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Focus on
"Trauma and Emergency Surgery"
and not only...

Official publication of

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# Postoperative leaks in esophagectomy and sleeve gastrectomy for obesity*

**Rifat Latifi MD, FACS, FICS[1] ; Agron Dogjani MD, PhD, FACS[2]**

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***Abstract***

Postsurgical gastro-intestinal or intestinal-intestinal anastomotic leaks while not frequent, are the most feared complications for any anastomoses performed in the gastrointestinal tract (GIT) by general surgeons. This is particularly important in the upper GIT, such as gastro esophageal anastomosis, where leaks can lead to severe sepsis and septic shock, need for re-operation, or stent placement. For this short review we will address post-operative leaks following esophagectomy and sleeve gastrectomy as the most frequent bariatric procedure today. The factors and causes responsible for Upper Gastro-Intestinal Anastomosis, as they relate to patient, surgeon or technique will be reviewed. Moreover, the diagnosis and current management will be examined.
***Keywords***: Esophago-gastro-intestinal leaks, management of leaks, esphagectomy

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***Anastomotic leaks following esophagectomy***

*Anastomotic leaks following esophagectomy are serious complications, but most recent developments in surgical techniques and management of such leaks has been substantial. The incidence of leak following esophagectomy ranges from 0%-35%. The main risk factors are cervical and hiatal location of the anastomosis, positive margins for malignancy, local ischemia and technical errors. Other important factors for anastomotic leak are higher American Society of Anesthesiologists (ASA) score, malnutrition, Diabetes Mellitus (DM), renal failure, steroids, obesity and smoking. In a series of 390 patients undergoing esophagectomies were performed (median age 65 (range 32-81) years), in which 96·7 per cent of patients this was a two-stage subtotal esophagectomy, 31 patients (7·9 per cent) developed a leak. Of these, only four (13 per cent) required immediate thoracotomy. The median length of stay for patients with a leak was 41·5 (range 15-159) days; none of these patients died (1). Surgeon's experience and the frequency that the operation is performed by individual surgeon as well as institutional overall experience are another important factor.*

*Moreover, whether the anastomosis is performed hand sewn or stapler influences the frequency of leaks. Recent evidence favors use of stapling in preventing anastomotic leak. The meta-analysis by Liu et al (2) of 15 RCTs (n=2,337) comparing stapling vs hand-sewn anastomosis use of stapler reduced the risk of leak by 34%. In another recent study by Ryan et al (3) of 21 RCT combining prospective/retrospective cohort studies (n=7167) comparing transthoracic vs trans-hiatal approaches (TTE) vs THE) there were no difference between TTE and THE. However, in a cohort studies leak risk there was significant (44%) reduction in risk of leak favoring TTE. One has to note though that this meta-analysis reported mixed results. Use of of omentoplasty to reduce the leak rate was reported as favorable by Schaheen et al (4). Interestingly, Zhou et al (5) reported no differences in leak if esophagectomy is done minimally invasive or open. Clinical presentation of the leak varies by the location of the anastomosis and other factors (preoperative status, co-morbid conditions, nutritional status), and it may present as sepsis from mediastinitis or peritonitis to large drainage from the site into the pleural space. Moreover, arrhythmias, upper abdominal or chest pain, bronchopneumonia, hypoxia, confusion and agitation to full respiratory failure, increased WBC, and deterioration of end-point resuscitation and finally the need for mechanical ventilation and tube thoracostomy. The diagnosis is usually made clinically, change in drainage character or amount, contrast esophagogram or flexible endoscopy, or probably most commonly by CT scan.*

*The management depends on clinical presentation and location of the anastomosis and extent of anastomotic disruption, i.e., grading of the leak that may be without clinical signs (Grade 1) to major leak (Grade 3) or Grade 4, with entire gastric conduit necrosis. Nonoperative, conservative management for occult (Grade I) leaks such as delayed initiation of oral feeding may suffice and antibiotics. However, general principles of management include systemic antibiotics, close or occlude the defect as soon as possible which could be done by stents or surgically. Drain associated fluid collections, prevent distal obstruction and ensure minimizing factors such as keeping perforation open (e.g., tumor, foreign body, persistent infection). In more serious situation, esophageal diversion or resection, if sepsis is poorly controlled with more conservative measures, should be done. In recent years, laser-assisted fluorescent-*

*dye angiography (LAA) has been used to assess perfusion in the gastric graft and to correlate perfusion with subsequent anastomotic leak. In a study of 150 patents undergoing esophagectomy with planned gastric pull-up (GPU reconstruction a leak was found in 24 patients (16.7%) and were significantly less likely when the anastomosis was placed in an area of good perfusion compared with when the anastomosis was placed in an area of less robust perfusion by LAA (2% vs 45%, P < 0.0001) (6). While management of leaks in this situation may be complex, the use of stents has been recently reported in 267 patients by van Boeckel et al (7) with success rate 81-94%. Placement of self-expanding metal stents (SEMS) or self-expanding plastic stents (SEPS) has emerged as a minimally invasive treatment option for benign esophageal ruptures and leaks, although the most common complication was stent migration, which occurred more often with SEPS [n = 47 (31%)]. Recent data suggest conservative management of esophageal leaks is associated with excellent outcomes without using esophageal stents and do not support the widespread adoption of endoscopic stenting (1). Yet, we suggest that both esophagectomy and management of complications should be performed by surgeons and in institutions with large experience in esophagectomy and with ability to deploy a multidisciplinary approach.*

***Leaks following laparoscopic sleeve gastrectomy (LSG) for morbid obesity***

*Morbid obesity has risen to true world-wide epidemic proportion. To this end, bariatric surgery has become a common procedure, particularly in the western world. While over the years a number of bariatric procedures evolved including gastroplasty, vertical banding gastroplasty (VBG), gastric banding, gastric bypass (Roux-en Y), partial biliopancreatic diversion and duodenal switch operations, with advances in stapler technology, laparoscopic and robotically assisted sleeve gastrectomy has become most common bariatric procedure world-wide. While, life saving for many obese and super obese patients, bariatric surgery may be associated with significant complications.. However, although post-operative complications are not common in all these procedures, they must be recognized and addressed promptly in order to minimize possible mortality and significant morbidity. Large published case series of open and laparoscopic cases the leak rate varies between 0.1% and 8.3% after gastric bypass (8), while the Laparoscopic Sleeve Gastrectomy (LSG) has become the procedure of choice in bariatric surgery, and leaks have been reported to be much lower, however. For example, data from 12799 LSGS, the International Sleeve Gastrectomy Expert Panel Consensus Statement 2011, the leak rate was 1.06% (9). Yet, as this procedure is becoming the most common bariatric procedure performed, even a small percentage of leak as suggested from this panel discussion, may be very significant and should be understood by those who perform it.*
*The etiology of the leaks is multiple but generally falls into mechanical/tissue causes or ischemic causes, both of which involve intraluminal pressure that exceeds the strength of the tissue and/or staple line [10]. Identifying the best technique with lowest complication such as reinforcement of the stapler resection of the stomach has been studied extensively. In a systematic review by Gagner and Buchwald (11) of 88 RCTs, retrospective/prospective studies (n=8,920), laparoscopic sleeve gastrectomy (LSG) was compared with 4 staple-line reinforcement methods. The study compared LSG staple-line leak rates of 4 prevalent surgical options: no reinforcement, over sewing, non-absorbable bovine pericardial strips (BPS), and absorbable*

*polymer membrane (APM). There were 191 leaks in 8,920 patients; overall leak rate 2.1%. Leak rates ranged from 1.09% (APM) to 3.3% (BPS); APM leak rate was significantly lower than other groups (p= 0.05). The percentage of leak was the lowest with absorbable membrane 1.09 (N/A); Over sewing 2.04 (p=0.02); No reinforcement 2.60 (p=0.001); while the highest leak rate was using bovine pericardium 3.30 (p=0.0006). Moreover, a meta-analysis by Parikh et al (11) of 112 studies (n=9,991), LSG, use of Bougie ≥40 Fr OR 0.53 (0.37, 0.77), significantly (47%) reduced odds of leak while there were no significant effects for distance to pylorus, use of buttressing.*

*The clinical presentation and the management of leaks post LSG depends entirely on the size of the leak and may involve conservative management such as nil per mouth, intravenous fluids, provision of enteral nutrition support distally to the leak (proximal small bowel most commonly) broad spectrum antibiotics to re-exploration (preferentially laparoscopically in the early days post op). In more severe cases of leaks conversion of what was LSG, should be converted into more complex procedure such conversion to Roux- Y gastro-jejunostomy.*

*In one study, fifteen (2.8%) patients presented with a leak after LSG. The diagnosis was made at a mean of 27.2±29.9 days (range, 1-102) after LSG. Eight (53.3%) patients underwent conservative treatment initially and 6 (75.0%) of these patients required stenting as secondary treatment. Although leaks from 3 patients resolved with stenting, the other 3 required restenting and 2 eventually underwent conversion to gastric bypass. Five (33.3%) patients underwent endoscopic intervention, closing the leak with fibrin glue (n=3) or hemoclips (n=2). Two (13.3%) patients who were diagnosed with a leak immediately after LSG before discharge had their leak oversewn laparoscopically with an omental patch. Leaks in 9 (60.0%) patients did not heal after the first intervention, and the mean number of intervention required was 2.3±1.7 times (range, 1-7) for the treatment of this condition.*

***Summary***

*Recognizing the leak early be it post esophagectomy or gastric sleeve resection and addressing it promptly must be done in a timely fashion, if complications and serious morbidity are to be minimized. Traditionally, any leak from the gastric pull-up anastomosis or any form of bariatric surgery would have been re-operating, wide draining or a combination off. The definitive management of these leaks depends on the location, patient's condition, and the ability to provide nutrition support enterally. Proper drainage, use of the stent, and provision of enteral nutrition support offer the highest chances that the leak will close. Recently the American Society for Metabolic and Bariatric Surgery issued position statement and recommendation on prevention, detection, and treatment of gastrointestinal leak after gastric bypass and sleeve gastrectomy, including the roles of imaging, surgical exploration, and non-operative management (7). While meticulous tissue handling, use of proper tissue thickness, and avoidance of inadvertent narrowing, undue tension, and twisting or kinking of the mesentery and tissues are most important, other elements in this statement should be examined by every surgeon doing GI anastomosis.*

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# The presence of a foreign body in the digestive tract - case reports and literature review.

**Daniel Houser[1], Mark H. Johnston, MD[2]***

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**Abstract**

***Background:*** The presence of foreign bodies in the digestive tract usually occurs in pediatric, adolescent and psychiatric patients. Current Protocols focus mainly on pediatricians and adults.
We present some cases mainly of feminine age. Most swallowed foreign bodies will harmlessly pass through the GI tract, but some will lead to health problems if they become lodged (too big to pass, such as a spoon, or small objects like a pill that adheres to a moist surface); traumatize the mucosa (sharp or pointed object, like a razor blade or pin), or cause burn-like illness (biologically active, such as a button battery or a medication patch) may cause problems.
which during X-Ray abdominal exfoliation show varying objects in the digestive tract at different levels. The following examinations highlighted the most accurate localization.
Asymptomatic clinical data continued to deteriorate, despite imaging evidence. This article discusses the challenges involved in the management of foreign troops in the digestive tract and the re-evaluation of literature
***Keywords***: digestive tract, foreign body, management, pediatric patient

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***Introduction***

*Foreign body (FB) ingestion and food bolus impaction is a common reason for people of all ages to visit the emergency room. Although nearly 80% of FBs pass spontaneously, 20% require endoscopic intervention and nearly 1% require a more invasive surgical procedure.*

*The majority of FB ingestion cases are in children between 6 months and 3 years. These cases are largely accidental, unwitnessed, and can be asymptomatic, suggesting that the incidence is actually higher than what is reported (Shah & Mamula, 2018). Adults present more often with a food bolus impaction secondary to a pre-existing condition, such as eosinophilic esophagitis, strictures, malignancy, post-GI surgery, hiatal hernia, or achalasia (Ambe et al, 2012) (Yuan, 2017). Another subset of cases that require special attention is those of intentional ingestion. Incarcerated persons, psychiatric patients, and those with behavioral problems have a higher incidence of ingestion with multiple objects and recurring ingestions, and more often require intervention. In one study, 69% of cases from intentional FB ingestion required endoscopic intervention, and 22% required surgery (Dalal et al, 2013).*

*The most common objects ingested by children are coins, magnets, batteries, small toys, plastics, jewelry and buttons (Shar & Mamula, 2018). Food impactions are more common in older children (>10 years) and true foreign bodies are more common in younger children (<10) (Sugawa et al, 2014). Adults more often present with food related ingestions, such as fish and chicken bones, chunks of meat, fruit seeds, and toothpicks. Other items may include metallic objects (ie rings) or dentures (Yuan et al, 2017) (Ambe et al, 2012) (ASGE, 2011). A study of intentional ingestions within the incarcerated population found a variety of objects such as pens, razorblades, utensils, hardware, bed springs, toothbrushes, glass, batteries, and various metal objects (Dalal et al, 2013). The location of impaction, perforation, or obstruction varies with object type, but not necessarily with age, and may be associated with physiological narrowing, underlying pathology, previous surgery, or congenital malformations (Geng et all, 2017) (Yuan et al, 2017) (Shah & Mamula, 2018).*

*Common sites of acute angulation or narrowing are the following:*

1. ***Cricopharyngeus muscle (cervical esophagus)***
2. ***Aortic arch (thoracic esophagus)***
3. ***Left main stem bronchus (thoracic esophagus)***
4. ***GE junction***
5. ***Pylorus***
6. ***Duodenal sweep***
7. ***Ileocecal valve***
8. ***Anus***

*According to two large studies done in China, 82-87% of FBs requiring intervention become lodged between the pharynx and the distal esophagus, primarily in the cervical and thoracic esophagus (Geng et all, 2017) (Yuan et al, 2017). In a study focused on cases of intentional ingestion, nearly 50% were in the stomach (Dalal et al, 2013). Fortunately, only ~20% require endoscopic intervention, less than 1% require surgery, and the rest pass spontaneously without complication (Yuan, 2017; Shah, 2018). Children make up the majority of FB ingestion cases in the U.S*. with approximately 85%, however in two studies conducted in China, adults were found to have*

*higher incidences of reported ingestions/impactions (Yuan, 2017; Geng, 2017).*

**includes U.S. territories of Guam, Puerto Rico, American Samoa, U.S. Virgin Islands, District of Columbia, and the Federated States of Micronesia.*

**Diagnosis**

***History and Physical Exam***

*Initial workup of a suspected FB ingestion must begin with a thorough history and physical exam. Adults most often present with food impaction secondary to a pathologic process such as in eosinophilic esophagitis. Patients with FB symptoms may or may not be aware that they ingested something. In communicative children and adults, the exact details of when and what type of FB was ingested may be conveyed to the physician. This information should be gathered from the caretaker in young children, mentally impaired, and older, non-communicative adults (Shah and Mamula, 2018). Additional information helpful to the determination of care include the size and configuration of the object to include a picture if possible, last oral intake, characterization of symptoms, and past medical history significant for gastrointestinal abnormalities, surgery, or disease. Inquiry of common FB associations should be made for patients who are not certain of an ingestion. A history of prior dysphagia or odynophagia, presence of dental prosthetics, and a patient's occupation may help in diagnosing an unknown ingestion (tailors with needles).*

*In some cases, the patient may indicate the perceived location of the FB. This is not shown to have a strong association with the actual location and should not be relied on for diagnostic purposes (Connolly et al, 1992). Patients may present within hours of FB ingestion, however if unwitnessed or unbeknownst, may not present for days, months or years after ingestion (Geng, 2017). Often the precipitating factor is the onset of symptoms.*

***Symptoms***

*Symptoms may or may not be present, and this can prolong the time to treatment. This is especially pertinent for pediatric patients who may be completely asymptomatic. Children brought in by an adult who witnessed or suspected an ingestion should be assumed to have ingested a FB until it is completely ruled out. Fortunately, most patients present with symptoms, many of which may help to localize where the impaction is. Children most often present with vomiting, drooling, and dysphagia, while adults more often present with odynophagia, FB sensation and sore throat. Other symptoms include retrosternal pain, abdominal discomfort, and respiratory symptoms of coughing, stridor, and choking (Jayachandra & Eslick, 2013) (Geng et al, 2017) (Shah & Mamula, 2018). In more severe pediatric cases, fever, aspiration pneumonia, and failure to thrive may indicate a prolonged ingestion period, perforation, or deep ulceration (Shah, 2018).*

***Imaging***

*Radiographs of the affected area are recommended in one or two planes to first, confirm diagnosis, and secondly to determine location, orientation, number, and size of the FB. Foreign bodies can be radiodense or radiolucent, and this should be considered before any imaging is done. Most large, dense FBs are easily identified on plain radiograph; however, small animal bones, wood, plastic, glass, and thin metal objects are difficult to distinguish. Although computed tomography (CT) is not the first choice for imaging FBs, it is recommended in circumstances of suspected complications or delayed presentation, where it should be the first-line mode of imaging (Shah, 2018). Where radiation*

*exposure is a concern, point of care (POC) ultrasound may play a part. POC ultrasound is rarely cited as a commonly used method, however it has been recommended for use as an adjunct diagnostic tool to determine esophageal measurements, persistence of intraluminal air-fluid level, and direct FB visualization (Singleton, 2017).*
*Metal detectors can be used to confirm a general location of a metal FB. Mainly used in children. Contrast studies, such as gastrografin, are contraindicated due to the increased risk of aspiration and impaired visualization during endoscopy which is frequently the next step in care.*

**Management**

***General***

*The European Society of Gastrointestinal Endoscopy recommends early referral to the Emergency Department (ED) and evaluation with X-Ray for anybody suspected of a FB ingestion, even if asymptomatic (ESGE). Since 80-90% of ingested FBs pass without any difficulty, conservative treatment is recommended in the absence of significant symptoms, especially those that are blunt, short (<6cm), and narrow (<2.5cm) (Ambe, 2012). However, certain objects run a higher risk of complications and must be removed.*
*Ingestion of batteries, magnets and sharp/pointed objects, or obstructive symptoms in adults and children are considered emergent and the FB must be removed as soon as possible (Shah, 2018; Ambe, 2012). Objects in the esophagus causing minimal symptoms or longer than 6 cm are considered urgent and should be removed within 24 hours. (Shah, 2018; Ambe, 2012). FBs more than 2.5 cm in diameter are non-urgent and may be removed if there is a clinical indication, or the patient elects to have it removed. (Shah, 2018; Ambe, 2012)*

***Equipment***

*The type of endoscopic equipment used is contingent upon the type of FB being removed. Overall, both flexible and rigid endoscopy are commonly used depending on where the impaction is located and additional considerations involved, such as the need to protect the airway, where rigid endoscopy may prevent the need for an over tube. Overall, there is a 98.3% success rate for removal of FBs by endoscopy (Geng, 2017). Over 85% of FBs were found by flexible endoscopy (Geng, 2017). Those not removed successfully were chicken, fish and pig bone FBs (31.6%), metal FBs (21.1%), and dental prostheses (15.8%). (Geng, 2017). Foley catheter, fluoroscopic balloon extraction (Rosenfeld, 2018)*
*Rat-tooth and Alligator tooth forceps, polypectomy snares, polyp grasper, Dormier basket, biopsy forceps, retrieval nets, magnetic probes, friction fit adaptors, banding caps, transparent caps, endoscopy scissors have all been used successfully to remove FBs. Single and double balloon enteroscopes for children have also been used successfully (Shah, 2018).*

***Food bolus impaction***

*Food bolus impaction makes up the majority of esophageal obstruction cases in adults and should*



***Figure 1 - Middle third of esophagus: Foreign body***

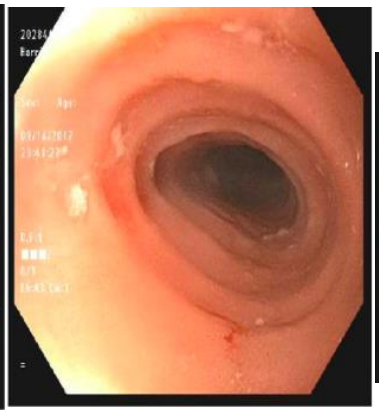


***Figure 2 - Eosinophilic esophagitis***



***Figure 3 - Upper third of esophagus***

*be considered a medical emergency. Often, the patient is reasonably comfortable, in which case intervention can be postponed, as passage of the food bolus will sometimes occur spontaneously. Regardless, obstructions should be cleared within 24 hours to reduce the risk of complications. Although some studies encourage biplane radiographs immediately to determine the presence or absence of bones, the European Society of Gastrointestinal Endoscopy (2016) suggests that a more conservative approach be taken if the patient is asymptomatic, and only resort to radiographic imaging when bones are suspected. Underlying pathology is strongly associated with adult food bolus impaction and may be as high as 93% (Truskaite & Dlugosz, 2016). A recent survey indicated that only 34% of gastroenterologists regularly perform a biopsy following removal of an esophageal food bolus, it is estimated that over 10,000 cases of eosinophilic esophagitis per year in the US may be missed as a result (Hiremath et al, 2017).*

*In another study, 40% of food bolus impactions were associated with an underlying diagnosis of eosinophilic esophagitis (Truskaite & Dlugosz, 2016). ood in esophagus due to eosinophilic esophagitis Lithium battery in 5 years old child's esophagus (Figures 1-3).*

**Batteries**

Batteries pose a special risk when ingested and require immediate attention. The majority of cases are children under 5 and involve small, round disk or button batteries found in small electronics such as toys, remote controls, and watches (Rosenfeld, 2018). Although some batteries pass through the GI system without complication, immediate intervention, including attempted removal and at a minimum close monitoring, is recommended due to the severity of possible complications. The most common of these are associated with esophageal impactions and include mucosal irritation, esophageal perforations, and in the most severe cases, hemorrhage due to trans-esophageal fistulas (TEF) impacting the aorta which often lead to death, especially in children under the age of 2 years (MMWR, 2012). Esophageal damage of any degree warrants hospitalization.

Diagnosis of battery ingestion has been successfully made using plain radiographs in 94% of patients (Rosenfeld, 2018), and been able to identify batteries in the esophagus, stomach, small bowel, and colon. Patients with esophageal battery impaction may present with sore throat, coughing, respiratory difficulties, and drooling, which retrospective studies have found to lead to incorrect diagnosis of an upper respiratory tract infection, prolonging critical treatment and increasing the risk for severe complications, especially in young patients. Early identification and imaging to confirm the diagnosis is key to timely treatment of patients with potentially fatal impactions.

Patients with esophageal battery impactions should always receive intervention. Common interventions are fluoroscopic balloon extraction and rigid or flexible endoscopy, although Foley catheter extraction is also used. When extraction is not possible from the esophagus, pushing the battery into the stomach and attempting retrieval from there is an alternative method (ASGE, 2011). Batteries that enter the stomach, bowel, or colon are less likely to become lodged and should be managed non-operatively. Serial radiographs should be taken every 3-4 days to observe progression, and in the event of non-progression for more than 48 hours, surgical removal may become necessary (ASGE, 2011) (Rosenfeld, 2018).

**Blunt objects**

The most common blunt objects are coins in children in US and China studies, followed by bony FBs, plastic bars and iron nails (Geng, 2017). (Figures 4-8) These should all be removed if in the esophagus, within 24 hrs if asymptomatic, 2 hrs if symptomatic or a button battery. If in stomach or below, follow if asymptomatic, remove if symptomatic (ESGE).




***Figure 4 - Penny in 2 years old esophagus***




***Figure 5 - Quarter stuck in 5 years old esophagus***

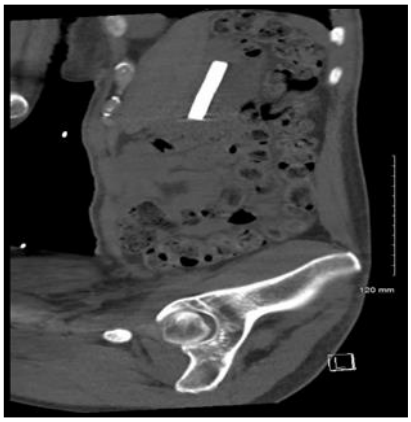



***Figure 6 - DOMINO in stomach (CT sagittal view)***



*Figure 7 - Two buttons in the esophagus (lateral view)*




*Figure 8 - Two buttons in the esophagus (AP view)*

**Sharp-pointed objects**

In Geng's series bony FBs made up 65% of cases and included fish, chicken, and duck bones (Geng, 2017)

**Long objects**

Objects longer than 6 cm should be removed endoscopically as they are unlikely to pass through the duodenal sweep (Pellerin, 1969). These include such objects as pens, pencils, toothbrushes, and eating utensils.

**Narcotic packets**

Concealment of illegal drugs via ingestion of balloons, condoms or wrapped in plastic has been reported in both children and adults. These are usually visible radiographically. Rupture or leakage of contents can be fatal. Thus, endoscopic removal is contraindicated. Surgical removal should be performed when the packets fail to pass or intestinal obstruction is apparent.

- ***One particular group of patients that pose a significant surgical challenge are FB ingested in the anus for pleasure seeking reasons. These usually end up having surgery…***
- ***The other group of patients are those who repeatedly swallow just about any FB to get surgical attention…***

**Conclusion**

Foreign body ingestion and food bolus impaction is a relatively common presentation to the ED. Emergent removal should be performed for all esophageal food impactions, foreign bodies with evidence of complete esophageal obstruction, disk batteries in the esophagus and magnets within reach of an endoscope. Removal should also be performed for objects with a diameter of 2.5 cm from the stomach, sharp-pointed objects or those longer than 6 cm. Removal of suspected drug containing packets should only be done surgically if packets are suspected to rupture or if they fail to progress radiographically.

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# Laparoscopic Radical Prostatectomy in Albania: Initial Experience in 25 Patients

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**Abstract**

Background: Laparoscopic or robotic assisted prostatectomy has become common world wide. However, to our knowledge, laparoscopic radical prostatectomy has not been reported in Albania.
Objective: To analyze the early perioperative and oncologic results obtained with the extraperitoneal laparoscopic prostatectomy (ELRP).
Patients and Method: A retrospective study of all the patients operated at Salus Hospital Tirana, Albania. All data were collected and evaluated retrospectively on the basis of thorough clinical and pathological examination. For data management and statistical analysis, all variables pre-, intra- and perioperative data were collected in a spreadsheet.
Results: In the 4-year period ( outline the period), 25 patients underwent the ELRP procedure. The average age of patients was 65 year-old and the PSA of 17.5 ng/dl. The total surgery time was 168 minutes on average. Only one patient was transfused after surgery, and limfocele was present in 2 patients. No other complications occured.
Pathological examination revealed pT2 and pT3 cancers in 72% (18/25) and 25% (6/25) of patients, respectively. One patient had regional lymph nodes infiltration. The incidence of positive surgical margins and biochemical relapse rate was 16 % (4/25) and 32 % (8/25), respectively.
Conclusion: The ELRP technique is safe and effective procedure in the treatment of prostate cancer, with low morbidity.
**Keywords:** Laparoscopy; prostate cancer; radical prostatectomy

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**Introduction**

Schuessler *et al.* (1) in 1992 introduced the laparoscopic approach for surgical treatment of prostate cancer, and Guillonneau and Vallancien (2) in 1999 standardized the technique, making it feasible and reproducible. Since then, the use of LRP has widely spread in throughout the world and, in some center has completely replaced the open prostatectomy. Many studies in the literature confirm the maturity of the laparoscopic technique: the results of oncological and functional outcomes are similar to those of traditional surgery, with all the advantages of minimal invasiveness.
The Urological Department of Salus Hospital Tirana, Albania first carried out a laparoscopic radical prostatectomy (LRP) in 2013. In the present study, we report our results after 4 years of procedures, analyzing in particular the oncological and functional aspects.

***Patients and Methods***

*Patients.* Between September 2013 and December 2017, 25 patients with prostate cancer, underwent extraperitoneal (Figure 1) LRP at our Center.
All procedures were performed by three surgeons. Qualitative and quantitative data were assessed and analized.

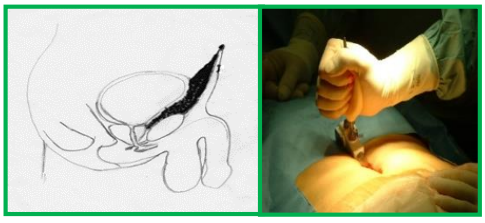


***Figure 1***

***Preoperative data are summarized in Table 1.***

| Preoperative data | |
|---|---|
| **Number of patients** | 25 |
| **Age (years) (median range)** | 65 (57 - 76) |
| **PSAng/mL (median, range)** | 17,5 (1 -170) |
| **Follow up months (median, range)** | 28 (2 - 50) |

Our criteria for performing a nerve-sparing procedure were: age and preoperative erectile function, absence of unilateral palpable nodule or involvement of the prostatic capsule at imaging, ipsilateral Gleason score ≤3+4, Prostate Specific Antigen (PSA) <10 ng/ml.
At our Clinic, the staging lymph node dissection is done to all the patients.

*Pathological examination.* All prostate specimens were analized by a dedicated pathologist who reported the following features: Gleason score, [pre-International Society of Urological Pathology (ISUP) 2005 (3)], (Table 2) pathological stage, seminal vesicle invasion, extracapsular extension (defined as the presence of neoplastic cells into adipose tissue), surgical margin status (cancer at the margin marked with ink) and lymph node invasion.
*Follow-up: recovery of continence, potency, cancer control.* Patients were discharged with a program of follow-up visits at 1, 3, 6 and 12 months. The recovery of urinary continence was evaluated on the basis of the number of pads/day.

| Clinical Gleason Score and Clinical Stage | Nr (%) |
|---|---|
| **Clinical Gleason score** | |
| **< 6** | 15 (60) |
| **3+4** | 4 (16) |
| **4+3** | 3 (12) |
| **8-10** | 2 (8) |
| | |
| **Clinical Stage** | |
| **T1a, b** | 4 (16) |
| **T1c** | 21 (84) |
| **cT2** | 0 |
| **cT3** | 0 |

*Table 2*

Patients free of pads were considered complete continent. The occasional loss of urine (one minipad per day) was classified as minimal stress incontinence. The use of two or more pads indicated moderate-to-severe incontinence. Good erectile function was defined as the ability to achieve an erection sufficient for penetration with or without the use of inhibitors of phosphodiesterase type 5 (PDE-5). Patients who reported erections only with intra-cavernous injection or vacuum devices were considered impotent. Biochemical relapse (BCR) was defined as a PSA value greater than 0.2 ng/ml, increasing from previous values.

