from the journal on personal websites or institutional repositories both prior to and after publication, while providing bibliographic details of the publication in *AJTES*. All articles are also available in PDF format on our website https://journal.astes.org.al/ and can be downloaded free of charge.

The *AJTES*'s mission is to distribute and expand worldwide good quality research, focused primarily on the medical and health care problems of the European and not only.

AJTES is open to publication for all the authors that comply with the scientific and ethical requirements of the journal. All manuscripts submitted for publication are strictly internally and externally peer reviewed for their originality, methodology, scientific relevance, quality, ethical nature and suitability for the journal. A similarity check is performed on all manuscripts submitted. All the articles published at *AJTES* will be fully accessed online. The open-access publication fee for this journal is EUR 200 for full-length articles and EUR 150 for case reports.

Submission of a manuscript implies that the submitted work has not been published before (except as part of a thesis or report, or abstract); that it is not under consideration for publication elsewhere; that its publication has been approved by all co-authors. If and when the manuscript is accepted for publication, the author(s) still holds the copyright and retains publishing rights without restrictions. Authors or others are allowed to multiply article as long as not for commercial purposes. For the new invention, authors are suggested to manage their patent before published.

Ethics

AJTES is committed to the highest standards of research and publication ethics. All submitted manuscripts are screened for plagiarism in order to detect instances of overlapping and similar text. The editors will act in accordance to the relevant international rules of publication and research ethics (COPE guidelines, WAME resources, WMA policies and ORI) if any ethical misconduct is suspected.

The journal recommends an approval of the research protocols by an ethics committee in accordance with international agreements "WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (last updated: October 2013, Fortaleza, Brazil)", "Guide for the care and use of laboratory animals (8th edition, 2011)" and/or "International Guiding Principles for Biomedical Research Involving Animals (2012)". This approval is required for all experimental, clinical and drug trial studies. For articles concerning experimental research on humans, a statement should be included that informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. The journal may request a copy of the Ethics Committee Approval received from the relevant authority. Informed consent must also be obtained for case reports. More details on the ethical principles of the journal may be found at the "Ethical Guidelines" and the "Instructions to Reviewers" pages. All reference for the ethical issues must be mentioned at the method section of the article.

Conflict of interest policy

The AJTES's editorial review process is in accordance with the Good Editorial Practice set by international editorial organizations (WAME, COPE). WAME indicates that "conflict of interest exists when an author, reviewer, or editor in the publication process (submission of manuscripts, peer review, editorial decisions and communication between authors, reviewers and editors) has a competing interest that could unduly influence his or her responsibilities (academic honesty, unbiased conduct and reporting of research and integrity of decisions or judgments) in the publication process".

The AJTES requires that each author, reviewer, and editor must disclose to the editor-in-chief any conflict of interest related to family, personal, financial, political or religious issues as well as any competing interest outlined above at the WAME's definition. Whether or not a conflict of interest and financial support exist, they must be declared at the Conflict of Interest Statement (signed and approved from all the authors) as well as at the end of the manuscripts (Conflict of Interest Statement, before the Reference Section). If a reviewer or an editor has a conflict of interest and/or believes that it is not appropriate to be a reviewer, or an editor for a given manuscript, the reviewer or the editor should resign from the assignment. The AJTES editorial board members may also submit their own manuscripts to the journal. However, they cannot take part at any stage on the editorial decision of their manuscripts. They will be treated like any other author and if any, final acceptance of such manuscripts can only be made by the positive recommendation of at least two external reviewers. Authors should not contact any of the editorial executive or scientific board members during the review process. All necessary information regarding the process of a manuscript will be regularly provided from the editorial office via the official e- mail addresses. The names of the handling editor and the reviewers are not disclosed to the author(s). Due to the AJTES's double-blinded review principles, the names of authors and reviewers are not known to each other. Please refer to

the "conflict of interest statement and copyright form" section below for the conflict of interest declaration for authors. For a conflict of interest statement for reviewers, please refer to the "Instructions to Reviewers" page.

