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# Postoperative Biological and Physiological Gastrointestinal Changes after Whipple Procedure

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## Abstract

In the last years there was an increased interest towards the pancreatic cancer, especially considering its growing incidence (rapidly becoming the fifth cause of death by cancer in the developed countries), lack of any sustainable markers and/or risk factors and the chilling fact that almost 95% of the patients with this disorder are presenting to the hospital in the advanced and unresectable stages. Even more, although known and developed for almost 70 years, the surgical approach for the pancreatic cancer is a subject of debate because its efficacy and postoperative biological changes. It is known that the most common surgery in chronic pancreatitis and pancreatic cancer is represented by the Whipple pancreaticoduodenectomy. Still, after an extended resection and reconstruction of the upper gastrointestinal tract, it seems that the digestive physiology can be disrupted. In this way, in the present mini-review we will describe some postoperative gastrointestinal biological and physiological changes after Whipple procedure, by mainly focusing on the gastrointestinal motility, bone demineralization, dumping and re-resection, as well as on the affected pancreatic function, postoperative weight loss and remnant pancreatic fibrosis and how the management of this related pathological aspects can be applied in these cases.

**Keywords:** Pancreatic cancer; Pancreaticoduodenectomy; Pancreatectomy; Whipple procedure; Gastrointestinal physiology

## Background

Lately the oncological research literature depicted an increased interest towards the pancreatic cancer, especially considering its growing incidence (rapidly becoming the fifth cause of death by cancer in the developed countries), lack of any sustainable markers and/or risk factors and the chilling fact that almost 95% of the patients with this disorder are presenting to the hospital in the advanced and unresectable stages [1].

Even more, although known and somehow developed for almost 70 years, the surgical approaches for the pancreatic cancer are only improving the morbidity and hospital postoperative mortality, with very few effects on survival rate. Moreover, there are still a lot of unknowns regarding the efficacy of the surgical approaches in pancreatic tumors and their postoperative biological changes [2].

In this way, it is known that the most common surgical technique in chronic pancreatitis and pancreatic cancer is represented by the Whipple pancreaticoduodenectomy, which represents the classical resection techniques for tumors and basically consists in removing the head of the pancreas, as well as the gallbladder, a part of the duodenum and the pylorus and antrum. Moreover, it is important to mention that in the aforementioned cases, after an extended resection and reconstruction of the upper gastrointestinal tract, the digestive physiology will be disrupted [1,2].

In this way, in the present mini-review we will describe some postoperative gastrointestinal biological and physiological changes after Whipple procedure, by mainly focusing on the gastrointestinal motility, bone demineralization, dumping and re-resection, as well as on the affected pancreatic function, postoperative weight loss and remnant pancreatic fibrosis and how the management of this related pathological aspects can be applied in these cases.

## The Gastrointestinal Motility

In this context, we will shortly describe some basal aspects regarding the gastric acid secretion and the gastrointestinal motility. Thus, regarding the gastric acid secretion, the main components of gastric juice are the

acid, the pepsin, the gastric lipase and the intrinsic factor. The acid has two major effects: facilitates peptide hydrolysis and reduces the number of bacteria in the stomach and in the proximal small intestine [3]. As a consequence, patients develop a B12 deficiency and require substitution [4]. Moreover, the gastric intrinsic factor is needed to absorb enough vitamin B12 from your normal diet and should therefore be substituted after Billroth I and II resections (e.g. operations in that the greater curvature of the stomach is connected to the first part of the jejunum in end-to-side anastomosis [5] after subtotal or total gastrectomies but not after any type of vagotomy.

With regards to the gastrointestinal motility, we could say that the normal gastric motility makes the stomach function as a reservoir (e.g. evacuating food in the small intestine in a controlled and regularly way). Moreover, the stomach digests and grinds food into smaller particles that are easily accessible to other enzymes in the small intestine, so as to obtain dietary nutrients which will be absorbed [6]. Still, the normal gastric emptying is a complex process. The stomach acts in series with the pylorus, duodenum and proximal jejunum. In this way, the evacuation of food from the stomach is controlled with a balance between propulsive motor activities and non-propulsive in the stomach and the resistance to evacuation of the pylorus and the duodenum [7]. Moreover, some scintigraphy studies on gastric emptying on humans indicated that both liquids and solids are initially stored in the proximal stomach and that the evacuation process only begins when food is propelled towards the gastric antrum where then it passes through the pylorus in the small intestine. Also, the size of the food fragment discharged from the stomach is well regularized [8].

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In this way, very well connected to what we are about to present here, the fragments of food that are passing into the duodenum are distributed by size, nearly all measuring less than 1 mm [9,10]. Thus, vagotomies (both truncal and supraselective) are altering the gastric motility by reducing proximal stomach relaxation and by increasing pressure in the stomach after food ingestion. Moreover, the gastric resections of the stomach alter the shredding process. As the gastric reservoir function is progressively destroyed with the increased resection, gastric emptying processes are profoundly modified. Moreover, after a Billroth I and II resection both gastric emptying of solids and liquids is increased [11,12].

Currently there is not sufficient data to document the differences between the two methods regarding gastric emptying, but existing records suggest that liquids leave the stomach faster than solid components [11]. Also, shredding food seems to be disturbed suggesting that solid fragments larger than 2 mm may leave the stomach [13].

Also, patients with antrectomy discharge solid foods rapidly, approximately 1/3 of the radioactively labelled fragments of the meat leave the stomach being at a size greater than 1 mm. By resecting the distal stomach, the controlled propel of solid food in the duodenum is destroyed. Instead, the discharge of solid foods does not seem to be impaired [8].

Selective vagotomy with pyloroplasty accelerates the gastric emptying of liquids, but does not affect the discharge of solid fragments [11]. Moreover, the grinding process is not affected since the fragments which are leaving the stomach are smaller than 1 mm indicating that the rate of gastric emptying of solids was similar both in healthy subjects and in these patients [11].

Truncal vagotomy, on the other hand, disrupts the entire stomach. These effects on gastric emptying are complicated. In most patients gastric emptying of solids is initially accelerated, but this initial fast process is followed by a slow evacuation phase. In up to 50% of patients slow evacuation is prevalent, which makes the total gastric evacuation to be delayed. Still, the shredding process is not affected by this procedure [14].

In addition, gastric surgery might affect not only the postprandial gastric emptying, but also the profound effects of gastrointestinal motility during dietary fasting could be affected. In this way, it was showed that after truncal vagotomy the migration of the motor complex myoelectric is either very low or absent [15]. Consequently, these patients are highly susceptible to develop bezoar, which is a mass found trapped in the gastrointestinal system [16].

Also, many of the problems appearing after the postprandial gastric surgery can be easily understood by the accelerated gastric emptying. For example, the lactose intolerance occurring after gastric surgery is related to the rapid occurrence of lactose in the small intestine. In this way, due to a limited capacity to hydrolyse lactose in adults, this massive appearance of lactose exceeds the hydrolytic capacity of lactase [17].

By analogy, postprandial hyperglycaemia after gastric surgery causes rapid entry of glucose in the small intestine, with a fast absorption of carbohydrates [18]. That is way many patients are losing weight after gastric surgery and as consequence to malnutrition and other nutritional deficiencies.

Also, mild steatorrhea is common after gastric surgery, but the daily amount of fat in the faeces rarely exceeds 15% of the ingested fat [19,20]. Factors contributing to this effect are considered to be the alterations in pancreatic and biliary secretion responses, biliopancreatic normal secretions and an unfavourable rate of food intake and digestive juices.

Moreover, there is an accelerated transit of the chyme through the small intestine, which generates an insufficient digestion, and as a

result, undigested food reaches the colon. Also, after distal gastrectomy, food fragments larger than 1 mm pass from the stomach into the small intestine. These "big" fragments can only be digested slowly. Thus, with an accelerated transit, time for digestion is insufficient.

In addition, pancreatic enzymes and bile salt concentrations are significantly decreased in the small intestine immediately after the ingestion of liquids in patients with subtotal gastrectomy [21]. This marked reduction is more likely the result of a dilution of the biliary and pancreatic secretions through the study of gastric emptying after the liquid lunch. Also, these results refer to liquid meals and are not observed in solid lunches.

Thus, the exocrine function of the pancreas appears to be close to normal after gastric surgery. On the other hand, several clinical studies have documented impaired exocrine pancreatic function after various gastric surgery procedures [22]. Alteration of exocrine pancreatic function was demonstrated both by analysing the fat in stools, as well as by indirect pancreatic function tests. Thus, it is preferable to use the term of impaired digestion rather than impaired exocrine pancreatic secretion, since the pancreas secretion is normal, but probably the digestion process was altered as we described above.

It also has to be mentioned that the most common clinical problems after gastric surgery are postprandial symptoms like precocious satiety, postprandial vomiting, alkaline or bile reflux gastritis and abdominal discomfort. In addition, the diarrhea, weight loss, maldigestion, anaemia and bone disease may be present. In this way, the weight loss can be caused by several factors and some conditions after gastric surgery, but an inadequate diet may be considered in patients with weight loss. Moreover, digestive insufficiency, with or without exocrine pancreatic insufficiency, and in excess multiplication of the bacterial flora in the small intestine could be another two factors contributing to weight loss [23].

Also, anaemia can occur after gastric surgery. In fact, in the absence of other complications, anaemia occurs after a period of several years after surgery. Thus, in a classic study of the 50' [24] anaemia developed gradually over the years with faster appearance of anaemia in patients which have lost blood. Anaemia can also develop as a result of iron deficiency, vitamin B12 and folate or a combination of these. In this way, the iron deficiency is the most common cause of postoperative anaemia. In addition, it has mentioned that two factors are the most important in regards to the high prevalence of postoperatively iron deficiency: a decrease in the availability of iron salts to be absorbed due to reduced post-surgical acid production and a disturbance of food digestion (especially meat), which is the main iron source for most of the people [25].

### **Bone Demineralization, Dumping and Re-resection**

Other aspects that could be described in the present context could be represented by the bone demineralization, dumping and re-resection processes.

In this way, the appearance of metabolic bone disease as a late complication after gastrectomy is well known [26]. For a long time, it was accepted that in patients with total or subtotal gastrectomy, a disturbance in calcium absorption and low levels of vitamin D occurs, without a plausible explanation.

As a consequence, the bone disease may develop over time. In this way, the bone demineralization is a physiological process that occurs with age and progresses faster in women than in men [27,28].

It seems that total gastrectomy accelerates bone demineralization more than a physiological process. Moreover, total gastrectomy induces a faster mineralization, as compared to the partial gastric resection [29]. In this way, in a study on 39 patients with total gastrectomy, as

compared with 59 patients with partial gastrectomy, the first group had higher incidence of bone demineralization (56% vs. 23%). The decline in bone mineral content was also related to age and more pronounced in women.

In addition, 10 years after surgery, many partially resected patients showed a marked decrease in bone mineralization, while in patients with total gastrectomy these changes occurred in 5 years. Also, approximately 30% of patients had abnormalities in serum minerals (calcium and phosphorus), alkaline phosphatase and 25-hydroxyvitamin D [26].

Even more, the importance of bone changes after gastric surgery is best illustrated by the observation that in the postoperative period fracture rate is 2-3 times higher, as compared to the healthy population of the same age and sex [30].

Regarding the dumping processes, it is considered that because part of the stomach is resected in standard Whipple operation, approximately 10% of patients suffer from the so called dumping syndrome (e.g. occurs when food, especially sugar, moves from the stomach into the small bowel too quickly) [31].