*Data collection and statistical methodology.*
All data were collected and evaluated retrospectively on the basis of thorough clinical and pathological examination. For data management and statistical analysis, all variables pre-, intra- and perioperative data were collected in a spreadsheet (Table 3)

| Perioperative data | |
|---|---|
| **Operative time min (range)** | 168 (110-260) |
| **Transfusion rate** | 1 (4%) |
| **Conversion rate** | 0 |
| **Median cateterizatin time (range) days** | 9,8 (6-15) |
| **Mean hospital stay (range) days** | 6,4 (3-12) |
| **Lymph node metastasis** | 1 (4%) |

*Table 3*

***Results***

*Pre- and perioperative clinical data.*
Most patients had a clinical Gleason score ≤6 (60 %), while high-grade (4-6) disease accounting for only 8 % of cases. At the time of surgery, all the 25 patients (100 %) had clinically-localized disease (T1-T2)

| Pathological Stage | nr | Positive Margins R+ (%) | Clinical Gleason score | N (%) |
|---|---|---|---|---|
| **T1a, b** | 0 | 0 | < 6 | 13 (52) |
| **T1c** | 1 | 0 | 3+4 | 9 (36) |
| **cT2** | 18 | 2 (8) | 4+3 | 1 (4) |
| **cT3** | 6 | 2 (8) | 8-10 | 2 (8) |
| | | Total 4 (16%) | | |

*Table 4*

An extraperitoneal approach was performed in all the patients.

*Pathological outcome and oncological follow-up.* Pathological characteristics are summarized in Table 4.

The follow-up ranged from 2 to 50 months (median= 28 months). The overall BCR rate was 32% (8/25) (Table 5).

| **Biochemical Relapse. Stage and Gleason Score** | tot 8 (32%) |
|---|---|
| Pathological stage (nr) | Pathological Gleason Score |
| pT2 (3) | < 6 (1) |
| pT3a (2) | 3+4 (4) |
| pT3b (3) | 4+3 (1) |
| | 8-10 (2) |

*Table 5*

None of the patients developed bone metastases or died from prostate cancer desease or other deseases.

*Functional outcome.*
*Urinary continence:* The rate of minimal stress incontinence is 40% (10/25) and no one has moderate-to-severe incontinence.

*Erectile function: We have no data about* erectile function.

*Complications.* Overall, we recorded 2 patients complicated by limphocele in 25 LRPs (8%). No one needed re-operation as both were absorbed spontaneously. None of the patients needed intensive care recovery after surgery.

***Discussion***

*Oncological outcome.* The cornerstones that have guided the development of LRP are maintaining quality of life, good oncological control, low morbidity, and the benefits of a minimally, invasive approach. A magnified view and the consequent better appreciation of the anatomical structures are closely linked to the achievement of these goals. Among them, the primary objective is to control cancer. Experience with the Heilbronn technique on 500 patients led to an overall postive margin rate of 19% (7.4% and 31.8% in pT2 and pT3 cases, respectively) (4). The experience on 1000 patients at the Charité Hospital in Berlin was as follows: 14.8% in pT2 and 54.4% in pT3 cases (5). In a series of 1,300 patients, the University of Leipzig reported a positive margin rate of 9.8% in pT2 and 34.3% in pT3 cases (6). Overall, considering the data reported in the most important series of LRP, the rate of positive surgical margins in LRP ranges from 11% to 30% (7).

In our study, positive surgical margins were identified in 16% of patients (4/25), in particular, in 8 % of pT2 and in 8 % of pT3 cases.

Regarding the evaluation of biochemical progression, different series use different PSA cut-offs in the definition of relapse, which vary from 0.1 to 0.4 ng/ml. Recently Hruza *et al.* published long-term oncological

results: the BCR-free survival rate 10 years after LRP was 80.2% in pT2, 47.4% in pT3a and 49.8% in pT3b/pT4 cases, confirming a better prognosis in patients with organ-confined disease ($p$<0.001) (8). The rate of clinical progression-free survival at 10 years were: 97.2% in pT2, 84.4% in pT3a and 78.1% in pT3b/pT4 cases, and estimates of cancer-specific survival were 100%, 97.3% and 90.6%, respectively.

In our series, the BCR-free survival at 3 years is 68%,
The major series report 94.4% of BCR-free survival at 3 years from LRP.
Functional outcome. Functional results (urinary continence and erectile function) are becoming increasingly important for many patients. One of the main advantages of a minimally-invasive approach is the control of bleeding. The magnified view and better hemostasis allow for accurate identification of the different anatomical and functional structures and, accordingly, a more respectful surgery.
The main problem, which can make any objective comparative analysis between the different series impossible, is the lack of uniformity in defining, evaluating and reporting functional outcomes after radical prostatectomy. This usually leads to a great variability in the results of the different published series.
In our experience, at a timepoint of at least 12 months after surgery, 15/25 patients (60 %) were completely continent, 10/25 (40%) reported minimal stress incontinence (one mini pad), no patients needed more than one pad.

Similarly, the erectile function recovery rate varies significantly in different reports as there is no consensus regarding the definition, the use of different data collection methods and the use of drugs for the treatment of impotence.
In literature, important prognostic factors for predicting a good recovery of erectile function are: patient's age, preoperative function, nerve-sparing technique, and duration of follow-up (9). The majority of series report data on small groups of patients, usually treated after the surgical technique was well-acquired (10).
Stolzenburg *et al.*, using the IIEF, reported their experience of 700 extra-peritoneal LRPs: follow-up was 6 months and a nerve-sparing technique was performed in 185 (26.4%) patients, potent before surgery, unilaterally in 114 patients (16.2%) and bilaterally in 71 (10.1%) (11). At 6 months, 8 out of 66 men with unilateral technique (12.1%) and 16 of 34 with bilateral sparing (47.1%) had erections sufficient for intercourse with or without the help of PDE5 inhibitors. Rassweiler *et al.* reported the results of their first 180 LRP in 2003: 10 patients were treated with nerve-sparing technique (two bilateral and eight unilateral). Four patients had erections sufficient with sildenafil (12). The Montsouris group reported functional data of 47 consecutive patients under the age of 70 years, potent before surgery and treated with bilateral nerve-sparing LRP: 31 (66%) of those were able to have intercourse with or without PDE5 (13).
In our series, we have no certain data on potency. This is due to the fact that our patents do not refere during the follow-up

visits about erectile function as they retain as primary end-point the oncological safety, secondly the preservation of urinary continence, and the erectile function not important. However we do not have patients who use intra-cavernous injections or vacuum devices.

*Perioperative outcome.* In literature, the only proven advantages of LRP over the open technique are reduced blood loss, transfusion rates, hospital stay, postoperative pain, and duration of catheterization (14). The average blood loss reported after LRP ranges between 200 and 390 ml. The Montsouris group reported an average blood loss of 380 ml and a transfusion rate of 4.9%. In our experience we transfused only one patient over 25 operated.

The data on the length of hospital stay are extremely variable and must be interpreted in the light of the economic differences of health systems in Europe and the USA. In the USA, the patient is discharged very quickly, in 90% of cases within the second day (15). The main non-comparative studies indicate a range of hospitalization between 2 and 10 days, while the duration of catheterization is 7-10 days. Several reference Centers prefer to remove the catheter around the sixth to seventh postoperative day. At our Clinic, the average duration of catheterization was 9.8 days. We remove the catheter after a retrograde cystography.

**Conclusion**

Four years after the first LRP performed at our Clinic, the first series reported in Albania, we can state that Laparoscopic radical prostatectomy is a a safe and effective procedure in the treatment of prostate cancer, with low morbidity. We do not perform open surgery for prostate cancer, and we can say that the “gold standard” in our hand is Laparoscopic radical prostatectomy for prostate cancer. In our experience, the benefits are all related to the less invasive approach: reduced hospital stay, blood loss and pain, with improved recovery and cosmesis. The major difficulty is overcoming a learning curve that may seem prohibitive. However, with increasing experience and thanks to technological advances, the true potential of laparoscopy is gradually emerging.

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# Minimally Invasive Hallux Valgus Surgery. A Systematic Review

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**Abstract**

**Background;** This systematic review aims to illustrate the published results of "minimally invasive" procedures for correction of hallux valgus. Based on former systematic reviews on that topic, the literature search was organised by two independent investigators. MEDLINE was systematically searched for available studies. The keywords used were "hallux valgus", "bunion", "percutaneous surgery", "minimally invasive surgery", "arthroscopy", "Bosch" and "SERI". Studies were assessed using the level of evidence rating. A total of 21 papers were included in this review. These studies described a total of 1,750 patients with 2,195 instances of percutaneous, minimally invasive or arthroscopic hallux valgus surgery. Clinical reports of results after minimally invasive hallux valgus surgery at meetings are common. Published results in peer-reviewed journals are less common and the majority of papers are level IV studies according to the level of evidence ratings. We found one level II and three level III studies. Reported complications seem to be less than one may see in one's own clinical practice. This possible bias may be related to the fact that most studies are published by centres performing primarily minimally invasive hallux valgus surgery.

**Keywords:** Minimally invasive procedures, hallux valgus, bunion, percutaneous surgery, arthroscopy

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**Introduction**

The earliest reports of surgical hallux valgus correction date back to Gernet in 1836. Procedures for resection of parts of the first metatarsophalangeal (MTP) joint by the colleagues Hueter, Mayo [1], Keller [2] and Brandes [3] became the most popular.

Since these techniques were proven to fail, correctional metatarsal osteotomies replaced them; again our ancestors in the nineteenth century had already thought the same way. The first reports date back to Reverdin [4] who described in 1881 a subcapital closing wedge osteotomy for the correction of hallux valgus deformity. It then became popular as the Hohmann [5] osteotomy.

From the beginning of the use of osteotomies for the treatment of hallux valgus deformities, surgeons distinguished between distal and proximal osteotomies. While Hohmann [5], Wilson [6], Mitchell [7] and chevron [8] osteotomies were representatives of the distal osteotomies, Loison [9], Balacescu [10], Ludloff [11], Trott [12] and crescentic Mann osteotomies [13] were representatives of the proximal osteotomies. One might think that after more 160 years of facing the problem of hallux valgus surgery the ideal treatment should have been found. In 1931 Peabody [14] thought that he had found it. He stated that all of his patients were happy and there were no complications. Unfortunately, he was wrong and surgeons are still seeking wisdom. Helal in 1981 [15] counted more than 150 different techniques and the number has continued to increase.

At least a minimum consensus among surgeons has been established. Minor and moderate deformities [rated by intermetatarsal angle (IMA) and hallux valgus angle (HVA)] may be treated by distal osteotomies, while more severe deformities are best treated by proximal metatarsal osteotomies, which have been mathematically proven to give the best corrections.

Ferrari [16] published a systematic review in 2002 and concluded that there was no compelling evidence for an advantage of any of these techniques over any other particular type of surgery.

The role of minimally invasive techniques

Minimally invasive surgery has gained popularity in all fields of orthopaedic and trauma surgery. The theoretical advantages are potentially decreased recovery and rehabilitation times, reduced surgical time and less stress to the patient.

One may distinguish between minimal incision surgery, percutaneous surgery and arthroscopic surgery [17]. Arthroscopic hallux valgus surgery is certainly not a standard procedure [18]. It is demanding, time-consuming and carries the potential risk of nerve injury [19, 20].

Early reports of percutaneous hallux valgus surgery date back to the 1940s [21] in the USA, where podiatrists were trying to circumvent the restrictive laws regarding surgery for podiatric physicians. Early power equipment for minimal incision metatarsal osteotomies was developed in the 1960s.

Peter Bösch modified the popular Kramer osteotomy after a conversation with the podiatrist O.T. New. His so-called subcapital osteotomy (SCOT) technique [22] became the origin of all percutaneous techniques of hallux valgus surgery that were later invented. The disadvantage of the percutaneous technique is the fact that surgery is performed without direct visualisation of the different tissue layers and intraoperative fluoroscopy is mandatory. The bony procedures are performed using a high-speed power bur which entails the disadvantage of bone loss which leads to shortening of the metatarsal.

The minimal incision hallux valgus surgery is a technique where the smallest necessary incision to create the osteotomy is performed by using a power saw blade. These techniques are generally not performed under fluoroscopy [21].
The current question is whether it is justifiable to use percutaneous or minimal incision hallux valgus surgery based on the actual medical literature.

***Literature search and data extraction***

Based on the systemic reviews by Mafulli et al. [17] and Roukis [21] the literature search was organised by two independent investigators. MEDLINE was systematically searched for available studies. The keywords used were “hallux valgus”, “bunion”, “percutaneous surgery”, “minimally invasive surgery”, “arthroscopy”, “Bosch” and “SERI”.
Once the relevant articles had been retrieved, they were hand-searched for further references fitting the search pattern. Only articles published in peer-reviewed journals were included. If a reference could not be obtained it was excluded from consideration. Studies were assessed using the level of evidence rating introduced by the Journal of Bone and Joint Surgery (American Volume) in 2003 [23].

**Results**

A total of 21 papers were included in this review. These studies described a total of 1,750 patients with 2,195 instances of percutaneous, minimally invasive or arthroscopic hallux valgus surgery. Almost all studies were level IV studies, three studies could be rated as level III and one study as level II (Table 1).
Bösch et al. [24] and Markowski et al. [25] published in 1990 and 1991 the preliminary results with the SCOT (percutaneous) technique in 45 patients and 64 feet. The average follow-up was 16 months (range eight to 32 months). The range of motion decreased from preoperatively 66.5 % of the patients presenting a range of motion between 70 and 110° to 35 % at final follow-up. There were also 9 % pin track infections.
In 2000 Bösch et al. [22] reported much better results in a seven to ten year follow-up study. Of the 98 feet the HVA was corrected from preoperatively 36° (range 14–54°) to 19° (range 7–40°), and the IMA was corrected from 13° (range 6–18°) to 10° (range 3–18°) at follow-up. Complications included four deep infections and four cases of delayed bone healing.
Portaluri [26] in 2000 published a series of the Bösch technique in 143 patients with 182 operated feet. The radio- logical results were almost identical to those Bösch et al. [22] reported. Only two patients had a pin track infection, two had early accidental pin removal and eight had reported superficial infections.
Magnan et al. [27] in 2005 reported on 118 consecutive percutaneous distal metatarsal osteotomies at an average of 35.9 months. Significant correction of all radiological parameters was reported. In 61 % either plantar or dorsal displacement of the capital fragment was noted. Only one deep infection at the osteotomy site and superficial skin irritation by the Kirschner wire were reported. First MTP joint range of motion of less than 30° was seen in seven patients (6.8 %).
In 2013 Iannò et al. [28] presented 72 patients (85 feet) treated with the Bösch method with an average follow-up of 73.3 months. HVA, IMA and sesamoid position were statistically significantly corrected ($p < 0.1$ for all). Complications included three cases of avascular necrosis (AVN) of the meta-tarsal head, malunion in four feet and two cases of skin irritation due to the Kirschner wire.

A multicentre study of the distal percutaneous metatarsal osteotomy according to Isham was presented by Bauer et al. [29]. A total of 189 feet were prospectively followed with a mean follow-up of 13 months (12–24 months). The osteotomies were percutaneously performed and no internal fixation was used. The American Orthopaedic Foot and Ankle Society (AOFAS) score improved from preoperatively 52 points on average to 93 points at follow-up. The median range of motion decreased from 90° preoperatively to 75° which is an average of 17 % loss of motion. Neither nonunion, AVN nor malunion of the capital fragment was reported. The authors state that their technique requires a learning phase before being able to produce reliable acceptable results.

In a single-institution study Bauer [30] reported his own results with the percutaneous Isham technique. A total of 104 cases in 82 feet were followed for a median of two years. AOFAS score, HVA and sesamoid position were significantly improved. Due to the philosophy of the Isham technique correction of the IMA is only possible to a limited extent. Besides two cases of limited range of motion, two cases of complex regional pain syndrome (CRPS) and six cases of distal metatarsal articular angle (DMAA) overcorrection, no complications were reported.

Radwan and Mansour [31] performed a comparative study between 31 percutaneous distal metatarsal osteotomies (Bösch technique) and 33 distal chevron osteotomies. The operative time results revealed on average seven minutes less surgical time with the percutaneous surgery. There was no difference in bony
healing and radiographic parameters. The mean range of motion was almost identical in both groups. They further described that limited dorsal range of motion occurred more often in the chevron group. According to the report there was no nonunion or malunion after the percutaneous distal metatarsal osteotomy.

Roth et al. [32] presented a retrospective comparative study of the percutaneous (Bösch) and the standard Hohmann techniques. There were 88 percutaneous and 36 open osteotomies performed. Radiological parameters revealed similar results in both groups. The complication rate with 15 % infection, 10 % nonunion and 6 % CRPS in the percutaneous group was much higher than in the open group.

In 2009 Maffulli et al. [33] compared a series of 36 Scarf osteotomies with a series of 36 Bösch osteotomies. The mean operative time for the Bösch technique was significantly less then for the Scarf osteotomy (19 vs 42). Radiographic evaluation revealed similar results with both techniques. Range of motion at follow-up was not reported in this series. There were three pin track infections after the Bösch technique.

Giannini et al. [34] performed a prospective comparative study of the SERI (simple, effective, rapid, inexpensive) and Scarf osteotomies. Twenty patients with bilateral hallux valgus deformities underwent a Scarf on one side and a SERI osteotomy on the other side. All patients underwent clinical and radiological follow-up at two and seven years. The results of the radiological correction between the two groups were similar in respect of HVA, IMA and DMAA. In this study there were no reported intraoperative or post-operative complications in either group. All osteotomies healed properly. Most interesting were the reported surgical times. A very short surgical time of 17 minutes on average with the Scarf osteotomy was even topped by the average surgical time of three minutes with the SERI.

Enan et al. [35] evaluated the early results of the minimally invasive hallux valgus correction using the minimal incision Hohmann-type technique. At a

mean follow-up of 21 months (12–36 months) 24 patients with 36 operated feet, a preoperative IMA≤18° (9–18) and an HVA of more than 17 and less than 40° formed the study group. Without knowing the pre- operative AOFAS score, the score at final follow-up was 91.1 points. In only 44.4 %, the position of the metatarsal head was found without plantar (47.3 %) or dorsal displacement (88.3 %). Shortening on an average of 2.2 ± 2.8 mm was noted. The HVA was corrected from an average of 27.7° (18–37) to 14.6° (8–24) and the IMA from 11.2! (10–18) to 5.8°(4–12). As complications only three feet with mild inflammatory skin reactions around the outlet of the K-wire were observed.

**Discussion**

Post-operative range of motion and stiffness after the percutaneous or minimally invasive Hohmann-type osteotomy [27, 35] is a matter for discussion. Despite the fact that a K-wire is inserted for six weeks beside the joint capsule and the first MTP joint has no range of motion for six weeks the reported numbers of stiffness are low [27, 35]. In their original paper Markowski et al. [25] reported a decrease of range of motion in 31 % of patients. Radwan and Mansour [31] compared the mean post- operative range of motion after the percutaneous Bösch method and distal chevron. Although the first technique includes fixation of the first MTP joint for six weeks while the distal chevron allows immediate range of motion and as described range of motion exercises after four weeks, the presented results showed almost identical mean post-operative range of motion at follow-up. Unfortunately most studies do not report the post-operative loss in range of motion [26, 32].
A potential disadvantage of the percutaneous and minimally invasive distal metatarsal osteotomies according to the Hohmann technique is the plantar or dorsal malalignment. While Bösch et al. [22], Scala and Vendettuoli [36], Sun et al. [37], Giannini et al. [34] and Radwan and Mansour [31] did not report metatarsal head position at follow-up, Magnan et al. [27] reported 61 %, Enan et al. [35] 55.6 % and Iannò et al. [28] 4.7 % dorsal or plantar malalignment.
Most studies did not mention the incidence of malunion or nonunion after percutaneous or minimally invasive distal metatarsal osteotomies. Kadakia et al. [38] planned a randomised prospective study. Due to their early complications with the minimally invasive technique they stopped the study. One may argue that despite the fact that the authors were extremely experienced foot and ankle surgeons, their experience in minimally invasive hallux valgus surgery was minimal and they started the study with the first patient they planned for surgery.
We found three comparative studies of minimally invasive distal metatarsal osteotomies vs open hallux valgus operations. All studies revealed similar corrections of all radio- graphic parameters. Maffulli et al. [33] reported a highly significant shorter surgical time with the percutaneous technique (19 vs 42 min), while in Radwan and Mansour's [31] study only a minimal but statistically significant difference (50 vs 58 minutes, $p = 0.015$) was reported. In Giannini et al.'s [34] study an extremely short surgical time was reported. Duration of surgery is an issue in hallux valgus correction; nevertheless, this should not be the only argument when choosing one procedure over the other.
Reported complications vary among the studies. While Giannini et al. [34] reported no complications at all in their comparative series, other authors noted complications. Bösch reported in 1990 pin track infection in 9.5 % and Roth et al. [32] in 15 %. Bösch et al. [22] stated in 2000 that the infection

rate decreased after completing the learning curve. Bauer et al. [29], Portaluri [26], Scala and Vendettuoli [36] and Iannò et al. [28] reported few incidences of pin track infections.
Correction of radiographically measured deformity is the objective aim of hallux valgus surgery. This can certainly be achieved using minimally invasive hallux valgus surgery. Comparisons of minimally invasive and open techniques revealed similar results of both techniques [17, 31, 32, 34, 44, 45].

**Conclusion**

Clinical reports of results after minimally invasive hallux valgus surgeries at meetings are common. Published results in peer-reviewed journals are less common and the majority of papers are level IV studies according to the level of evidence ratings. We found one level II and three level III studies. Reported complications seem to be less than one may see in one's own clinical practice. This possible bias may be related to the fact that most studies are published by centres performing primarily minimally invasive hallux valgus surgery. Correction of deformity is certainly similar to open hallux valgus surgery. One definite advantage is the reduced time of surgery, and the disadvantage especially with the Bösch technique is the potentially reduced range of motion after surgery. Studies of higher levels of evidence with larger numbers of cases should be conducted.

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# Misdiagnosed Appendicitis in Children

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**Abstract**

**Background:** Appendicitis is the one of the most common emergency abdominal operation in children. It is estimated that appendicitis is diagnosed in about 2 % of children who present to emergency department because of acute abdominal pain[1]. Timely diagnosis and appendectomy can prevent abscess formation, perforation as well as reducing early and late postoperative complication.
**Methods:** This study is a retrospective review of all children diagnosed with acute appendicitis in our emergency department between January 2015 – 2018. We have compared the clinical features and the results of examinations between two group of patients - those who were diagnosed correctly and have been operated, and those who were misdiagnosed and operated later respectively more than 24 hours after initial control.
**Results:** This study includes fifty-nine children less than sixteen years old, admitted in our clinic and operated due to acute appendicitis. Fifty three (89.9%) of them were hospitalized after the first control, whereas the remining six (10.1 %) were discharged home after the initial control. The misdiagnosed patients were returned in our department less than twenty hours after the first control. Compared with the patients in which the diagnosis was made correctly the misdiagnosed patients in general had lower levels of leukocytes, CRP and temperature.
**Conclusion:** The diagnosis of appendicitis in children can be very difficult because of the atypical features. According to our experience and the data from other studies, still there is not a single test or combination of clinical and laboratory examinations, able to discriminate children with and without acute appendicitis with a high percentage of accuracy.
**Keywords:** Children, appendicitis, misdiagnosed

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**Introduction**

Appendicitis is the most common abdominal emergency which demands the surgical intervention. Despite the relatively high incidence of this emergency and a great knowledge about appendicitis, sometimes the diagnosis can be a true challenge even for an experienced surgeon especially in the case of elderly patients and children[1,2]. Early diagnosis can prevent perforation as well as decrease the rate of postoperative complications. The rarity of acute appendicitis among children is the main reason for the difficulty in diagnosis and the increased rate of perforation[3,4,5].

**Aim of the study:** The aim of this study is to to present our experience in the management of acute appendicitis in children focusing on pathogenesis, diagnosis, and current management strategies.

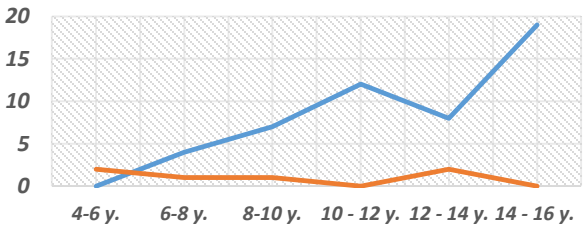
**Material and methods**

In this retrospective study we've included all the children less than 16 years, admitted in our clinic between January 2015 – 2018 with the diagnosis of acute appendicitis. The diagnosis was confirmed after surgical intervention and histopathological examination. The patients that were sent home after the first control and afterwards hospitalized and operated within 24 hours of their discharge were considered to be misdiagnosed. All the important datas, such as age, gender, signs and symptoms during initial control, clinical examination and interval between the initial visit and the surgical intervention were analyzed and processed.

**Results**

From fifty-nine children included in this study 31 of them (52 %) were girls and 28 boys (48 %). The mean age of children was 9.6 years (range, two to fifteen years). Most of the children respectively 47 of them (79 %) were over five years of age.

*Distribution of patients by age*




After the first control in our department fifty-three patients (89.9 %) were diagnosed correctly with acute appendicitis and operated, whereas six of them (10.1 %) have been sent home with the advice that they should immediately come back in the event of a deterioration of their condition – (misdiagnosed patients).

The misdiagnosed patients were controlled twice or more in our clinic before the diagnosis of acute appendicitis was confirmed.

In all misdiagnosed children the interval between first control and surgical intervention was more than 24 hours.

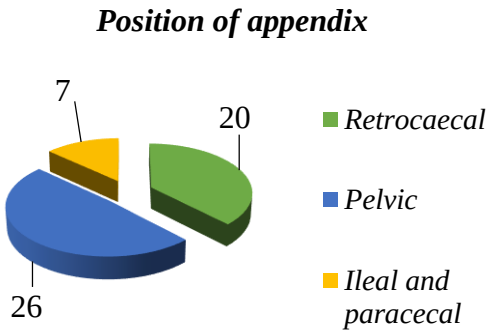
The main complaint of the patient correctly diagnosed were abdominal pain and pain in the RLQ, whereas in case of misdiagnosed patients the pain was localized in the epigastric region or scattered diffusely into the abdominal cavity.

The signs of acute tonsillopharyngitis were present in three of misdiagnosed patients at their first control.

| *Complaints* | *Misdiagnosed group* | *%* | *Correctly diagnosed group* | *%* |
|---|---|---|---|---|
| ***Abdominal pain*** | 50 | 94 % | 4 | 67 % |
| ***Migrating pain*** | 44 | 83 % | 3 | 50 % |
| ***RLQ tenderness*** | 46 | 86 % | 1 | 17 % |
| ***Muscle guarding*** | 21 | 40 % | 0 | 0 % |
| ***Fever*** | 19 | 36 % | 1 | 17 % |
| ***Vomiting*** | 25 | 47 % | 3 | 50 % |
| ***Diarrhea*** | 10 | | 2 | 33 % |
| ***Duration of symptoms*** | < 12 h | | > 18 h | |

*Table 1*

Abdominal ultrasonography was performed in 29 correctly diagnosed children and in 14 of them free periappendicular or pelvic fluid collection was detected. Abdominal ultrasound was normal in three misdiagnosed patients.
In correctly diagnosed patients, position of appendix was retrocaecal in 20 (37 %) of them, pelvic in 26 (49 %) patients, whereas ileal and paracecal position was found in 7 (13 %) patients. In five misdiagnosed children the appendix was in retrocecal position whereas in one of them in pelvic position.




Postoperative complications have been observed in both groups of patients although their incidence was greater in the misdiagnosed group of children. Wound infection was the most common complication in both groups respectively in eight correctly diagnosed patients (15 %) and in two misdiagnosed patients (33 %). Pelvic abscess was found only in one misdiagnosed patients and was treated by open drainage.

Length of hospital stay was shorter in correctly diagnosed patients (about 4 days) compared to misdiagnosed patients (about 8 days).

**Discusion**

Recent advances in the management of appendicitis seem to be not sufficient for accurate diagnosis of this condition in children. For these reasons, despite the multiple diagnostic modalities, misdiagnosis of acute appendicitis still remains a problem in pediatric surgery. The data from many studies report that the misdiagnosis rates vary from 7.5% to 37% for children[5,8,9] respectively nearly 100 % for those younger than two years[6,7,12]. In our study most of the patients were aged between 7 and 15 years old with an average age of 10.5 years[10,11]. Abdominal pain especially in RLQ was the most common complaint of children with acute appendicitis in our study, whereas in the misdiagnosed group the most frequent complaint was epigastric or diffuse abdominal pain. In many others studies, RLQ pain is the most common complaint of children with acute appendicitis[13]. CRP

and white blod cell count are very helpful in establishing the diagnosis of acute appendicitis [14,16,17,18]. In our study about 90 % of well diagnosed patients had leukocytosis (< 12.5 x $10^4$ L) while in the misdiagnosed groups the high level of leukocytes was found only in 60 % of children (> 11 x $10^4$ L). We always have to consider the fact that increased white blood cell count (WBC)[15,26,29] is also present in other conditions such as gastroenteritis, mesenteric lymphadenitis, pelvic inflammatory disease and certain other infections, and that the the WBC count alone without other investigations cannot differentiate between a complicated and an uncomplicated acute appendicitis[29]. In different studies the sensitivity of increased white blood cells to diagnose acute appendicitis varies from 65 to 85%[19,20,21,22,23], whereas a normal count of WBC cannot exclude the diagnosis of acute appendicitis[26,29].

Although C-reactive protein (CRP) is a good indicator for bacterial infection and rises earlier than WBC count, most studies show that leukocyte level had a better diagnostic value in the diagnosis of acute appendicitis[26,15,29].