INSTRUCTIONS FOR AUTHORS

AJTES is based on independent and unbiased double-blind and peer-reviewing principles. Only unpublished papers that are not under review for publication elsewhere can be submitted. The authors are responsible for the scientific content and the ethical compliance of the material to be published. *AJTES* reserves the right to request any research materials on which the paper is based. It is highly recommended that all manuscripts must be checked from a native English speaker with experience in Scientific English writing. The executive editorial board is committed to a rapid publishing process. The authors will be kept informed about all the stages of the reviewing process.

Manuscript formatting

The manuscript format must follow the guidelines described below that are in accordance with the ICMJE (Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals - updated in August 2013 - http://www.icmje.org/icmje-recommendations.pdf. The manuscript must be submitted to the following address: ajtes.editor@gmail.com

Papers that do not comply with the format of the Journal and submission requirements will be returned to the author for correction without further review.

General Format

The manuscript should be typed in a Microsoft Word™ file, single-column format, double-spaced with 2.5 cm margins on each side, and 11-point type in Times New Roman font.

All abbreviations must be defined the first time they are used and should be displayed in parentheses after the definition. Abbreviations should be limited to those defined in the AMA Manual of Style, current edition. Authors should avoid abbreviations in the title and abstract and limit their use in the main text.

Decimal points should be used in decimals throughout the manuscript. Measurements should be reported using the metric system according to the International System of Units (SI). Consult the SI Unit Conversion Guide (New England Journal of Medicine Books, 1992). An extensive list of conversion factors can be found at http://www.unc.edu/~rowlett/units. For more details, see:

http://www.amamanualofstyle.com/oso/public/jama/s i_conversion_table.html.

When a drug, product, hardware, or software is mentioned within the main text product information, it should include the name of the product, the producer of the product, and the city or the country of the company. It should be provided in parenthesis in the following example format: "Examination BIO- AUTO analyzer (Beckman-Coulter, New Jersey, NJ, USA)".

Article Type

Identification of the article type is the first step of manuscript preparation and submission. The article type dictates the rules that should be followed, including formatting and word limits of the manuscript. The main categories of article types are outlined below:

Original Article: Original contributions are manuscripts containing substantial novel research. These articles can include randomized controlled trials, observational (cohort, case-control or cross-sectional) studies, diagnostic accuracy studies, systematic reviews, and meta-analyses, non-randomized behavioral and public health intervention trials, experimental animal trials, or any other clinical or experimental studies. Abstracts must begin on a separate page and should not exceed 300 words.

Abstracts should be structured with the following subheadings: *Background, Aims, Study Design* (case-control study, cross-sectional study, cohort study, randomized controlled trial, diagnostic accuracy study, meta-analysis and systemic review, animal and in vitro experimentation, non-randomized study in behavioral sciences and public health, etc.), Methods, *Results, Conclusion, and Keywords.*

The main text should be structured with the following subheadings:

Introduction, Material and Methods, Results, Discussion, Conclusions, Acknowledgments, Conflict of Interest statement, Authorship contribution, References, Tables, and Figure Legends.

The main text should not exceed 4500 words, excluding the abstract, references, tables, and figure legends. There should be a maximum of 100 references.

Review Article. A review article is an article that summarizes the current state of understanding of a particular topic. A review article surveys and summarizes previously published studies, rather than reporting new facts or analysis.

Review articles are sometimes referred to as survey articles or, in news publishing, summary articles.

Academic publications that specialize in review articles are known as review journals.

Review articles learn about:

- *Main people who were/are working in a field*
- *Recent major advances and discoveries*
- *Significant gaps in the research*
- *Current debates*
- *Ideas on where the research might go next.*

Review articles in journals analyze or discuss research previously published by others, rather than reporting new studies results. An expert's opinion is valuable, but an expert's assessment of the literature can be more valuable. When reading individual articles, readers could miss features that are apparent to an expert clinician-researcher. Readers benefit from the expert's explanation and assessment of the validity and applicability of individual studies.