Also, in regards to the re-resection, our group found in the literature 4 documented cases [32] of reanastomosis for anastomotic stenosis after PCD, which had as symptoms upper abdominal pain, diarrhea and impaired results at the glucose tolerance test. Moreover, after the reanastomosis symptoms have disappeared. Moreover, there are descriptions for a repeated surgery for local recurrence or hepatic metastasis in pancreatic cancer after an initial cephalic duodenopancreatectomy [33].

## Postoperative Gastrointestinal Physiology after a Pancreatic Resection

Exocrine pancreatic insufficiency which is installed after pancreatic surgery may be due to a pre-existing preoperative pathological process, such as chronic pancreatitis, which is aggravated by the pancreatic resection leading to the loss of functional parenchyma [34].

Also, the insufficiency may result from the lack of activation for the pancreatic enzymes in the small intestine. It is also important to mention that the general assumption that once the pancreatic insufficiency is installed, pancreatic function is deteriorating rapidly over the years; it is not entirely true, at least for a substantial number of patients. In this way, pancreatic insufficiency in these patients may remain stable or may even improve due to alcohol abstinence and/or due to a pre-existence of a mild or moderate preoperative insufficiency [34].

Clinically, the evolution stages of exocrine pancreatic insufficiency can be divided into compensated and uncompensated. Moreover, the substantial reserve capacity of the pancreas enables an alteration of the exocrine pancreatic secretion of up to 90%, without clinical signs of malabsorption. In addition, steatorrhea and azotorrhea occur when the amount of lipase and trypsin drops to less than 10% of normal [35].

Still, in the literature we could find some contradictory observations to other two groups of patients: those who had exocrine secretions of the pancreatic higher than 10%, but had diarrhea and those with almost no lipase in the pancreatic juice, but with the daily excretion of fat being normal [36].

While the first situation can be explained by a wide variability in the exocrine secretory capacity of the pancreas, the second may be due to effective the action of the non-pancreatic lipases. These may originate in the serous salivary glands and in the gastric mucosa, while lipase activity is higher in the upper portion of the great curvature of the stomach, as compared to the proximal one. According to this finding, patients with exocrine pancreatic insufficiency can absorb more than

50% of ingested fat despite the absence of a measurable lipase activity.

In fact, it has been found that the pancreatic insufficiency was associated with significantly increased activity of the non-pancreatic lipolytic in the duodenum in fasting conditions. However, no significant difference was found between the tested groups regarding the postprandial non-pancreatic lipolysis activity. This situation was present in 90% of patients with total lipolytic activity at the level of Treitz ligament in patients with exocrine pancreatic insufficiency, in contrast to the healthy controls. This fact may explain why some patients do not require enzyme replacement even after total pancreatectomy.

In the case of pancreatic carcinoma, pancreatic insufficiency rapidly occurs and usually coincides with ductal obstruction in the pancreatic head. However, 40% of the otherwise healthy proximal pancreatic part is able to maintain the necessary secretion of enzyme. Although theoretically all pancreatic function tests may be performed after the operation, direct testing which involves duodenal intubation, such as the secretin-pancreozymin Lundh test, are not possible after right conventional resection of the pancreas with antrectomy (Whipple operation).

Looking at things in a pragmatic manner, postoperative testing for steatorrhea as a sign of exocrine pancreatic insufficiency is sufficient. The problem is to appreciate at what level of steatorrhea, enzyme replacement therapy should be initiated. As a rule, the administration of enzymes is initiated only when the excretion of fat exceeds 15 g/day or the patient loses weight or has diarrhea or dyspepsia [37].

There are also studies showing that the pancreatic function in chronic pancreatitis does not deteriorate over time in all patients. In this way, Sato et al. after a follow-up of 7 years observed in 4 of 11 patients who had performed different surgical procedures and secretin-pancreozymin test pre- and postoperatively, that it improves postoperative exocrine pancreatic function. Moreover, Dohi et al. observed the same facts 12 months after pancreatic resection or pancreatic-jejunal anastomosis. Malfertheiner et al. diagnosed the exocrine pancreatic insufficiency when steatorrhea occurred. In this way, postoperative steatorrhea occurred in 24 patients after resection surgeries, but only in 4% after drainage procedures. Similar results were also reported by Gooszen et al. In this way, exocrine pancreatic function deteriorated in 44% of 23 patients after partial pancreatic resection, but in none of 22 patients who received surgical drainage.

Moreover, Frey et al. have demonstrated that postoperative steatorrhea depends on the type of operation and the extent of the resection. After the Whipple operation the percentage of patients with steatorrhea increased from 5% to 55%, from resecting 80-95% of the left pancreatic, steatorrhea has increased from 9% to 38%, and after resecting of 40% - 80% of the left pancreas steatorrhea increased from 4% to 19%. In addition, Prinze and Greenlee have carried out drainage procedures on 87 patients with chronic pancreatitis. 20% of them have required preoperative enzyme replacement due to severe exocrine pancreatic insufficiency and 33% postoperatively.

Moreover, in a study of Lankisch et al. on exocrine pancreatic function, 25 patients were investigated for 25 months after surgery. 44% had an improvement in exocrine function after different types of surgery; another 44% had a steady trend and 12% deterioration. Also, monitoring these patients for a median period of 37 months showed that 46% of 26 patients had an improvement of exocrine function. In addition, this was more frequent after drainage operations, than after resections. 35% had a steady evolution, while in 19% a deterioration was observed.

In fact, only one study attempted to assess which preoperative condition of the exocrine function is necessary to be met to expect an improvement in postoperative evolution. In this way, the authors



reported that pancreaticojejunostomy performed on patients with Wirsung duct and late emergence of pathological changes as well as exo- and endocrine insufficiency, determines a belated damage mixed insufficiency, regardless if the patient gives up alcohol or not. These results are consistent with those found by Miyake et al. which also reported unoperated patients presenting an improvement in exocrine insufficiency, if this was mild or moderate at the time of diagnosis. In conclusion, experience in the postoperative exocrine pancreatic function is limited, but lately there seems to be an improvement. Moreover, postoperative exocrine function deterioration appears to be more common after resection operations, rather than after surgical drainage [38,39].

## Testing Pancreatic Function

It is known that exocrine pancreatic insufficiency causes malabsorption, the main symptoms being steatorrhea (fat in stool > 7 grams/day), abdominal pain and weight loss [40]. Moreover, exocrine insufficiency mechanism can be an isolated or a general reduction of the pancreatic enzymes or on the contrary, these could be quantitative normal, but no longer active in the small intestine [37].

In this way, there are two different ways to test the exocrine pancreatic function in non-operated patients, but this test is also necessary after surgery, especially in pancreatic carcinoma to assess what is left of exocrine pancreatic function. Moreover, both tests (e.g. pancreozymin secretin test (SPT) and Lundh test) require intubation of the duodenum and thus are not possible after Whipple operation. The SPT test measures the concentration of bicarbonate and the secreted amount as well as the enzymes such as amylase, lipase and trypsin in duodenal liquid after the stimulation of the pancreas with secretin and cholecystokinin-pancreozymin, CCK-PZ or caerulein, a pancreatic peptide that stimulates the secretion of isolated secretin from the frog skin with a structure similar to CCK. Also, the performance of the test was not standardized and each centre has its own procedures and different benchmarks.

On the other side, in Lundh test [41] stimulation is made by a well-defined lunch. However, even in this case, each centre has its own values. While CPS test gives the values of the submaximal response to exocrine pancreas stimulation, at the Lundh test we obtained a physiological response. Also, there are some false results in celiac disease and after vagotomy or gastric resection.

Regarding the indirect testing of the pancreas, there are urine tests, faeces tests and faecal fat analysis. The only urine test remained in use is PLT (pancreolauryl test). In fact, patients are receiving the test lunch along with acid test and dialuric- fluorescein, which is cleaved by pancreatic arylesterases. Also, part of the substance (fluorescein) is absorbed and then excreted through urine. Two days later the test is repeated with fluorescein to exclude individual absorption impairments or metabolic liver disease or kidney failure. In this way, the final result is obtained by making excretion rate on the testing day compared to control day. In addition, the administration of pancreatic enzymes should be interrupted 5 days before the test. Also, we should note that false results can occur in patients with Billroth II operation.

## Postoperative Weight Loss and Remnant Pancreatic Fibrosis

Regarding the postoperative weight loss, in a prospective study on a group of 26 resected patients between 2000 and 2001, 61% presented steatorrhea during the study and 20% at 12 months after surgery. There was also a significant increase in median Body Mass Index (BMI) from 6 weeks ( $22.9 \pm 4.4$ ) and 12 months ( $26.5 \pm 4.3$ ) after surgery. Median value of stool fat was 8.9 grams/day, 6.3 g/day, 7.1 g/day and 6.7g/ ay at 6 weeks, 3 months, 6 months and 12 months, respectively. Also, there were significant correlations between fat stools and their frequency, stool consistency and BMI. In this way, the authors concluded that there

might be a role for enzyme substitution in these patients after pancreatic resection to relieve symptoms and quality of life [41]. Moreover, in a study of 35 patients which received cephalic duodenopancreatectomy with preservation of the pylorus, gastric emptying was delayed shortly after surgery (1-2 months) and then returned to preoperative values in the long term (6-12 months). Moreover, body weight returned to normal if both faecal chymotrypsin and fasting blood sugar were preoperative normal, but this effect was not present if any of them was modified before the operation [41].

With regards to remnant pancreatic fibrosis, it is believed that the fibrosis of the pancreatic remnant after PCD at 12-18 months after surgery can be better evaluated using the time- signal intensity curve of dynamic MRI. Also, mucosa-to-mucosa pancreaticojejunal anastomosis was found to be more advantageous, with a low risk of fibrosis of the pancreatic remnants, as compared to pancreaticojejunal end-to-side anastomosis, in a study on 36 consecutive patients.

## Conflict of interest

The authors are stating that they do not have any conflict of interest to disclose.

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# Study of Fast Track Surgery in Patients with Biliary Intestinal Anastomosis in China

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## Abstract

**Objective:** To investigate the feasibility. Safety and economical aspects of fast-track surgery (FTS) in patients with biliary intestinal anastomosis application security, effectiveness and its advantages.

**Methods:** 31 patients were randomly divided into FTS group (n=16) and the control group (n=15). Control group using conventional perioperative treatment, guided by the idea of FTS group use the FTS perioperative measures, analysis and comparison of postoperative day 1 bad psychological emotions, exhaust and defecation time, postoperative hospitalization days and the hospitalization expenses and so on. Postoperative complications and adverse reactions in the groups.

**Results:** Compared with the photographic, FTS group exhaust and defecation time in advance, and shorten hospitalization time, hospitalization expenses reduced ( $P < 0.05$ ), complications and adverse reaction is similar between the two groups has no statistical significance ( $P > 0.05$ ).

**Conclusion:** Fast-track surgery in patients with biliary intestinal anastomosis, with a safe, effective, economic and other characteristic, can accelerate the rehabilitation of patients.

**Keywords:** Biliary; Gastrointestinal; Nutrition; Outcomes

## Introduction

Fast track surgery (FTS) concept refers to the preoperative, intraoperative and postoperative application has been proven effective methods to reduce stress and operation, patients with complications, accelerate the postoperative recovery [1,2]. At present in colorectal surgery, efficacy and safety of gastric cancer, liver cancer surgery has also been confirmed [3,4]. FTS start is concerned by more and more surgeons. The application of FTS principle in the choledochojunostomy patients, and to evaluate the safety, effectiveness and advantage.