One of the most characteristic signs of acute appendicitis is the presence of pain and tenderness in right lower abdominal quadrant[11,25]. In our study this sign was present in approximately 86 % of patients, whereas only in 17 % of misdiagnosed children group. Our results are similar to most of other studies from literature[11]. Our experience shows that the misdiagnosed children alongside the lack of characteristic pain in the RLQ had a shorter duration of symptoms. Several authors also stress this data in their studies[10,11].

Postoperative wound infection was the most common complication in our study. It was present in 7.6 % of correctly diagnosed patients and 16.6 % of misdiagnosed ones. Pelvic abscess occurred in only one misdiagnosed patient. According to different studies the rate of this complication ranges from three to eight percent[1,2]. Although C-reactive protein (CRP) is a good indicator of bacterial infection and rises earlier than WBC count, most studies show that leukocyte level has a better diagnostic value in the diagnosis of acute appendicitis.

**Conclusion**

The diagnosis of acute appendicitis in children remains a challenging and difficult procedure. Nowadays, no single test or combination of clinical and laboratory examinations can be reliable in differentiating children with and without acute appendicitis. Misdiagnosis predominantly was associated with a shorter duration of symptoms, failure to elicit physical signs in irritable children, atypical presentation, less relevant physical findings, and more often happens in children less than five years old. Diagnosis of children in this age often requires a serial physical and laboratory examinations and a high level of suspicion, which aid to
establish the correct diagnosis at the initial visit.

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# Frequency of Gastrointestinal Diseases in Patients with End-Stage Renal Disease Treated with Long Term Dialysis

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**Abstract**

**Background: G**astrointestinal complications are frequent in patients with renal disease and are responsible for substantial morbidity and mortality among these patients in developing countries. Many times, these patients are subjected to endoscopic evaluation and mucosal biopsies are taken for definitive diagnosis. Long before the routine uses of dialysis, patients dying of uremia were found to have a high incidence of gastrointestinal abnormalities (1).

**Matherials and methods**: The survey included 240 persons; 120 of them were dialysis patients, while the remaining 120 were healthy individuals who served as a control group. 54 (45%) of the patients with hemodialysis were females while 66 (55%) of them were males with mean age: 58.20 ± 18.00 years. These patients had been in dialysis for more than 12 years at the Clinic for Nephrology in Skopje and the Clinical Hospital in Tetovo.

**Results:** Gastrointestinal complications were present in 20 (37.0%) out of 54 females while 26 (39.4%) out of 66 males presented with duodenal bulbar ulcers. 84 patients [(females-38/54 (70.4%) and males-46/66 (85.2%)] of the total number of 120 examined patients were found to have chronic gastritis.

**In conclusion**, we found that the incidence of PUD was more than 10 times higher in CKD patients than in those without CKD over a 3-year period between 2008-2010. CKD patients receiving HD, NSAID, or clopidogrel had an increased risk of PUD, compared to CKD patients not receiving these treatments.

**Key words:** Gastrointestinal disease**,** chronic gastritis,peptic ulcer disease, hemodialysis.

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**Introduction**

Gastrointestinal (GI) complications are well known in patients with renal disease. The etiologies of GI complications in CKD are likely to be multifactorial. Urea increases back diffusion of hydrogen ions across the mucosal barrier. Elevated gastrin levels, partly due to the decreased renal clearance of gastrin (4-6) and partly due to the enhanced gastrin synthesis,6 act as an important stimulus for acid secretion. The above mentioned factors increase gastric mucosal injuries in patients with renal failure. Since gastrin decreases pyloric sphincter tone, high gastrin levels may lead to biliary reflux, thus worsening mucosal injury (7,8). Other mechanisms may contribute to the mucosal abnormalities in ESRD. For example, biliary reflux can worsen gastro-duodenal inflammation. Since gastrin can decrease pyloric sphincter tone, high gastrin levels may worsen biliary reflux, thus worsening mucosal injury. For duodenal ulcers, impaired pancreatic bicarbonate secretion (35,36) and increased pepsinogen release (9,10) in renal failure might also play a role. Several studies have also noted that upper gastrointestinal hemorrhage in dialysis patients is often associated with the use of ulcerogenic drugs such as steroids, iron and especially non-steroidal anti-inflammatory agents, but this is also true in the general population. Although Helicobacter pylori infection is clearly important in causing gastroduodenal lesions in all patients, the infection rates have not been found to be increased in patients with renal failure (11-13,). Gastrointestinal disorders are frequent complications in patients with chronic renal failure treated with hemodialysis.Long before the routine use of dialysis, patients dying of uremia were found to have a high incidence of gastrointestinal abnormalities. Mallory-Weiss tears seem to have a prevalence that is independent of renal function, while esophageal varices may be less frequent in the dialysis population . Patients with renal transplants are at increased risk of esophagitis from opportunistic infections such as Candida, cytomegalovirus and herp|es simplex. Therefore, dialysis patients still tapering immunosuppressive therapy after failed allograft should be carefully watched for these infections. Although uremic patients not on dialysis may have delayed gastric emptying, end stage renal disease itself generally does not cause delayed emptying. However, slower gastric emptying has been documented in patients with intraperitoneal dialysis. Gastrointestinal symptoms related to decreased motility are common in diabetic patients, a group which comprises a large proportion of many dialysis populations.

The routine measurement of gastrin has no clinical role, but the literature documenting gastrin elevations in renal failure should be kept in mind if searching for a gastrinoma in a dialysis patient (14-18).Improvements in dialysis technique and changes in the patient population undergoing dialysis have modified the spectrum of gastrointestinal diseases seen in patients with end-stage renal disease (ESRD), also called chronic kidney failure, a term that describes the gradual loss of kidney function.

**Matherials and methods**

The survey included 240 individuals in total. Half of them (120 patients) were dialysis patients and the other half were healthy individuals who served as a control group. Overall our "cross-sectional" study included, 108 (45%) women of average age of 59.50 ± 14.50 years and 132 (55%) men of average age of = 56.40±12.80 years. The gender distribution for the dialysis patients was as follows: 54 (45%) of them

were females and the remaining 66 (55%) were males, with mean age: 58.20 ± 18.00 years. The patients had been on dialysis for more than 12 years in the Nephrology Clinic -Skopje and the Tetovo Clinical Hospital. The control group of healthy examiners (volunteer blood donors) had also the same female to male ratio: 54 (45%) females : 66 (55%) males. The two groups were also the same concerning their age, gender, religious affiliation and national affiliation. All patients with gastrointestinal complications examined H: B, as well as a small number of gastroscopies.

| *Gender* | *Number* | *The Average age ±SD* |
|---|---|---|
| *Men* | 66 (55%) | *56.40 ±12.80* |
| *Females* | *54 (45%)* | *59.50 ±14.50* |

***Table no 1. Number of patients presented by sex and average age***

| *Gender* | *Macedonian (45%)* | | *Albanian (55%)* | |
|---|---|---|---|---|
| | Nr | % | Nr | *%* |
| *Men* | 30 | 25.0 | 36 | *30.0* |
| *Females* | *24* | *20.0* | *30* | *25.0* |

***Table no 2: Distribution of patients according to nationality***

Out of the total number of patients, 54 (45%) of them were Macedonians and 66 (55%) were Albanians. The gender distribution for the Macedonian patients (45%) was as follows: 25% males and 20% females. The male to female ratio for Albanian patients was 30% males: 25% female. Concerning their religious affiliation, 66 (55%) patients were of Islamic faith and 54 (45%) of the Catholic religion.

**Statistical analysis of the examined material**

Statistical basic methods such as the arithmetic mean value and standard deviation (X±SD) were used. Comparative statistics parameters between the two groups were analyzed by using specific statistical tests called StudentoV, Mann-Whitney and Wilcoxon's test. The results were presented in the form of tables and in the form of processed diagrams.

**Results**

Gastrointestinal disorders are frequent complications in patients with chronic renal failure undergoing hemodialysis. In our study gastrointestinal complications were present in 20 (37.0%) out of 54 females while 26 (39.4%) out of 66 males presented with duodenal bulbar ulcers. 84 patients [(females-38/54 (70.4%) and males-46/66 (85.2%)] of the total number of 120 examined patients were found to have chronic gastritis, verified by clinical, ventricular, gastroscopic and CLO-tests. In the group of examiners a positive presence of serum HbsAg was observed in 10 (14.8%) females and 12 (18.2%) males. Anti HbsAg-positivity was found in 26/54 (48.1%) of females and 35/66 (57.6 %) of males. Those findings were result of contact and previous infection with Hepatitis-B. Virus virion of the manifested clinical hepatitis was not observed in the group of examined patients.

| *Gastrointestinal complications* | *Females* | | *Men* | |
|---|---|---|---|---|
| | Nr. | % | Nr. | *%* |
| *Duodenal ulcer* | 20 | 37,0 | 26 | *39.4* |
| *Chronic gastritis* | 38 | 70.4 | 46 | *85.2* |
| *Ascites* | *8* | *14.8* | *12* | *18.2* |

***Table no. 3. Gastrointestinal complications of patients treated with hemodialysis***

The highest percentage of gastrointestinal complications of the examined patients were chronic gastritis with = 82.8%, duodenal ulcers with = 79.4% and ascites with = 38.2% ***(tabl. 3).***

**Discussion**

CKD patients receiving hemodialysis treatment comprise more than 1.2 million people in the world, and this population is expanding at a rate of 7% per year according to the progress in medical and dialysis technology.1 GI complications are known to commonly occur in patients with renal failure. Uremia and dialysis have been found to increase the risk of lesions in the GI tract. Gastrointestinal disorders are frequent complications in patients with chronic renal failure treated with hemodialysis. Long before the routine use of dialysis, patients dying of uremia were found to have a high incidence of gastrointestinal abnormalities.

Mallory-Weiss tears seem to have a prevalence that is independent of renal function, while esophageal varices may be less frequent in the dialysis population. Patients with renal transplants are at increased risk of esophagitis from opportunistic infections such as Candida, cytomega-lovirus and herples simplex. Therefore, dialysis patients still tapering immunosuppressive therapy after failed allograft should be carefully watched for these infections. While uremic patients not on dialysis may have delayed gastric emptying, end stage renal disease itself generally does not cause delayed emptying. However, slower gastric emptying has been documented with inperitoneal dialysis patients during a dialysis fluid dwell period. Furthermore, gastrointestinal symptoms related to decreased motility are common in diabetic patients, a group which comprises a large proportion of many dialysis populations. Most investigators have concluded that gastrin elevation does not explain the mucosal lesions in patients with ESRD. The routine measurement of gastrin has no clinical role, but the literature documenting gastrin elevations in renal failure should be kept in mind for the possibility of gastrinoma in a dialysis patient (14-18).

Improvements in dialysis technique and changes in the patient population under-going dialysis have modified the spectrum of gastrointestinal diseases seen in patients with end-stage renal disease (ESRD), also called chronic kidney failure, a term that describes the gradual loss of kidney function. Peptic ulcer disease (PUD) is still a common disease in elderly patients and patients with multiple comorbid conditions. Evidence suggests that *Helicobacter pylori*infection and use of non-steroidal anti-inflammatory drugs (NSAID) are the primary causes of PUD in the general population. However, compared to the general population, patients with chronic kidney disease (CKD) have distinct causative factors and clinical outcomes of gastro-duodenal ulcers. Population-based studies have demonstrated that CKD patients have a higher risk of peptic ulcer bleeding and bleeding-related

morbidity and mortality. Tseng et al. reported a high recurrence rate of PUD among hemodialysis (HD) patients even after *H. pylori* eradication. Another longitudinal study also reported that PUD occurred in a significant number of long-term HD patients despite a low prevalence of *H. pylori* nfection. Both PUD and CKD are leading public-health issues , and many studies have described associations between them (19-29). Despite this, limited information is available about temporal trends in PUD among CKD patients (5,6,7). Another limitation of existing evidence is the focus on hospitalized patients with peptic ulcer bleeding, preventing generalization to the entire CKD population . It is also unclear if CKD patients differ from non-CKD peptic ulcer patients with respect to the ulcer location (gastric or duodenal mucosa) and patient status (inpatient or outpatient). Finally, it remains uncertain whether CKD patients taking ulcerogenic medications (e.g., NSAIDs or aspirin) are more likely to develop PUD (30,31). In addition, we determined the incidence of PUD over a 10-year period, compared between CKD patients and patients without CKD. More specifically, the effects of gastroduodenal mucosa and ulcerogenic medications on CKD-related PUD were investigated. Dialysis treatment, including the mode and length of the treatment, was recorded.

Because the different dialysis modalities can affect the risk of ulcerous duodenal CKD patients were specifically divided into patients who had never received HD treatment (non-HD CKD) and patients who received HD treatment at any time, regardless of the duration of treatment (HD-CKD). HD-CKD patients included patients who had HD for <3 months (temporarily HD-CKD) and those who underwent HD for ≥3 months (HD-CKD maintenance). Depending on the location of the ulcer and the upper part of the endoscopy (eg, in the outpatient department or during hospitalization), these groups were further stratified to observe the effect of CKD on the stomach and duodenal mucosa. H. pylori peptic ulcer has been identified by receiving H. pylori eradication therapy during or after the date of the index. H. pylori eradication was defined as administration of proton pump inhibitors or H2 receptor antagonists plus clarithromycin or metronidazole plus amoxicillin or tetracycline and with or without bismuth. The use of drugs has been documented for aspirin, NSAIDs (except aspirin), warfarin, clopidogrel, and cilostazol.

NSAIDs consisted of cyclooxygenase-2-specific inhibitors (COXIBs) and traditional NSAIDs (except COXIBs (24-28)). More importantly, there was a rapid increase in the incidence of PUD in elderly patients with CKD, compared to a decrease in younger CKD patients. Several factors, including HD therapy, patient access (inpatient vs. outpatient), and the use of NSAID and clopidogrel, further affected peptic ulcer risk in CKD patients. In addition, CKD patients undergoing mainte-nance HD were likely to develop GU following long-term HD therapy. Overall, we suggest that CKD itself is a strong independent risk factor for PUD, and the incidence of PUD among elderly CKD patients is substantially increasing.Well-developed studies have demonstrated that CKD patients with peptic ulcer bleeding were more likely to have adverse outcomes such as prolonged hospital days and increased mortality rates(111,18,19).The incidence of PUD in the general population is reported to be decreasing , while our results indicate that the incidence is increasing in patients with CKD. The decrease in PUDs in the general population may be the result of a decrease in *H. pylori* infections (18). Given that the prevalence of *H. pylori* infection in CKD patients is lower than in those with normal renal function (7), the increase in PUD in this population is likely due to other causes. In recent

decades, CKD has been associated with increasing age, the presence of a greater number of comorbidities, and an increased use of NSAID (21,22). Therefore, we thought that these factors are probable explanations for this increasing incidence of PUD in CKD, particularly as they are also well-known risk factors for PUD.Our results indicate a deleterious influence of HD therapy on peptic ulcer risk, regardless of dialysis duration. Anticoagulant use during HD may contribute to this risk (3,6,9,10). In addition, intradialytic hypotension and hemodynamic changes might play a role in the occurrence of PUD. Intradialytic hypo-thension remains one of the most common HD problems and occurs in approximately 20–30% of HD sessi-ons (23).The majority of CKD cases (96.3%) in this study received endoscopic diagnoses and treatments in the inpatient setting instead of the outpatient department. Yang et al indicated that approximately 10% of upper gastrointestinal bleeding episodes in the dialysis population were managed in the ambulatory care department (5). It should be noted that PUD may be the primary cause of admission or may be a complication in those already hospitalized for another condition . Even though CKD patients are considered to have a high risk for ulcer rebleeding and require more surveillance in hospitals (4,12), this heigh-tened awareness does not fully explain this result.Further studies might be warranted to investigate the effects of the above factors on the association between CKD and PUD. CKD patients receiving hemodialysis trea-tment consist of more than 1.1 million people in the world, and the size of this population is expanding at a rate of 7% per yearaccording to the progress in medical and dialysis machine technique. GI complications are known to commonly occur in patients with renal failure. Uremia and dialysis have been found to increase the risk of lesions in the GI tract. Predominant biopsy findings included erosive gastritis, ulcerative esophagitis, esophageal candidiasis, and duodenitis/duodenal ulcerations. None of these patients were documented to be on any gastric irritant drugs.

The low incidence of esophageal candidiasis in this study is probably due to the fact that they are not routinely biopsied in our hospital. This study exposes the wide spectrum of GI pathology in patients with kidney disease. Opportunistic infections are well known in allograft recipients; however, morphological effects of drug toxicity remain underreco-gnized since these patients are not always biopsied.With the emerging reports of rather specific drug-related biopsi changes, endoscopic mucosal biopsies play unquestionable role in the management of these patients. H. pylori is a major cause of gastritis in the gjeneral population. H. pylori is a major cause of gastritis in the gjeneral population. The increase in the availability of urea, asubstrate for H. pylori metabolism, might be expected to increase the prevalence of H. pylori infection in the CKD population. The prevalence of infection decreases as dialysis periods progressed, in particularwithin the first 4 years after the start of treatment, suggestingthat hemo-dialysis treatment, but not uremia,plays a role in the lower prevalence of H. pylori infection(32-37). Renal failure patients on hemodialysis or peritoneal dialysis are prone to develop this complication due to repeated bouts of hypotension during dialysis.

**Conclusions**

In conclusion, we found that the incidence of PUD was more than 10 times higher in CKD patients than in those without CKD over a 3-year period between 2008-2010. CKD patients receiving HD, NSAID, or

clopidogrel had an increased risk of PUD, compared to CKD patients not receiving these treatments. Peptic ulcer risk might be influenced by ulcer location, HD therapy, inpatient status, and ulcerogenic medications.

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# Sachse Laser in post-trauma urethral stricture: a valid alternative before Urethroplasty.

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**Abstract**

**Introduction**: The most commonly used treatment modality for urethral strictures is the direct visual internal urethrotomy method according Sachse cold knife, but with low long-term success rate. Alternative method after failure is isurethroplasty with preputial flap or Buccal mucosa. The aim of this presentation is to report the efficacy of the Internal Urethrotomy with Holmium Laser (Sachse laser).

**Material and methods**: We report three cases of urethral stenosis after trauma which treated with Internal Urethrotomy with Holmium Laser (Sachse laser) after failure of multiple treatments with Sachse cold knife. We evaluated and compared the uroflowmetry parameters before and after Sachse laser.

**Results:** The average of uroflowmetry parameters before incision were: Q max 4.5 ml/sec, Q med 3 ml/sec. Voided Volume 323 cc, while after incision with Sachse laser were: Q max 30 ml/sec, Q med 12 ml/sec. Voided Volume 363 cc.No patients relapsed during follow-up time from 3 to 24 months.

**Conclusion:** Even though these are only a few cases, we think that Sachse laser is a valid alternative after unsuccessful Sachse cold knife and before Urethroplasty, even in patients with urethral stricture after trauma.

**Keywords:** Treatment modality, urethral strictures, alternative method

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**Introduction**

Urethral stricture is one of the most difficult urological problems to cure adequately and is known to mankind since ages as it has been documented in ancient literature of the Hindus,[1] Egyptians and Greeks.[2] Minimally invasive surgical approaches are utilized efficiently and safely in the treatment of various disorders in urological practice. However, treatment options for urethral strictures have been limited both in number and level of success, as judged by the high recurrence rates. Treatment options for urethral strictures include self-catheterization, bougie dilation, balloon dilation, cold-knife optical internal urethrotomy (OIU), laser urethrotomy methods and open reconstructive urethroplasty, which is generally reserved for cases which did not benefit from endoscopic approaches [2]. OIU, described by Sachse in 1974, is still the preferred method due to the practical and minimally invasive nature of the procedure [3]. One of the alternative approaches is the correction of the stricture using laser energy, which was first used in urology in 1984 and established as a common method in internal urethrotomy since the nineties [4].

***The aim*** of this retrospective study is to report our experience with the treatment by Holmium Laser Internal Urethrotomy (HIU) of three cases of urethral stricture after trauma multi treated before by cold-knife optical internal urethrotomy (OIU),and compare the pre- and post- operative uroflowmetry results.

**Materials and Methods**

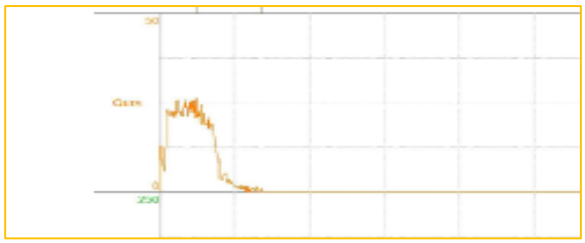
This is a retrospective study of 3 patientswhopresentedto our Clinic for urethral stricture disease after trauma multi treated before by cold-knife optical internal urethrotomy (OIU), between 2013 - 2016.
We extracted data from medical records and our Medarchiver system on uroflowmetry and cystoscopyfindings, including the site and length of stricture, number of previous urethrotomies or other surgeries for the treatment of urethral stenosis.
All patients with symptoms or signs suggestive of urethral stricture underwent auroflowmetry (UFM) and cystourethroscopyto confirm the diagnosis and determine urethral stricture length.
One urologist performed the urethrotomies using a single incision at the 12 o'clock position or using a modified procedure including multiple radial incisions at the 3, 9,
and 12 o'clock positions; the incisions were made with a cold knife and laser.
Follow-up data included subjective and objective results as Uroflowmetry parametersand whether subsequent intervention was needed. All patients underwent a uroflowmetry after 3, 6, and 12 months from surgery.
Symptoms of recurrence included decreased force of the urine stream, feelings of incomplete bladder emptying, or recurrent urinary tract infections.
Signs of recurrence were a significant
increase in postvoid residual urine on bladder ultrasound or bladder scan, decreased urine flow rate (<15 mL/second), or stricture as determined by diagnostic cystoscopy or retrograde urethrogram.
Absence of symptoms or signs of recurrent stricture in any patient at last follow-up defined
the success of the procedure. The end point of the follow-up was the last visit that showed failure of treatment or being recurrence-free for minimum 24 months.

**Results and Discussion**

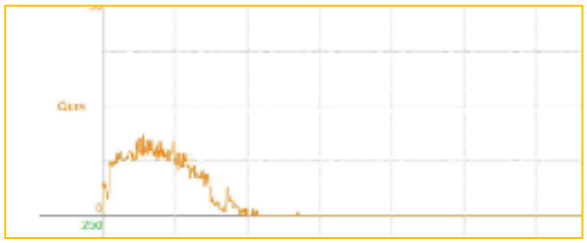
The mean age was 48 years (range: 44-53). Three male patients with urethral stricture disease after trauma were treated from 2013-2016.

***Patient 1***: 53 years old, after a car incident and urethral rupture he had a termino-terminal anastomosis of the bulbar urethra. For urethral stenosis after surgery, he underwent a Cold knife sachse incision in another hospital which failed and 6 months after it presented at our hospital in urinary retention.

We decided to do a Holmium Laser Internal Urethrotomy (HIU).



*UFM after 1 month from the Incision: Q max 24 ml/sec, Q med 13 ml/sec. Voided Volume175 c*



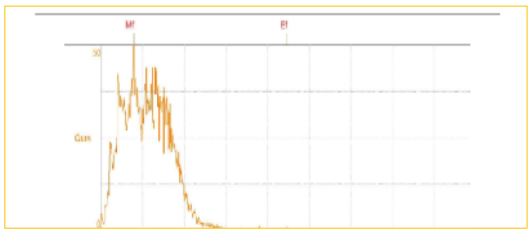
*UFM after 6 months from the Incision: Q max 14 ml/sec, Q med 9 ml/sec. Voided Volume180 c*

***Patient 2***: 44 years old, after a car incident and bulbar urethral stenosis he had 3 cold-knife optical internal urethrotomy (OIU) in three different European Centers (Spain, Italy, France) from September 2014 to September 2015. He presented to us with LUTS, sensation of non-emptying his bladder after micturition, reduction of the urinary stream. We performed a uroflowmetry and this is the result before surgery.



*UFM before Incision Q max 2 ml/sec, Q med 1 ml/sec. Voided Vol 233 cc.*

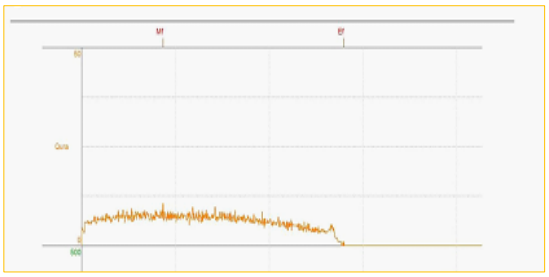
After a Holmium Laser Internal Urethrotomy (HIU) of a pre sfinteric annular stenosis of 3 mm long this is the result of the uroflowmetry.



*UFM after 3 months from the Incision: Q max 38 ml/sec, Q med 19 ml/sec. Voided Vol 550 cc.*

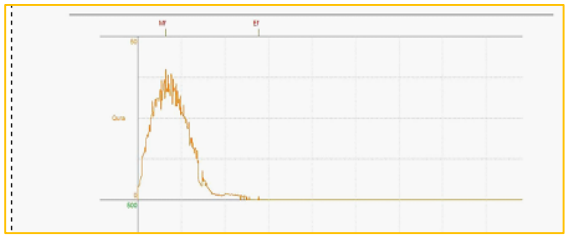
We don't have any other information of thi;s patient after three months.

***Patient 3***: 48 years old, 5 years before he underwent different urethral dilatation for urethral stenosis. He presented to us with LUTS, sensation of non-emptying his bladder after micturition, reduction of the urinary stream. We performed a uroflowmetry and this is the result before surgery.

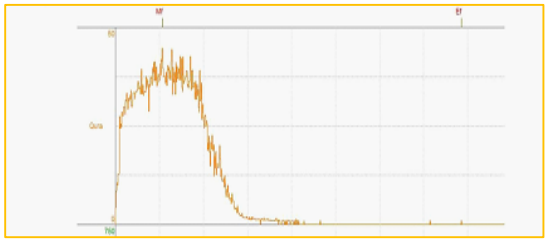


*UFM before Incision Q max 7 ml/sec, Q med 5 ml/sec. Voided Vol 422 cc.*

Theurethrocystoscopy evidenced multiple stenosis of the penile urethra from two cm from the external meatus until the internal sphincter where we performed a Holmium Laser Internal Urethrotomy (HIU). These are the results of uroflowmetry after the surgery.



*UFM after 1 month from the removal of the catheter: Q max 35 ml/sec, Q med 13 ml/sec. Voided Volume 311 cc*



*UFM after 1 year from the Incision: Q max 40 ml/sec, Q med 17 ml/sec. Voided Vol 600 cc*

In our results the average of uroflowmetry parameters before incision were: Q max 4.5 ml/sec, Q med 3 ml/sec. Voided Volume 323 cc, while after incision with Sachse laser were: Q max 30 ml/sec, Q med 12 ml/sec. Voided Volume 363 cc.No patients relapsed during follow-up time from 3 to 24 months.

Urethral strictures are often treated withurethrotomy, most commonly direct visual internal urethrotomy [5]. With the introduction of lasers, holmium laserurethrotomy was subsequently used in many centers withequal recurrence outcomes as achieved with VIU [6, 7, 10, 11].

Many urologists prefer VIU over urethral reconstructionbecause of its ease to perform, low cost, short hospital stay,and perceived low complication rate. They may opt to repeatVIU several times to avoid complex urethral reconstruction,which requires significant surgical experience. This trend
continues despite the moderate success rate reported inthe selected patients.

Several studies have examined the cost-effectiveness ofmanaging anterior urethral strictures. Urethroplasty as theprimary therapy was cost-effective only when the expectedsuccess rate of the first VIU was less than 35% [8], whereasVIU became more favorable when the long-term risk of stricture recurrence was less than 60% [9]. If a repeaturethrotomy is required, open urethroplasty is the treatmentof choice for recurrent urethral stricture

**Conclusions**

Both, cold knife and holmium laser, have been effective in providing immediate relief to patients with urethral strictures. Holmium laser is technically more demanding than cold knife for internal urethrotomy. The complications of both modalities

are low and easily manageable. Lack of a significant difference between recurrence rates and complication rates of HIU and OIU suggests that both are safe and effective treatment methods in urethral strictures.

Even though we report only a few cases, we think that Sachse laser is a valid alternative after unsuccessful Sachse cold knife and before Urethroplasty, even in patients with urethral stricture after trauma. Larger studies encompassing cases with different characteristics may help to identify the variables that may favor or discourage the use of either method in future studies

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# The Diagnostic Value of C-Reactive Protein and Total Leucocytes Count in Patients with Acute Abdominal Pain In Children

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**Abstract**

**Background:** C-reactive protein (CRP) is one of the acute-phase proteins which increases during inflammatory conditions. Nowadays, C-reactive protein (CRP) is a commonly used biomarker especially in emergency department (ED) for diagnostics of febrile and infectious patients. It is almost impossible to distinguish the bacterial from nonbacterial (viral) infection by CRP level only - so the detailed history of onset of disease is very important to establish the diagnosis of bacterial infection as a cause of acute abdominal pain.
**Objective:** The aim of this study was to establish the diagnostic value of leucocyte and CRP count in in diagnosing acute abdominal pain.
**Material and methods:** We retrospectively evaluated 159 patients with acute abdominal pain admitted to the surgical department of the Clinical Hospital of Tetova and PHO "Alba – Med" over a period of 2 years respectively from January 20016 to January 2018. All patients included in this study was aged between five to 15 years old.
**Results:** During the study period there were 158 patients (96 were females and 56 males). All the patients suffered from acute abdominal pain, whereas 45 of them had a surgical condition, respectively in 42 of them acute appendicitis as a cause of pain, Meckel's diverticulitis, jejunal intussusception and ruptured ovarian cyst in three other patients. In 105 patients nonsurgical condition was the reason of acute abdominal pain. CRP was performed within 24 h after admission in all the patients. In the group of patients with surgical disease in 41 of them (91 %) the value of CRP was more than > 5g/L.
**Conclusions:** According to our experience we conclude that the CRP level is not sufficient to predict patients with acute abdominal pain that require surgical treatment.
**Key words:** CRP, acute abdominal pain, surgery

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**Introduction**

C-reactive protein (CRP) represents one of the acute-phase proteins (APPs), which serum level changes rapidly in the presence of inflammatory conditions, by at least 25%[6,]. C reactive protein (CRP) was discovered in 1930 whereas this name received because reacts with the C-polysaccharide of the pneumococcus bacteria in the acute phase of pneumococcal pneumonia[1,4]. CRP can be useful to screen many inflammatory conditions but without the possibility to distinguish accurately the etiology of the inflammation process because increased values of CRP are registered not only in infectious diseases, but also in the presence of systemic inflammation caused by rheumatoid arthritis, myocardial infarction, necrotising soft tissue infections, multiple trauma, neoplastic processes , pancreatitis etc., This is why it is not recommend to use CRP to differentiate inflammatory conditions from infectious diseases[2.3].