Literature reviews provide a summary of what the authors believe are the best and most relevant prior publications.

Systematic reviews determine an objective list of criteria, and find all previously published original papers that meet the criteria; they then compare the results presented in these papers.

Some journals likewise specialize in the review of a field; they are known as review journals.

The concept of "review article" not need to do peer-reviewed or is non-peer-reviewed.

Abstracts must begin on a separate page and should not exceed 350 words.

Abstracts should be structured with the following subheadings: *Background, Aims, Methods, Results, Conclusion and Keywords.*

The main text should not exceed 4500 words, excluding the abstract, references, tables, and figure legends. There should be a maximum of 20 tables and/or figures and 150 references.

Commentaries articles:

are usually by invitation only, are short, narrowly focused articles that are usually ordered by the journal. These articles are generally not reviewed.

A comment generally takes one of two forms:

- The first form aims to highlight one or more exciting research articles or clinical trials recently published in a journal or other one, to discuss specific issues within a subject area, rather than across the field, and to explain the clinical implications of the article rather than new findings in context. Opinions are welcome as long as they are based on fact.
- The second form is more editorial in nature and includes an aspect of an issue that is relevant to the purpose of the journal. Examples of this type of comment could be a discussion on the impact of new technology on research and treatment or a discussion on peer review changes or grant application procedures and their effect on research. By their nature, the second form of comment is less common. Comments are usually commissioned by well-known experts in a particular field, and authors are asked to provide a balanced summary of the field, to cover only the work that has been published (or is still in print at the time of writing), and not to discuss and mention mainly their work or that of their close colleagues.

Abstracts must begin on a separate page and should not exceed 250 words.

Abstracts should be structured with the following subheadings: *Background, Aims, Methods, Discussion, Conclusion, and Keywords.*

Commentaries articles must be a maximum of 2000 words and have a maximum of 40 references. Typically, do not contain pictures or tables. For more information click here https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4789530/

Perspective articles; have an important role in academic research. They stimulate further interest in presented topics within the reader audience.

They are different from other types of articles because they present a different take on an existing issue, tackle new and trending issues, or emphasize topics that are important but have been neglected, in the scholarly literature.

In some scientific fields, they bridge different areas of research that the journal publishes, while in others they bring new issues and ideas to the forefront. In general, their role is to enlighten a general audience about important issues.

It gives researchers the opportunity to contribute to their discipline in different ways, while at the same time enhancing their own professional work.

A perspective article is a way for young researchers to gain experience in the publication process that can be often arduous and time-consuming. It can be a way in which they learn from the publication process while they are working on their original research articles that often take years to complete.

In the case of experienced researchers, provides them at least two distinct benefits:

- The first, it allows them to step back and reflect on a significant issue that they may know a lot about, but that they have never had the time to address.
- The second benefit is that the researcher gets the opportunity to give their own authorial voice to a published article that will reach a wide audience.

Before one decides to write and submit a perspective research article to an academic journal, it is important to become familiar with the article's expectations of the target journal.

Although academic journals hold a similar definition and purpose of a perspective article, there are differences in the technical requirements each journal has. When it comes to the length of the perspective article, some journals have strict limitations while others allow articles to vary the length within a given range. The perspective article has a limitation of 2,500, with defined reference and figure limits. Abstracts must begin on a separate page and should not exceed 250 words.

With respect to the structure of the perspective article, journals define their expectations in different terms. The perspective article emphasizes the structure of the article, requiring sections such as the *abstract, introduction, topics, and conclusion.*

Opinion articles allow readers of a newspaper to voice their thoughts and ideas on topics ranging from local happenings to international controversy. Most opinion articles are about 1500 words long, with a professional tone. If you want to try your hand at writing an op-ed, you can learn to choose a compelling topic, write an effective draft, and finish off your op-ed like a professional editor. The perspective article emphasizes the structure of the article, requiring sections such as the *abstract, introduction, topics, and conclusion.* Abstracts must begin on a separate page and should not exceed 250 words.