## Materials and Methods

### Patient enrolment

Thirty-one patients were implemented choledochojunostomy in our hospital from January 2011 to December 2015 were. Inclusion criteria: less than 70 years of age, preoperative diagnosis, undergoing biliary intestinal anastomosis in patients without severe organ dysfunction, hypertension, diabetes.

### Study design

Thirty-one patients were randomly divided into FTS group and control group (Table I). The FTS group (n=16): 9 male, 7 female, age ( $46.7 \pm 2.2$ ) years. Intrahepatic bile duct stones 12 cases, bile duct cyst 4 cases. The control group (n=15): 9 male, 6 female, age ( $47.1 \pm 1.5$ ) years; Hepatolithiasis 11 cases, bile duct cyst 4. There was no statistically significant difference in gender, age, basic diseases, operation, basic medication etc. between groups ( $P > 0.05$ ). FTS group accepted the FTS treatment. All subjects have signed informed consent (Table I).

### Clinical observations

Observational index According to the POMS-SF [5] on patients of questionnaire or question and answer survey score, patients with postoperative first day bad psychological state were compared between the two groups. Patients with exhaust and defecate time, and postoperative length of hospital stay, cost of hospitalization, adverse reaction and complication were record and compared with two groups.

Discharge standards without intravenous fluids, by oral medication that can meet the pain control, normal temperature, after eating no abdominal distension, nausea, vomiting and other discomfort, with their own toilet, the going home desire can be discharged.

**Follow-up** After discharge within 7 days every day by attending their telephone contact, understanding of the disease and provide medical treatment. Outpatient treatment on a regular basis. 7 days after the surgery, take out stitches outpatient service.

### Statistical analysis

The measurement data is represented by mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ),  $P < 0.05$  has significant difference,  $P < 0.01$  has obviously significant difference.

## Results

Two groups of patients were cured. Compared to the control group, postoperative day 1 tension, anxiety, fear and other negative emotions significantly reduced in the FTS group ( $P < 0.05$ ), (Table II).

In the FTS group, exhaust and defecation time is shortened, decreased length of hospital stay, hospitalization costs were reduced, the difference is statistically significant ( $P < 0.05$ ), (Table III).

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**Table I:** Comparison of perioperative treatment measures between the FTS group and the control group

Measures	FTS group (n=16)	Control group (n=15)
<b>Preoperative education</b>	Preoperative 2d started with health education, psychological nursing, the treatment process, reduce anxiety and fear of mental patients	Routine preoperative 1d conversation, inform surgery, preoperative preparation and its significance
<b>Preoperative fasting</b>	Preoperative fasting 6 h, preoperative 2-4 h. 500 mL 10% glucose drink	Preoperative fasting 12 h, forbidden to drink 6 h.
<b>Catheter</b>	Indwelling after anesthesia, pulling surgery	within 24 h after Preoperative indwelling, postoperative 3 ~ 5d extraction
<b>Nasogastric tube</b>	Indwelling after anesthesia, awake within 6 h after pulling out	Routine preoperative indwelling, ventilation after removal
<b>Bowel preparation</b>	No bowel preparation	The night before surgery or oral cleaning enema for Magnesium Sulfate
<b>Anesthesia</b>	General anesthesia (short acting anesthetic) combined with epidural anesthesia	General anesthesia (short acting anesthetic)
<b>Liquid control</b>	The input amount of per hour is 5 ~ 10 mL/ kg input, after 2500 mL/d or so, after eating, water reduction	Without special attention
<b>Drainage tube</b>	Peritoneal drainage tube indwelling drainage fluid, bile, non-bloody liquid and less than 100 mL/d extraction	Abdominal drainage tube out 5 ~ 7 d after the operation
<b>Postoperative analgesia</b>	Multimodal analgesia, such as epidural analgesia, patient-controlled intravenous analgesia (PCA), oral non-steroidal analgesics.	Opioid analgesics
<b>Get out of bed</b>	Active demand early ambulation, postoperative first bed day 2 h, second days to get out of bed every day at least 6 h.	Voluntary patient ambulation
<b>Postoperative fasting</b>	Early postoperative 6 h started eating, drinking a little water, second day eating semifluid food, transition to a normal diet as early as possible.	Exhaust and defecation after drinking water, gradually return to normal diet

**Table II:** On the first day after surgery POMS- SF between the two groups (x ± s, score)

Group	n	Nervous	Anxiety	Fear	Depression	Lonely
FTS group	16	4.20 ± 1.52 $\Delta$	3.61 ± 1.78*	3.65 ± 1.56*	3.82 ± 1.73	3.44 ± 2.66
Control group	15	5.82 ± 1.31	4.88 ± 2.12	5.20 ± 2.08	4.33 ± 1.66	3.71 ± 2.10

\*: P<0.05,  $\Delta$ : P<0.01, compared with the control group.

**Table III:** Comparison of postoperative recovery between the two groups (x ± s)

Group (hr.)	n (hr.)	Exhaust time (d.)	Defecation time (million)	Hospitalization	Hospital costs
FTS group	16	54.2 ± 14.3 $\Delta$	88.9 ± 30.1*	6.0 ± 1.0*	1.8 ± 0.3*
Control group	15	70.4 ± 12.2	101.0 ± 23.7	7.0 ± 1.3	2.1 ± 0.4

\*: P<0.05,  $\Delta$ : P<0.01, compared with the control group.

The incidence of nausea, vomiting, abdominal distension after operation and infection had no statistically significant difference in the two groups (P>0.05), (Table IV). Thirty-one patients were a good quality of life in followed up.

## Discussion

FTS concept refers to the preoperative, intraoperative and postoperative application has been proven effective methods to reduce the operation of excitation and complications, accelerate the patient's postoperative rehabilitation. It is the combination of a series of effective measures of the synergy as a result, many measures have been in clinical application, such as perioperative nutritional support, attaches great importance to the oxygen supply, no regular application early nasogastric tube decompression, feeding, growth hormone, minimally invasive surgery, and so on [1,6]. FTS new fasting and eating plan, no bowel preparation, not retained or early removal of all kinds of indwelling catheter, postoperative early activities etc. perioperative treatment measures seem to have the risk of increased postoperative aspiration, pneumonia, anastomotic leakage and abdominal infection and other complications, in patients with biliary enteric anastomosis is safe, effective, worthy of discussion.

Biliary intestinal anastomosis belongs to the biliary tract surgery, because surgery can cause trauma and even life-threatening, patients before there are varying degrees of tension, anxiety, fear and other negative emotions, which is not conducive to postoperative rehabilitation. The traditional preoperative education and psychological nursing is actually limited to relatively simple disease health education and regards, comfort level. It is necessary to further optimize. The FTS treatment of patients to accept, in addition to the

conventional education and psychological nursing, preoperative 2d started to patients and their families with the FTS treatment processes, through the oral and written form the operation will take the treatment and nursing measures, patients and their families gathered in the FTS treatment considerations that FTS treatment has accelerated postoperative body recovery, shorten the hospitalization time, alleviate the negative emotions of patients, reduce the psychological stress. The postoperative day 1 score PMOS-SF results show tension, anxiety, fear and other negative emotions significantly reduced, indicating that the optimization of the FTS operation before education and psychological nursing can significantly reduce or eliminate the negative emotions of patients, reduce the psychological stress in the FTS group. In the past to prevent inhalation pneumonia will preoperative fasting 12h, ban water 4 h as perioperative preoperative preparation of routine, but for a long time of fasting, water easily lead to low blood sugar and insulin resistance and increased intraoperative and postoperative fluid volume and increased stress. European and American modern anaesthesiology guide pointed out that reduce preoperative fasting time to reduce the surgery patient's thirst, hunger, a bad mood and tense, preoperative 6h. Fasting before operation, 2-3 h. eating sugary carbohydrates is not only safe, but also can increase the glycogen content, reduce postoperative insulin resistance, and can shorten the time of hospitalization [7]. This study used preoperative fasting drink 2-4 h. 500 mL 10% glucose solution during anaesthesia without vomiting, aspiration, does not increase the risk of anaesthesia at preoperative 6h in the FTS group,. is generally believed that after abdominal surgery patients with anal exhaust before eating. Sagar [8] study shows, abdominal surgery after 6h of small intestine returned to normal peristalsis, postoperative early intestinal liquid began to be absorbed and postoperative 24 h gastric motility has returned to normal. Therefore, exhaust, defecate is not

**Table IV:** The incidence of adverse events between the two groups

Adverse events	FTS group (n=16)	Control group (n=15)
Nausea (%)	2 (12.5)	2 (13.3)
Vomiting (%)	2 (12.5)	2 (13.3)
Abdominal distension (%)	2 (12.5)	2 (13.3)
Incision infection (%)	1 (6.3)	0
Urinary tract infection (%)	0	1 (6.7)

eating the necessary premise. Postoperative early oral feeding not only does not increase the anastomotic leakage risk [2], but can promote intestinal peristalsis, the maintenance of intestinal mucosa barrier, postoperative gastrointestinal function recovery time of normal early [9,10], reducing the infusion time and accelerate the rehabilitation of patients. The study of postoperative 6h. after drinking a little water, eating for a semi liquid diet for 2 days, to patients can be tolerated, no nausea, vomiting, abdominal distension and other adverse reactions as the standard, the gradual transition to semi liquid diet, normal. 2 patients with postoperative nausea and vomiting, abdominal distension after operation were improved after given symptomatic treatment, not again line of gastrointestinal decompression in the FTS group. There was no complications such as anastomotic leakage, anastomotic bleeding. Incidence of postoperative adverse reaction and complication was not statistically significant in two groups ( $P>0.05$ ). Therefore, FTS new fasting and eating plan in patients with biliary enteric anastomosis peri operative is safe.

Preoperative bowel preparation is designed to remove luminal contents, avoid postoperative abdominal distension, but easily lead to dehydration, nutritional status and intestinal bacteria shift down. Studies have shown that excessive bowel preparation can increase postoperative abdominal infection and the incidence of anastomotic leakage. In addition to biliary enteric anastomosis surgery, hepatobiliary surgery can enter the intestinal tract, especially the lower digestive tract without bowel preparation [11]. Our results show that minimally invasive surgery is the core content of FTS; precise anastomosis technique is the key to avoid anastomotic leakage. At present, biliary enteric anastomosis and technical proficiency has been greatly improved. Part of the biliary enteric anastomosis has been through the stapler, agreement is more safe and reliable [8]. There is no need for routine bowel preparation, but for old years with chronic constipation patients using oral tomato leaf and paraffin oil, glycerine anal therapeutic laxative and no mechanical bowel preparation were more secure. There were not underwent bowel preparation and the incidence of anastomotic leakage in the FTS group. There was no significant difference in postoperative abdominal infection in the two groups [11]. The traditional view of requirements before the operation of abdomen routine indwelling nasogastric tube and prevent postoperative nausea and vomiting, relieve gastrointestinal dysfunction caused by abdominal distension, until postoperative anal exhaust, in order to increase the safety of abdominal surgery. FTS philosophy thought that abdominal surgery not routinely placed nasogastric tube can reduce postoperative patients with oropharyngeal discomfort reaction, reduce the risk of pulmonary infection, patients with early recovery after eating, and does not increase the incidence of postoperative complications of nausea, vomiting, abdominal distension, fistula and so. If intraoperative bloating evident or anesthesia resulted in air into the gastric lumen, the placement of gastric tube in operation, but should strive for removal at the end of surgery [12]. For abdominal distention, nausea and vomiting after eating, also there is no need to immediately gastrointestinal decompression and application of gastrointestinal drugs, symptomatic treatment can not only achieve good results, but also reduce the stress of indwelling gastric tube. To estimate the long operation time can indwelling catheter after anaesthesia, but catheter placement will increase the chance of infection and discomfort, the limitation of activity, without urinary retention in postoperative 24 h extraction.