CRP is predominantly synthesized by the liver and its level in the blood starts to rise four to six hours after the inflammation and it duplicates every eight hours, while the maximum value is registered within 36 to 50 hours.

The plasma half-life of CRP is about 19 hours whereas it may take several days to return to the baseline level[20]

Due to its long half-life in the serum, CRP may remain high during recovery phase, but if reduction of CRP is not registered 72 hours after treatment a re-evaluation of the course of the disease is recommended [16,17].

Leucocyte count still remains the most frequently used laboratory test in diagnosing acute abdominal pain. The range of sensitivity and specificity of WBC for the diagnosis of acute abdomen in several clinical studies have been reported to be between 67% and 97.8%[7], whereas in this context neutrophil count has been detected as a superior diagnostic marker for differential diagnosis of acute abdomen. In most studies it is estimated that a neutrophil ratio above 85% is a safe sign of advanced acute appendicitis[9, 11 .]

The aim of this study was to evaluate the diagnostic value of leucocyte and CRP count in in diagnosing acute abdominal pain.

**Materials and methods**

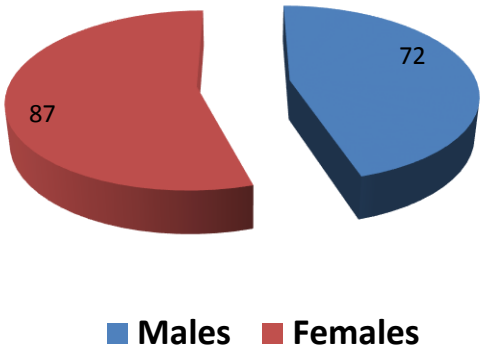
All patients admitted in our clinic with a clinical sign of acute abdominal pain between January 2015 - 2018 were studied retrospectively. After admission the diagnosis of patients with acute abdominal pain was established by medical history, physical examination, CRP level, white blood cell (WBC) count and sometimes imaging tests such as plain abdominal radiography, ultrasonography and abdominal CT scan.

According to the results of physical examination, laboratory results as well as ultrasonography and abdominal computed tomography examination, patients were divided into two groups.

The first group included the patients with non-surgical conditions, whereas the second group all the patients with surgical diseases (in total 45 patients).

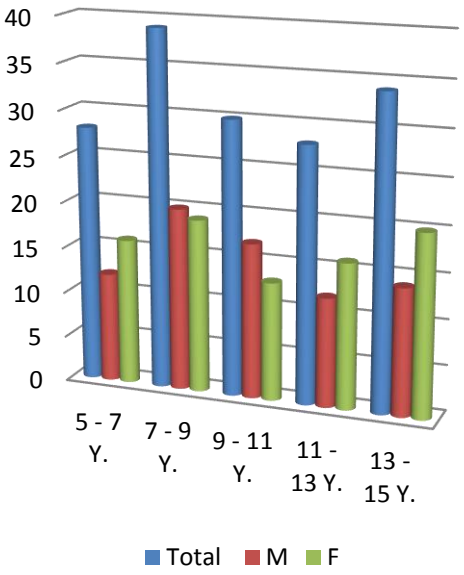
**Results**

During the study period there were 159 patients (72 of them were males and 87 females) *(Diagram 1).*




*Graph 1*

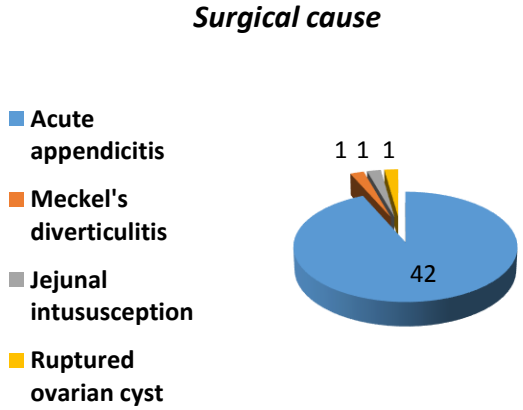
The mean age of children included in this study was 10.01 years, ranging from
five to fifteen years (*Diagram 2).*




*Graph 2*

All the patients included in this study complained for acute abdominal pain. After careful examination and clinical evaluation it was noticed that in 47 patients a surgical condition was the cause of acute abdominal pain, whereas in 108 children a non-surgical disease was the reason of complaint. Anamnestic data revealed that in children with surgical conditions the pain usually begins in the periumbilical region and then was localized in the RLQ region, whereas during examination all the patients had a rebound tenderness in the right iliac fossa. In the group of patients with non-surgical disease pain started mainly in the epigastrium or around umbilicus and then scattered across the abdominal cavity.

The most common cause of acute pain in the group of children with surgical disease was been acute appendicitis – in 42 of them, whereas Meckel's diverticulitis, jejunal intussusception and ruptured ovarian cyst was a cause of acute abdominal pain in the remaining three patients.




*Graph 3*

In the group of children with non-surgical abdominal pain, mesenteric lymphadenitis, dyspepsia, acute gastroenteritis and pelvic inflammatory disease was the most common cause of pain.

In all the patients after admission blood samples were obtained and CRP level and WBC were determined. In the group of patients with surgical disease the level of CRP more than 5 g/L was

registered in 33 patients or 73 %, whereas in a group with non-surgical conditions the level of CRP > 5 g/L was registered in 75 children or 65 %. Repeated measurements of CRP were performed in all patients with surgical condition and in 33 of them CRP was steadily high, whereas in twelve others was registered a decrease in CRP level.

WBC count was also performed in all patients and moderate leukocytosis ≤ 15.000/mm3 was registered in 39 patients (86 %) with surgical conditions and in 81 children (70 %) with non-surgical diseases.
Abdominal plain radiography was performed in 59 patients included in our study, 18 of which was been with surgical diseases whereas 41 with non-surgical conditions. Our assessment was that plain radiography does not show a high sensitivity or specificity for the diagnosis of acute appendicitis and should not be ordered in this group of patients, but my be of particular importance in differential diagnosis of the acute abdominal pain.

Abdominal CT has been shown to have a greater sensitivity and accuracy not only for the diagnosis of acute appendicitis but also for the diagnosis of other causes of acute abdominal pain. We have performed totally 39 abdominal CT in patients of this study, 11 of which were from the first group and 28 from the second.
According to our experience it seems that ultrasound examination has a great sensitivity and accuracy rate for acute appendicitis and intussusception.

**Discusion**

Despite the recent advances in the diagnostic modalities the diagnosis of acute abdomen still remains a challenge in pediatric practice. For this reason, different diagnostic techniques such as abdominal ultrasound, CT scanning, and laboratory examinations have been used to improve the diagnostic accuracy.
Recently one of the most used biomarker in the emergency department to facilitate the diagnosis of acute abdomen is the C-reactive protein (CRP)[6,8,12]. Prospective studies showed that this marker may be useful not only in establishing the diagnosis of acute appendicitis, but also plays a diagnostic role in acute abdominal pain[16,17,18,19]. Another parameter that helps to determine the etiology of acute abdominal pain is also white blood cell count (WBC)[24,5]. It is estimated that C-reactive protein and WBC count can be helpful in the diagnosis of acute abdomen[9,10,11].

In many studies conducted over the last years it is estimated the diagnostic value of CRP in acute abdominal pain and most of them have concluded that CRP alone is not useful in differentiating between surgical and non-surgical causes of acute abdomen[13,14,15]. Other studies emphasize the role of white cell count and C-reactive proteins in the diagnosis of acute appendicitis and they report a high sensitivity and specificity of these parameters in the diagnosis of acute abdominal pain[21,22].
Our study shows that the specificity of CRP to diagnose the cause of acute abdominal pain was very low, but combination of WBC count and C-reactive proteins give a more valuable information for the diagnosis of acute appendicitis during acute abdominal pain[5,7]. It is estimated that patients with high value of CRP and WBC are highly suspected to have acute appendicitis and should be followed carefully until the decision on surgical intervention is undertaken.

Many authors as Anderson et al.[13] studied the value of CRP and WBC count in patients suspected for

acute appendicitis and found that a normal value of this parameters should be a good indication to postpone the operation.

Other authors like Chi *et al*.[12] studied the role of CRP in patients with acute abdominal pain and concluded that CRP was helpful in decision making in patients with an acute abdomen.

Ultrasonography and computed tomography (CT) helps in setting up a diagnosis in patients with abdominal pain, considering that CT is likely more accurate than ultrasonography[26]. However according to the experience of many clinicians of the emergency department, ultrasonography is most useful in diagnosing of some group of the diseases such as PID, renal colic, advanced periappendicular inflammation etc[29]. Concerning CT it is recommended if excessive bowel gas precludes ultrasonography examination, or in the case of diseases of small and large intestine[28,30].

**Conclusion:** Increased level of CRP concentration is not sufficient to differentiate between surgical and non-surgical diseases in patients with acute abdominal pain, while the combination of CRP and WBC count provides safer data about the etiology of acute abdominal pain. However, CRP level and WBC count should be used only in adjunctions with clinical data and if possible with ECHO examination or abdominal CT-scan.

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# Identifying and Treating Ascending Cholangitis: A case report and review of literature.

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***Abstract***

Acute cholangitis is an infection of the biliary system that typically results from obstruction. Common causes include choledocholithiasis, strictures, foreign bodies (such as biliary stents) parasitic worms (e.g. ascarids) and compression from an external structure. Obstruction allows for higher bacterial concentrations and bacterial proliferation. With biliary stasis and increases in intraductal pressure, bacteria migrate into the venous and lymphatic systems with subsequent bacteremia. The rate of gallstone development is 3-4 % annually in those >60 years old with up to a 15% overall prevalence in the US. In the US, 85% of ascending cholangitis cases are a consequence of choledocholithiasis. The gram-negative bacteria E coli, Klebsiella, Pseudomonas and Enterobacter are the most commonly identified pathogens. Anaerobes are less common.

Ascending cholangitis is classically diagnosed by the presence of Charcot's triad – fever, right upper quadrant pain and jaundice. Though very specific, the presence of Charcot's triad is only 26% sensitive and thus its absence does not rule out the diagnosis. All patients with suspected ascending cholangitis should undergo appropriate fluid resuscitation, be given broad spectrum antibiotics to cover the likely enteric pathogens, and closely monitored for worsening in their clinical condition.

Once initial assessment is complete and resuscitative efforts begun, imaging is often helpful in confirming the diagnosis of ascending cholangitis. After the diagnosis has been confirmed, ERCP and biliary drainage is indicated.

***Keywords***: Ascending cholangitis, treatment, diagnosis

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***Introduction***

Case Example/; A 48-year-old man with one prior episode of gallstone pancreatitis and subsequent cholecystectomy presented to a community hospital Emergency Room complaining of one day of progressive epigastric pain with bilious, non-bloody vomiting. The pain was non-radiating and not associated with fevers or obvious jaundice. Initially his heart rate was in the 80s and blood pressure 120s/80s. His WBCs on admission were 7300/uL, his total bilirubin was 2.3 mg/dL, AST/ALT were 516/388 U/L, GGT 335 U/L and his alkaline phosphatase was 130 U/L. His lipase was normal at 49 U/L. CT abdomen/pelvis with contrast was performed and the initial review suggested possible, though not obvious, biliary pathology. He was admitted for observation.

Though our patient had a relatively benign initial presentation, he developed a fever to 101.9 degrees Fahrenheit on his first day of admission. A repeat review of his CT scan at our facility suggested a 4 mm filling defect in the common bile duct suspicious for CBD stone. Piperacillin-tazobactam and IV fluids were given and the patient quickly defervesced though his bilirubin increased to 4.3 mg/dL.

In cases such as this, it is important to rapidly determine (1) if the patient has ascending cholangitis and (2) how quickly intervention is required. In the article below, the authors discuss the approach to suspected ascending cholangitis including special situations including anticoagulation and pregnancy.

***Epidemiology***

Acute cholangitis is an infection of the biliary system that typically results from obstruction. Common causes include choledocholithiasis, strictures, foreign bodies (such as biliary stents) parasitic worms (e.g. ascarids) and compression from an external structure. Obstruction leads to increased pressure in the biliary tree and biliary stasis with subsequent malfunction of normal biliary defenses and increase in bacterial concentration. In health, there is typically minimal migration of duodenal bacteria past the ampulla in a patient with no prior biliary intervention. Bacteria which do migrate upstream are generally flushed back out via normal bile flow. Obstruction allows for higher bacterial concentrations and bacterial proliferation. With biliary stasis and increases in intraductalpressure, bacteria migrate into the venous and lymphatic systems with subsequent bacteremia [1]. Since normal flow of bile moves bacteria out of the biliary system to prevent infection, restoring a normal flow of bile is the cornerstoneof treatment.

The rate of gallstone development is 3-4 % annually in those >60 years old with up to a 15% overall prevalence in the US. Multiparity, female gender, obesity, and certain ethnic backgrounds also predispose to cholelithiasis. Seventy-five percent of female Pima Indians, for example, have gallstonesas adults [2]. Migration of gallstones distally in the common bile duct may lead to ductal obstruction and cholangitis. In the US, 85% of ascending cholangitis cases are a consequence of choledocholithiasis [3]. Additional risk factors include primary sclerosing cholangitis, biliary stricture, and recurrent pyogenic cholangiopathy. Patients with prior biliary intervention such as biliary stent placement are at increased risk for cholangitis due tobiofilm formation and eventual stent obstruction [4]. Of patients admitted with gallstone disease, up to 9% are for acute (ascending) cholangitis. The gram-negative bacteria *E coli*,*Klebsiella*, *Pseudomonas*,and *Enterobacter* are

the most commonly identified pathogens. Anaerobes are less common.

***Diagnosis of Cholangitis***

Ascending cholangitis is classically diagnosed by the presence of Charcot's triad – fever, right upper quadrant pain and jaundice. Though very specific, the presence of Charcot's triad is only 26% sensitive and thus its absence does not rule out the diagnosis [5]. A high percentage of patients with acute cholecystitis will also present with positive Charcot's triad, meaning that it also lacks specificity. In severe cholangitis with sepsis, Reynold's pentad, which includes hypotension/shock and altered mental status in addition to the triad, is found in fewer than 7% of patients [6]. While it is vital to consider and exclude ascending cholangitis in such cases, it is also important to remember that a number of other conditions may lead to RUQ and jaundice, and that some of these conditions may be associated with fever as well. (table1)

| |
|---|
| Ascending cholangitis |
| Choledocolithiasis |
| Acute Cholecystitis |
| Mirrizzi's syndrome |
| Lemmel's syndrome |
| Biliary Strictures/Secondary cholangitis |
| Primary Sclerosing cholangitis |
| Chronic Pancreatitis |
| Choledochal cyst |
| Autoimmune/IgG4-related cholangitis |
| Duodenal, ampullary, biliary or pancreatic malignancy |
| Viral hepatitis |

*Table 1: Causes of right upper quadrant pain and jaundice.*

A more clinically applicable tool for diagnosis may be the Tokyo guidelines [5]. These guidelines divide cases into suspected or definite based on three categories of criteria: systemic symptoms, laboratory results, and imaging findings. (Table 2) For suspected disease, one must have systemic symptoms as well as suggestive imaging or lab findings. Definitive diagnosis calls for systemic symptoms and both suggestive imaging and lab findings.

It is important to remember that in acute cholecystitis, a leukocytosis and mild bilirubinemia may be present, though bilirubin greater than 4 mg/dL suggests common bile duct obstruction [7].A common bile duct measuring greater than 6 mm also suggest a mechanical biliary obstruction, though prior cholecystectomy may enlarge the common bile duct, creating a diagnostic dilemma. Acute viral hepatitis may also present with jaundice and RUQ pain, though significant elevations in WBCs and CRP are rare[4]. In such cases, imaging of the biliary system should be normal. Acute viral hepatitis serologies should be performed when transaminase elevation is present and there is no obvious biliary pathology.

| | | |
|---|---|---|
| *A* | **Fever or chills** | **SIRS** |
| *B* | Direct hyperbilirubinemia | Elevated aminotransferases (> 1.5 ULN) |
| *C* | Biliary ductal dilation | Definitive etiology seen (e.g. biliary stone) |

*Table 2: Tokyo diagnostic criteria for ascending cholangitis. ULN= upper limits of normal.*
***SIRS**: Systemic Inflamatory Response Syndrome; A: Systemic symptoms; B: Lab. findings; C: Imaging findings*

**Management**

Initial steps should include a rapid assessment of clinical severity including vital signs as well as mental status. Basic laboratory evaluation is performed to assess for end organ dysfunction and to confirm etiology. These labs should include complete blood count, complete metabolic panel, and INR/PT. In those who are febrile, blood cultures should be performed prior to the initiation of antibiotics. In patients with SIRS or evidence of end organ dysfunction, admission to an intensive care unit is recommended.

All patients with suspected ascending cholangitis should undergo appropriate fluid resuscitation, be given broad spectrum antibiotics to cover the likely enteric pathogens, and closely monitored for worsening in their clinical condition.
Risk stratification is imperative to determine the timing of interventions to decompress the biliary system such as ERCP or percutaneous drainage. The Revised Tokyo guidelines provide a three-tiered grading system for this purpose (table 3).

| | |
|---|---|
| **Grade III: severe** | **Cholangitis with dysfunction in *at least one organ or system*:**<br>**1. Cardiovascular dysfunction: hypotension requiring pressor support**<br>**2. Neurological dysfunction: altered mental status**<br>**3. Respiratory dysfunction: $PaO_2/FiO_2$ ratio <300**<br>**4. Renal dysfunction: oliguria, serum creatinine >2.0 mg/dl**<br>**5. Hepatic dysfunction: INR >1.5**<br>**6. Hematological dysfunction: platelets <100,000/mm³** |
| **Grade II: moderate** | Cholangitis *with any two* of the following:<br>1. Abnormal WBC count (>12,000/mm³ or <4,000/mm³)<br>2. High fever (≥39°C)<br>3. Age (≥75 years old)<br>4. Hyperbilirubinemia (total bilirubin ≥5 mg/dl)<br>5. Hypoalbuminemia (< 0.7 x lower limit of normal) |
| **Grade I: mild** | Cholangitis that does not meet criteria for moderate or severe disease |

*Table 3: Revised Tokyo criteria for determining the severity of cholangitis.*

Patients with severe disease should receive ERCP as soon as they are medically stabilized. All others can receive the procedure safely within 24 hours, though the exact timing is not certain [5].

Once initial assessment is complete and resuscitative efforts begun, imaging is often helpful in confirming the diagnosis of ascending cholangitis.

Right upper quadrantultrasound (RUQUS)is often the first imaging study performed given its ease of access,low cost, and lack of radiation exposure. Biliary dilation on RUQUS is often seen, but its absence does not rule out cholangitis. In those in whom the diagnosis remains in doubt after RUQ US, MRCP is the best cross-sectional imaging modality to define a definitive etiology given its high-resolution reconstruction of the biliary tree without contrast or radiation exposure. CT scan may also be used in those who are not candidates for MRCP or where MRCP is not readily available, though it has less sensitivity for choledocholiths which is the most common etiology. While ERCP is highly accurate as a diagnostic test, its higher risk profile makes is most appropriate as a therapeutic rather than a diagnostic tool.

Once the diagnosis has been confirmed, ERCP and biliary drainage is indicated. The timing of endoscopy depends on the severity as illness as discussed above. In those with category III(severe) disease, biliary drainage should be performed as soon as the patient has been stabilized. For those in the moderate and mild categories, the timing is less clear. The Tokyo guidelines suggest that the lowest severity patients can safely receive biliary drainage in 24 hours [8]. This is largely based on expert opinion as well as a study by Chak and colleagues which showed that delay beyond 24 hours was associated with worse outcomes [9]. This study, however, did not stratify subjects by severity and so it is possible that the results were confounded by a higher number of severely ill patients. Recent studies indicate that the safe window of ERCP may in fact be longer. Khashab and colleagues retrospectively examined 90 patients with ascending cholangitis treated with ERCP and drainage. They found that after 72 hours both total costs as well as the composite endpoint of death, persistent organ failure, and ICU days were higher [10]. Hou, et al. performed a somewhat larger study looking at the impact of ERCP timing on outcome in 199 patients. While no difference in mortality was found, delays of greater than 48 hours led to a disproportionate increase in length of stay and that at greater than 72 hours patients had more hypotension requiring vasopressor support [11]. One reason for delay in ERCP in some centers is the impression that cases done on the weekends may have worse outcomes than those done during the work week, presumably due to less experienced teams performing these procedures. Tabibian, et al. retrospectively examined this possibility, comparing outcomes in 181consecutive ERCP at the Mayo Clinic [12] There were no differences in any of the examined outcomes in ERCPs performed on the weekend versus weekdays. While highly quality prospective studies on the matter would be welcome, it appears that ERCP is equally safe and effective on the weekend, and that most ERCP for biliary decompression in mild to moderate cases should be done within 48 hours and certainly no later than 72 hours after admission. Of course, careful observation to detect clinical deterioration warranting earlier intervention is critical.

Given that ERCP can be delayed 24-48 hours in non-severe cases responding to medical therapy, some consideration should be given to transferring patients to a center that performs a high volume of ERCP. When patients receive ERCP by endoscopists and at centers with high volume of ERCP, the likelihood of success increases and the likelihood of adverse events decreases significantly [13]. This principle must be balanced with the patients' wishes, clinical stability and regional availability of ERCP.

**Special Situations:**

While ERCP with stent placement is a low-risk for bleeding complications per ASGE guidelines [14], sphincterotomy is high risk and the endoscopists must take caution in patients currently receiving anticoagulation or dual antiplatelet therapy. Bleeding occurs in up to 2% of sphincterotomies and the risk increases with anticoagulation, antiplatelet agents or acute inflammation [15]. For an elective high-risk procedure, warfarin would be stopped five days prior and the novel anticoagulants stopped at least 2 days prior depending upon creatinine clearance [14]. Aspirin can be continued peri-procedurally, though clopidogrel should be discontinued at least 7 days prior to sphincterotomy. Clearly, one does not have the luxury of such time in cases of acute cholangitis.

As such, the endoscopist has two choices – to reverse the effects of the anticoagulants/antiplatelet agents or to avoid or minimize the size of sphincterotomy. The precise manner of reversing these agents is beyond the scope of this article and the reader is directed to several excellent articles on the topic. (16) If a patient is in need of biliary drainage and the risk of reversal is deemed unacceptably high, one may avoid a sphincterotomy and a place a 7-french plastic biliary stent. This stent is of sufficient size to effect adequate drainage in most cases, but small enough to be easily passed through an intact sphincter of Oddi. There is some data that avoiding sphincterotomy may decrease the risk of post-ERCP pancreatitis (PEP) as well [17]. If the endoscopist desires to remove a choledocholith at the same setting, this generally cannot be done via an intact papilla. Options in this case include making a small (2-3mm) sphincterotomy and performing a papillary balloon dilation. This is associated with fewer bleeding complications and the limited eliminates the increase risk of PEP induced by balloon dilation in western population[18]. If stone extraction is incomplete or not performed, follow up ERCP may be accomplished after clinical recovery from cholangitis, typically in 3-4 weeks.

Pregnancy is a unique clinical situation where risks to the unborn child must be weighed against the benefits of treatment. Pregnancy itself increases the risk for biliary stones [19]. Up to 10% of women post-partum have evidence of new cholelithiasis, though only 1% of those will develop symptoms. Pregnancy is also a risk factor for post-ERCP pancreatitis, occurring in 12-16% of patients; prophylaxis with indomethacin is restricted as this can be teratogenic. In addition, MRCP is contra-indicated in the first trimester. Sedation, radiation, and the procedural risk of pancreatitis involved with ERCP can pose harm to both mother and child. Acute cholangitis, however, poses a higher risk to the patients and ERCP is therefore indicated even in pregnancy.(20)

According to the American College of Obstetricians and Gynecologists, radiation exposure of less than 50 mGy has not been shown to be harmful to a fetus, and ERCP exposes a fetus to less than 6 mGy, though 'as low as reasonably achievable' should be the goal. If surface ultrasound fails to confirm biliary stones, EUS could be used provided the benefits were found to outweigh the risks of sedation. If there is strong clinical suspicion for cholangitis, ERCP can be attempted without fluoroscopy and several different approaches have been described. Wire placement can be confirmed, aspiration of bile through the sphincterotomy or balloon, or in rare instances, via cholangioscopy. Once successful biliary cannulation has been confirmed, a plastic biliary stent can be placed that

will allow for appropriate bile drainage. Alternatively, a sphincterotomy could be performed. Either of these options may result in spontaneous extraction of biliary stones; if stones remain, as long as biliary drainage occurs, removal can be attempted after delivery if late enough in pregnancy.

Sedation to the mother does pose risk to the child, and thus the ASGE recommends an Obstetrics consult prior to any procedure as well as the use of an anesthesiology providerfor the procedure itself [20]. There are currently no available medications that are class A, though meperidine and propofol areclassB; fentanyl and midazolam have not been shown to be teratogenic in humans at usual doses but are not preferred.

If ERCP is unsuccessful or unavailable, biliary drainage must be accomplished by other means. An interventional radiologist can perform percutaneous trans-hepatic biliary drainage under ultrasound guidance [5]. This is most likely to be successful when there is significant biliary dilation for the radiologist to target. A percutaneous drain placed this way can be temporizing until definitive removal of the obstruction can take place when the patient is more stable. Another option is the so-called rendezvous procedure where the interventional radiologist advances a percutaneously placed guidewire trans-hepatically into the duodenum [21]. The endoscopist then retrieves the wire and performs the remainder of the ERCP in standard fashion.

In patients with surgical altered anatomy such as those post-roux-en-Y gastric bypass or pancreaticoduodenectomy (Whipple procedure), endoscopic access to the bile duct can be more challenging. Options in these cases include balloon-assisted enteroscopy, ERCP via surgically placed gastrostomy, EUS guided biliary access, and IR-directed transhepatic drainage [22]. Selection will be based on local expertise. If none of the aforementioned options were successful, surgical biliary drainage may be performed, though this is a much more morbid procedure, especially in a patient with severe cholangitis.

**Prognosis and follow up**

Prior to ERCP, mortality from severe cholangitis was nearly 50% [23], though modern data suggests mortality ranges from 3 - 11% [24,25] with much of it coming from severe cases. If a plastic stent is placed, this needs to be removed within 8 weeks of placement as there is a high rate of stent occlusion if they are left in place longer with more narrow stents more likely to occlude [26]. In patients with an intact gallbladder in whom choledocholithiasis was the etiology of the cholangitis, cholecystectomy is recommended due to a significantly increased morbidity, often due to recurrent cholangitis, when surgery is foregone [27]. Due to the associated inflammation, most surgeons prefer a reasonable interval between the episode and subsequent cholecystectomy. Li and colleagues compared patients undergoing surgery within 6 weeks of AC to those with a longer delay. Surgical delay was associated with significantly more intraoperative (28.8% vs 9.4%) and postoperative (42.5% vs 15.6%) complications [28]. In those with cholangitis due to biliary strictures, ascertaining the etiology of the stricture through directed sampling by brushing, biopsies, and or EUS/FNA is critical, though this is often best performed after the resolution of the acute episode.

**Case Example Conclusion**

ERCP was performed on hospital day 2 and revealed an 8 mm stone in the distal common bile duct. A sphincterotomy was performed and a brown and black pigment stone was removed – likely a retained stone left in place during his cholecystectomy. Balloon sweep did not reveal any additional stones. PCR testing detected *Enterobacteriaceae* and *Escherichia coli* in his blood, though standard blood cultures were negative, and the patient recovered uneventfully on a two-week course of oral ciprofloxacin

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# Sebaceous carcinoma in situ as a diagnostic entity. Case report and review of the literature.

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**Abstract**

**Background:** The concept of carcinoma in situ was first introduced by Broders in 1932 [1] and has been accepted as a well-established notion and diagnostic category in many organs and systems. However, sebaceous carcinoma in situ (SCIS) has not yet been recognized as a concept and diagnostic entity in general pathology or dermatopathology. Such lesions have been commonly misinterpreted as either a benign neoplasm or sebaceous carcinoma. Tumors that do not necessarily arise in pre-existing sebaceous glands are usually invasive at the time of diagnosis, and like their ocular counterparts, can exhibit pagetoid intraepidermal spread. Cases of purely in-situ extraocular sebaceous carcinoma are extremely rare and yet controversial until now.
Recognizing sebaceous carcinoma in situ as a valid concept and diagnostic entity that will certainly help to avoid misinterpretation and subsequently under or over treatment of such lesions.
In this article, we provide a case report presentation with histopathological examination and a critical review of the literature.
**Keywords**: SCIS, sebaceous adenoma, sebaceous carcinoma, extraocular sebaceous carcinoma in situ, histopathology diagnosis.

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**Introduction**

The benign "tumor-like" enlargements of the sebaceous glands have a histologic appearance which may not differ appreciably from that of the normal gland. There is no clear histologic distinction between the so-called adenoma of sebaceous gland and the hyperplastic and hypertrophic glands. The abnormality is chiefly one of increase in size, number and location of the glands with minor aberrations such as absence or atrophy of basal cells, variations in the tendency for the central cells to degenerate or absence of ducts.

Regarding the origin of sebaceous neoplasms, Kazakov et al. stated that "whereas in periorbital sebaceous lesions, it is accepted that sebaceous lesions arise from Meibomian glands and glands of Zeis, sebaceous glands elsewhere in the skin practically never appear to give rise to a sebaceous carcinoma". Sebaceous skin tumors can be sporadic or syndromic, as seen in association with Muir-Torre syndrome (MTS).

Circumscribed lesions have been described according to their clinical characteristics:

(a) those occurring in old age, (b) congenital lesions or appearing during puberty and (c) lesions associated with other cutaneous and visceral pathologies forming the syndrome of Pringle's disease.