The latest articles discuss the current or recent news of general interest (the problem of the day) or of a specific topic (of interest to the general public and its results are quite welcome). A final article may include randomized and non-randomized (complete and partial) of scientific data in the interest of a local, national, regional, continental, and global study. The Latest articles emphasize the structure of the article, requiring sections such as the *abstract, Background, Aims, Study, Methods, Results, Discussions, and Conclusion.*

The main text should not exceed 4500 words, excluding the abstract, references, tables, and figure legends. There should be a maximum of 20 tables and/or figures and 100 references.

Abstracts should be structured with the following subheadings: *Background, Aims, Study, Methods, Results, Conclusion, and Keywords.* Abstracts must begin on a separate page and should not exceed 250 words**.**

Short Report:

Short reports or short communications are short versions of research, applications, or work in progress limited to 1500 words. These articles can include clinical or laboratory work, collected case reports of scientific significance, etc.

Abstracts must begin on a separate page and should not exceed 250 words.

Abstracts should be structured with the following subheadings: *Background, Aims, Study, Methods, Results, Conclusion, and Keywords.*

The main text should be structured with the following subheadings: *Introduction, Material and Methods, Results, Discussion, Conclusions, Acknowledgments, References, Tables, and Figure Legends.* The main text should not exceed 1500 words, excluding the abstract, references, tables, and figure legends. There should be a maximum of 8 tables and/or figures and 25 references.

Invited Review or Medical education articles*:* Invited review and Medical education articles are comprehensive analyses of specific topics in medicine, which are written upon invitation due to the extensive experience and publications of authors on the review subjects. They can also be articles focused on clinical teaching and guidelines.

All invited review articles will also *undergo peer-reviewing prior to acceptance.* Review articles must not exceed 5000 words for the main text (excluding references, tables, and figure legends) and 250 words for the unstructured abstract. A review article can be signed by no more than 6 authors and can have no more than 50 references.

Case Report: Interesting cases demonstrating new findings can be reported. Cases should be unique, representing a diagnostic or therapeutic challenge, and having a learning point for the readers.

Abstracts of case reports should mainly include information about the case and should be limited to a maximum of 250 words.

The abstract must begin on a separate page and should be structured with the following subheadings: *Background, Case Report, Conclusion, and Keywords.*

The main text of case reports should be structured with the following subheadings: *Introduction, Case Report, Discussion, Acknowledgments, and References.*

Case reports must not exceed 1500 words (excluding references, tables, and figure legends).

Case reports can be signed by no more than 6 authors and can have no more than 15 references and 6 figures or tables. It is highly recommended that the Case reporting must follow the CaRe (Case Report) guidelines.

Clinical Reasoning*:* Clinical reasoning represents rational thinking through the various aspects of patient care to better define the medical strategy regarding the diagnosis and/or treatment of a clinical problem in a specific patient. Conducting a physical exam, taking a medical history, ordering complimentary exams, and describing safe and effective treatment are necessary steps in gathering clinical data from a patient before engaging in the process of clinical reasoning. The latter represents a critical thinking process about all the important clinical information using personal skills and abilities often achieved from the experience.

This article type is intended to help clinicians think differentially and take the next step which determines the best course of action to take based on what is known or what can reasonably be hypothesized from clinical data.

The authors are encouraged to present clinical cases from their experience which has generated a real diagnostic dilemma.

The first section, case presentation, should include the patient's complaints as well as historical and clinical data enough to present an initial differential diagnosis.

The second section, complementary exams, is dedicated to pertinent and necessary complementary examinations according to previous topographic and clinical differential diagnosis.

In the third section, the authors should present all steps (surgery, biopsy, pathological exam) needed in defining the final diagnosis.