## Conclusion

Fast-track surgery in patients with biliary intestinal anastomosis, with a safe, effective, economic and other characteristic, can accelerate the rehabilitation of patients.

## Conflict of interest

Authors have no conflict of interests to declare.

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# Predictors of Malignancy in Patients with Solitary and Multiple Thyroid Nodules

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## Abstract

**Introduction:** Ultrasound (US) and Fine-needle aspiration (FNA) are the main methods used for investigating thyroid nodules, with questionable predictive values in multinodular goiter (MNG) compared to solitary thyroid nodule (STN).

**Objective:** To detect the independent predictors of malignancy in patients with solitary and multiple nodules.

**Patients and methods:** Medical records of patients who were admitted for thyroidectomy at Alexandria Main University Hospital and Medical Research Institute Hospital between January 2014 and January 2016 were reviewed. Demographic and clinical data, US reports, FNA reports (Bethesda "B" system), and final histopathological results were recorded and analyzed. Patients with hyper- or hypo-thyroidism, previous history of thyroid cancer or those with incomplete data were excluded.

**Results:** Collectively, 20% (111/554) of the study population proved to have malignancy on final histopathology, 19.3% (82/422) with MNG and 22% (29/132) with a STN. Combining gender and age showed that significantly more male patients with MNG under the age of 45 years had thyroid cancer ( $X^2=11.75$ ,  $p=0.003$ ). Statistically significant US features in the MNG Group included micro-calcifications, solid composition, echogenicity, incomplete halo, ill-defined margins, and suspicious cervical lymph nodes (LNs). In STN, significant US features included complex composition of nodules, peri-nodular vascularity, and also suspicious cervical LNs. The FNA results of BII-V reports showed that 16.9% (69/408) and 17.6% (22/125) of patients with MNG and STN, respectively, had false negative results. The risk of malignancy showed a significant rise from BIV to BVI lesions in both Groups. Multivariate analysis revealed that, in MNG, the highest malignancy predictor was micro calcification, followed by FNA (BVI) and then suspicious cervical LNs. In STN, the features that retained significance in multivariate analysis were suspicious LNs & BVI-FNA.

**Conclusion:** Based on the data presented, it may be concluded that the independent predictors of malignancy were US findings of micro-calcification in patients with MNG, suspicious cervical LNs and Bethesda VI on FNA in patients with both MNG and STN.

**Keywords:** Predictors; Malignancy; Multinodular; Goiter; Solitary nodule; Ultrasound; FNA

## Introduction

Thyroid nodules are a common clinical finding, with an estimated prevalence of 3% to 7% on the basis of palpation [1-3]. They are more common in the elderly, in women, and in presence of iodine deficiency and history of exposure to radiation [1]. Diagnosis of multinodular goiter (MNG) should rely on ultrasound (US) examination since approximately 20%-50% of patients diagnosed clinically as having a solitary thyroid nodule (STN), are found to have additional nodules on US [1,4,5]. The mean incidence of malignancy in thyroid nodules is 14% [6,7], which increased markedly in recent years due to the wide application of high resolution US and fine-needle aspiration (FNA) [8,9]. While patients with MNG have been reported to have the same risk of malignancy as those with STN [10-12], Other authors reported a higher likelihood of malignancy for STN [10,13]. The present study was conducted to detect the independent predictors of malignancy in patients with MNG as compared to STN.

## Patients and Methods

### Study population

The medical records of 1217 patients who were admitted to Alexandria Main University Hospital and Medical Research Institute Hospital, between January 2014 and January 2016, were retrospectively reviewed. After excluding patients with hyper- or hypo-thyroidism or

history of thyroid cancer, and those with incomplete data, patients who underwent thyroidectomy for euthyroid MNG (Group 1,  $n=422$ ) or STN (Group 2,  $n=132$ ) were included in the present study, and constituted the study population ( $n=554$ ).

### Demographic and clinical data

Age, gender, family history of thyroid cancer, previous history of irradiation or thyroid surgery, clinical presentation on admission, and retrosternal extension were all recorded.

### Imaging data

The solitary nodule and the largest or most suspicious nodule (in case of MNG) were evaluated in the reviewed reports regarding the

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following parameters; echogenicity, calcifications, halo, margins, composition (solid, cystic, mixed), size (divided according to maximum diameter/nodule into <2 cm, 2-4 cm, >4 cm), vascularity (Doppler examination), and the presence of suspicious cervical lymph nodes (LNs) (rounded, >0.5 cm, lost hilum, peripheral vascularization, cystic changes, and calcification).

## Histopathological data

The Bethesda system for reporting thyroid cytopathology (BI-BVI) was adopted in this study, where BI is non-diagnostic or unsatisfactory, BII is benign, BIII means atypical or follicular lesion with undetermined significance, BIV is follicular neoplasm, BV is suspicious of malignancy and BVI is malignant. Predictive indices of FNA were calculated to detect the utility of (B-VI) in diagnosing malignancy. All of the available data for each patient were compared to final histopathology.

## Statistical analysis

Data were analyzed using IBM SPSS software package version 20.0 (Belmont, Calif 2013). Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square ( $\chi^2$ ) was conducted using Fisher's exact test or Monte Carlo correction. Quantitative variables were presented as mean and standard deviation of the mean and were compared using the Student t test. Univariate and multivariate logistic regression were used. A p-value of <0.05 was considered to be statistically significant.

## Results

Collectively, 20% (111/554) of the study population proved to have malignant disease on final histopathology (Table 1), 82 patients (19.3%, 82/422) belonged to the MNG Group and 29 (22%, 29/132) belonged to the STN Group, with no significant differences between both ( $\chi^2=0.404$ ,  $p=0.525$ ). Table 2 shows the demographic and clinical data of patients with thyroid cancer in both Groups. Male patients with MNG had insignificantly more cancer than female patients (29.5% versus 18.3%, respectively). In the STN Group, female patients had insignificantly more cancer as compared to male patients (23% versus 13.3%, respectively). Family history of thyroid cancer was significantly more in patients with STN ( $\chi^2=4.156$ ,  $p=0.042$ ). Combining gender and age with a cut-off point at 45 years (Table 3) showed significant differences in MNG only, where more male patients under the age of 45 years (47.1%) had cancer as compared not only to female patients in the same age group (14.8%) ( $\chi^2=11.75$ ,  $p=0.003$ ), but also to male patients above the age of 45 years (18.5%) ( $\chi^2=4.08$ ,  $p=0.043$ ). On the other hand, thyroid cancer was encountered more in female patients above the age of 45 years (24.4%) as compared to those below 45 years (14.8%) ( $\chi^2=5.39$ ,  $p=0.020$ ). The majority of patients (95.1%) presented with a slowly progressive neck swelling with or without dyspnea and/or dysphagia not related to any other systemic disease. None of the patients presented with hoarseness of voice. There was no statistically significant difference in malignancy occurrence between patients with retrosternal extension (RSE) (9.7%) and those without (17.5%) ( $\chi^2=1.237$ ,  $p=0.266$ ) in the MNG Group. Only two patients with STN had RSE, and they proved to have benign thyroid pathology ( $\chi^2=0.530$ ,  $p=1.000$ ). Table 4 summarizes the US features in both Groups. As may be seen, statistically significant features predictive of cancer in the MNG Group included micro calcification, solid composition, echogenicity, incomplete halo, and ill-defined margins. In addition, 11 patients out of 21 (52.4%) with suspicious cervical LNs had malignant disease ( $\chi^2=19.09$ ,  $p<0.001$ ). Statistically significant US features in the STN Group included complex composition of nodules and peri-nodular vascularity. Moreover, all 5 patients with suspicious cervical LNs in this Group proved to have malignant thyroid disease ( $\chi^2=20.229$ ,  $p<0.001$ ). Although, largest nodules (> 4 cm) in patients with MNG or STN had

the highest rate of malignancy (22.4% and 31.8%, respectively), yet, there was no statistically significant difference regarding nodule size and occurrence of malignancy. The collective reports of BII-BV FNA results (non-malignant) revealed that 17.4% (91/523) turned out to be malignant on final histopathology. Accordingly, 16.9% (69/408) and 17.6% (22/125) of patients with MNG and STN, respectively, had false negative results. On the other hand, BVI FNA (malignant), showed one false positive case (1/14, 8.3%) in patients with MNG as compared to none in those with STN (Table 5). The risk of malignancy showed a significant rise from BIV to BVI lesions in both Groups as shown in Figure 1. Multivariate analysis of predictors of malignancy in MNG revealed that the highest predictor was micro-calcification, followed by FNA (BVI) and then the presence of suspicious cervical LNs (Table 6). In STN, predictors that retained significance in multivariate analysis were the presence of suspicious cervical LNs and BVI FNA.

## Discussion

The clinical importance of thyroid nodules rests with the need to exclude thyroid cancer [2,10,14-16]. In the current study, 19.4% of MNG patients and 22% of STN patients had malignant disease on final histopathology. Similar results were reported by other authors, with a malignancy rate of 5.7%-31% in MNG [2,13,15,17-31] and 17% in STN [32] with no significant difference between both [13,19,32-38]. Thus, the likelihood of thyroid cancer seems to be independent from the number of nodules [13-39]. The difference in the reported rates of malignancy among patients with MNG and STN in the above studies undoubtedly reflects differences in the selection criteria used for analysis, as well as geographic differences in the population studied [19]. Several authors reported that detection of malignancy did not correlate with patient's gender, which is in accordance with the current findings [12,20,40,41]. Other studies however, reported higher rates of thyroid carcinoma in male patients [13,31] especially in patients with follicular neoplasm (BIII, BIV) [13,15,27,31,42-47]. While some authors reported that older age is an independent risk factor of malignancy [29,31,45,46,48-51], others, in accordance with our findings, found no correlation with age in patients with solitary or multiple nodules [12,13,15,18,20,40,41]. In a study by Luo et al. [15], age lost its significance as an independent risk factor for thyroid malignancy when included in a multivariate analysis, suggesting that age is not a very strong independent risk factor for malignancy and will likely not be helpful in predicting the risk of malignancy in a given patient. On the other hand, some investigators found that older age is significantly correlated with the presence of benign neoplasms in thyroid nodules [42,52]. This wide contradiction is probably due to differences in patients selection and numbers of the study population [1,10,13,53]. It is conceivable that both gender and age are weak independent risk factors, but perhaps they add value when combined together as a single index of risk prediction, as shown in the present study that showed a higher risk in male patients with MNG less than 45 years. Combining high resolution US with FNA in evaluating thyroid nodules is considered the modality of choice in investigating nodular