From the first classification of neoplasms with sebaceous differentiation proposed by Warren and Warvi in 1943 [2], to the one by Rulon and Helwig in 1974 [3], Lever in 1949 and 1989 [4, 5], Elder et al in 1997 and 2005 [6, 7], Prioleau and Santa Cruz in 1984 [8], Troy and Ackerman in 1984 [9] and Steffen and Ackerman 1994 [10], Mehregan and Hashimoto in 1991 and 1995 [11,12] and Burgdorf in 1990 [13], Farmer and Hood in 2000 [18], McKee in 1996 and 2012 [14,15], and Weedon in editions from 2002 to 2017 [19–22] The diagnostic entity of "sebaceous carcinoma in situ" was never mentioned in their classifications.

Classification of sebaceous neoplasms up to date has been made into three categories:

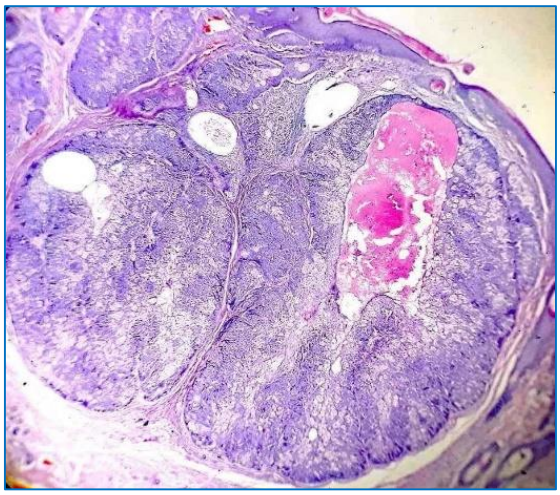
- Sebaceoma (a benign neoplasm with well-defined architecture and no atypia),
- Borderline sebaceous neoplasm (low-grade SC tumor with well-defined architecture and nuclear atypia)
- Sebaceous Carcinoma (a malignant tumor with invasive growth and evident nuclear atypia).

**Case presentation**

A 56-year-old male presented with a history of a rapidly-growing lesion in the lateral aspect of his nose. Upon examimation, the dermatologist noted another lesion in his mental region showing an elevated yellowish, exophytic nodule measuring 0.9 cm in greatest diameter. The surgeon decided to remove the mental lesion too (Figure 1).




***Figure 1.*** *The marked lesion is the main complaint that brought the patient to the dermatologist. A second lesion is noted on the right aspect of the mental area, which according to the patient, is an old lesion that has been slowly growing over the past years.*



**Microscopic examination**

***Figure 2. H&E stain on low magnification reveals:***

*Lobular pattern neoplasia in the deep dermis. The lobules are composed of sebaceous cells preserving the original structure of the sebaceous glands. It is noted a peripheral population of hyperchromatic cells in all the lobules. The lobules do not demonstrate any focus of disruption of the basal membrane. Surgical margins are free of disease.*

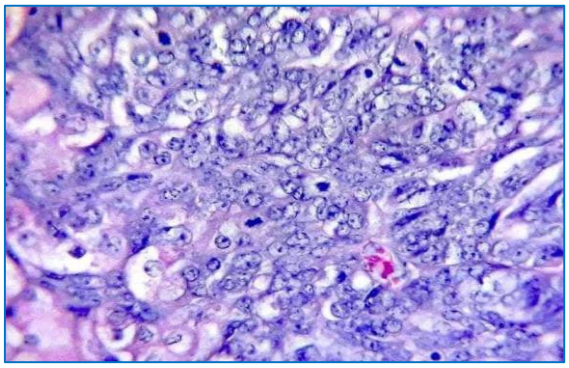


***Figure 3. H&E stain on high power reveals:***

*Increased population of atypical cells with high nuclear/cytoplasmic ratio, eosinophilic cytoplasm preserving the central granular clarification typical of sebaceous cells, enlargement of the nuclei and prominent nucleoli. The mitotic index is increased, as noted in the picture.*

**Histopathological diagnosis:**

The first lesion was diagnosed as well-differentiated invasive squamous carcinoma, keratinized type. Lateral margins and depth are free of neoplasia.

The final diagnosis of the second lesion as described in the figures 1, 2, 3 was:

**Sebaceous carcinoma in situ.** Lateral margins and depth are free of neoplasia.

**Discussion**

Like the definition for any other type of carcinoma in situ, the definition of SCIS would be a sebaceous neoplasm with these microscopic features:

1. Architectural findings such as: no invasive growth, population of neoplastic cells still confined in epithelium not extending the basal membrane (within surface epithelium, infundibular epithelium, sebaceous gland, sebaceous duct or follicular epithelium);
2. Cytological features consistent of malignancy such as: nuclear atypia, enlarged nuclei, hyperchromasia, increase of N/C ratio, increase of mitotic activity and/or presence of necrosis.

These histopathologic findings fit the exact definition of carcinoma in situ, a malignant epithelial neoplasm confined in the epithelium of origin, which was introduced by Broders in 1932. According to some authors, SCIS has a number of different histopathologic manifestations. There are three histopathologic types: flat, nodular and cystic types.

Well- and moderately-differentiated SCIS were initially called sebaceous adenoma by some authors [3, 28] and has been called this way by many authors up to this day. However, in an article published in 1998, Nussen and Ackerman revised this concept and stated that the so-called

sebaceous adenoma is not a benign neoplasm but a sebaceous carcinoma [29]. This notion was mentioned in the second edition of a book dedicated to neoplasms with sebaceous differentiation published in 2009 [26]. Although this notion has been accepted by some authors, it is not shared by many others in the field of dermatopathology. In an article published in 2010, Chen proposed a different view and asserted that the so-called sebaceous adenoma is really SCIS based on the abovementioned definition of SCIS [23].

Diversely, poorly-differentiated or high nuclear grade nodular/cystic SCIS is often misinterpreted as sebaceous carcinoma. For example, a study by Kazakov et al. with five cases of sebaceous neoplasms showing architectural findings of benignancy and cytologic features of malignancy stated that "the classification of such lesions as sebaceoma (with atypia) or sebaceous carcinoma remains unresolved" [32]. This opinion was in contrast to that of Resnik, who reviewed the slides of the five neoplasms [33]. In Resnik's opinion, 4 out of the 5 cases represented sebaceous carcinoma and one sebaceoma. Based on the architectural features of benignancy (well-defined borders of the lobules with no invasive growth) and cytological features of malignancy (presence of nuclear atypia, increased mitotic figures including atypical ones and necrosis), Kramer and Chen thought most, if not all, of the five sebaceous neoplasms presented by Kazakov et al. are in fact examples of sebaceous carcinoma in situ [24].

**Conclusions**

In summary, we can justify sebaceous carcinoma in situ as a valid concept and diagnostic entity. Additionally, this also explains why this neoplasm does not recur or metastasize after simple complete excision. Since it is merely an "in situ" lesion, simple complete surgical excision will result in a cure rate that is essentially 100%. Thereby, surgery is the treatment of choice for these patients.

Accordingly, for the reasons mentioned above, the so-called sebaceous adenoma is neither an adenoma nor an invasive carcinoma, but rather sebaceous carcinoma *in situ.* The histopathological criteria for diagnosing such lesions are clear, accurate and comprehensible.

Recognizing sebaceous carcinoma in situ as a distinct entity must be considered in order to prevent diagnostic misinterpretation, consequently avoiding under or over treatment of these patients.

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# Early and Late Outcome, Mortality and Major Morbidity After Lung Cancer Surgery for Primary Carcinoma

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**Abstract**

Background: Radical surgical resection of lung cancer with or without adjuvant treatment is still a prerequisite for cure. Advances in operative and postoperative care led to a decline in complications and mortality rates during the last decades. In spite of different additional modes of treatment, survival is still poor.

The aim of study: To examine the operative mortality and morbidity after lung cancer surgery and to identify factors associated with an adverse outcome.

Material and methods: The study comprised 968 consecutive patients referred to University Hospital of Lung Disease, "Shefqet Ndroqi" Tirana, Albania, for lung carcinoma, during a 13-years period (January 2004-December 2017). All patients underwent routine laboratory examinations spirometry and preoperative CT- scan of the thorax and upper abdomen. PET-CT, EBUS–EUS, Mediastinotomy or Mediastinoscopy wasn't performed as routine.

Results: Of 968 patients, 690 (70.5%) were male and 278 (28.7%) female. Mean age 65.5±9.4 years (range 15 - 87 years). Lobectomy was the most used surgical modality in 566 (58.5%) patients, meanwhile pneumonectomy was performed in 112 (11.6%) of patients. Minor complications during surgery occurred in 45 (11.7%) of patients. Continuous air leakage was the most complication after surgery in 25.3%, followed by lung atelectasis in 21.3% and cardiovascular complications in 17%.

Conclusion: our results show low mortality and morbidity after lung cancer surgery. However, patients with reduced lung capacity, older age and those undergoing pneumonectomy should be treated with great care.

**Key words**: Outcome, complications, lung cancer, thoracic surgery.

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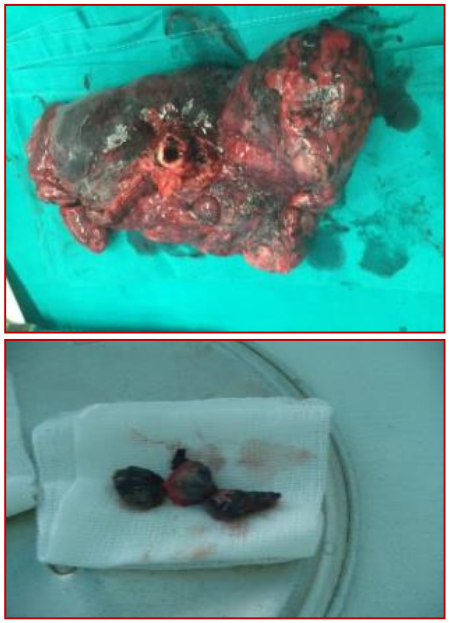
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**Introduction**

Lung cancer *(Figures 1-5)* is the most common form and cause of cancer death world-wide. Radical surgical resection, with or without adjuvant treatment, is still a prerequisite for cure. In European countries the proportion of patients who undergo surgery for this disease varies between 10 and 20%. Advances in operative and postoperative care have led to a decline in complications and mortality rates during the last two decades (1).
In spite of different additional modes of treatment, survival is still poor. To be able to improve the quality of operative procedures it is important: to identify patients running the highest risk, optimizing the patient's condition, medication and respiratory status before surgery, to have knowledge of peri and postoperative mortality and morbidity, and also of risk factors prior to surgery.





*Figures 1-5: 1- X-ray view; 2,3-Operative view; 4,5-Macroscopic specimens*

**Results**

Of 968 patients, 690 (70.5%) were male and 278 (28.7%) female. Mean age 65.5±9.4 years (range 15

- 87 years), of them 271 (27.9%) patients were over 70 years. No differences is seen in death between gender (female vs. male 3.6% vs. 3.9% respectively; p=0.476).

| ***Demographic characteristic*** | ***Patients*** | ***Death within 30 days*** | | ***Major complications*** | |
|---|---|---|---|---|---|
| | N (%) | N (%) | P-value | N (%) | P-value |
| ***Age*** | 697 (72.1) | 18 (2.6) | 0.039 | 23 (3.3) | 0.0024 |
| *< 70 years* | 271 (27.9) | 19 (7.0) | | 25 (9. 2) * | |
| *≥ 70 years* | | | | | |
| ***Gender*** | 278 (28.7) | 10 | 0.476 | 20 (7.1) | 0.984 |
| *Female* | 690 (70.5) | (3.6) | | 28 (4,0) | |
| *Male* | | 27 (3.9) | | | |
| ***Co morbidity*** | 257 (26.6) | 17 (6.8) | 0.064 | 29 (11.2) * | 0.0001 |
| *Yes* | 711 (73.4) | 20 (2.8) | | 9 (1.24) | |
| *No* | | | | | |
| ***Total cases*** | 968 | 37 (3.8) | | 48 (7.2) | |
| | (100) | | | | |

***Table 1:*** *Patient characteristics in relation to death within first 30 days of surgery and major complications*

According to histopathology most of patients result squamous cell carcinoma (56%), followed by adenocarinoma (36%) and the rest other types. Significant difference in mortality within 30 days is seen between adenocarcima, squamous cell carcinoma and other type of cancer ((2, 7%, 3.8% vs. 12.6% respectively; p< 0.01). In spite major complications were in other group of cancer no significant differences is seen between groups. Over 2/3 of patients 78% were current smokers and only 22% never smokers. No differences are seen in term of death or major complications among the groups (2.6% vs. 2.0% and 6.4% vs. 9.4% respectively). Lung function is the parameter of particular importance as a prognostic factor in evaluation of patients after surgery. A significant difference in patients is seen with FEV1< 70% compared with them with FEV1> 70% in term of mortality and major complications (10.7% vs. 2.3% and 23, 8% vs. 2.6% respectively.

| | ***Patients (Nr.%)*** | | ***Mortality (≤ 30-days) (Nr. %)*** | | ***Major complications (Nr. %)*** | |
|---|---|---|---|---|---|---|
| ***Histopathological type*** | | | | | | |
| *Adenocarcinoma* | 348 | 36 | 9 | 2.7 | 26 | 7.6 |
| *Squamous cell ca.* | 542 | 56 | 21 | 3.8 | 35 | 6.4 |
| *Other types* | 78 | 8 | 9 | 12.0* | 9 | 12.0 |
| ***Smoking habits*** | | | | | | |
| *Smoker* | 756 | 78 | 20 | 2.6 | 48 | 6.4 |
| *Never smoked* | 212 | 22 | 4 | 2.0 | 20 | 9.4 |
| ***Lung function (FEV1, %)*** | | | | | | |
| *FEV1 > 70%* | 765 | 79 | 17 | 2.3 | 20 | 2.6 |
| *FEV1 < 70%* | 203 | 21 | 22 | 10.7** | 49 | 23.8*** |

***Table 2:*** *Mortality and major complications, tumor and patient characteristic, (nr. %);* *******statistically significant*

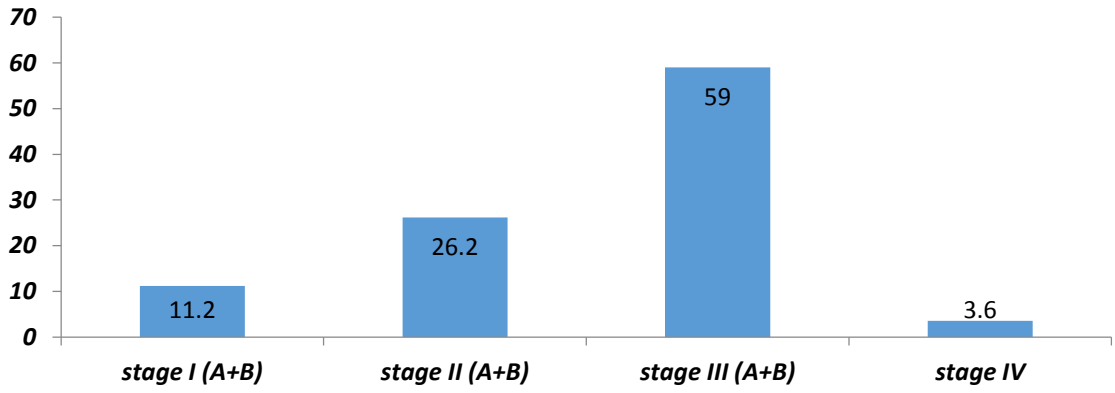



***Table 3:*** *Stage of diseases and surgery modality.*

It is noted that the largest number of patients belonging to stage III + IV (63%) of cases, compared to 37% in stages I + II. Single lobectomy (58%) predominate significantly versus other types of surgery.

Lobectomy was the most used surgical modality in 566 (58.5%) patients, meanwhile pneumonectomy was performed in 112 (11.6%) of patients. Minor complications during surgery occurred in 45 (11.7%) of patients.

| *Surgery approach* | *Patients (N, %)* | | *Mortality within 30-days, (N, %)* | | *Major complications (Nr, %)* | |
|---|---|---|---|---|---|---|
| *Pneumonectomy* | 112 | 13.4 | 15 | 13.4 | 30 | 26.7 |
| *Right* | 42 | 4.4 | 11 | 26.1 | 20 | 39.2 |
| *Left* | 70 | 7.2 | 4 | 5.7 | 10 | 14.3 |
| *Lobectomy* | 566 | 58.5 | 7 | 1.2 | 16 | 2.8 |
| *Bilobectomy* | 126 | 13 | 7 | 6 | 8 | 8 |
| *Explorative thoracotomy* | 51 | 5.3 | 5 | 9.8 | 5 | 9 |
| *Wedge, Segmentectomy* | 107 | 11 | 3 | 3 | 3 | 3 |
| ***Total*** | **968** | **100%** | **37** | **3.8** | **62** | **6.4** |

***Table 4:*** *Patient characteristics according surgery modalit*

The 30 days mortality rate was 3.8% (37) patients, 1.2% after single lobectomy and 13.4 % after pneumonectomy.

Continuous air leakage was the most complication after surgery in 25.3%, followed by lung atelectasis in 21.3% and cardiovascular complications in 17%. Of the life-threatening complications respiratory failure was the most events in 20.0% of patients,

followed by Broncho-pleural fistula in 18.7% and pulmonary edema in 15% of patients.

| *Minor complications* | *Nr.* | *%* | *Major Complications* | *Nr.* | *%* |
|---|---|---|---|---|---|
| ***Supra-ventricular arrhythmias*** | 13 | 17.3 | Respiratory failure | 10 | 20.8 |
| ***Continuous Air leakage*** | 19 | 25.3 | Broncho-pleural fistulas | 9 | 18.75 |
| ***Lung Atelectasis*** | 16 | 21.3 | Pulmonary edema | 7 | 14.6 |
| ***Obstructive symptoms*** | 11 | 14.6 | Cardiac failure | 6 | 12.5 |
| ***Paresis of recurrent Nerve*** | 1 | 1.3 | Tumor embolism | 5 | 10.4 |
| ***Insufficient wound healing*** | 4 | 5.3 | Myocardial infarction | 3 | 6.25 |

| | | | | | |
|---|---|---|---|---|---|
| ***Diaphragmatic paresis*** | 6 | 8.0 | Chilothorax | 3 | 6.25 |
| ***Mediastinal Shift displacement*** | 5 | 6.6 | Postoperative bleeding | 4 | 8.3 |
| | | | Cerebral infarction | 1 | 2.0 |
| ***Total*** | 75 | 7.7% | Total | 48 | 4.9% |

***Table 5:*** *Minor and Major Complications within first 30 days after surgery, (7.7% vs.4.9%)*

**Discussion**

Bronchial cancer today represents a health problem all over the world and one third of them meet at the age of 70 **(1-3).** In our study there have been 70.5% male and 28.7% female. This is closely related to the smoking habit which is widespread in males. The number of tobacco users affected by pulmonary cancer in our country in a study conducted at our hospital by Vakeflliu. Y and al. results up to 86.6% of cases. We found differences is seen in death between gender (female vs. male 3.6% vs. 3.9% respectively; p=0.476).

In this study, the age of the intervening pulmonary carcinoma varies from 15 to 87 years. Of 968 cases in total 271 patients were over 70- years old. Mortality and major complications result with significant differences comparing to those under 70 years old (p=0.03 and 0.0024 respectively). Nevertheless, old age alone does not appear to be a definite contraindication to surgery

There are surgical experiences in patients over 70 years, which indicate that this therapeutic strategy can be performed with good results (11-13). Shirakuza et al. (11), in a series of 33 patients older than 80 years, operated for pulmonary tumor, conclude that, in an elderly subject, not age, but the spread of the disease and the cardio-pulmonary reserve should guide the choice of intervention. Also significant differences are seen according to patients with co morbidity. Furthermore, previous studies have indicated that concomitant diseases such as ischemic heart disease, diabetes mellitus or chronic obstructive lung disease represent significant risk factors for an adverse outcome.

The histological examination of the material in this study shows the significant predominance of the squamous cell carcinoma and adenocarcinoma versus other types. However, based on the sex of the patients, predominance of adenocarcinoma is observed in females, due to the increase in the number of smokers.

Surgical treatment of pulmonary cancer is the method chosen for stage I and II. Procedures that save pulmonary parenchyma offer lower mortality and morbidity than pneumonectomy and instability when complete resection has taken place. (12)

Lung function is the parameter of particular importance as a prognostic factor in evaluation of patients after surgery. In this study a significant difference in patients is seen with FEV1< 70% compared with them with FEV1> 70% in term of mortality and major complications (10.7% vs. 2.3% and 23, 8 % vs. 2.6% respectively.

According to the extent of pulmonary resection, the largest number of cases is treated with lobectomy (58%) followed by bilobectomy and pneumonectomy (13%) and segmentectomy (11%), less is performed explorative thoracotomy [p <0.001].

As expected, the mortality was higher following pneumonectomy (13.4%) than other type of surgery.

The major complications most often related to a postoperative death were respiratory failure (20.0%) followed by Broncho-pleural fistula in

18.7% and pulmonary edema in 15% of patients. These data are in accordance with other reports. In several studies risk factors for major complications after lung resections have been identified, namely: age, male sex, smoking and concomitant disease. As confirmed in the present study, a low respiratory capacity, assessed as FEV1% and pneumonsctomy, appears to be the most important predictor of a high risk of complications after lung resections.
Our results confirm that low mortality 3.8% and an acceptable level of major morbidity 6.4 % can be achieved after surgical resections for lung cancer, especially after single lobectomies (1.2%).

**Conclusion**

Our results show low mortality and morbidity after lung cancer surgery. However, patients with reduced lung capacity and those undergoing pneumonectomy should be treated with great care, as they run a considerable risk of major complications or death during the first 30 days postoperatively. Older age (>70 yrs), does not appear to be a contraindication to lung cancer surgery, but patients in this group should undergo careful preoperative evaluation.
Pneumonectomy sinister et systemic mediastinal lyphonodulectomy ca bronchopulmonare hilare sinister,post neoadjubvant chemiotherapy.

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# The Diagnostic Role of Hyperbilirubinemia in Complicated and Non -complicated Appendicitis

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**Abstract**

Background: Acute appendicitis is one of the most frequent causes of abdominal pain. Early diagnosis is the key to success for the surgeon, followed by the treatment with operation or conservative treatment as a new approach, before the stage of gangrenous appendicitis or perforation occurs.

Aim: This study aims to establish he role of hyperbilirubinemia as a laboratory marker in prediction of acute appendicitis in the early diagnosis.

Materials and methods: This is a cross-sectional study; it included 201 patients admitted in the emergency ward with suspicion for acute appendicitis. All patients that participated in this study have been subject to appendectomy. The blood samples were taken from all patients in order to analyze the level of total/direct bilirubin.

Results: The study samples of 201 patients consisted of 67.7% with complicated appendicitis and 32.3% with non-complicated appendicitis. The sensitivity, specificity, PPV, NPV for laboratory marker, as predictor for complicated vs non-complicated cases of appendicitis was as follows: Total bilirubin; specificity (72.3%), sensitivity (54.4%), PPV (80.4%), NPV (43.1%),

Conclusion: Elevation of total/direct bilirubin level in patients with clinical signs of acute appendicitis might predict the stage of acute appendicitis, such prediction may help surgeons to provide accurate treatment of the disease without delay in the diagnosis. This accuracy can be further supplemented by using Alvarado scoring model during the clinical approach.

**Keywords:** Acute appendicitis, total/direct bilirubin, appendectomy, examination, clinical approach, Alvarado score.

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**Introduction**

Acute appendicitis is defined as an inflammation of the appendix vermiformis. It is a common cause of abdominal pain and still remains a diagnostic and therapeutic challenge for surgeons in the emergency ward. Less than five percent of children diagnosed with acute appendicitis are younger than five (5) years old (1). Up to 40 % of cases with appendicitis occur in the age-group between 10 and 29 years(2). Although, it is frequently seen in second through fourth decades of life, it can be diagnosed in any age. Appendicitis is more frequent in males rather than females (8.6% vs. 6.7%) (3).
The common cause of appendicitis is usually obstruction of lumen with nonspecific factors(4, 5).This obstruction occurs from the undigested food, fecaloma, lymphoid inflammation or even any twist around. In a small percentage of cases, bacteria from enteric part may infect appendix with direct spread or may cause hyperplasia in the lymphoid part of appendix with consequent obstruction.(6) More than 14 organisms are reported in patients with perforative appendicitis. Different agents including adenoviruses (Montgomery EA and al) Rubella(8) ,Epstein-Barr virus, Actinomyces Israeli (8, 9),Ascaris lumbricoides and Enterobius vermicularis(10, 11) are involved in this polymicrobial infection. *Escherichia coli* and *Bacteroides fragilis* are two organisms which equally found in normal appendix as well as in acute and perforated appendicitis(12, 13). In the later stages of the inflammation, mucosal ulceration occurs, followed by Escherichia coli dissemination to the portal blood system. Studies in animal models have shown that bacteria can interfere with microcirculation on the hepatocyte, thus inducing hepatic damage with impaired acid bile secretion within the hepatobiliary system(14). E. coli affects also the intravascular hemolysis, second mechanism by which bilirubin levels increase in the blood circulation (15).
Recently, the use of imaging methods was associated with increased diagnostic accuracy in daily practice and decreased rate of negative appendectomy.
This way, SCOAP trial with 3540 appendectomies performed, found significant decrease in negative appendectomy with increased CT and ultrasound use(16).
Different scoring systems are available and the most commonly used are: the Alvarado Score, Acute Inflammatory Response Score, the Pediatric Appendicitis Score (PAS) (17) and the Lintula score (18).
The first score was presented by Alvarado in 1986 and furthermore modified Alvarado score was accessible by Kalan and colleagues (19). Their score ranged from 0-9 points.
The use of Alvarado score is important during the clinical evaluation of patient suspicious for acute appendicitis. Every patient with high Alvarado score needs further assessment and evaluation.
There are many systems that numerous authors proposed for use during the clinical assessment of patients with abdominal pain but the Alvarado score with its modification is widely favored (19, 20).
The Alvarado score was constructed by Alvarado in 1986 and is expressed up to maximum10 points. It is also known as a MANTRELS, which is an acronym for Alvarado score (Table 1).

| Feature | Point |
|---|---|
| **Migration of pain** | 1 |
| **Anorexia** | 1 |
| **Nausea** | 1 |
| **Tenderness in right lower quadrant** | 2 |
| **Rebound pain** | 1 |
| **Fever** | 1 |
| **Leukocytosis** | 2 |
| **Shift of white blood cell count to the left** | 1 |
| Total | **10** |

**Table 1: Structural criteria of the Alvarado Score**
*Modified from: Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med 1986; 15:557.*

Scores from 1 to 4 correspond to low risk for acute appendicitis and subsequently patient can be discharged from the Emergency Ward, whether the score from 5 to 6 needs further observation. Finally, in cases when the score is 7 up to 10,surgical intervention is considered(20). Currently, the clinical approach for all cases suspicious for acute appendicitis, include CBC (complete blood count) particularly leukocyte count, serum C - reactive protein and pregnancy test for women in childbearing age, for the purpose of excluding pregnancy.

**Differential Diagnosis**
Different inflammatory processes can simulate the acute appendicitis manifestation with similar and overlapping signs and symptoms, such is Meckel's diverticulitis, acute ileitis, cecal diverticulitis, crohn's disease, urologic disorders, gynecologic disorders, tubo-ovarian abscess.

**Treatment**
The treatment of acute appendicitis is appendectomy with open approach, appendectomy with laparoscopic approach and non-operative treatment. The operative treatment is widely used for treatment in patients with acute appendicitis. This can be performed with classical operation or laparoscopic approach depending on the experience of surgeon. The newest studies suggest the treatment of non- complicated acute appendicitis with conservative approach. This approach is usually applied in the initial phases of the inflammation and include the use of antibiotics, rehydration and dynamic follow-up. (21, 22). Acute appendicitis without complication can be managed successfully with antibiotics, without surgery. In cases where the recurrence of inflammation occurs (14 % of them), surgical treatment is performed (22, 23).

**Aim of the study**
The overall aim of this study is to determine role of the hyperbilirubinemia in early triage and diagnosis of complicated versus non-complicated appendicitis in patients following clinical assessment such as the Alvarado Scoring system.S pecific aims of the research
1. To determine sensitivity and specificity of bilirubin levels in early assessment of acute appendicitis.
2.To establish bilirubin level as a standard laboratory marker for diagnosis of appendicitis.

**Materials and methods**
**1.Ethics**
The Ethical Committee of the University Clinical Center of Kosovo approved the study protocol (with reference number 1/86/2016). The signed informed

consent of the patients were obtained from all subjects that participated in this study.

**2.Inclusion criteria**

1. *Patients admitted in emergency ward and surgery unit, clinically suspicious for acute appendicitis (all patients included in this study were operated for acute appendicitis).*
2. *Patients from 14 years old and above.*

**3.Exclusion criteria**

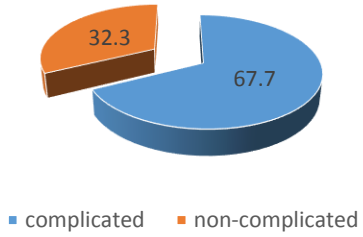
1. *Children with abdominal pain younger than 14 years.*
2. *Patients with liver disease, hepatitis and jaundice.*
3. *Patients with hemolytic anemia and consequent hyperbilirubinemia.*
4. *Patients with abdominal trauma injury.*

**4.Statistical Analysis**

Statistical analysis was performed by using statistical package SPSS 17.0 version software. All categorized variables were presented as proportion in percentages with their 95% confidence interval (95%CI). The mean values of all continuous variables will also present with their 95% CI. X2-analysis or Fisher exact test will perform to test the difference in proportions of qualitative variables between groups. The diagnostic performance of a test used as primary outcomes was evaluated using Receiver Operating Characteristic (ROC) curve analysis. The level P <0.05 was consider as the cut-off value for significance.

**Results**

A total of 201 subjects with acute appendicitis were enrolled in this study. In all 201 patents appendicitis was the final diagnosis. They were randomized in two groups. Complicated acute appendicitis was found in 136 patients (67.7%) participating in this study. While 65 patients (32.2%) were identified with non-complicated appendicitis. The percentage difference is statistically significant with p <0.05 (p=0.0000-Difference test) (Graph 1).