A supplementary section should include an overview of the final diagnosis.

The maximum lengths of the text and the references should not exceed 2500 words and 30 references, respectively. No abstract is required.

Clinical Image: The journal publishes original, interesting, and high-quality clinical images having a brief explanation (maximum 500 words excluding references but including figure legends) and of educational significance. The figure legend should contain no more than 100 words.

It can be signed by no more than 5 authors and can have no more than 5 references and 2 figures or tables. Any information that might identify the patient or hospital, including the date, should be removed from the image.

An abstract is not required with this type of manuscripts.

The main text of clinical images should be structured with the following subheadings: Case, and References.

Letter to the Editor*:* Letters in reference to a journal article must not exceed 600 words (excluding references). Letters not related to a journal article must also not exceed 600 words (excluding references). An abstract is not required with this type of manuscripts. A letter can be signed by no more than 5 authors and can have no more than 5 references and 2 figures or tables.

Other*:* Editorials, reviewer commentaries, book reviews, reports on publication, and research ethics, Opinions and View-Points are requested by the Editorial Board.

A summary of the article type's characteristics is given in the table below.

	Limit of				
Article Type	***Word***	***Abstract word***	***Reference***	***Author***	***Tables/Figures***
Original Article	4500 [1]	300 [4]	100	None	20
Review Article	4500	350	150	6	20
Commentaries articles	2000	250	50	6	-
Perspective articles	2500	250	40	2	2
Latest articles	4500	250	100	10	20
Invited Review	5000 [1]	250	50	6	6
Case Report	1500 [1]	250 [5]	15	6	6
Clinical Image	500 [2]	N/A	5	5	2
Letter to the editor	600 [3]	N/A	5	5	2
Clinical reasoning	2500 [3]	N/A	30	5	3
Short report	1500	250 [4]	25	4	8

[1] This should not includet the abstract, references, tables or figure
[2] This should include the figure
[3] This should not include the
[4] Should be structured with the following subhjeadings: Background, Aims, Study Design, Methods, Results, Conclusion, and Keywords.
[5] Should be structured with the following subhjeadings: Background, Case Report Conclusion, and Keywords.

Preparation and submission of a manuscript

All manuscripts should be submitted via email to the following address: *ajtes.editor@gmail.com*; *ajtesjournal@gmail.com*

The submission should be divided into SEPARATE files in the following order:

1. *Cover Letter (separate file). https://drive.google.com/file/d/1pKueirCkP2-DNd6RsY5Lk-NzQOBjQnKO/view?usp=sharing*
2. *Authorship Contributions, Copyright Transfer, and Conflict of Interest Statement Form (separate signed file). https://drive.google.com/file/d/1lVGYfpvqsXruNwFeKothDX0zt2WGiXxb/view?usp=sharing*

https://drive.google.com/file/d/1_53doLRgxRIp1kVbiyYVh9XDLzaDtjv_/view?usp=sharing

https://drive.google.com/file/d/1hB-5WsprQAiwsqWNiL4Yqrr0Zkm2tf-I/view?usp=sharing

3. *Manuscript (Title page, Abstract page, main text, references, tables, and figure legends).*
4. *Figures (if applicable).*

1. Cover Letter

The cover letter addressed to the Editor in Chief from the corresponding author, should include:

the article title and type of article he/she is submitting (for example original article, case report, review article, or clinical image).

The corresponding author should briefly summarize why their work is a valuable addition to the scientific literature. Furthermore, there should be a statement that the manuscript has not already been published, accepted, or under simultaneous review for publication elsewhere.

AJTES does not accept multiple submissions and duplicate submission. For manuscripts that have been presented orally or as a poster, this must be stated on the title page with the date and the place of the presentation.

An example of a cover letter can be found on the journal's webpage (AJTES Cover Letter). https://drive.google.com/file/d/1pKueirCkP2-DNd6RsY5Lk-NzQOBjQnKO/view?usp=sharing

2. Authorship Contributions, Copyright Transfer and Conflict of Interest Statement Form

This is a statement of scientific contributions and responsibilities of all authors.