**Table 1:** Final histopathology of malignant tumors in patients with MNG and STN

US Features	MNG (N=422)		STN (N=132)		
Final Histopathology	N	%	N	%	$\chi^2$ (p)
Papillary thyroid carcinoma (PTC)	70	85	21	72.5	2.43 (0.118)
Follicular thyroid carcinoma (FTC)	8	9.8	5	17.2	0.76 (0.382)
Medullary thyroid carcinoma (MTC)	2	2.4	2	6.9	1.23 (0.268)
Hurthle cell carcinoma (HCC)	1	1.2	0	0	0.36 (0.55)
Anaplastic thyroid carcinoma +PTC	1	1.2	0	0	0.36 (0.55)
Anaplastic thyroid carcinoma (ATC)	0	0	1	3.4	2.85 (0.091)
<b>Total</b>	<b>82</b>	<b>100</b>	<b>29</b>	<b>100</b>	<b>0.404 (0.525)</b>



**Table II:** Demographic and clinical data of patients with malignant disease in both Groups (MNG and STN)

Demographic and clinical data		MNG (82/422)	STN (29/132)	X <sup>2</sup> (p)
Gender	Male	13/44 (29.5%)	2/15 (13.3%)	1.55 (0.213)
	Female	69/378 (18.3%)	27/117 (23%)	1.3 (0.249)
X <sup>2</sup> (p)		3.210 (0.073)	0.736 (0.391)	
Age (years)	< 45	44/260 (16.9%)	15/80 (18.8%)	0.142 (0.706)
	> 45	38/162 (23.5%)	14/52 (26.9%)	0.257 (0.612)
X <sup>2</sup> (p)		2.722 (0.099)	1.228 (0.268)	
Previous surgery		12/58 (20.7%)	1/2 (50%)	0.979 (0.322)
Family history of thyroid cancer		0/11	2/6 (33.3%)	4.156 (0.042*)
Radiation history		0/2	0/0	-

\* P&lt;0.05

**Table III:** Incidence of malignancy in patients with MNG and STN in relation to gender and age combined together

	MNG (N=82)		X <sup>2</sup> (p)	STN (N=29)		X <sup>2</sup> (p)
	< 45 y N = 260	> 45 y N=162		< 45 y N = 80	> 45 y N=52	
Male	8/17 (47.1%)	5/27 (18.5%)	4.082 (0.043*)	1/8 (12.5%)	1/7 (14.3%)	0.01 (0.920)
Female	36/243 (14.8%)	33/135 (24.4%)	5.39 (0.020*)	14/72 (19.4%)	13/45 (28.9%)	1.391 (0.238)
X <sup>2</sup> (p)	11.750 (0.003)*	0.440 (0.623)		0.228 (1.000)	0.657 (0.659)	
Total	44/260 (16.9%)	38/162 (23.4%)		15/80 (18.8)	14/52 (26.9%)	

**Table IV:** Ultrasound (US) features in patients with MNG and STN

	N		%		N (p)	%		(p)		N (p)
	N	%	N	%		N	%	N	%	
Hypoechoic	87	78.4	24	21.6	2.109 (0.155)	16	73	6	27.3	0.757 (0.390)
Micro-calcification	16	53.3	14	46.7	19.575 (<0.001)*	6	60	4	40	2.544 (0.121)
Solid	18	64.3	10	35.7	7.140 (0.016)*	13	68	6	31.6	1.698 (0.219)
Complex	139	81.3	32	18.7	0.420 (0.517)	46	90	5	9.8	6.144 (0.013)*
Incomplete halo	0	0	2	100	9.602 (0.03)*	0	0	1	100	3.912 (0.205)
Ill-defined margins	10	62.5	6	37.5	4.751 (0.029)*	5	63	3	37.5	1.520 (0.359)
Peri-nodular vascularity	17	77.3	5	22.7	0.478 (0.489)	7	50	7	50	8.452 (0.009)*
Intra-nodular vascularity	9	64.3	5	35.7	3.436 (0.064)	9	60	6	40	3.995 (0.080)
Cervical LNs	10	47.6	11	52.4	19.075 (<0.001)*	0	0	5	100	20.229 (<0.001)*

χ<sup>2</sup>: Chi square test

\*: Statistically significant at p ≤ 0.05

**Table V:** FNA (Bethesda System) [6] results as diagnostic test for malignancy

Bethesda System	MNG (N=417**)				STN (N=129**)			
	Benign (N=340)		Malignant (N=82)		Benign (N=103)		Malignant (N=29)	
	N	%	N	%	N	%	N	%
B (II-V)	337	83.6	66	16.4	100	82.0	22	18.0
BVI	1	7.1	13	92.9	0	0	7	100.0
X <sup>2</sup> test	33.232 (p<0.001)*				9.075 (p=0.003)*			

χ<sup>2</sup>: Chi square test

\*: Statistically significant at p ≤ 0.05

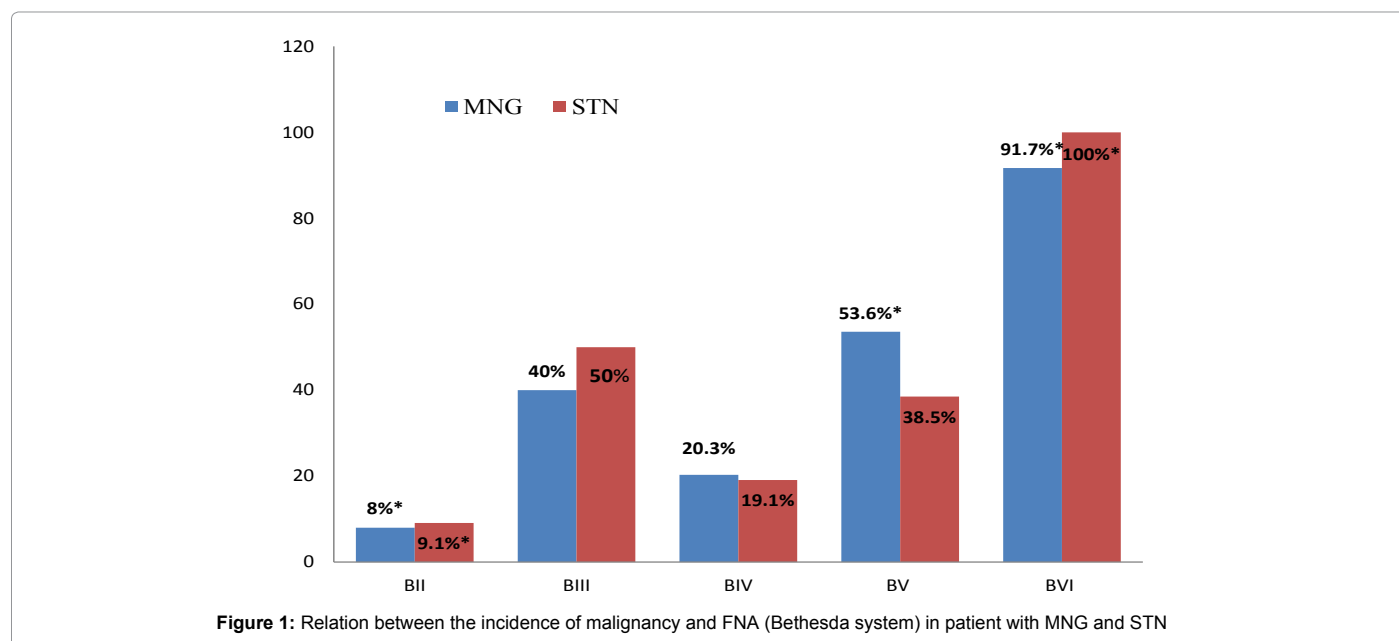
\*\*: Patients with BI-FNA were not included (MNG Group, n=5 – STN Group, n=3)

thyroid gland [1,26]. Out of the analyzed US features in this study, micro calcification, solid composition, incomplete halo, and ill-defined margins were significant risk factors in patients with MNG, in addition to suspicious cervical lymph nodes in both Groups. Similar results were reported by other studies that investigated the risk of malignancy in MNG alone [20,54-57], or in both MNG and STN [51,54,58-61]. Ultrasound features cannot accurately distinguish between benign and malignant thyroid disease. Although certain sonographic features are associated with increased risk of malignancy, the predictive value of these criteria are not sufficiently high or low to preclude the missing of FNA, and it is recommended that US features are used in combination with FNA and clinical presentation to reach the proper management [12,13,51,58,62,63]. Cytopathological examination is the corner stone in appraising the malignant potential of a given thyroid nodule. A meta-analysis study reported non-diagnostic incidence rate (BI)

between 1.8% and 23.6%, with a collectively reported malignancy rate of 16.8% [8]. In the current study, three of 9 patients (33.3%) who were classified as BI had cancer. This high rate could be attributed to several factors; not all FNA in the present study were obtained under US guidance, no on-site smear adequacy assessment was adopted, not all reviewed FNA reports were performed by same pathologist, and most of biopsied nodules were large in size (≥ 4 cm), which may be associated with a high malignancy rate, reaching 27% as reported by Pinchot et al. [31] and Gharib et al. [1]. In this study, 8.4% of BII patients had false negative results (i.e. malignant disease). The false negative rate of 0-8% was reported by several authors [8,10,17,64,65], with the rate being higher in large nodules (≥ 4 cm) [10,31,66]. In this study, the rate of malignancy increased with increasing in Bethesda rating from BIV to BVI. Similar findings were reported in the literature with an average rate of malignancy of 1.2%-25.3% in BIV [6,8,17,46,67,68] 60%-75%

**Table VI:** Multivariate analysis logistic regression of predictors of thyroid malignancy in patients with MNG

Predictors of Malignancy	B	SE	P value	Odds Ratio	95.0% CI	
					Lower	Upper
Microcalcification (US)	1.452	0.453	0.001*	4.270	1.758	10.374
FNA (B VI)	3.079	1.189	0.010*	21.736	2.114	223.491
Suspicious cervical LN (US)	1.538	0.599	0.010*	4.655	1.438	15.072
Ill-defined margin (US)	1.056	0.64	0.099	2.876	0.82	10.088
Solid composition (US)	0.794	0.495	0.108	2.212	0.839	5.832
Intra-nodular vascularity (US)	0.909	0.713	0.202	2.481	0.613	10.035

**Figure 1:** Relation between the incidence of malignancy and FNA (Bethesda system) in patient with MNG and STN

in BV [6,8,39,69], and 97%-99% in BVI [6,70]. Ideally, false positive cases in BVI reports should be less than 1%, ranging from 0.5%-10% [17,71,72].

## Conclusion

Based on the data presented, it may be concluded that (1) thyroid nodules in MNG may harbor malignancy similar to those of STN, (2) the most significant independent predictor of malignancy is the presence of micro-calcifications (by US) in MNG in addition to suspicious cervical LNs by US, and FNA (Bethesda VI) in both MNG and STN, and (3) other predictors of malignancy include solid composition of the nodule, incomplete halo and ill-defined margins in MNG, as well as complex composition and peri-nodular vascularity in STN; however, these are only significant on univariate analysis.

## Conflict of Interest

Authors have no conflict of interest to disclose.

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# Evaluation of Preoperative Nutritional Status in Gastric Cancer Patients

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## Abstract

**Background:** Malnutrition is a common feature in gastric cancer patients and it is directly correlated with tumour stage. The goal of our study was the assessment of nutritional status in a large series of gastric cancer patients.

**Methods:** We performed a retrospective study which included all the patients newly diagnosed with gastric cancer which were submitted in our unit in a 2 year period. We performed a comparative analysis between the patient in which radical resection was performed and the patient in which a palliative procedure was made.