*Graph 1. Distribution of patients with complicated and non-complicated appendicitis*

***Age Distribution***

The average age of patients with complicated appendicitis is 30.7 years old, while the average age of patients with non-complicated appendicitis is 21.9 years old (Table no.2). According to the Mann-Whitney U test, the difference between two groups is statistically significant for p <0.05 (p=0.000009).

| *RANK SUM - GROUP 1* | *RANK SUM - GROUP 2* | *U* | *Z* | *P-LEVEL* |
|---|---|---|---|---|
| *15444,50* | *4856,500* | *2711,500* | *4,428981* | *0,000009* |

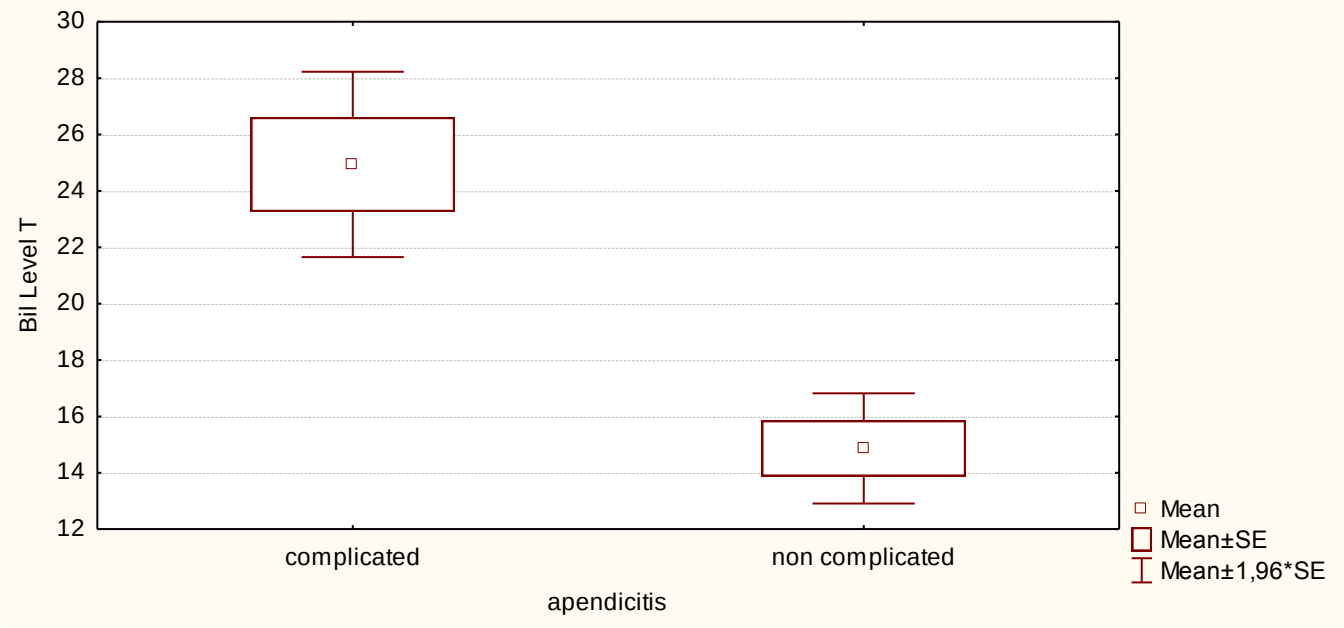
*Table 2. Difference between age, complicated and non-complicated appendicitis determined by Mann-Whitney U Test 1*complicated appendicitis. 2* non-complicated appendicitis*

Bilirubin level between two groups of studies

The average level of total bilirubin in the group with complicated acute appendicitis is 24.9 mg/l, higher than the reference value (18.8 mg/L). Average value of total bilirubin in the group of non-complicated appendicitis is 14.9 mg/L and it is in line with the reference value (18,8 mg/L), (Tab.3 and Graph.2). The difference between the average values of total bilirubin according to the Mann-Whitney U test is statistically significant; p <0.05(p=0.000022).

| | Mean - 1 | Mean - 2 | Valid N - 1 | Valid N - 2 | Std.Dev. - 1 | Std.Dev. - 2 |
|---|---|---|---|---|---|---|
| **Bil Level T** | 24,9 | 14,9 | 136 | 65 | 19,56050 | 8,04453 |

*Table 3. Average value of total bilirubin in complicated and non-complicated group*
*1*complicated appendicitis2* non-complicated appendicitis*




*Graph 2. The average value of total bilirubin in complicated and non-complicated appendicitis*

| | Rank Sum - Group 1 | Rank Sum - Group 2 | U | Z | p-level |
|---|---|---|---|---|---|
| **Bil Level T** | 15373,50 | 4927,500 | 2782,500 | 4,244926 | 0,000022 |

***Table 4. Mann-Whitney U Test (total bilirubin and appendicitis)***
1*complicated appendicitis 2* non-complicated appendicitis

The accuracy of total bilirubin as a diagnostic test (predictor marker) for the detection of early complicated and non-complicated acute appendicitis, is analyzed in Table 4. From the total

number of 201 patients with appendicitis, true positive were 74 patients, false positive 18. From 109 negative findings, 47 true negative and 62 false negative results.

The accuracy of total bilirubin: sensitivity 54.4%, specificity 72.3%, positive predictive value 80.4%, negative predictive value 43.1%. Total accuracy 60.2%.

ROC analysis shows that total bilirubin participates in establishing the diagnosis in complicated appendicitis with 68.5% (p=0,000) (good predictor for complicated appendicitis) (Figure 1).

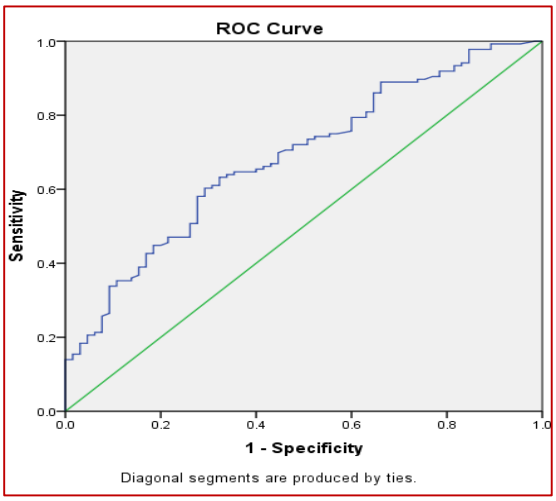



*Figure1. ROC curve for total bilirubin as a predictor for complicated appendicitis*

Average value of direct bilirubin in the group of complicated appendicitis is 7.9mg/Land is higher than the reference value (5.1mg/L). The average value of direct bilirubin in the group of non-complicated appendicitis is 4.8mg/L and it is in line with the reference value(5.1mg/L). The difference between the average values for direct bilirubin according to the Mann-Whitney U test is statistically significant with the value of p<0.05(p=0.000251), (Table 5).

| | ***Rank Sum - Group 1*** | ***Rank Sum - Group 2*** | ***U*** | ***Z*** | ***p-level*** |
|---|---|---|---|---|---|
| ***Bil Level D*** | 15148,50 | 5152,500 | 3007,500 | 3,661654 | 0,000251 |

**Table 5. Direct bilirubin level according to Mann-Whitney U Test**

1*complicated appendicitis. 2* non-complicated appendicitis

The accuracy of direct bilirubin as a diagnostic test (predictor marker) for the detection in early complicated and non-complicated appendicitis, is analyzed in Table 20. From 201 patients with acute appendicitis, true positive were 76, false positive 60. From 65 negative results, 46 were true negative and 19 false negative results. The accuracy of direct bilirubin: sensitivity 80.0%, specifity 43.4%, positive predictive value 55.9%, negative predictive 70.7%. Total accuracy is 60.7%.

ROC analysis shows that direct bilirubin participates in establishing the diagnosis in complicated

appendicitis with 68.5% (p=0,000), (good predictor for complicated appendicitis) (Figure 2).

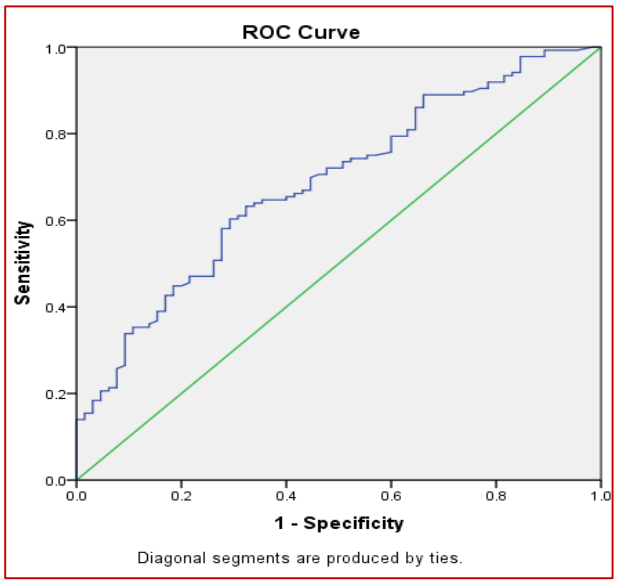


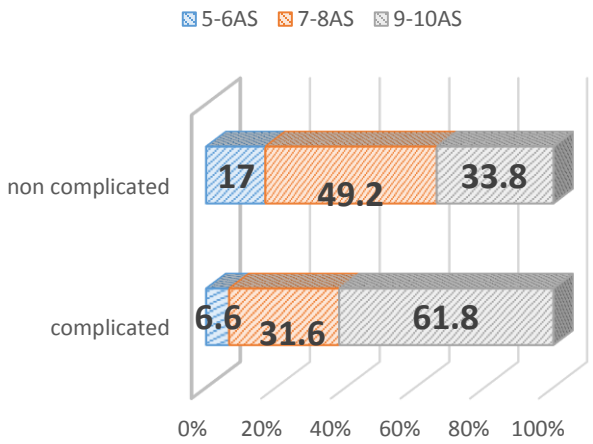

*Figure2. ROC curve for direct bilirubin as a predictor for complicated appendicitis*

**Alvarado scoring model between complicated vs non-complicated appendicitis**

According to the Alvarado Score, the largest percentage of patients with complicated appendicitis consist of patients with definitive diagnosis of acute appendicitis, who require a surgical intervention (61.8%). 31.6% of them comprise patients with acute appendicitis, and finally, the remaining 6.6% consist of patients with a possible diagnosis of acute appendicitis.

According to the Alvarado Score, the largest percentage of patients with non-complicated appendicitis consisted of patients with presence of acute appendicitis (49.2%). The percentage of 33.8% of the patients is comprised of patients with definitive diagnosis, required surgical intervention, and finally, the percentage of 17.0% consisted of patients with a possible diagnosis of acute appendicitis based on the Alvarado Score (Graph 3).

The difference in percentage which is registered in two groups of the study in relation with Alvarado Score is statistically significant for p<0.05(p=0.0002; p=0.0158, p=0.0212).




*Graph 3. Diagnosis based on the Alvarado Score model*

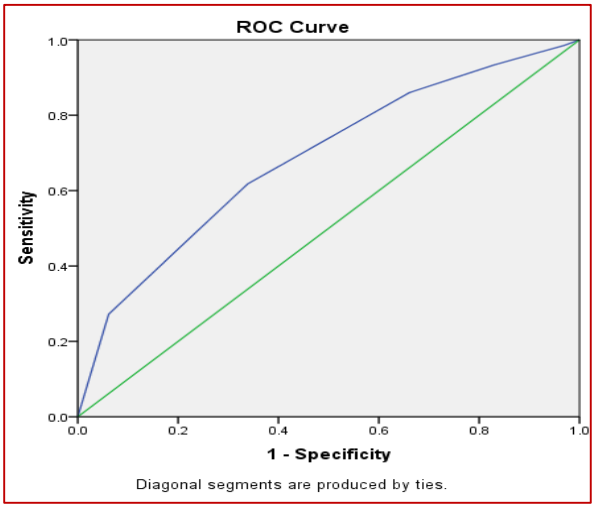



*Figure3. ROC curve for Alvarado score as a predictor for complicated appendicitis*

ROC analysis shows that Alvarado score participates in establishing the diagnosis for complicated appendicitis with 68.6% (p=0,000), (good predictor for complicated appendicitis) (Figure 3).

**Disscusion**

Data from our study revealed bilirubin level and Alvarado score as reliable markers in the diagnosis of the complicated versus non-complicated appendicitis.

Diagnostic test accuracy (ROC) in the present study ranged from 68.6 % for bilirubin and Alvarado score. The incidence of acute appendicitis is different, but the prevalence is around 7.5 up to 22 out of 10 000 citizens.(3, 24, 25) Delayed diagnosis and complication are important outcome measures during the surgical evaluation.

In this study, we intended to analyze the laboratory marker such as: bilirubin level total/direct, gender, Alvarado scoring and histopathologic results in patients, divided in two groups with complicated and non-complicated appendicitis.

Complicated appendicitis is defined as gangrenous appendicitis, perforation, abscesses and peritonitis whereas non-complicated appendicitis were phlegmonous and catarrhal appendicitis.

In our study, we have analyzed 201 patients with acute appendicitis in which appendectomy was performed.

From the total number of patients that participated in this study 67.7% or 136 patients were diagnosed with complicated appendicitis and 32% or 65 patients with non–complicated appendicitis, therefore statistically significant difference was recorded for patients with complicated vs non-complicated appendicitis.

According to the retrospective cohort study conducted by Serres SK and al, the rate of complication for patients with acute appendicitis was around 23% in their study (26).

Contradictory, in our study, the rate of complications in patients with acute appendicitis were much higher compared to the above-mentioned study. This main finding in our study might be partially explained by non-appropriate and over-use of different analgezics during the initial phases of the disease which may mask or mimic clinical appearance and therefore delay the prompt diagnosis of acute appendicitis. Delayed referral from the primary health care as well as limited access to the medical services are among frequent determining factors for the disease outcome.

Statistically significant dependence was recorded between the gender, age and the form of appendicitis. The average age for patients with complicated appendicitis was 30.7 years (mean-1) while in patients with non-complicated appendicitis the average age was 21.9 years (mean-2). Although the majority of the published studies revealed predominantly male gender in acute appendicitis, to our current knowledge, association between the male gender and complicated form of appendicitis was not previously described. Therefore, Mann-Whitney-U test showed statistically significant difference ($p<0.05$) regarding the patient gender and form of the acute appendicitis in the present study. 74.3 % of patients with acute complicated appendicitis were male and only 25.7 % were female hence, statistically significant difference was found between males and females and complicated appendicitis (($p<0.05$)

The role of hyperbilirubinemia as a laboratory marker that may contribute in the diagnosis of acute appendicitis has been analyzed in numerous studies (27-29). Different studies, recently have tried to explain the role of hyperbilirubinemia in patient with sepsis and small number of authors have hypothesized the connection between hyperbilirubinemia and acute appendicitis and its complication (29, 30).

In our cross-sectional study 201 patients with acute appendicitis were enrolled in total. From the total number of patients that participated in this study,

67.7% of them were patients with complicated acute appendicitis while 32.3 % were patients with non-complicated acute appendicitis. Based on our study, the level of total bilirubin was elevated in the group of patients with complicated appendicitis with average level of bilirubin 24.9 mg/l and according to the Mann-Whitney U test this result is statistically significant. For direct bilirubin the average value is 7.9 mg/l, also statistically significant. For complicated appendicitis, sensitivity of total bilirubin was 54.4%, specificity 72.3, positive predictive value 80.4, negative predictive value 43.1 while global accuracy reaches up to 60.2%. Poras Chaudhary et al, in the prospective study of 50 cases have concluded that bilirubin is an important marker during the diagnosis of appendicitis and complicated appendicitis(31). According to the same results from this study hyperbilirubinemia was present in perforated and gangrenous appendicitis. The level of serum bilirubin reported was above 3 mg/dl, sensitivity and specificity of hyperbilirubinemia in gangrenous appendicitis was 100% and 92.9 % respectively, with high positive and negative predictive value (72.7% and 100%, respectively) according to this study(31).

The role of hyperbilirubinemia in revealing complicated or perforative appendicitis was also demonstrated in another study conducted by Khan and co-workers. Reported sensitivity and specificity of the total bilirubin level in predicting the perforative appendicitis according to this study was 88% and 80 % respectively(32). D'Souza N et al in their study suggest that hyperbilirubinemia in patients with acute appendicitis and complicated cases of appendicitis had higher specificity compared with WBC and CRP.(33)

We have evaluated the accuracy of total bilirubin and according to our study the sensitivity of total bilirubin is 54.4%, specify 72.3% positive predictive value 80.4% and negative predictive value 43.1%. The study from D'Souza N et al, concluded that serum bilirubin in acute appendicitis is marker with higher sensitivity but with low sensitivity.(33)

The serum bilirubin analysis with receiver-operating characteristic curve (ROC) in our study have shown that bilirubin marker is good predictor for complicated appendicitis (68.6%). Based on a study from Andrew Emmanuel et al, where the bilirubin level was analyzed using ROC curve the sensitivity were 57% and specificity 72% (34). In 201 patients enrolled in our study, we have concomitantly performed total bilirubin as well as direct bilirubin measurement. In this study statistically, significant difference was found regarding the total bilirubin level in complicated vs non -complicated appendicitis (24.9mg/L vs 14.9mg/L, respectively). Statistically significant difference was also found regarding the direct bilirubin measured in our subjects (7.9mg/L vs 4.8mg/L) between the complicated and non-complicated appendicitis.

One of the most interesting findings in the present study is that sensitivity of the total bilirubin for differentiating complicated vs non-complicated appendicitis was only 54.4% and 80.0% for direct bilirubin. This way the combination of those two markers can improve clinical diagnosis in Emergency Ward and classify patients with acute need for surgery.

Although PPV was similar for total and direct bilirubin (80.4 vs 70.7), the total accuracy for total and direct bilirubin resulted with 60.2 vs 60.7 respectively.

Therefore, hyperbilirubinemia is strongly suggestive of complicated appendicitis based on the data from the previous studies and in the same line are correspondingly results from the present study. (35)

The Alvarado scoring system was used in our study to determine the role of this model in reducing the mismatch diagnosis. According to the ROC analysis

preformed during our study, Alvarado score is very good predictor in cases of complicated appendicitis with 68.6%. Based on our study the use of the scoring system in patients with suspicion for acute appendicitis ensures high rate of sensitivity and specificity. Also the study from Memon ZA et al, showed that Alvarado scoring system can contribute in decreasing the negative appendectomy.(36).

In this study all appendectomy samples were referred for histopathologic evaluation and diagnosis which also included patient follow-up. Results from our study showed a strong correlation between the primary clinical assessment and final diagnosis.

Hence, gangrenous changes in histopathological examination were found in 99.3 % of complicated appendicitis and phlegmonous changes in 87.7 % of non-complicated cases.

Important finding from the present study is also statistically highly significant correlation between the histopathologic diagnosis and total and direct bilirubin ($p<0.05$).

To summarize, the above mentioned relationships between each variables used in the study, reveal hyperbilirubinemia and Alvarado scoring system as the most reliable biomarkers for early diagnosis and prognosis of acute appendicitis, pointing out the obvious discriminatory strength of the bilirubin level and scoring system to categorize complicated from non-complicated appendicitis.

**Conclusion**

1. Data from the present study found out high rate of complications in patients diagnosed with acute appendicitis in our study sample.
2. Our results demonstrated a strong correlation between the male gender and complicated appendicitis (male 74.3 % vs female 25.7 %).
3. Hyperbilirubinemia poses moderate diagnostic and prognostic test accuracy principally for the complicated appendicitis (ROC=68.6%).
4. Combination of total and direct bilirubin can improve clinical diagnosis in Emergency Ward and classify patients with acute need for surgery.
5. Alvarado scoring system is a good diagnostic predictor in complicated appendicitis (ROC=68.6%).
6. A strong correlation between the clinical diagnosis and histopathological result was evidently demonstrated.
7. Total and direct bilirubin level showed statistically significant correlation with the final histopathological diagnosis ($p<0.05$).

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# CELLUTOME™ Epidermal Harvesting System

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**Abstract**

Introduction: Treatment of acute and chronic wounds are a major challenge. In modern medicine, numerous approaches to wound healing are known. One of them is the use of epidermal autologous grafts. The purpose of this article is to present the use of automated epidermal harvesting system (CELLUTOME™ Epidermal Harvesting System; KCI, an Acelity company, San Antonio, TX, USA) in General Hospital dr. Jože Potrč Ptuj, Slovenija.
Case presentation: Treatment of a patient with a chronic wound after ruptured varicose veins on the right shin, a patient with a chronic wound after crash injury and a patient with nonhealing postoperative wound using CELLUTOME™ Epidermal Harvesting System are described.
Conclusion: Our results showed the positive effects of epidermal autologous grafts on the healing process of various types of wounds and confirmed the advantages of this system for the production of epidermal autologous grafts.
**Keywords:** Wound healing, autologous epidermal grafting, chronic wound, acute wound

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**Introduction**

Acute and chronic wounds are a significant challenge for wound care specialists. While acute wounds proceed through the normal stages of healing, chronic wounds usually do not follow an orderly process of regeneration and repair (1, 2) The healing process can be lengthy, requiring frequent office visits and dressing changes (1). Today there are many known methods of treating acute and chronic wounds. Skin grafts have been used to achieve successful wound healing when primary wound closure is not a feasible repair option (3). Split-thickness skin grafts (STSGs) have long been the gold standard for the management of acute wounds but have not gained favor in the treatment of chronic wounds for several reasons: discomfort associated with the donor site, the creation of a second wound (donor site) in a patient with poor wound-healing potential, and a lack of documented efficacy for the procedure (1). Traditional types of autografts include full-thickness and split-thickness skin grafts. Some disadvantages of autografts include the need for a surgical procedure with anesthesia, creation of a second wound on donor site, difficulty in obtaining uniform graft thickness, pain, and challenges with graft take and graft rejection (3, 4). Problems with the donor site may include excessive pain, pruritus, infection, dyschromia, delayed healing, and hypertrophic scarring, particularly in patients with poor healing properties due to various comorbidities (5, 6). Another drawback to traditional skin grafting techniques is the cosmetic outcome, including hypopigmentation, hyperpigmentation, and hypertrophic scarring (7).
Dermatologists first used epidermal grafting in 1964 and later for the treatment of hypo pigmented lesions (8). Epidermal skin grafts differ from full-thickness and split-thickness skin grafts in that they only contain the epidermal layer of the skin, which is comprised of 5 layers and 4 cell types. Despite the challenges of harvesting epidermal grafts, successful use has been reported in the treatment of burns and chronic wounds (9, 10). Epidermal grafting does not have any of the limitations encountered with STSG, however, it has not gained wide acceptance, as previous harvesting techniques were cumbersome and time-consuming (1). Epidermal grafting or using autologous epidermis that has been minced to expand and cover wounds much larger than the donor site, are an alternative to traditional autografts using only a minimal amount of autologous tissue from the donor site (11, 12). Only the epidermal portion of the donor area is grafted. This means that the graft acquires the epidermal architecture and characteristics of the recipient site, not the donor site, what potentially leads to better color match and cosmetic outcome (12, 13).
In 2013 an automated epidermal harvesting system (CelluTome Epidermal Harvesting System; KCI, an Acelity company, San Antonio, TX, USA) that applies negative pressure to harvest epidermal microdomes was commercially introduced (1). This system is also used in General Hospital dr. Jože Potrč Ptuj, Slovenia, since 2016.

The CELLUTOME™ Epidermal Harvesting System is a minimally invasive tool for harvesting epidermal micrografts and is designed for use in the office or outpatient setting. This system combines suction and warmth and produces consistent thin sections of epidermal skin. The technology of the device involves splitting the dermal-epidermal junction to form microdomes (ie. blisters), which are harvested into epidermal micrografts. These micrografts consist of undamaged epithelium with keratinocytes (Kci). The system yields up to 128 epidermal micrografts (1).

Epidermal grafting provides an approach in the treatment of acute and chronic wounds. The epidermal grafts can be used on wounds that have a clean granulating base that is free of nonviable tissue. The inner thigh is the preferred donor site; any hair on the inner thigh should be clipped and the skin prepared with 70% isopropyl alcohol. The harvester should be positioned on the donor site with the blue handle orientated in the upwards position and secured with the provided Velcro strap (Figure 1, 2).



*Figure 1: Positioning of harvester*




*Figure 2: Positioning of harvester*

The physician should visually confirm complete contact with the skin and reposition if necessary. Alternate corners of the vacuum head-harvester complex should be pressed to ensure a good seal.

Next, the 'Start' button should be pressed on the control unit. The system heats the skin to between 37°C and 41°C and applies 400– 500mmHg of negative pressure. The vacuum head also provides illumination so that the site can be observed through the view window. The microdome preparation takes from 15 to 60 minutes; the preparation is complete when round epidermal microdomes form (Figure 3,4).

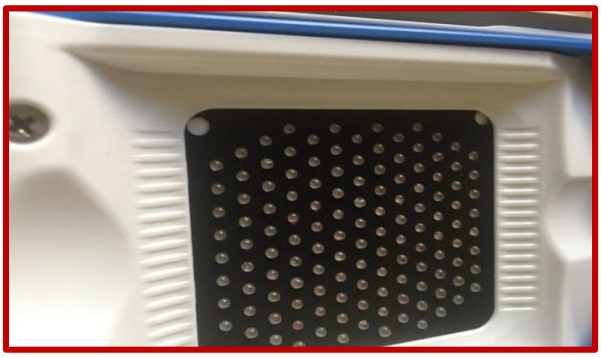


*Figure 3: Formation of microdomes*



*Figure 4: Microdomes*

To collect the microdomes, the control unit is turned off and the vacuum is removed from the vacuum head. The vacuum head is unlatched from the harvester by pressing the blue handle on either side. A dressing is then inserted into the harvester and pressed firmly against the microdomes. The choice of dressing can be left to the discretion of the physician—Tegaderm film dressing (3M Company, St. Paul, MN, USA) is recommended for

wounds with low levels of drainage. If using the film dressing, it is suggested that the dressing be rubbed gently against microdomes. Next, holding the harvester in place, the blue handle is retracted upwards until a click is heard, and then the handle is slowly returned to the start position. The dressing is carefully removed from the harvester and transferred to the recipient site (Figure 5).

The microdomes are secured in place by using compression wrapping, a bolster dressing, or with NPWT. The donor site (Figure 6) can be treated with a film dressing (1).

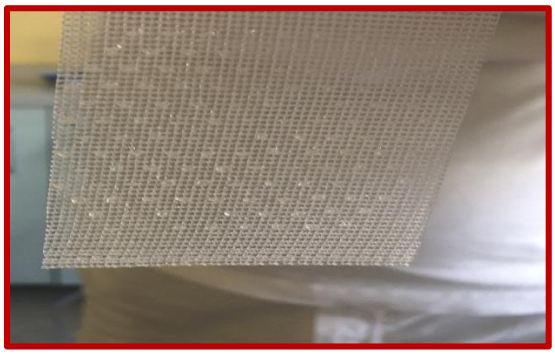


*Figure 5: Microdomes for transmission*



*Figure 6: Donor site*

Several advantages of epidermal grafting are noted over traditional split-thickness skin grafting. While split-thickness skin grafting necessitates the use of anaesthesia, with this automated system, epidermal grafts can be harvested easily by physicians in an out-patient setting. Patients experience little or no discomfort during the harvesting procedure. This novel automated epidermal harvesting system has simplified suction blister grafting, making epidermal grafting available to clinicians as an option for acute and chronic wounds. Early results from 17 cases have indicated decreased wound area of chronic wounds in a variety of patients, including those with comorbidities and in patients where an STSG was contraindicated (1). Epidermal grafting for dermatological use is well-documented in the literature, specifically in treating vitiligo (14, 15) and lesions of chronic discoid lupus erythematosus (16).

(17) reported their initial clinical experience using the CELLUTOME™ Epidermal Harvesting System for harvesting epidermal grafts when they treated 7 Haitian patients with chronic lower extremity wounds. Of the 7 wounds, 3 closed completely in 4 weeks and 3 showed marked improvements. All donor sites healed without any visible scarring. The harvesting of epidermal grafts using CELLUTOME™ Epidermal Harvesting System was accomplished in an outpatient setting and did not require anaesthesia or specialized surgical technique. Thus, epidermal grafting may provide a promising option for patients in resource-poor countries.

(18) provided a general overview of epidermal grafting and reported results of 4 patients treated with epidermal grafts harvested by the CELLUTOME™ Epidermal Harvesting System from the patient's thighs. Complete reepithelialisation was achieved in 3 wounds: a heat burns to the right radiated breast, right scalp melanoma excision site, and wound created after removal of a sacral tattoo. The fourth wound was a diabetic foot ulcer of 8 years' duration that maintained 50% reepithelialisation at the 2-month follow-up. All

donor sites healed without scarring within 1-2 weeks.

(19) treated 5 patients with chronic recalcitrant lower extremity ulcers (pyoderma gangrenosum) with epidermal grafts harvested by the CELLUTOME™ Epidermal Harvesting System. All patients continued to receive medical care for pyoderma gangrenosum. Three of the 5 wounds achieved full reepithelialisation at 5, 7, and 12 weeks, respectively. The remaining 2 wounds reduced in size by 64% and 99%, respectively, within 8 weeks. Minimal pain was associated with the procedure, and all donor sites healed within 1 week. There were no complications at the donor and recipient sites. In this series the authors noted that reepithelialisation moved in from the wound edges, and the epidermal grafts did not appear to "take" to the underlying tissue.

The purpose of this article is to present case examples of patients, treated in the wound care ambulatory setting in General Hospital dr. Jože Potrč Ptuj, Slovenia. Case examples of three patients where autologous epidermal graft, obtained by CELLUTOME™ Epidermal Harvesting System has been used to treat chronic wounds are described.

## Case presentations

### Case example 1

Patient ŠM (woman, born 1927) with heart failure, arterial hypertension, atrial fibrillation on anticoagulant therapy was previously treated because of spontaneous bleeding from right shin, because of ruptured varicose veins. Haemostasis was performed with regular wound treatments. The extent of necrosis was not determined. A month later, the patient was hospitalized with local necrosis of right shin sizing 15 x 10 cm (Figure 7).