The form is available for download at the journal's webpage. https://journal.astes.org.al/

The ICMJE recommends that authorship has to be based on the following 4 criteria:

- *Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work.*
- *Drafting the work or revising it critically for important intellectual content.*
- *Final approval of the version to be published.*
- *Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

A contributor should meet all four criteria to be identified as an author. If a contributor does not meet all four criteria, he/she should be acknowledged in the acknowledgments section of the manuscript. All authors must sign the corresponding declaration.

For more details please refer to the ICMJE's definition of the role of authors and contributors at http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html

AJTES recommends that the author ranking in the authorship list has to follow the importance of the contribution of the individual co-authors in the study, with the exception of the last author who is generally the author group coordinator or leader and whose contribution is comparable with the first author.

The authors must state in the section dedicated to the Author Contribution Form and in the main text (before the Reference section) if they have agreed for another ranking order (for example authors A.B and C.D. have an equal contribution to this study, etc).

The specific contribution of each author must be stated at the end of the manuscript, before the references.

All contributing authors must sign the ***Authorship Contributions, Copyright Transfer, and Conflict of Interest Statement Form*** and submit it through the submission system during submission. Please see Authorship Contributions**,** Conflict of Interest Statement and Copyright form for detailed information regarding "Acknowledgement of Authorship, Exclusive Publication Statement, Conflict of Interest Statement, and Transfer of Copyright Agreement".

Please refer to the "conflict of interest policy" for more information. https://drive.google.com/file/d/1hB-5WsprQAiwsqWNiL4Yqrr0Zkm2tf-I/view?usp=sharing

1 - Manuscript must contain: **Title Page (separate page)**

This should include:

a) The complete manuscript title (no more than 150 characters). https://drive.google.com/file/d/1YznkUnqHJR9NWah39QOe6gWfUfX1njk3/view?usp=sharing

b) The running head (no more than 50 characters).

c) Word counts for the abstract and text (the text word count does not include references, tables, and figure legends).

d) The number of references and the number of figures and/or tables.

e) All authors' full names.

f) Detailed affiliations and e-mail addresses (all authors should meet the ICMJE's requirements for authorship – see details at "author contribution form"). http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html

g) The name, address, telephone and fax numbers, and email address of the corresponding author.

h) Key-words: (3 to 6 key-words) from the list provided in Index Medicus under "Medical Subject Heading (MeSH)". https://www.nlm.nih.gov/mesh/meshhome.html

i) Information about where and when the study has previously been presented.

Abstract Page (separate page)

Original articles, invited review articles, and case reports should include an abstract on a separate page.

Abstracts for original articles and short reports should be structured with the following subheadings: *Background, Aims, Study design, Methods, Results, and Conclusion.*

Abstracts for case reports should be structured with the following subheadings: *Background, Case Report, and Conclusion.*

Abstracts for review articles should not be structured. *Clinical images, clinical reasoning, Editorials, Letters to the Editor, and Commentaries or Opinions/Viewpoints* should not contain an abstract.

Main document

The main document should include the main text, acknowledgments, conflict of interest disclosure, authorship contribution description, references, tables, and figure legends, in that order.

Main text

The main text should be structured according to the article type, as described in the Article Type section above.

Acknowledgments

All contributors who do not meet the criteria for authorship (ICMJE: authorship and contributorship: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html

should be mentioned in this subheading.

https://drive.google.com/file/d/1s-yaIzH5B36WKsr9U8VzvrFzDlsjU86B/view?usp=sharing

Conflict of interest disclosure: The authors should disclose any potential conflict of interest.

Statement about specific author contribution at the study (including concept, design, supervision, resource, materials, data collection and/or processing, analysis and/or interpretation, literature search, writing, and critical reviewing).