**Results:** There were 136 gastric cancer patients; radical resections were performed in 81 patients (34 total gastrectomies and 47 subtotal gastrectomies). Palliative procedures included 17 gastroenterostomy, 13 feeding jejunostomy and 25 exploratory laparoscopies. Patients in which radical resection was performed presented higher Karnofsky ( $P=0.006$ ) and Charlson ( $P=0.007$ ) indexes, higher BMI ( $P=0.017$ ), higher albumin ( $P=0.001$ ), lymphocytes ( $P=0.03$ ) and Onodera index ( $P=0.0032$ ).

**Conclusion:** An accurate clinical and biological nutritional assessment of newly diagnosed gastric cancer patients could identify the subgroup of patients with more advanced or metastatic lesions in which a thorough stadialisation should be performed.

**Keywords:** Gastric cancer; Nutritional status; Gastrectomy; Gastroenterostomy; Jejunostomy; Karnofsky index; Charlson score; Onodera index

## Introduction

Although the incidence have decreased in western world, gastric cancer represents a major health care problem worldwide and remains one of the leading causes of cancer related deaths. Prognosis of gastric cancer is relatively poor with 5-year survival rates around 27% [1] for all stages and 63% for localised disease. Surgery plays the major role in the multidisciplinary treatment of gastric cancer and gastric cancer surgery is regarded as one of the most demanding and high risk surgery. The main goals of gastric surgery are the complete resection of the disease with local lymphadenectomy in order to increase survival without the increase of postoperative morbidity and mortality. Gastric cancer patients are at high risk for malnutrition [2], the most common causes of malnutrition are tumour volume with early satiety or obstruction and metabolic alterations [3]. Malnutrition is associated with increase morbidity and mortality after major gastric surgery and a thorough nutritional screening of potentially surgical candidates for gastrectomy is mandatory as intervention prior to surgery can improve the nutritional status and surgical outcomes. An easy non-invasive method for nutritional status assessment is the questionnaire such as: The Short Nutritional Assessment Questionnaire (SNAQ) and Malnutrition Universal Screening Tool (MUST) which are mandatory in some western countries. Questionnaires are subjective methods to investigate nutritional status and methods that objectively measure patient's status are used: plasma serum markers and imaging studies. The aim of this study is the assessment of nutritional status of a large cohort of gastric cancer patients using objective markers and the correlation with the extent of the disease.

## Materials and Methods

We conducted a retrospective study using a prospective collected database of consecutive patients diagnosed with gastric cancer in a single institution (1<sup>st</sup> Surgical Unit, Regional Institute of Oncology Iași) between May 2012 and 2014. All the patients had histological confirmed disease. In all cases was performed preoperative staging which included:

upper gastrointestinal endoscopy with biopsy, abdominal computed tomography and staging laparoscopy (where indicated). Functional status of the patients was assessed in all patients by routine blood tests, electrocardiogram, chest radiography and cardiac ultrasound in patients with impaired cardiac function. Based on the results of preoperative staging all patients were suitable for surgical treatment in absence of distant metastases or peritoneal carcinomatosis. Types of surgery included: total or subtotal gastrectomy depending on the localisation of the tumour, reconstruction was performed in all cases using a Roux-en-Y anastomosis. Locally advanced tumours involving surrounding organs were not considered unresectable; in those cases a multiorgan resection was performed. In patients with total gastrectomy a D-2 lymphadenectomy was performed and in cases with subtotal gastrectomies a modified D-2 lymphadenectomy. For cases in which peritoneal carcinomatosis was found, or the tumour was locally advanced but non-resectable, a palliative procedure was performed: gastroenterostomy or feeding jejunostomy. In patients without tumour obstruction a laparoscopy/laparotomy was performed. We considered two groups of patients: patients in which resection was performed and patients in which a palliative procedures due to tumour extent or extensive carcinomatosis. Patient's functional status assessment included: ASA physical status [4], Charlson score [5] Karnofsky index. Indicators of immune and nutritional status of the patients were: body mass index (BMI), haemoglobin, white blood cells, lymphocyte

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counts, total proteins and albumin levels, Onodera index (prognostic nutritional index) calculated as  $10 \times \text{albumin (g/dl)} + 0.005 \times \text{total lymphocyte count (per mm}^3\text{)}$ . All nutritional factors were measured prior to surgery.

## Statistical Analysis

Continuous data were expressed as median and interquartile range. Categorical data were compared among the two groups using Fisher's exact test and continuous data using Mann-Whitney U test. A p-value less than 0.05 was considered significant. Statistical analysis was performed using MedCalc v.4.0.

## Results

During the study period there were 136 patients operated for gastric cancer (86 males (63.23%) and 49 females (36.02%)) with a mean age of 66.9 (65.24-68.69) years. Radical resections were performed in 81 patients (59.55%). There were performed 34 total gastrectomies and 47 subtotal gastrectomies. Palliative procedures included: gastroenterostomy in 17 cases, feeding gastrostomy/jejunostomy in 13 cases and laparoscopy / laparotomy in 25 cases. Patient's characteristics are described in Table I. According to the UICC TNM classification of malignant tumours 7<sup>th</sup> Edition, stage I tumours were present in 2.9% of cases, stage II was present in 18.38% of cases, stage III was present in 46.32% of cases and stage IV in 32.35% of all cases. Only 4 patients underwent preoperative chemotherapy, despite the fact that most of the patients were diagnosed with locally advanced tumours (stage III-IV). By performing a comparative analysis of the clinical and biological characteristics of the resected and unresected patients we observed no difference in terms of age ( $P=0.6$ ), preoperative haemoglobin ( $P=0.49$ ) and white blood cells counts ( $P=0.23$ ). Also there were no differences regarding the histological type (intestinal type vs. Signet ring cell,  $p=0.11$ ) and the localisation of the tumour ( $P=0.16$ ). The characteristics of those two subgroups of patients are summarised in Table II. By comparing the clinical and functional status of the patients there were statistical highly significant differences regarding the Charlson score ( $P=0.006$ ), Karnofsky score ( $P=0.007$ ) and the BMI ( $P=0.017$ ). Although there were no statistical significant differences regarding the blood total protein levels ( $P=0.09$ ), the patients in which resection was performed presented higher levels of albumin ( $P=0.0032$ ).

## Discussion

One of the most important predictor factors for postoperative morbidity or mortality and overall survival in cancer patients is represented by the nutritional status. Malnutrition is frequent encountered in gastric cancer patients, mainly due to the increased metabolic demands (especially after surgical intervention), insufficient nutrient intake (depression-associated anorexia, mechanical intake difficulties and the side effects of the chemotherapy). A significant weight loss (above 10% of the usual weight) is considered to be a indicator of severe malnutrition and it can be encountered in up to one third of the newly diagnosed gastric cancer patients [6]. In other studies, the significant weight loss varied was encountered in 21.6 and 50% [7,8]. We included in our study all the patients newly diagnosed with gastric cancer referred to our unit in which a form of surgical treatment was needed. Based on the results of our study, the respectability rate was 59.55%, lower than the reported radical resection rates for gastric cancer [9]. Surgery does not give any benefit in terms of survival for patients with metastatic disease (either peritoneal or in distant organs), therefore, it is important to evaluate the curability and to avoid an unnecessary exploratory surgery for those patients. Most of the patients diagnosed with gastric cancer presented locally advanced or metastatic tumours, due to the lack of screening programs and the late onset of diagnosis in a symptomatic patient. Based on the actual guidelines recommendations and the results of previous

randomised studies in gastric cancer patients [10,11], most of the patients with locally advanced tumours are candidates for preoperative chemotherapy. Beginning from 2015 all the patients with locally advanced gastric tumours (diagnosed on preoperative imaging or on staging laparoscopy) are submitted to neoadjuvant chemotherapy. One of the main purposes of our study was to see if there are any differences in the clinical and biological nutritional status in patients with resectable tumours and those with unresectable or metastatic gastric tumours. In our study the patients in which resection was not suitable presented lower Karnofsky indexes and lower Charlson comorbidities indexes, this was mainly caused by the effect of the advanced tumour on body biology (including the effects of malnutrition). Those patients presented lower albumin plasmatic levels, one of the most accurate tools to investigate the nutritional status. Moreover, the immune response was altered in those patients, they presented lower lymphocyte levels. The combination of albumin and lymphocytes formula (Onodera Index or Prognostic Nutritional Index) was, as expected, statistically significant different in the two subgroups of patients. This nutritional index was directly correlated with greater tumour depth, lymph node metastases, lymphatic permeation and venous invasion for gastric cancer patients [12]. Moreover, this index could be a novel indicator of the malignant potential of human tumours [13]. The fact that there were no differences of the nutritional status between those two subgroups regarding the tumour localisation on gastric wall, could be an indicator that the nutritional impairment mechanism in gastric cancer is more complex and it is not correlated with the possible mechanical effect of the tumour localised in the proximity of the cardia or the pylorus. Our study presents several limitations. We included in our study all the patients which were referred to our unit with a specific indication for surgery, and we excluded the patients diagnosed with gastric cancer which were not suitable for surgery (patients with metastatic disease or patient unfitted for surgery). The effect of those patients, with a probable impaired nutritional status could sustain the results of our study. Another limitation is represented by the indication of surgical treatment in patients with locally advanced tumours; those patients, based on the current recommendations, should have been submitted to neoadjuvant chemotherapy. The effect of the neoadjuvant chemotherapy on the nutritional status of those patients previous to surgery could be investigated in a future study with standardized and uniform procedures. Nonetheless, the present study gives an insight regarding some indicators of nutritional status in a relative large subgroup of patients. In conclusion, preoperative serum albumin levels and the prognostic nutritional index are significant predictors of unresectability in gastric cancer patients. This could be an indicator of a more advanced disease, such as local involvement or peritoneal/hepatic metastases which were not suspected on the initial staging of the patient. In our opinion, for a gastric cancer patient with an impaired nutritional status, in which the initial imaging examination

**Table I:** Patient's characteristics.

<b>Age</b>	<b>66.9(65.24-68.69)</b>
Gender(male /female)	86 / 49
Charlson score	4
Stage I	4 pts
Stage II	25 pts
Stage III	63 pts
Stage IV	44 pts
<b>Type of resection</b>	
Total gastrectomy	34 pts
Subtotal gastrectomy	47 pts
<b>Tumour location</b>	
Distal stomach	57 pts
Body	80 pts
Upper stomach	26 pts



**Table II:** Comparative analysis of the resected and unresected patients.

	Resected patients (N=81 pts)	Unresected patients (N=55)	P value
Age	65.5 (63.45-67.7)	69 (66.1-71.8)	0.6
Charlson score	3	4	0.006
Karnofsky score	90 (80-90)	80 (70-80)	0.007
BMI	25.16 (24.06-26.25)	22.61(21.55-23.66)	0.017
Hb	10 (9.39-10.66)	10.9 (10.1-11.7)	0.49
WBC	7853 (7365-8340)	7363 (6675-8050)	0.23
Lymphocytes	1647 (1502-1791)	1271 (1116-1426)	0.001
Total proteins	66.7 (65.02-68.38)	63 (60.7-65.3)	0.09
Albumine levels	37.76 (36.40-39.06)	36.17 (34.7-37.55)	0.03
Onodera index	45.9 (44.29-47.64)	42.53 (40.9-44.15)	0.0032
<b>Hystological type</b>			0.11
Intestinal	60	38	
Signet ring cells	12	10	
Undifferentiated	9	7	
<b>Tumour location</b>			0.16
Distal stomach	33	17	
Body	35	25	
Upper stomach	13	13	

do not reveal a locally advanced tumour or a metastatic disease, the staging procedures should include a PET/CT or a echoendoscopy for a more accurate diagnosis.