*Figure 7: Wound after necrectomy (28. 9. 2016) (Case example 1)*

Necrectomy was performed and negative pressure system was installed. During the hospitalization, patient received regular negative pressure wound treatment and the wound regularly healed. After discharge in home care, he continued with negative pressure wound treatment and ambulatory wound management. After three weeks, the patient returned to hospital due to the planned operative procedure (20). Because of comorbidities and

general health condition patient was not suited for a surgical procedure under general anaesthesia. Therefore, on the 26th of October 2016 we performed skin cell extraction with CELLUTOME™ Epidermal Harvesting System from medial left thigh and covered skin defect. Skin defect was covered with polyurethane foam. First wound dressing was performed after four days, while continuing treatment with Vaseline gauze. Vaseline gauze was later replaced by polymer membrane in a hydrophilic polyurethane matrix and used until healing (Figure 8).



*Figure 8: Wound after skin cell transplant, first wound dressing (Case example 1)*

Cleaning of the wound was performed using saline solution. Wound care was performed three times weekly. A donor site for cell transplant was treated with film dressing and healed within 7 days. On 4th




*Figure 9: Healed wound (4. 1. 2017) (Case example 1)*

of January 2017 (70 days after skin cell transfer) wound healed (Figure 9).

**Case example 2**

Patient KM (male, born 1946) with arterial hypertension and rheumatic disease had a crush injury on the 29th of September 2017. First visit in our ambulatory setting was three weeks after the injury. There were two wounds on medial side of right thigh, dermacated necrosis with mild redness. Necrectomy and cleaning of the wound were performed. On 25th of October 2017 negative pressure wound system was installed (Figure 10). Patient regularly visited the ambulatory setting for wound care negative pressure wound system changes. On 1th of November 2017 skin defect was covered with clean granulation tissue. We performed skin cell extraction with CELLUTOME™ Epidermal Harvesting System from medial left thigh and covered skin defect measuring 6.0 cm x 5.0 cm. After cell transplant skin defect was covered with polyurethane foam. First dressing change was done after four days while continuing wound treatment with polymer membrane, followed by medical honey. Cleaning of the wound was performed using saline solution. Wound care was performed three times weekly.

A donor site for cell transplant was treated with film dressing and healed within 7 days. On 27th of December 2017 (57 days after skin cell transfer) wound healed (Figure 11).

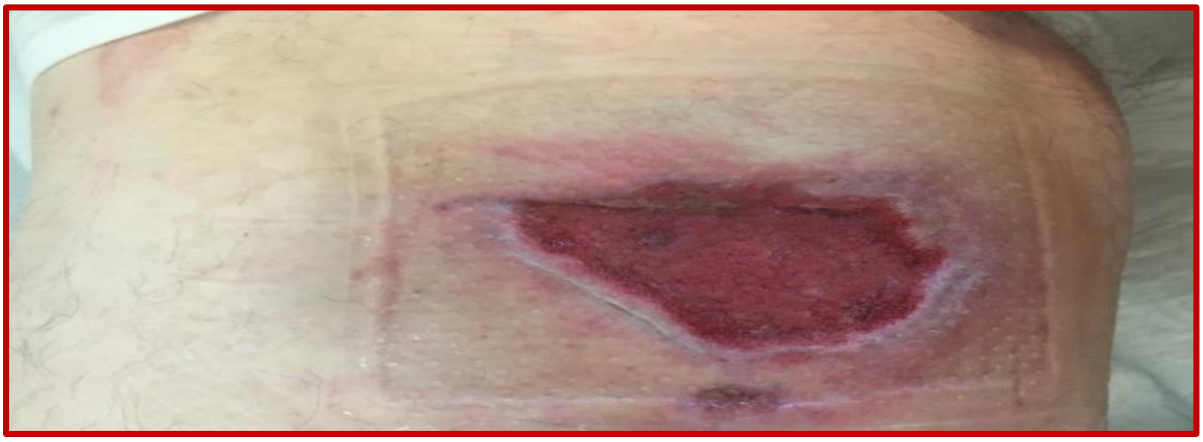


*Figure 10: Wound after necrectomy (25. 10. 2017) (Case example 2)*



*Figure 11: Healed wound (27. 12. 2017) (Case example 2)*

**Case example 3**

Patient LN (woman, born 1961) with osteoporosis fell on the 15th of April 2017 and gained communitive fracture of right distal femur resulting in surgery. After surgical procedure, we treated skin defect using a negative pressure wound treatment which resulted in granulation of wound bottom. On 12th of May 2017 we performed skin cell extraction with CELLUTOME™ Epidermal Harvesting System from medial left thigh and covered skin defect (Figure 12).

Defect measured 10.0 cm x 5.0 cm. Again, polyurethane foam was used to cover skin defect. A first dressing change was made after four days while continuing wound treatment with a polymer membrane in the hydrophilic polyurethane matrix, which was used until the last treatment in our ambulatory settings (Figure 13).

Cleaning of the wound was performed using saline solution. Dressing change was three times weekly. A donor site for cell transplant was treated with film dressing and healed within 7 days. On 28th of June 2017 (47 days after skin cell transfer) wound measured 1.0 cm x 2.8 cm (Figure 14).

Unfortunately, the patient ended her visits in our ambulatory setting without knowing the reason. The end result is not known.

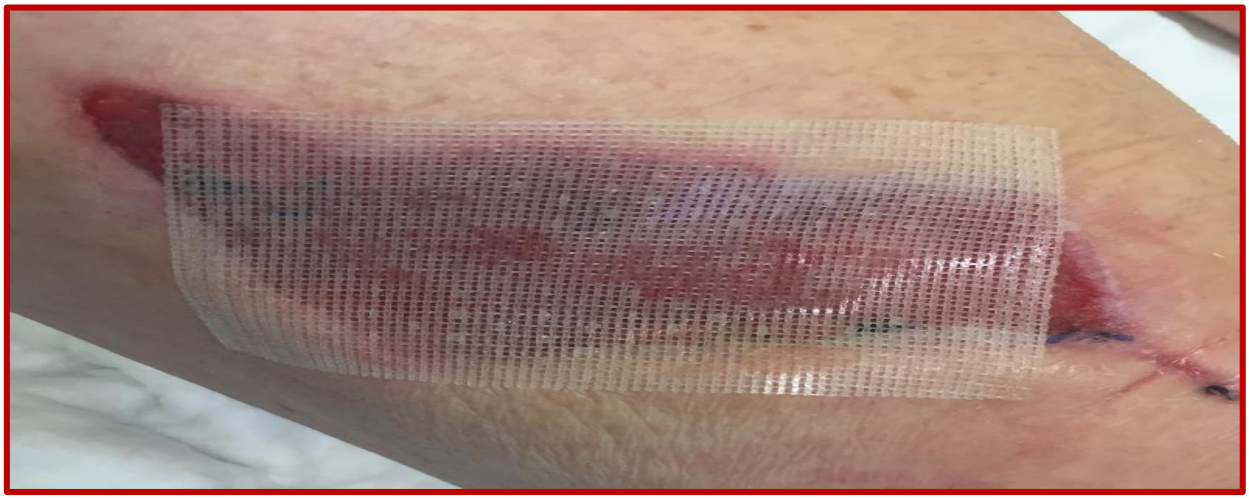


*Figure 12: Application of microdomes to the wound (12. 5. 2017) (Case example 3)*



*Figure 13: Wound after skin cell transplant, second wound dressing (19. 5. 2017) (Case example 3)*




*Figure 14: Wound 47 days after skin cell transplant (28. 6. 2017) (Case example 3)*

**Conclusion**

We found that two out of three wounds completely healed. The average time from cell transfer to healing was 64 days. In the third case, the patient for unknown reasons did not come to the control in the ambulatory setting, but we find that during the period of 47 days after the transfer of cells in the area of the wound was reduced by 94%.
The procedure was carried out in the ambulatory setting by a physician and nurse. We found the procedure of cell transfer using the CELLUTOME ™ Epidermal Harvesting System short and simple. None of the patients needed hospitalization and the procedure was performed without anesthesia, what is a great advantage for polymorbid patients. The patients did not have any pain or unpleasant sensations in the take-off site during and after the procedure. The take-off sites completely healed in all patients within 7 days. The wound management after cell transfer was carried out with latest wound dressings, which reduced the number of shifts and visits in the ambulatory setting. We found lower economic burden for the patient and the health system and improved the quality of life of patients. CELLUTOME ™ Epidermal Harvesting System can be successfully used in the treatment of various types of wounds, as the results of the different studies shown positive effects on healing processes. However, randomized controlled trials are needed on a larger sample of patients in order to be able to finalize the safety and efficacy of this system. In addition, the effects of other factors that influence the wound healing process should be studied as part of the integrated treatment of patients.

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# Apolipoprotein c-iii (apo-$c_3$) Metabolism in Patients with End Stage Renal Disease Treated with Long Term Hemodialysis

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**Abstract**

Background: End Stage Renal disease (ESRD) as it was historically termed is a term that encompasses all degrees of decreased renal function, from damaged–at risk through mild, moderate, and severe chronic kidney failure. ESRD is a worldwide public health problem. In the United States, there is a rising incidence and prevalence of kidney failure, with poor outcomes and high cost (see Epidemiology).

Material and Methods: The blood sample for routine analysis (lipidogram) and specific analysis was taken at 08 o'clock in the morning with the room temperature that variated from 19 to 24°C, before the hemodialysis session, minimum 12 hours of fasting - with tendency to avoid the absorption effect of food by the intestine as well as avoid absorption of lipids and formation of chilomicrones. In all samples regardless of their group, the concentration of ApoC-II and lipids were analyzed in a period of 12 months in a period of 12 months (the measurements were made every three months, it means we totally made 3 measurements in 9 months).

Results: The results from patients and controlling group for Apo-$C_3$ and lipid profile (ChT, TG, HDL-ch, LDL-ch) are given in table number 3. A significant statistical difference with $p<0.0001$ is found from the results of the lipidic profile and ApoC-III of patients with ESRD treated with HD compared with the results of the controlling group for the same parameters.

Conclusion: In this study patients with ESRD treated with HD have high parameters of ApoC-III, TG, LDL-ch but low concentrations of HDL-ch due to impaired catabolism of apolipoproteins in this specific group of patients. In all patients symptoms of CDV (myocardial infarction, angina pectoris, ischemia), acute coronary syndrome were noticed.

**Key words:** Apolypoprotein-$C_3$ (Apo-$C_3$), End stage renal disease.

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**Introduction**

Lipid metabolism disorders in patients with chronic terminal renal insufficiency were prescribed for first time in 1827 by Dr Bright, especially in the patients with nephrotic syndrome (10). It is a known fact that patients with chronic renal terminal insufficiency (CTRI) present clinically with early atherosclerosis and serious cardio-vascular complications, cerebro-vascular and peripheral arterial injuries more frequently in very large number in younger population compared to the healthy population. Recently it has been verified that uremic hyperlipidemia persists in the early stages of kidney weakening, prior to treatment with hemodialysis (HD) and it is presented as basic factor of the beginning of atherogenic processes in patients with chronic terminal renal insufficiency. Determination of lipid and apolipoproteins profile in particular of their abnormalities in patients with chronic terminal renal insufficiency (CTRI) in the early stages of the disease, and analysis of ethiopathogenic mechanisms can significantly help in proposing preventive measures (dietary, treatment) with which there will be reduced visible frequent appearance of dyslipidemia, atherosclerotic lesions and reduced incidence of atherosclerosis in patients with CTRI randomized by gender and age (11). Patients with terminal chronic renal failure (TCRF) mostly appear with the type IV type of secondary hyperlipoproteinemia (according to Frederickson's classification) where high concentrations of triglycerides dominates (hypetrigly-ceridemia values of 28-100%} (12,13). Apolipoprotein-$C_3$ also known as apo-CIII is a protein that in humans is encoded by the Apo-$C_3$ gene. Apo-CIII is a component of very low density lipopro-tein (VLDL). Apo-$C_3$ is a relatively small protein containing 79 amino acids that can be glycosylated at threonine-74. The most abundant glycoforms are characterized by an O-linked disaccharide galactose linked to N-acetylgalactosamine (Gal-GalNAc), further modified with up to 2 sialic acid residues. Less abundant glycoforms are characterized by more complex and fucosylated glycanmoieties.

Apolipoprotein C-III (apo-$C_3$) is an 8.8 kDa glycol-protein synthesized by the liver and intestines. APOC3 inhibits lipoprotein lipase and hepatic lipase; it is thought to inhibit hepatic uptake of triglyceride-rich particles.The Apo-$A_1$, Apo-$C_3$ and Apo-$A_4$ genes are closely linked in both rat and human genomes. The Apo-A-1 and Apo-A-4 genes are transcribed from the same strand, while the A-1 and C-III genes are convergently transcribed. An increase in apoC-III levels induces the development of hyper-triglyceridemia. Recent evidences suggest an intracellular role for Apo-$C_3$ in promoting the assembly and secretion of triglyceride-rich VLDL particles from hepatic cells under lipid-rich conditions.

However, two naturally occurring point mutations in human apo $C_3$ coding sequence, namely Ala23Thr and Lys58Glu have been shown to abolish the intracellular assembly and secretion of triglyceride-rich VLDL particles from hepatic cell. ApoC-III is highly associated with hypertriglyceridemia and is a powerful independent predictor of CVD risk in subjects without renal disease. In the circulation, apoC-III is associated with TRL and HDL exchanging rapidly between these lipoproteins. In vitro studies demonstrate that apoC-III inhibits LPL and HL activities and the uptake of TRL and their remnants by hepatic lipoprotein receptors (14,15). ApoC-III may also stimulate apoB and triglyceride synthesis and, hence, drive hepatic overpro-duction of VLDL particles. Elevated plasma apoC-III concentration, specifically its accumulation in TRL and their remnants, is a consistent feature of dyslipidemia in

CKD (16,17). Of note, we recently reported that moderate CKD is associated with hypertriglyceridemia related to delayed catabolism of triglyceride-rich VLDL and IDL particles. In CKD subjects, plasma apoC-III concentration was significantly elevated and was an independent predictor of impaired VLDL catabolism (18,19). The underlying mechanism for the increased plasma apo-$C_3$I concentration in these CKD subjects, however, has not been examined. A better understanding of the metabolism of apoC-III may clarify the association between dyslipidemia and CVD, with implications for better therapeutic management in the CKD population. In the present study, we investigated the kinetics of plasma apo-$C_3$ in predialysis, moderate CKD subjects (defined as those with an estimated glomerular filtration rate [eGFR] of 30–60 ml/min). We hypothesized that subjects with moderate CKD would exhibit catabolic defects in apo-$C_3$ metabolism. We also explored associations between the kinetics of plasma apo-$C_3$ and VLDL apoB and other markers of TRL metabolism, including apoA-V.

**Material and Methods**

The blood sample for routine analysis (lipidogram) and specific analysis was taken at 08 o'clock in the morning with the room temperature that variated from 19 to 24°C, before the hemodialysis session, minimum 12 hours of fasting - with tendency to avoid the absorption effect of food by the intestine as well as avoid absorption of lipids and formation of hilomicrones.

In all samples regardless of their group, the concentration of ApoC-II and lipids were analyzed in a period of 12 months (the measurements were made every three months, it means we totally made 3 measurements in 9 months). In the study we had totally 240 subjects, 100 of them were treated with HD, 100 were healthy that served as a controlling group. From the patients treated with hemodialysis 45(45%) were females, 54 (55%) were male, the average age was 58.00 ±18.00, treated more than 12 years with hemodyalisis in Clinical Hospital of Tetovo.
The controlling group consists 100 individuals 45 (45%) female and 55 (55%) male (table nr.1.) equal as the examined group in age, gender and nationality. In the cohort - prospective study (cross-section) total female participants were 100 (45%) the average age 59.60±12.80, 102 (55%) man with the average age of 58.70 ±14.60 (Table 1).

| ***Gender*** | **Nr.** | **Average age ± SD** |
|---|---|---|
| ***Male*** | 55 (55%) | 59.60±12.80 |
| ***Female*** | 45 (45%) | 58.70 ±14.60 |

*Table 1: Presentation of patients with ESRD according to genderand average age*

| Parameter | Reference values | Autors |
|---|---|---|
| **LT** | 4-10 g/l | Zollner & Kirsch (20) |
| **TG** | 0.68 – 1.70 mmol/l | G. Bucolla & H.David (21) |
| **ChT** | 3.1 – 5.2 mmol/l | CCAllain et al. (22) |
| **LDL-ch** | < 3.4 mmol/l, high risk> 4.1 mmol/l | Friedewalde & Frederickson (23) |
| **HDL-ch** | 1.6 mmol/l, high risk <0.9mmol/l | G.Warnick et a l (24) |
| **ApoC-III** | *5.5 – 9.5 mg/dl* | Tilly P.et al.(25) |

Table 2. Normal parameter of lipids and Apo-$C_3$ in the serum, and list of the author's name of the used method.

**Statistical processing of the examined materials**

From the basic statistical methods we have used: average arithmetical value and standard deviation X±SD. Statistical comparision of parameters of lipids and ApoC-III between two groups was analyzed with "Studentov t" test, while for the dependent or independent examples as well as for the nonnumeric tests we used: Mann-Whitney test. The differences of the statistical significance between the examined and the controlling group for the gained lipidic and ApoC-III values were analyzed with Anonova Two - Factor test, with statistical value for "p"< 5%=0.0005. The statistical dependence between the examined parameters were calculated with the linear regression formula (y=A+B) with statistical accuracy for "p" <1%=p<0.0001. The results of lipidic profile and apolipoproteine values are presented with graphs, tables, diagram processed with standard statistical program (statistic for windows).

**Results**

The results from patients and controlling group for Apo-$C_3$ and lipid profile (ChT, TG, HDL-ch, LDL-ch) are evidenced in table 3.

| ***Examined parameters*** | **ESRD patienients treated with HD** | **Controlled group** | ***p*** |
|---|---|---|---|
| ***TG mmol/l*** | **3.90 ± 0. 80↑** | **1.14 ± 0.50** | **<0.0001** |
| ***ChTmmol/l*** | **5.70 ± 0.90** | **4.30 ± 1.80** | **<0.0001** |
| ***LDL-chmmol/l*** | 4.70 ± 0.30 | 2.90 ± 0.50 | <0.0001 |
| ***HDL-chmmol/l*** | 0.80 ± 0.50↓↓ | 1.50 ± 0.80 | <0.0001 |
| ***Apo C-III mg/dl*** | 12.80 ±3.80 ↑↑ | 5,80± 0.90 | <0.0001 |

*Table 3*

From the results of the lipidic profile and ApoC-III of patients with ESRD treated with HD and from the results of the controlling group for the same parameters it can be noticed a significant difference with p<0.0001. The concentration of ApoC-III in the examined sample containing patients with ESRD were presented with average values 12.80 ±3.80

mg/dl in their plasma, in the controlling group the average values of ApoC-III were 5,80± 0.90 mg/dl. The difference between these two groups has a significant statistical meaning for p<0.0001. Facts that dovetail with various number of studies (citated in the study) of the metabolic disorders and high concentration of ApoC-III in patients with ESRD treated with HD. compared with the results gained from the co controlling group the patients with ESRD have 82- 85% higher levels of ApoC-III.
Table 4. Statementof Mann-Whitney U test parameter values displayed examine female patients and male patients treated with HD.

| *Parameters* | U | Z | p-level |
|---|---|---|---|
| *ApoC-III* | **1896.00** | **0.80** | **0.65** |
| *LT* | **1345.50** | **2.30** | **0.02** |
| *TG* | **1701.50** | **0.42** | **0.67** |
| *Ch* | **1651.00** | **-0.69** | **0.48** |
| *HDL-ch* | **1705.00** | **0.40** | **0.68** |
| *LDL-ch* | **1676.50** | **0.55** | **0.58** |

The difference between the value that was recorded average patients treated with dialysis in both sexes (Table 4) is nosignifikant for p <0.005 for larger number of parameters examined, significant statistical difference was verified only at LT with p = 0.0213

| *Report* | The correlation coefficient | *p* |
|---|---|---|
| *LDL-ch/HDL-ch* | **- 1.27** | **0.17** |
| *LDL-ch/Apo $A_1$* | **- 0.11** | **0.90** |
| *Apo $A_1$/ Apo$C_3$* | **0.04** | **0.66** |
| *Apo $A_1$/ Apo$C_2$* | **0.08** | **0.42** |
| *Apo $A_1$/Apo E* | **0.01** | **0.28** |
| *Apo$C_3$/Apo E* | **0.04** | **0.96** |
| *Apo$C_2$/Apo E* | **0.19** | **0.03** |

*Table 5. The correlation coefficient between the examined parameters*

Statistically significant positive correlation between the value recorded ApoC-III with Apo-E: Apo$C_2$ / ApoE: 0.96.

**Discussion**

Moderate chronic kidney disease (CKD) (defined by an estimated glomerular filtration rate of 30–60 ml/min) is associated with mild hypertriglyceridemia related to delayed catabolism of triglyceride-rich lipoprotein particles. Altered apolipoprotein C-III (apoC-III) metabolism may contribute to dyslipidemia in CKD. Dysregulation of lipoprotein metabolism may develop early in CKD with altered apolipoprotein concentrations despite normal plasma lipid concentrations. Of note, Kimak and Solski (25) reported that elevated plasma apoC-III concentrations, particularly the accumulation of apoC-III in VLDL particles, occur in moderate CKD (26).
Compositional changes in apoB-containing lipoprotein may render these particles less suitable as substrates for hepatic receptor-mediated uptake (27). Consistent with this notion, cellular studies report that apoC-III can abolish apoB- and apoE-mediated binding of lipoproteins to the LDL receptor, either by masking or altering the conformation of apoB and apoE (28,29). Elevated apoC-III concentration in moderate CKD was primarily a function of impaired apoC-III fractional catabolism. Holdsworth et al. (30) showed that renal impairment was associated with excess sialylation of apoC-III, which may render apoC-III-containing TRL particles less suitable as substrates for lipolytic degradation. Furthermore, the kidney is partly involved in the removal of apoC-III from plasma.

Decreased apoC-III fractional catabolism was associated with decreased VLDL particle catabolism in moderate CKD. The potential coupling of apoC-III and VLDL apoB metabolism is consistent with the role of apoC-III as a key regulator of apoB transport, as shown by recent studies using anti-apoC-III immu-noaffinity chromatography that demo-nstrates kinetic and structural hetero-geneity of apoB-containing lipopro-teins, based on apoC-III content.

Hence, the reduction in apoC-III fractional catabolism could partly be a consequence of moderate CKD. Pooled analysis of controls and CKD subjects showed a strong positive association between apoC-III catabolism and eGFR ($r$ = 0.569, P< 0.0001). Similar associations were observed in CKD subjects but failed to reach statistical significance. In addition, protein carbamoylation and accumulation of advanced glycation end products in the setting of CKD have been shown to alter protein structure, enzymatic activities, and binding to cell surface receptors. Hence, modification of apoC-III structure and binding could contribute to altered apoC-III catabolism in CKD (31,32). Elevated apoC-III concentra-tion is a common feature of dyslipidemia in CKD subjects. In addition, it is increasingly recognized as an important risk factor for CVD in the general popu-lation and may be an important target in CKD subjects. Moderate CKD subjects have elevated plasma apoC-III concentrations, a consequence of delayed apoC-III catabolism. Altered apoC-III catabolism in moderate CKD may also impair apoB metabolism, resulting in decreased catabolism and accumulation of TRL and their remnants in vivo. Modification of apoC-III catabolism may be a new therapeutic target for reducing CVD risk in moderate CKD. Future studies to assess the effects of statins and/or fibrates on apoC-III metabolism will provide better understanding of the cardiovascular benefits of such interventions in moderate CKD. A decrease in apolipoprotein-C-II/C-III ratio due to a disproportionate increase in plasma apolipoprotein-$C_3$ is a possible cause of lipoprotein lipase inactivation in uremia. It was also suggested that secondary hyper-parathyroidism is involved in the impaired catabolism of triglyceride-rich lipoproteins, provided an additional mechanism by which CKD may raise plasma triglyceride concentrations. Except of the low catabolic rate, the increased hepatic production of triglyceride-rich lipoproteins may also play a contributory role in the pathogenesis of dyslipidemia in renal disease. It is well known that CKD causes insulin resistance which can, in turn, promote hepatic VLDL production.

Thus, it could be hypothesized that the insulin resistance-driven overpro-duction of VLDL may significantly contri-bute to the development of hypertigly-ceridemia in patients with CKD. Hyperti-glyceridemia [due to accumulation of VLDL and remnant lipoproteins such as intermediate-density lipoprotein (IDL)], is also the predominant lipoprotein abnormality in a considerable number of cases with nephrotic range proteinuria. Synthesis of apolipoprotein it is direct impacted and controlled by genes unlike lipidic components that directly depend on the food consumption and lipometabolism.

**Conclusion**

In this study patients with ESRD treated with HD have high parameters of ApoC-III,TG,LDL-ch but low concentrations of HDL-ch approve for impaired catabolism of apolipoproteins in this specific group of patients. In all patients we had symptoms of CDV(myocardial infarction, angina pectoris, ischemia), acute coronary syndro-me.Most common dislipidemy was hipertri-gliceri-demy 90.0-

95.0%) in samples with ESRDI treated with HD-allow necessarily should be treated with fibrate, bezafibrate, clofibrate not with statine. Concentrations of ApoC-III in the examined group were 5-6 times higher compared to the controlling group. The role and clinical examination of apolipo-protein means early diagnostification and preve-ntion of visceral and peripheral atheroscle-rosis as accelerator for cardio/neuro vascular diseases. Determination of apolipoproteinic and lipidic concentrations enables preven-tive measurements for avoiding at least on etiopatho-logical factor for accelerate atherosclerosis. That's why we can conclude that exami-nation and treatment of apolipoproteine in the early stages of the diseases should be the first postulate in the treat-ment of CKD patients, this approach to the disease significantly will reduce the risk for CDV. Hypertrigliceridemy in uremic patients treated with HD is associated with genetic variations.

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# Management Strategy of Hyperthermic State in Critically Ill Patient.

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**Abstract**
Pyrexia is a protective physiologic response of the body against external and internal aggression. Temperature control is safe in and effective in septic shock but remain controversial in sepsis. Treating pyrexia to reduce oxygen consumption appears to have beneficial in cardiac arrest, low cardiac output and acute brain injury. Multiple therapeutic options are available for managing pyrexia, with precise targeted temperature management. Notably, the use of pharmacotherapy versus surface cooling has not been shown to be advantageous. When these two-therapy failed to control the extra-corporal method of cooling should be started. Renal replacement therapies are not typically indicated for temperature control but, in patients requiring renal support, they contribute to heat loss and participate in pyrexia control. Renal replacement therapies may represent a confounding factor in comparative trials on temperature control.
**Keywords:** Pyrexia. CRRT. SIRS. Aortic dissection.

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**Background**

Pyrexia is a common problem in ICU patients. The presence of pyrexia frequently results in the performance of diagnostic tests and procedures that significantly increase medical costs and expose the patient to unnecessary invasive diagnostic procedures and the inappropriate use of antibiotics. The main diagnostic dilemma is to exclude noninfectious causes of pyrexia and then to determine the site and likely pathogens of those with infections. ICU patients frequently have multiple infectious and noninfectious causes of fever [1] necessitating a systematic and comprehensive diagnostic approach. Around 35 % of in-hospital patients will develop pyrexia [2], increasing up to 70 % amongst the critically unwell [3], Pyrexia has long been thought of as a protective physiological response to help host defenses, although this is now being challenged. Despite recent advances, it remains unclear whether pyrexia or the physiological response to pyrexia causes morbidity and mortality and whether management of pyrexia with pharmacological agents or physical cooling actually confers benefit.

**Pathophysiology**

The process of tightly regulating body temperature within a specified range (±0.2 °C), or thermoregulation, is an essential homeostatic mechanism. Thermoregulation consists of afferent signaling via warm and cold thermoreceptors, central processing within the hypothalamus and efferent response. These responses include regulation of peripheral blood flow, diaphoresis and shivering. Whilst there is strict control there is also rhythmic temperature variabilityover a 24-h period [4], This circadian rhythm is altered in critically ill patients with both temporal shifts and a larger magnitude of variation, both increasing with disease severity [5]. Pyrexia secondary to the systemic inflammatory response should be distinguished from hyperthermia resulting from excessive heat production, as observed in heatstroke and malignant syndromes, or from ineffective heat loss. Here we will present two cases of life threating hyperpyrexia in severe ill patient. Case **one**; Ventricular septal defect (VSD) is a rare but lethal complication of myocardial infarction (MI). The event occurs 2-8 days after an infarction and often precipitates cardiogenic shock. Male patient 62 years old was diagnosed with interventricular septal defect after anteroapical myocardial infarction. Hemodynamic situation was very bad, in cardiogenic shock because of low cardiac output with low EF 30%. After coronary angiography, Intra-Aortic Ballon Pump (IABP) was inserted (Arrow set 40 cc balloon) via left femoral artery for circulatory support. After preparation the patient was immediately put in operation room. The operation consisted in closure of VSD with synthetic patch Dacron, left ventricular aneurism repair and two aorto-coronary bypass. Weaning from heart lung machine was easy with little hemodynamic support from vasoactive drugs. Urine output during whole operation and early hours was normal. Hours later after operation the temperature arrived till 39.9° C associated with elevated heart rate, low blood pressure, elevated vasoactive drugs and no urine output (septic shock). Four hours after installation of acute kidney injury Continuous veno-venous hemofiltration (CVVHF) was started via left femoral vein (12 FR double lumen Arrow catheter was inserted). Hemofiltration was performed with Prismaflex -Gambro machine and M-100 AN-69 Filter membrane and with effluent dose 25 ml/kg/hour. After renal recovery, 48 hours later, hemofiltration was stopped and patient continued to have good urine output and

good hemodynamic performance. Amiodarone iv was started also due to paroxysmal atrial fibrillation with high frequency, initially 300 mg loading dose, and after 1000 mg for first 24 hour. In third postoperative day, after termination of hemofiltration, the temperature reached again high value 40° C associated initially with high heart rate, rhythm disorder till life threating arrhythmia ventricular fibrillation multiple times (4 times in hour), converted with electric cardioversion. Physical method of cooling and antipyretic medication was started but without success, meanwhile patient continued to develop ventricular fibrillation. So, we decided to start again CRRT, without warming lines, to cool down the patient. After restarting the hemofiltration, the temperature slowly went down and heart rate was stabilized in normal sinus rhythm with no more life threating arrhythmia. After three days of hemofiltration, IABP was removed and hemofiltration was stopped and patient was disconnected from ventilator. The patient was discharged from ICU in normal hemodynamic situation, good urine output and without fever.