For example A.B (concept, design, data collection, etc); B.C. (data collection, analysis, writing, reviewing, etc).

They should comply with ICMJE recommendations that authorship be based on the following 4 criteria: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html#two

- *Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work.*
- *Drafting the work or revising it critically for important intellectual content.*
- *Final approval of the version to be published.*
- *Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

A contributor should meet all four criteria to be identified as an author. If a contributor does not meet all four criteria, he/she should be acknowledged in the acknowledgments section of the manuscript.

References

Authors are encouraged to cite primary literature rather than review articles in order to give credit to those who have performed the original work. Reference listings must be in accordance with ICMJE standards and numbered consecutively at the end of the manuscript in the order in which they are mentioned in the text. While citing publications, preference should be given to the latest, most up to date publications. Full papers must be clearly differentiated from abstracts presented in scientific meetings and published as supplements in scientific journals (see below: Abstract example).

If an ahead of print publication is being cited the DOI number should be provided. The authors are responsible for the accuracy of references.

Journal titles should be abbreviated in accordance with the journal abbreviations in Index Medicus/ Medline/Pub Med (for journal abbreviations consult the List of Journals Indexed for MEDLINE, published annually by NLM).

When there are 6 or fewer authors, all authors should be listed. If there are 7 or more authors, the first 6 authors should be listed followed by "et al". In the main text of the manuscript, references should be cited using Arabic numbers in parentheses.

The reference styles for different types of publications are presented in the following examples:

Journal article*:* Bendo Hysni, Halimi Omer, Traka Luan, Sakakushev Boris, Zago Mauro. Blunt abdominal trauma management… P 321 genes in three ethnic groups from Albania. Albanian Journal of Trauma and Emergency Surgery 2018; 2 (2): 84-92.

Book: Skibe Michal Ocular manipulation. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

Book chapter: Moor Ernest. the relationship between PATI and ISS score. In: Mos F, Thompton J, Peitersen E, editors. Trauma Management. New York: Springer Verlag; 2012:325-30.

Abstract: Erion Spaho, Artid Lame et al. Management of C4-C5 Fracture with Approach 360□ Without the Spinal Instrumentation 2018; 36: (abstract).

Article in electronic format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2626828/pdf/8903148.pdf.

For other reference styles, please refer to "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References".

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Tables should be presented within the main document and after the reference list. All tables should be referred to within the main text and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title should be provided for all tables and the titles should be placed above the tables. Abbreviations used in the tables should be defined below the tables (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide an easy reading.

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Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format). They should not be embedded in a Word document. When there are figure subunits, the subunits should be labeled in small letters (a, b, c, etc.). Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures should be blind too. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process all submitted figures should be clear in resolution and large in size (minimum dimensions 100x100 mm).

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Checklist

Before submission, the corresponding author should ensure that all files mentioned below meet the journal requirements:

- *A cover letter containing*
- *The article title and type*
- *A brief statement describing the novelty and importance of the work*
- *A statement declaring the absence or presence of a conflict of interest*
- *A statement that the manuscript has not been previously published or accepted for publication and is not submitted or under simultaneous review for publication elsewhere.*

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A title page including

- *Title (less than 150 characters), running title (less than 50 characters)*
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- *A statement of the date and place of the meeting where the manuscript was presented orally or as a poster, if*
- *Structured Abstract (on a separate page-see above)*

Structured main text (see above)

Ethical approval and/or informed consent has to be mentioned in the text (Methods)

References are in the correct format and cited sequentially in the text

All Tables and Figures have been included and appear correctly

***Permission for reprinted figures**,* tables, materials or photographs has been obtained (if available)

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Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option will be automatically cancelled. If the submitting author(s) believe that additional time is required, they should request a 2-week-extension before the initial 30 days period is over.

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Documents to download

a) Cover Letter

b) Authorship Contributions,

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The reviewed manuscripts are then re-reviewed by the Executive Editorial Board and a decision of rejection or acceptance is taken.