## Conclusion

An accurate clinical and biological nutritional assessment of newly diagnosed gastric cancer patients could identify the subgroup of patients with more advanced or metastatic lesions in which a thorough stadialisation should be performed.

## Conflict of Interest

The authors report no conflict of interest. All the authors had a significant contribution to this paperwork.

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# Re-Rupture of Abdominal Aortic Aneurysm after Endovascular Repair from Infected Endograft

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## Abstract

**Introduction:** Successful endovascular aortic aneurysm repair (EVAR) aims to prevent catastrophic rupture, however despite technical excellence at index operation, long term follow up remains and atory. This is due to the fact that delayed aortic rupture may occur in certain patients after EVAR. We present a technically challenging case which illustrates this concern.

**Case report:** An 82 year old man underwent successful EVAR using a redesigned, clinical trial graft (Medtronic, Minneapolis, MN), five years prior to presentation. He was lost to follow after the initial procedure. At presentation to us, he demonstrated a 13.5cm, ruptured infrarenal aortic aneurysm due to proximal aortic neck enlargement and endograft slippage. Emergency repair included a proximal supra-renal endograft extension (Endologix, Irvine, CA), femoralfemoral bypass (PTFE), and open abdomen with negative-pressure therapy (Abthera, KCI, San Antonio, TX) He survived and was discharged with close follow-up. He re-presented six months later with flank pain and a WBC 22,000. A CT Scan was concerning for a new contained aortic rupture (16cm) and a recurrent proximal endograft slip.

High clinical suspicion resulted in a return to operating room for axillary to femoralfemoral artery bypass (PTFE), followed by explantation of the endograft system, aortic sac resection, and omental flap coverage. Operative cultures yielded *Staphylococcus epidermidis*. He survived again and was discharged on a plan for long term antibiotics on post-operative day 10.

**Conclusion:** Long term follow up after EVAR may help to identify patients at high risk for endo-graft failures. Aortic neck enlargement leading to rupture may result from primary aneurysm growth, however infection can be an important cause. Time honored open aortic surgical techniques remain an important tool for every vascular surgeon.

**Keywords:** Rupture aneurysm; Endograft infection; Abdominal aortic aneurysm; Infected endograft; Re-ruptured abdominal aneurysm after EVAR; EVAR for ruptured AAA

## Introduction

Aortic aneurysm repair has evolved since it was described by Parodi and colleagues in 1991 [1]. Currently endovascular graft repair is the main method used for Abdominal Aortic Aneurysmal (AAA) repair with lower morbidity; mortality and hospital stay [2]. Patients undergoing EVAR encounter unique complications such as endoleaks. The overall incidence of early and late type I endoleak is thought to be up to 20%, depending on the series, device, and local practice patterns, with intraoperative type I endoleaks reported at a rate of 3% to 7% [3]. Endoleaks are associated with increased morbidity and mortality, hence close follow up is of paramount importance. Patients with incomplete follow-up have higher fatal complication rates than patients with frequent follow-up [4]. Clinical follow-up schedules have generally reflected the protocols in many clinical trials of EVAR, with post procedure surveillance CT scans being performed at approximately 1 month, 6 months, 12 months and annually thereafter [5]. AAA ruptures after EVAR is one of the complications secondary to endoleaks. Management of AAA rupture after EVAR can be done by intravascular means and it is well described in the literature [6]. Re-rupture after endovascular repair is a very rare event that can be secondary to multiple risk factors including larger initial aneurysm size, poor sealing zones, female gender, presence of aorto-enteric fistula, and stent-graft infection [5]. Infection of the Endograft is a rare entity however it has a devastating complication with high mortality. Infection is reported to be below 1% following EVAR and less than 5% after TEVAR [7,8]. This data arise from multiple single center retrospective studies. We present a patient that had a re-rupture of an AAA, and its etiology was

confusing due to the presence of a possible infection of the endograft requiring explanation with extra-anatomical bypass.

## Case Report

An 82-year-old male, with history of infrarenal AAA, presented to the emergency department in our hospital with sudden onset of abdominal and back pain. It is important to mention that Five years prior he had undergone successful EVAR using a redesigned, clinical trial graft (Medtronic, Minneapolis, MN), at an outside hospital. Computer tomography was obtained which showed a 13.5 cm ruptured infrarenal aortic aneurysm with a type I endoleak secondary to proximal aortic neck enlargement and endograft migration. In order to save his life emergency repair included a proximal supra-renal endograft extension (Endologix 34 × 80 mm, Irvine, CA) with a suprarenal fixation that was deployed into the left limb, effectively creating an aortouniliac device. Left to right femoro-femoral bypass (PTFE) was then created. His repair was complicated by abdominal compartment syndrome which was managed with decompressed laparotomy and negative pressure wound vac therapy (Abthera, KCI, San Antonio, TX). Patient recovered satisfactorily and was then discharged with close follow-up

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including serial imaging. As recommended per guidelines our patient had follow up CT scans at 1 month, and before 6 months showing stable appearance to the infra renal abdominal aortic aneurysm. No evidence of leak was seen. The previously described right-sided pelvic fluid collection likely representing resolving hematoma after aortic rupture further was decreased in size. Patient was stable clinically and on his images. Ten months after the procedure patient presented to the emergency department in our hospital complaining of mild back pain with 2 weeks of duration with mild gait disturbance and no other associated symptom. Repeated CT scan was performed that showed aortouniiliac stent graft in place with mild distal migration of the proximal portion of the graft. No evidence of endoleak. Infrarenal abdominal aorta aneurysm minimally increased in size compared to the prior study. Faint haziness around the abdominal aorta, most pronounced around the aneurysm that was increased since the prior study suggesting aortitis. No evidence of aneurysm rupture. Patient was admitted to the surgical intensive care unit for observation and was discharged home when clinically stable. Eleven months after the index procedure for AAA rupture, the patient presented with another episode of flank pain and leukocytosis of 22,000. CT angiogram showed a new contained 16.5 cm infrarenal aortic aneurysm rupture and a recurrent proximal endograft migration. With the high suspicion for infected endograft the patient was taken to the operating room for extra anatomic bypass and explantation of endograft. An axillary to femoral-femoral bypass (PTFE) was preformed followed by an excision of the endograft, which was completely detached proximally. The aneurysmal sac contained a foul smelling purulent material indicative of an infectious process. The aortic sac was resected; ligation of the infra renal abdominal aorta with omental flap coverage was performed. Operative cultures yielded *Staphylococcus epidermis*. Post-operatively patient was monitored in the surgical intensive care unit showing remarkable recovering and was discharged home.

## Discussion

Endovascular aneurysm repair has gained wider acceptance as a feasible alternative to conventional open repair. As more number of EVARs is performed, increased number of complications has been reported. Infected endovascular graft is a feared and devastating complication that's associated sepsis, hemorrhaging, and dissociation of arterial and graft interface with high morbidity and mortality [9]. The incidence of infected endograft is rare and has been reported in literature from 0.2-3% [10]. Ducasse et al. reported a 0.4% incidence of AEI in 9,739 procedures. Similarly, the review by Fiorani et al. of the literature and international practitioner survey yielded a 0.4% AEI incidence. Mortality rates after AEI have been reported as high as 18%. In this case report we present a patient with evidence of infected endograft which may be the etiology of multiple recurrent endograft failure and rupture. At the third presentation for abdominal aneurysm rupture, he presents with classic signs and symptoms of ruptured aortic aneurysm. The leukocytosis and history of vague weakness raised our suspicion for infected endograft. *Staphylococcus Epidermis* was isolated from OR culture and confirmed our suspicion. Although the most common organism causing endograft infections are caused by *S. aureus*, other common organism associated with AEI includes *S. epidermidis*, *Enterococcus*, *E. coli*, *Streptococcus* species [11]. Fungal infections are extremely rare [12]. Currently there are no standard of care for the management of infected endograft. However, the general consensus in many small reported cases suggests that surgical excision with intravenous antibiotics is the mainstay therapy [2,11]. The standard surgical approach includes two parts: explantation of the infected endograft and revascularization with extra-anatomic bypass [8,9]. Conservative management with IV antibiotic alone may be the only option for patients that will not survive an open procedure. In

selected cases, simple resection of the aneurysms sac and leaving the stent graft behind has been described. Unfortunately the mortality in these frail patients can be up to 40% [10]. Appropriate follow up for patients with EVAR presents another challenge. The current SVS recommendation for surveillance post EVAR after the first year is CT scan at one month and 12 months. Recommendation for long-term follow up after one year is ambiguous and depends on several risk factors. Re-rupture of AAA after EVAR is extremely rare. Rates are described to be 1.2% per patient per year depending on the type of endograft and degree of follow-up [5]. 50% of AEI presents between 25-70 months post EVAR [13]. Our patient presented 11 months after the 2<sup>nd</sup> procedure with ruptured aneurysm. He had extremely close follow-up. This underscores the importance of regular and long-term surveillance to detect evidence of impending rupture and prevent catastrophe.

## Conclusion

Long term follow up after EVAR may help to identify patients at high risk for endo-graft failures. Aortic neck enlargement leading to rupture may result from primary aneurysm growth, however infection can be an important cause. Time honored open aortic surgical techniques remain an important tool for every vascular surgeon.

## Conflict of Interest

Authors have no conflict of interest to disclose.

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# A Rare Cause of Painless Haematuria- Adenocarcinoma of Appendix

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## Abstract

Neoplasms of the appendix are rare, accounting for less than 0.5% of all gastrointestinal malignancies and found incidentally in approximately 1% of appendectomy specimen. Carcinoids are the most common appendicular tumors, accounting for approximately 66%, with cystadenocarcinoma accounting for 20% and adenocarcinoma accounting for 10%. Appendiceal adenocarcinomas fall into one of three separate histologic types. The most common mucinous type produces abundant mucin, the less common intestinal or colonic type closely mimics adenocarcinomas found in the colon, and the least common, signet ring cell adenocarcinoma, is quite virulent and associated with a poor prognosis. Adenocarcinoma of appendix is most frequently perforating tumour of gastrointestinal tract due to anatomical peculiarity of appendix which has an extremely thin subserosal and peritoneal coat and the thinnest muscle layer of the whole gastrointestinal tract. In addition to the risk of perforation, mucinous adenocarcinoma of appendix have peculiar tendency for fistula formation. Many of unusual presentations reported for primary appendicular carcinoma are the results of fistula formation into the adjacent viscera such as the urinary bladder, bowel or vagina as well as extraperitoneally into retroperitoneal tissues or directly to the skin surface.

**Keywords:** Adenocarcinoma; Appendix; Haematuria; Urinary bladder; Hemicolectomy

## Introduction

Neoplasms of the appendix are rare, accounting for less than 0.5% of all gastrointestinal malignancies and found incidentally in approximately 1% of appendectomy specimen. Carcinoids are the most common appendicular tumors, accounting for approximately 66%, with cystadenocarcinoma accounting for 20% and adenocarcinoma accounting for 10% [1]. We present a case of adenocarcinoma of appendix presenting only with a recurrent painless haematuria.