*Case* **two*;*** Aortic dissection remains a devastating vascular catastrophe with a high mortality rate if not diagnosed and managed promptly. However, its signs and symptoms are unpredictable. As the dissection progresses, other organs can be affected and can obscure the inciting diagnosis. Acute aortic syndromes have a mortality as high as 1% per hour for acute type A aortic dissections. A 67-year-old male with no significant past medical history presented to the emergency room with the chief complaint of sudden onset of substernal chest pain radiating to his back. Acute aortic dissection was suspected and then confirmed with contrast CT. After diagnosis, patient was transferred in cardiac surgery department and was prepared for emergency surgery.

Blood test and creatinemia was normal before CT. Urine output, blood pressure, blood gas and electrolytes were normal before surgery. Extra-corporal circulation was instituted in retrograde way via right femoral artery and right atrium. Cooling down in 25°C rectal temperature aortic arc was inspected releasing the aortic clamp, to find the entry intimal point. After 22 minutes circulatory arrest, hemi-arc aortic replacement was performed and 5 minutes retrograde perfusion via superior vena cava. After rewarming the patient was disconnected from heart lung machine with no circulatory support. Due to massive bleeding, a large quantitative blood and fresh frozen plasma was transfused in immediately postoperative period. High doses of noradrenalin e dopamine were used to maintain normal blood pressure and urine output. 48 hours after operation, the fever was installed with elevated temperature till 40,5° C. Decreasing temperature with physic and pharmacologic failed and the temperature remained elevated. In this situation CRRT was started via left femoral artery with no warming blood lines. The temperature gradually decreased, in normal value. During this period, we didn't use antipyretic drugs and the temperature was maintained in normal values. During the hemofiltration, urine output was normal and vasoactive drugs dose were minimal. Hemofiltration was stopped four days later when the patient didn't t had any more fever. After ten days of mandatory ventilation the patient was disconnected from ventilator in good situation but with motoric neurologic sequel. The patient was transferred in the ward for physiotherapy treatment.

**Discussion**

***Should we treat pyrexia?***
***The cost of pyrexia***

The cost of pyrexia should be considered in several ways. Pyrexia has a metabolic cost such that cooling febrile ICU patients will reduce oxygen consumption by 10 % per °C [6], Small studies in sedated patients demonstrated a significant reduction in V02 (the rate of oxygen consumption) and VC 02 (the rate of carbon dioxide elimination) during cooling [6, 7], In septic shock, temperature lowering by ibuprofen was associated with increased lactate clearance [8]. In patients with acute brain injury, pyrexia may increase intracranial pressure and worsen secondary ischemic damage [9], These suggest the possibility of therapeutically offloading the cardiorespiratory system and preserving brain function at times of stress. Whether the cost of pyrexia translates to unfavorable outcomes remains unknown. The incidence of pyrexia is decreasing over time with an absolute reduction of 35 % found in Canadian ICUs [10]. This did not coincide with an appreciable decrease in mortality, suggesting that important outcomes may not be affected by the incidence of pyrexia. Perhaps the question should not be "should we treat pyrexia?" but "in what conditions is it beneficial to treat pyrexia?". This is highlighted in a large observational study where fever within the first 24 h of ICU admission was significantly associated with decreased mortality in patients with infection while peak fever >40 °C was associated with increased mortality in patients without infection [11], An observational study on 1400 non-neurological critically ill patients also revealed different associations between the maximal peak temperature and mortality according to the presence of sepsis or not [12]. Fever >39.5 °C was associated with increased mortality in non-septic patients while moderate fever (37.5-38.4 °C) was associated with decrease mortality in septic patients. Moreover, this study highlights different impacts of fever treatment. Physical cooling did not alter the mortality risk and the use of antipyretic agents did not alter mortality in the non-septic group but did increase 28- day mortality in the septic group (adjusted odds ratio 2.61 (P = 0.028) for nonsteroidal anti-inflammatory drugs (NSAIDs) and 2.05 (P = 0.01) for paracetamol [12].
In patients with acute brain injury, pyrexia has been identified as an independent risk factor for increased mortality and poorer neurological outcome [10, 13-14].
Results are, however, inconsistent as fever could be a marker of brain injury severity [15]. The presence or not of infection may also alter the relationship between body temperature and outcome [16, 17]. In more than 100,000 patients, a negative association between early peak fever above 39 °C and hospital mortality was found in patients with traumatic brain injury and stroke but not in patients with central nervous system infection [17].

***Pharmacological methods of cooling***

Nonspecific medication used to reduce heat production in the critically ill patient includes sedative agents and neuromuscular blocking agents. More specific antipyretic medications include paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs). Paracetamol acts by selective inhibition of the cyclooxygenase-3 enzyme (COX-3); this results in reduced production of fever generating prostaglandins. With a relatively limited side-effect profile in most patients, paracetamol is widely used in critical care patients with fever. The other major group of antipyretics are NSAIDs—the risks of exacerbation of renal impairment and gastric ulceration with the use of these drugs mean

that they are often relatively contraindicated in the critically ill population.

***Physical methods of cooling***

Initially simple methods can be instituted, such as uncovering the patient whilst preserving their dignity and using cold towels placed across the patient or in the axillae. If ice packs are used, care must be taken to ensure that the ice does not come into direct contact with the patient's skin and cause subsequent thermal injury. Cooling blanket systems utilize circulated cold water and a feedback control system monitoring the patient's core temperature to achieve and maintain normothermia. In refractory cases of hyperthermia, more invasive methods of cooling may need to be implemented. This begins with rapid infusion of cooled i.v. fluids. Other invasive methods of cooling include the installation of cold fluid into body cavities such as the stomach, pleura, bladder, and peritoneum. Continuous renal replacement therapy (CRRT) is often regarded as one of the more important advances in intensive care medicine in recent years. The use of CRRT in critically ill patients with acute renal failure, combined with cardiovascular instability, severe fluid overload, cerebral edema or hyper catabolism and high fluid requirements, is widely accepted. CRRT is also used in some non-renal indications, and these are less well established. These non-renal indications are based on the (presumed) elimination of inflammatory mediators [such as systemic inflammatory response syndrome (SIRS) and sepsis, acute respiratory distress syndrome (ARDS), and cardiopulmonary bypass (CPB)], on the removal of fluid (ARDS, CPB, chronic heart failure), or on the elimination of other endogenous toxic solutes (inborn errors of metabolism, lactic acidosis, crush injury, tumor lysis syndrome).

In our cases there was no indication to start again CRRT for acute kidney injury, because the patient had good urine output and little bit alteration of renal markers. Because we failed to decrease the elevated temperature with pharmacological and physical method, only CRRT had wonderful result non-only in temperature control but also in hemodynamic and rhythm stability.

***Pharmacological versus non-pharmacological methods.***

A meta-analysis of 11 trials, from 48 reviewed, considered pharmacological versus non-pharmacological antipyretic treatments with outcome measures being targeted temperature and haemodynamic effects [20]. It found that intravascular as opposed to surface cooling had better target temperature results, although there was a non-significant trend towards higher mortality. Only three small studies consisted of a head-to-head comparison of pharmacologic and non-pharmacologic methods, for which the analysis was inconclusive [20], In sepsis, the three largest RCTs compared ibuprofen [8], paracetamol [19] and surface cooling [18] against placebo or no treatment. The maximal between-group differences in temperatures reported were 0.6 °C on day 1, 0.9 °C at 10 h and 1.6 °C at 12 h, respectively. Although inconclusive, these data may suggest that controlling fever by surface cooling is more efficient than by antipyretic agents.

***Summary***

Temperature is not only an important clinical marker of severity of illness but also an independent predictor of morbidity and mortality in critically ill patients. Close monitoring and regulation to avoid extremes of body temperature

is particularly important in the critically ill patient. This will prevent the uncontrolled disruption of homeostasis and associated subsequent organ dysfunction and failure. Additional studies are needed to explore and clarify the role of antipyretic treatments in febrile critically ill adult patients (pharmacological vs non-pharmacological treatment)

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# Managing the Patient Evidence Base Through Trauma Cases in Military University Hospital of Albania

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**Abstract**

**Background** The level of management of traumatic health care services in Albania as a service of the Military University Hospital in Emergency Care differs in relation to other university hospitals across the country, mainly due to changes in the public health of the population. The article aims to present the management of traumatic patients at the Military Hospital in Albania, providing examples of the number of cases that have been addressed in the spread of this disease as epidemiology in Albania. The literature review and data statistics will be carried out by using the hospital records that will be used for further research in Albania. In addition, there is a study of international reports on Trauma management issues, trauma care and quality in Trauma. Much of the results consider the necessity of adopting a comprehensive traumatic system, focusing on quality management and improving trauma care to increase survival and reduce complications to the wounded. Urban conditions and public health policies are the most important factors in developing and implementing programs to improve emergency trauma care services. The heterogeneity of the population and its geographical distribution, the complexity of road accidents, are challenging factors for quantitative research on trauma management and the effectiveness of its care. Staff training in all areas, combined with the existence of modern vehicles and equipment, means of communication and timely transfer of the ambulance, contribute to the treatment of patients with urgent trauma, life saving and prevention of all types of disabilities.
**Keywords.** Military University Hospital, health trauma management, information, quality of trauma patients

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## Introduction

In Albania, roads are a local public concern and are the main cause of trauma from accidents. Road safety is the goal of national, regional interventions aimed at preventing trauma. (Hughes et al, 1995). Albania, for its bad luck, is far behind the provision of road safety in relation to the EU average, the number of accidents[1] the number of deaths from car accidents. Road traffic accidents are a consequence of the loss of resources, resources and human resources. At one time, there is a considerable cost to society. This abstract realizes a presentation and assessment of the trend of trauma in Albania, the results of which can be used as a reference guide for designing and evaluating trauma management elements in the country.

## Chapter I

### University Hospital of Trauma & Military Hospital

In Albania, the Central Military University Hospital is a tertiary hospital which provides a specialized poly trauma health care. The Central Military University Hospital has the university status from the beginning of year 2002[2] The Trauma & Military Hospital is the only specialized hospital in the country, qualified with the mission "trauma management at the national level". The hospital has specialty basis: Emergency, Surgery, Orthopedics, Neurosurgery, ENT, Ophthalmology and Maxillofacial, ICU, Reconstructive Surgery, Therapy and Rehabilitation services. It has a capacity of 192 beds, but in emergencies, disasters and catastrophes the capacity increases up to 250 beds with 321 people as staff (81 doctors, 200 nurses, technicians pharmacists, 40 administration & logistics). In a Military Hospital, the emergency department receives an average of 7 – 8 patients with poly trauma every day, of these patients, some present directly and many are referred from other hospitals from the different regions because the hospital is located in a strategic geographic position. It is nearby crucifying the national road north-south, which makes possible the transportation of the wounded in a car accident on time. At the moment various problems are faced in the management of patients with poly trauma. In EU[3], road accidents annually lead to the death of more than 40,000 people, while the number of people involved exceeds 1.7 million. The most vulnerable group of people is 14 to 25 years old, where accidents in the streets are the cause of death. The main indicators of road safety in Albania have shown improvement, however, what they are doing in comparison with the EU.

## Chapter II

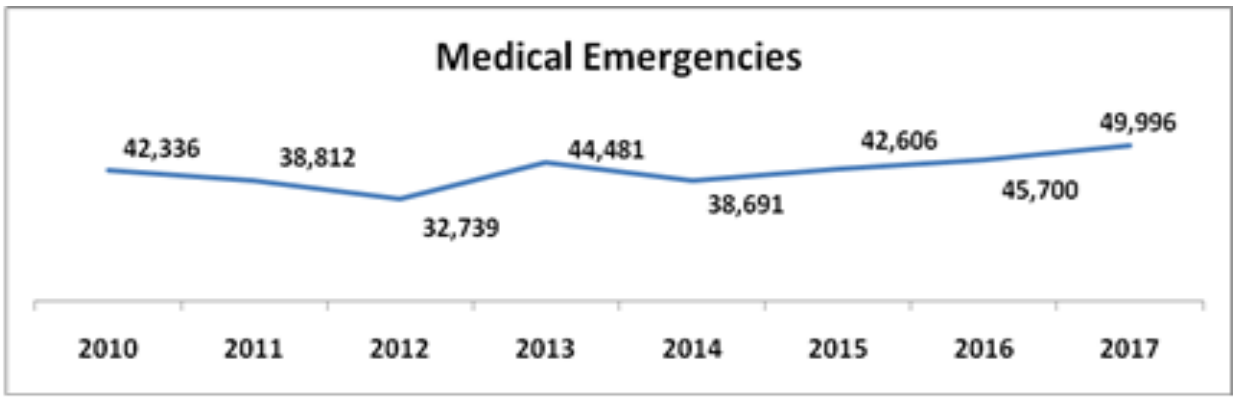
### Trauma cases in Albania: the period of 2010 – 2017 years

Our study has found a high percentage of admissions for hospital trauma for the period 2010 - 2017. In order to manage this situation, the number of traumas increases is a reflective and retrospective study of trauma management in the hospital. The studies are pointing to the statistical statistics of the Hospital, reviewing the clinical patient screenings that have been presented to the Emergency

[1] European Commission, Annual Accident Report. European Commission, Directorate General for Transport, June 2016.
[2] Council of Ministers no. 375, date 13.07.2002

[3] Accidents at work statistics, Eurostat Statistics Information, November 2016

Hospital during the last few years. Emergency service has received 335 361 emergency patients, from 2010 to 2017. 64% of them have had surgical emergencies and 36% of them therapeutical urgencies.




| Years | Total | Surgery | Medicine in Emergency |
|---|---|---|---|
| 2010 | 42.336 (12.62%) | 24.849 (11.58%) | 17.487 (14.49%) |
| 2011 | 38.812 (11.57%) | 22.173 (10.33) | 16.639 (13.79%) |
| 2012 | 32.739 (9.76%) | 19.312 (9%) | 13.427 (11.12%) |
| 2013 | 44.481 (13.26%) | 22.100 (10.29%) | 22.381 (18.54%) |
| 2014 | 38.691 (11.54%) | 26.847 (12.51%) | 11.844 (9.81%) |
| 2015 | 42.606 (12.70%) | 30.392 (14.16%) | 12.214 (10.12%) |
| 2016 | 45.700 (13.63%) | 32.334 (15.06%) | 13.366 (11.07%) |
| 2017 | 49.996 (14.91%) | 36.661 (17.08%) | 13.334 (11.05%) |
| Total | 335.361 (100) | 214.668 (100) | 120.693 (100) |
| Average | 41.920 ˜ 42.000 | ˜ 27.000 | ˜ 15.000 |

*Graph 1, Table 1 The medical emergencies (2010 – 2017)*

In 2017, there were 103.360 people out of which 62.2% males, with average age of 54.12 years. A total of 48.65% are emergency examiners, 46.90% of Intervention and Microsurgery in Emergency ODS, 4.44% of patients are treated with daily card (24 hours), with cardiac admissions from hospital emergency to 66.7% of cases. In most cases, this may be related to a study that would last long.

However, we do not consider that any day occasion was avoided by the hospital. The average time devoted to the study was on average 30 days, a little higher than expected, due to the high spread of the number of traumas in recent years. It was decided to study 80% of patients admitted in emergencies for 2017, their diagnosis was identified in all cases treated in emergencies because of 80% of the total number of patients. According to the census in medical emergencies during the past three years, etiology of trauma in UTMH emergency is (i) car accidents 12%; (ii) gunshot wound 4.8%; (iii) work trauma 38.8%; (iv) wound caused by blind and sharp tools19.4%. In Albania, the number of deaths by main causes period 2015, 2016, 2017 show that the number of accidents in Albania has been increasing. In 2017, the number of accidents increased by 38.23% compared to 2016. The number of deaths in Albanian roads during the period 2000-2017 was 37.1%. However, although there has been a significant increase in the number of deaths, there has been a significant deviation from the goal set in Albania, this can be described as a period that is not used enough to reduce the number of accidents.

| *Causes of death* | *2015* | *2016* | *2017* |
|---|---|---|---|
| *Natural* | 86,8 | 87,4 | 86,5 |
| *Accident* | 2,2 | 2,1 | 3,4 |
| *Suicide* | 1,0 | 1,1 | 1,5 |
| *Homicide* | 0,4 | 0,4 | 0,4 |
| *Accidentwork* | 0,3 | 0,2 | 0,2 |
| *No information* | 9,3 | 8,8 | 8,00 |
| *Total* | 100,0 | 100,0 | 100,0 |

*Table 2 The percentage of deaths by main causes: 2015-2016-2017*

| *Year* | *Hospitalization* | *Morbidity* |
|---|---|---|
| *2010* | 7.423 (14.94%) | 2.1 |
| *2011* | 6.023 (12.11%) | 2.5 |
| *2012* | 5.770 (11.62%) | 2.1 |
| *2013* | 4.835 (9.73%) | 2.2 |
| *2014* | 5.827 (11.72%) | 2.0 |
| *2015* | 5.870 (11.81%) | 3.0 |
| *2016* | 6.472 (13.02%) | 2.0 |
| *2017* | 7.475 (15.04%) | 2.0 |
| ***Total*** | **49.695 (100)** | **2.2** |
| ***Average*** | **6.200 ˜ 6.500** | **˜ 2.2** |

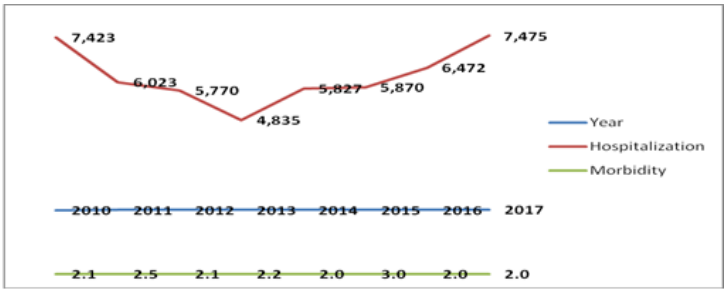



*Table 3, Graph 2 The trauma hospitalization by period 2010-2017*

It turns out that the mortality is constant while the number of cases hospitalized by Trauma is growing; 13.41% compared to 2016. And in the total of the period 2010-2017, their average/1000 is 6,200 patients (2.2 morbidity).

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|---|---|---|
| Hospitalization | 7,423 | 6,023 | 5,770 | 4,835 | 5,827 | 5,971 | 6,620 | 7,475 |
| Surgery Hospitalization | 5,421 | 4,639 | 4,516 | 4,108 | 5,033 | 5,269 | 5,784 | 6,678 |
| Trauma in Total | 2,597 | 2,272 | 2,418 | 2,354 | 2,432 | 3,135 | 3,204 | 4,971 |
| Incidence (Trauma ÷ Emergency) | 61,3% | 58.5% | 73.8% | 53% | 62.8 % | 73.5 % | 70,1 % | 99,4 % |

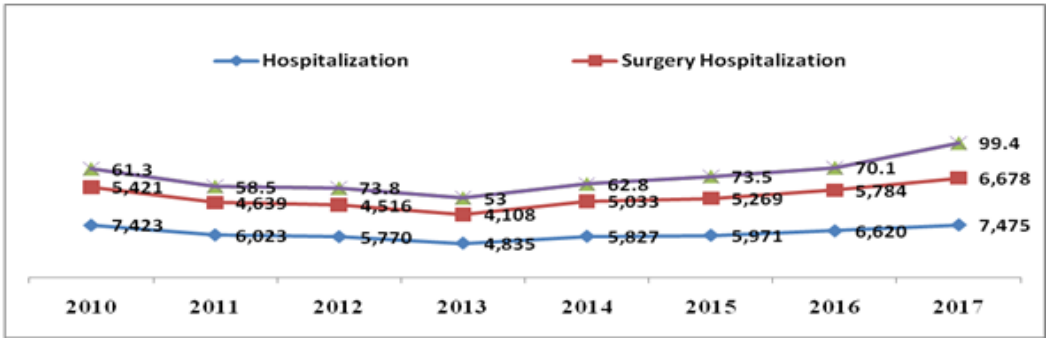



*Table 4, Graph 3 The surgery hospitalization and the incidence by period 2010-2017*

The incidence of traumas in Albania has been rising considerably by 99.4% for 2017, from which 6,678 patients have undergone operational interventions and 7475 patients have been hospitalized. The incidence trend is growing considerably for the country. WHO (2016), estimated that, 1.2 million deaths occurred due to road accidents, 3242 deaths per day and over 20 million injured each year. The World Bank is working closely with the Global Road Safety Facility for the Strategic Plan 2013-2020, this strategic plan sets out how it will contribute to the broader policy. All transport programmers will have a road safety component as it is expected that deaths due to third country road accidents up to 2020, (daly index) (Murray J. et.al. 1996). Traffic accidents do not have the same meaning among them. As far as accidents are concerned, accidents have been classified as: (i) fatal accidents, (ii) light / light injuries, and (iii) accidents with wounds. In Albania, official accidents are registered from the category (i) serious fatalities and (ii) light injuries.

## Chapter III

## The management of patient trauma care

According to (Donabedian's theory, 1988) of emergency services, many believe that the "boarding" of emergency patients awaiting inpatient beds compromises quality of care. To assess the quality of care for boarded patients, we used the "structure-process-outcome" framework described

by (Donabedian, 1988). His three part approach makes quality assessment possible assuming structure (attributes of material or human resources and organizational structure) influences process (what is actually done in giving and receiving care), which influences outcome (health status) (Liu et.al., 2011). To better study the quality of care of boarded patients, one should identify and understand the mechanisms accounting for any potential differences in care three components are identified: (i) the structure (facility - infrastructure and human resources), (ii) the processes (organization, operation, organization and provision of social services), (iii) of actions and services). In the Traumatic Hospital, patients are managed based on organizational activity to reduce the patient's waiting time and to improve the quality of trauma care. This is done in the first contact with the patient, where the first clinical practitioner evaluates, treats, and recommends the patient to other services in a safe manner (NSV Health 2012). The provision of quality in the Trauma Hospital implies an assessment of the actual level of services offered and attempts to change them when necessary (Black, 1990). Quality can be measured and the purpose of measurement is (i) confirmation that the full benefits of medical knowledge are successfully applied to the needs of the patients. (ii) maintaining and improving the level of care. (iii) the ongoing assessment with which the profession maintains and defines its standards and remains responsible for the public concerned. (EU, 2016).

## Recommendations

Albania is at risk of spreading traumatic epidemics in the country. Trauma work, car accidents occupy a leading place in the epidemiological profile. For this purpose, the steps of defining the Trauma Benchmarking model should be considered to clearly identify what needs to be measured, the quality standards for treating trauma patients, and the electronic database with the patient data to be analyzed and to set the performance gap, set the objectives of action plans according to trauma staff specialties, staff training in all areas, combined with the existence of modern vehicles and equipment, the means of communication and timely transfer of the ambulance, contribute to the treatment of patients with urgent trauma, life saving and prevention of all types of disabilities in Albania.

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# ESTES Congress 2019




## *Important Dates*

| | |
|---|---|
| Start abstract submission | **Mon, August 27, 2018** |
| Deadline abstract submission | Fri, October 19, 2018 |
| Start online registration | Mon, November 26, 2018 |
| Notification abstract acceptance | Fri, December 14, 2018 |
| Deadline for early bird registration, registration cancellation | Fri, February 15, 2019 |
| End of regular fee | Fri, April 19, 2019 |
| Congress ECTES 2019 | **May 5-7, 2019** |

# *Event Calendar*

Endorsed = Events taking place in ESTES member countries and/or organized by ESTES institutional members; discount for ESTES members is granted
Recommended = Events taking place in non-member countries; discount for ESTES members is granted
Recommended = National events by institutional members or other recommended events

## August 2018

[26]AUG- [29]**MRMI Course** Bangkok, Thailand. *Event Type:*Endorsed

## September 2018

[6]SEP- [8]**37th Annual Meeting of the European Bone and Joint Infection Society**Helsinki, Finland. *Event type:*Endorsed

[17]SEP- [18]**Workshop on Visceral Trauma (Definitive Surgical Trauma Care – DSTCTM)** Universitätsklinik Graz - Department of Surgery, Auenbruggerplatz 29, 8036 Graz, Austria. *Event Type:*Endorsed

[24]SEP- [25]**Advanced Cadaveric Trauma Surgery** Newcastle Surgical Training Centre. *Event Type:*Endorsed

## October 2018

[4]OCT- [6]**54. Jahrestagung der ÖGU** UNTERARM UND HAND Wyndham Grand Conference Centre Hotel, Salzburg, Austria. *Event Type:*Endorsed

[23]OCT- [26]**DKOU 2018** Messe Berlin, Jafféstraße, 14055 Berlin*Event Type:*Endorsed

## November 2018

[2]NOV- [3]**Trauma 2018** Moscow, Russia..*Event Type:***Endorsed**

# Congress Co-Secretary

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# Guidelines of Abstract Submission

- Abstracts are to be submitted through the internet websitehttp://astes.org.al/astes/congressand from email; *abstractsubmission@astes.org.al; astesorg@gmail.com; actes2018@gmail.com; medical.conference@unite.edu.mk* following strictly the specific guidelines.
- Abstracts may be submitted in English only. Authors are free to finalize their texts and submit their abstracts at any time before Friday, August 31, 2018 12:00 CET+1
- No changes can be made after this deadline.
- Confirmation of acceptance by the Program Committee will be published at http://www.astes.org.al/congres1.php by SEPTEMBER 15, 2018.
- In order to avoid disruption of Session by "no-shows", accepted Abstracts will only be integrated in the Final Program if the CONFERENCE registration form and payment of the Presenting Author have been received by NOVEMBER 1, 2018!
- Length of the abstract text is limited to 2'500 characters (incl. blanks). Text shall be structured: ***Introduction – Materials & Methods – Results – Conclusion.*** One table and one picture only may be included.
- Abstracts must include at least 50% new data if previously published or presented at a meeting.
- After acceptance, exchange of the Presenting Author will only be possible in case of approval of the written request by the Program Committee ACTES 2018.
- You may list up to eight (8) Co-Authors and four (4) institutions/ countries on the abstract form.
- The Presenting Author's Name must be identical to what will be written in the Conference Registration Form.
- Mailing Address - Any communication regarding the acceptance will only be given to the Submitting Author at the address respectively at the e-mail address as registered.
- Each Abstract can be used for one presentation only.
- Each Presenting Author of an accepted abstract must submit a Disclosure Form showing commercial, financial or research relationships or interests.
- Delegates registering in the category of "Student" may present abstract at ACTES 2018.
- All Abstracts become the property of the Albanian Society for Trauma and Emergency Surgery (ASTES). Submission of an Abstract represents permission to duplicate, publish and disseminate the work.
- ***NOTE:*** In case you should encounter any difficulties with the submission of your Abstract or with the publication of accepted Abstract presentations, please contact the Abstract Secretariat ACTES 2018 at Phone: ***+355692056123, +355672743431*** e-mail: ***secretary@astes.org.al; astesorg@gmail.com***

# *PRELIMINARY TOPICS*

*The published programme is subject to change. Regularly updated information can be found on www.astes.org.al*

*Polytrauma – Definition revisited & Trauma registries*
*Education and organization systems in trauma and emergency surgery*
*Update in prehospital care of trauma and emergency surgery*
*Emergency Medicine & Emergency Surgery & Acute care surgery& Trauma management in the same or separate unit...*
*Skeletal trauma & Sports medicine*
*New developments in fracture care.*
*Complex hip and pelvic fractures.*
*Reconstruction surgery and plastic surgery as integral part trauma management.*
*Are the burns services part of trauma services?*
*Head and Spine injuries in polytrauma.*
*Thoracic trauma management*
*Damage control principles in all specialities*
*Vascular Trauma management.*
*Minimally invasive techniques in trauma and emergency surgery*
*Blunt abdominal trauma versus penetrating abdominal injuries – differences in management?*
*Abdominal trauma: diagnostic algorithm and decision parameters for surgery treatment*
*Anaesthesia and resuscitation in trauma and emergency surgery. Advanced techniques for non-invasive & invasive monitoring.*
*Advances in Intra abdominal infection management*
*Point of care ultrasound, CT, MRI in trauma and emergency surgery*
*Acute elderly patients*
*Pediatric trauma*
*Controversies in Disaster & Military medicine. Disaster medicine, is it a surgical problem?*
*Updating in Nurses services in Trauma Care & Acute care surgery*
*Quality control in trauma cases*
*Outcome of rehabilitation procedure after head and skeletal trauma...*
*Innovations in Emergency Surgery & Trauma management... Telemedicine... new trends in Emergency Surgery & Trauma management*

# ACTES 2018 CONGRESS VENUE





Metropol Lake Resort
OHRID

*Settlment Konjsko B.B. 6000 Ohrid - Macedonia*
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***Email****: info@metropol-ohrid.com.mk*

# ACTES 2018 IMPORTANT DATES

| | |
|---|---|
| *Start abstract submission* | Thur, February 01, 2018 |
| *Deadline abstract submission* | Fri, August 31, 2018 |
| *Start online registration* | Mon, August 20, 2018 |
| *Notification abstract acceptance* | Sat, September 15, 2018 |
| *Deadline for early bird registration, registration cancellation* | Mon, October 15, 2018 |
| *End of regular fee* | Thur, November 01, 2018 |
| *Congress ACTES 2018* | November 8-10, 2018 |

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Albanian Society for Trauma and Emergency Surgery
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# 2nd Annual Albanian Congress of Trauma & Emergency Surgery

&

# 3rd Conference of Faculty of Medical Sciences, University of Tetova

**OHRID MACEDONIA**

**8-10 November 2018**

Submit your abstracts now



## Abstract Submission Deadline

## Friday 31 August

Submit abstracts online at: astes.org.al, abstractsubmission@astes.org.al

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