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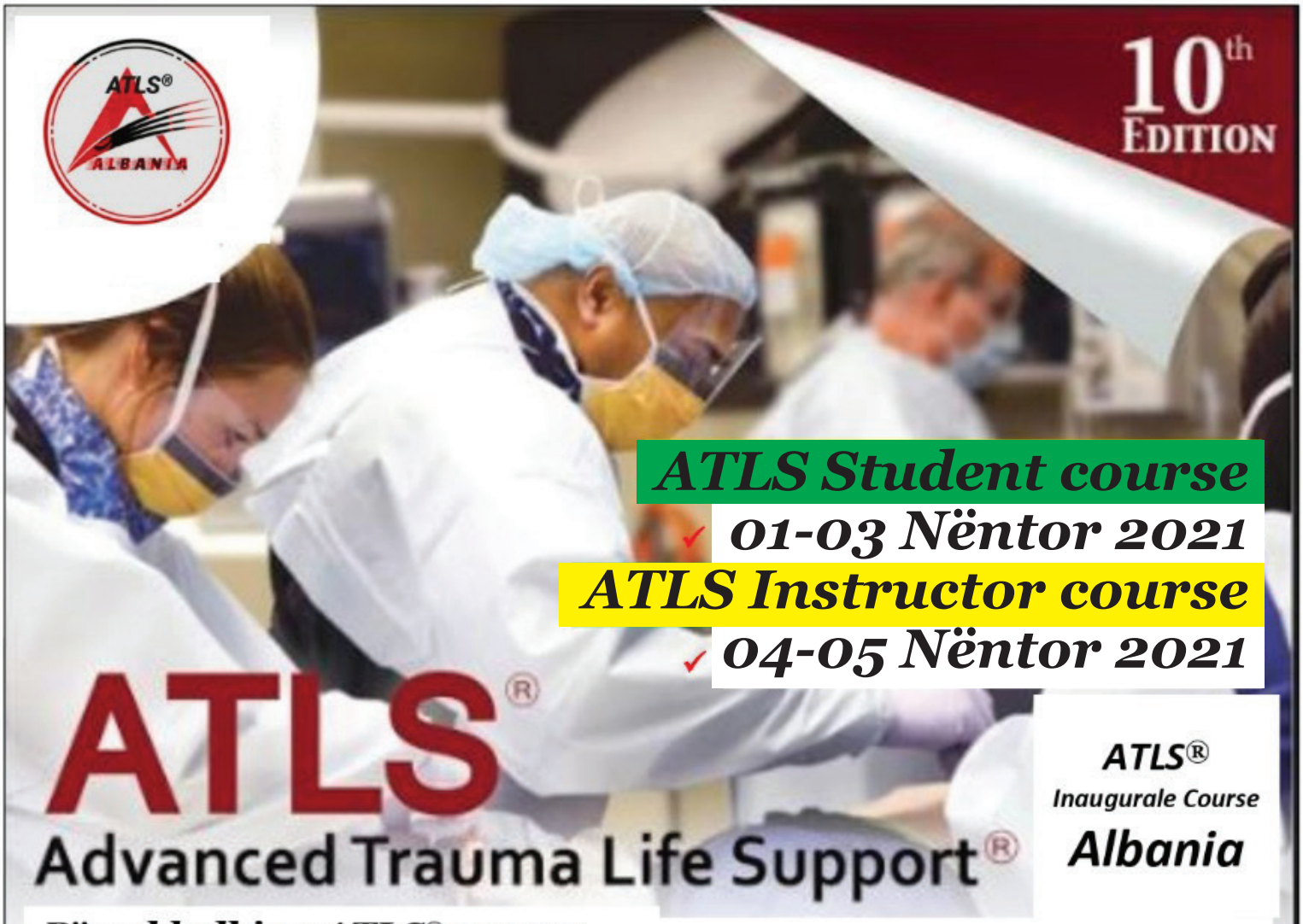
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