## Case Report

A 79 year male presented to our surgical clinic with history of recurrent attacks of painless haematuria since last 5 months. There was no history of any fever, pain abdomen or any other urinary complaints. Patient had history of similar attacks 5 months back for which he was investigated by routine haemogram and urine analysis. During that time his total leukocyte count was around 9000 cu/mm with urine analysis showed 15-20 red blood cells without any pus cells. He was taken up for cystoscopy which revealed a congested area in the bladder mucosa suggestive of cystitis. Then oral and intravenous contrast enhanced CT scan abdomen was planned which was reported to be acute appendicitis complicated by cystitis. Conservative management in the form Oshner Sherren's regiment with a plan of subsequent interval appendectomy was planned. Patient then had an uneventful recovery then with that conservative management. General physical examination at this time of presentation was unremarkable. Examination of abdomen showed mild tenderness in the suprapubic and right iliac fossa region without any palpable mass. Complete haemogram showed haemoglobin 13.23 g/dl, total leukocyte count- 7000 cu/mm with differential leukocyte count showing neutrophil- 72%, lymphocyte- 18%, monocyte- 10%. Routine urine test showed 5-7 red blood cells/high power fields. Liver function test and renal function test was within normal limits. Oral and intravenous contrast enhanced CT scan of abdomen was planned which showed a heterogeneously enhancing oblong mass lesion measuring

approximately 6 × 2.5 cm replacing the appendix with the tip of the lesion having an ill-defined interface with the dome of the urinary bladder suggestive of infiltration. No evidence of intrinsic mass lesion was seen within the urinary bladder. No abdominal lymphadenopathy or free intraperitoneal free fluid was detected. Interface between the mass lesion with bowel loops, right iliac vessels and right ureter was well maintained (Figure 1). Patient was planned cystoscopy followed by exploratory laparotomy. On cystoscopy an external bulge in the anterior urinary bladder wall with an area of mucosal erosion showing mild bleeding was seen. No intrinsic mass lesion was detected in the urinary bladder (Figure 2). Exploratory laparotomy was done. Appendicular growth was seen invading the dome of the urinary bladder (Figures 3 and 4). Right hemicolectomy with en bloc resection of invasion in urinary bladder was done. Primary ileo transverse anastomosis with repair of the urinary bladder wall was done under the cover of suprapubic cystostomy. Patient had an uneventful postoperative recovery. On post operative day 16 cystogram was done which revealed no leakage of contrast from the urinary bladder. Suprapubic cystogram was removed on post operative day 19. Histopathology of the specimen was suggestive of moderately differentiated mucinous adenocarcinoma with regional nodal metastasis with 4/15 lymphnodes showing metastatic deposits with perinodal extension. All resected margins were free from tumor (Figure 5). Patient was discharged with a plan of subsequent adjuvant chemotherapy.

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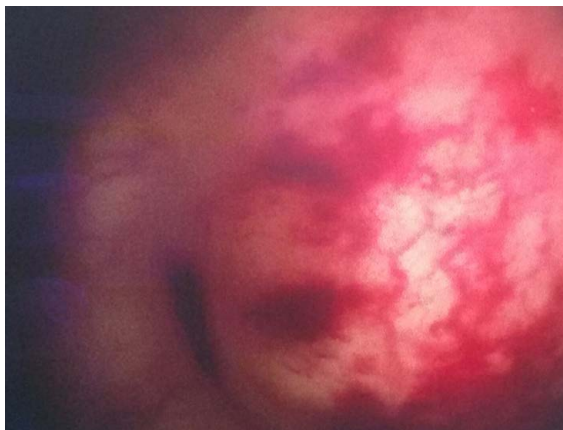
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**Figure 1:** CECT abdomen showing a heterogeneously enhancing oblong mass lesion with the tip of the lesion having an ill defined interface with the dome of the urinary bladder suggestive of infiltration.

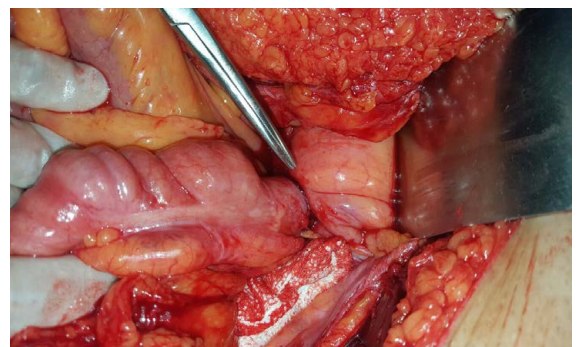


**Figure 2:** Cystoscopy showing an external bulge in the urinary bladder with a small area of mucosal congestion.

## Discussion

A tumor of Appendix is a rare entity and was first reported by Berger in 1882. On review of literature only about 250 cases of appendicular adenocarcinoma have been reported since Berger first described it in 1882 [2]. Carcinoids are the most common appendicular tumors, accounting for approximately 66%, with cystadenocarcinoma accounting for 20% and adenocarcinoma accounting for 10%. Appendiceal adenocarcinomas fall into one of three separate histologic types. The most common mucinous type produces abundant mucin, the less common intestinal or colonic type closely mimics adenocarcinomas found in the colon, and the least common, signet ring cell adenocarcinoma, is quite virulent and associated with a poor prognosis [1,3]. Then there are the rare forms of cancers which include adenocarcinoid, non-Hodgkin's lymphoma, ganglioneuroma, and pheochromocytoma. Malignant tumour normally spreads intraperitoneally through lymphatic. Hematogenous spread is rare. Benign primary processes are mainly mucinous epithelial neoplasms, also called adenomas, cystadenoma, and benign neoplastic mucocoele [3]. The majority of primary cancers of the appendix occur in 55-65 years of age, except for malignant carcinoid, which has a mean age of diagnosis of 38. Men and women seem to be at equal risk for all

appendiceal neoplasms except for malignant carcinoid which may have woman to man ratio in excess of 3: 1. Adenocarcinoma of the appendix is usually seen in the 6<sup>th</sup> to 7<sup>th</sup> decade with a male preponderance [2,4]. Appendicular adenocarcinoma usually presents as appendicitis with or without appendicular abscess, palpable abdominal mass, intestinal obstruction and pseudomyxoma peritonei [5]. Adenocarcinoma of appendix is most frequently perforating tumour of gastrointestinal tract due to anatomical peculiarity of appendix which has an extremely thin subserosal and peritoneal coat and the thinnest muscle layer of the whole gastrointestinal tract. In addition to the risk of perforation, mucinous adenocarcinoma of appendix have peculiar tendency for fistula formation [2]. Many of unusual presentations reported for primary appendicular carcinoma are the results of fistula formation into the adjacent viscera such as the urinary bladder, bowel or vagina as well as extraperitoneally into retroperitoneal tissues or directly to the skin surface. Extraperitoneal spread is associated with relatively good prognosis by preventing the development of peritoneal carcinomatosis [6,7]. Unusual presentation includes haematuria due to bladder infiltration, direct invasion of ascending colon detected on colonoscopy, intussusception, hydronephrosis due to ureteric infiltration, retroperitoneal abscess, vaginal bleeding, lower gastrointestinal bleed, epididymitis in case of metastases to the spermatic cord or testicles, ovarian mass due to Krukenberg tumor and cutaneous infiltration [5,8-14]. Management of appendiceal neoplasms should follow oncosurgical principles same as colorectal adenocarcinomas. If the patient presents electively, routine tumour markers including CEA, CT scanning and colonoscopy should be performed. Soft-tissue thickening and irregularity and thickening of the appendix wall and surrounding fat infiltration are nonspecific findings that suggest malignancy of appendix in CT scan abdomen. Gonzalez-Moreno and Sugarbaker found that those patients with mucinous type cancer had no survival benefit from hemicolectomy versus appendectomy.

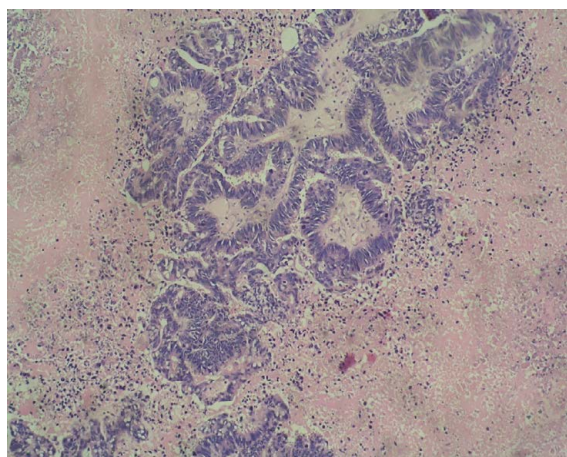


**Figure 3:** Intraoperative photo showing appendicular infiltration into the urinary bladder.



**Figure 4:** Specimen of right hemicolectomy with appendicular growth and wedge resected specimen of urinary bladder entoto.





**Figure 5:** Histopathology of the specimen suggesting moderately differentiated mucinous adenocarcinoma of Appendix.

They further mention that hemicolectomy is recommended in those patients where (1) it is necessary to clear the tumor or perform complete cytoreduction; (2) lymph node involvement is demonstrated by histopathological examination of the appendiceal or ileocolic lymph nodes; or (3) a nonmucinous subtype is identified by histopathological examination. In a study done by Pahlavan and Kanthan adenocarcinoid tumors, he states that even though Goblet cell carcinoma is an aggressive tumor, a simple appendectomy is appropriate in most cases. However, he further states that a right hemicolectomy should be performed in the following scenarios: (1) cellular undifferentiation, (2) increased mitotic activity, (3) involvement of the base of the appendix, (4) lymph node metastasis, or (5) tumor size greater than 2 cm.

Surgical treatment of appendicular adenocarcinoma with right hemicolectomy has been reported as the treatment of choice because it facilitates lymph node resection to enable accurate tumour staging. Post-operative histopathological diagnosis after appendicectomy requires second surgery in form of right hemicolectomy. Several studies have showed significantly better 5 year survival rates in patients treated with right Hemicolectomy compared to appendicectomy alone. In advanced disease, peritonectomy and intraperitoneal chemotherapy should be considered. Once pseudomyxoma peritonei secondary to the tumour occurs, patient requires aggressive surgical debriement of all deposits on peritoneum besides right hemicolectomy and excision of neighbouring compromised organs. Oophorectomy has been described in female patients with appendicular adenocarcinoma for the dual purpose of staging and removing a potential site of recurrence. Adenocarcinoma of appendix with extraperitoneal and intraperitoneal extensions to different organs requires partial or complete excision of the involved organ and fistulous truck besides right hemicolectomy. The presence of nodal involvement, systemic and intraperitoneal chemotherapy regimens should be used. Prognosis of adenocarcinoma of appendix depends on the subtype and extent of disease. Mucinous adenocarcinoma is considered to have a more favorable prognosis [14-20].

## Conclusion

Neoplasms of the appendix are rare, accounting for less than 0.5% of all gastrointestinal malignancies and found incidentally in approximately 1% of appendectomy specimen. Appendicular adenocarcinoma usually presents as appendicitis with or without appendicular abscess, palpable abdominal mass, intestinal obstruction and pseudomyxoma peritonei and is the most frequently perforating tumour of gastrointestinal tract due to anatomical peculiarity of appendix which has an extremely thin subserosal and peritoneal

coat and the thinnest muscle layer of the whole gastrointestinal tract. Management of appendiceal neoplasms should follow oncosurgical principles same as other colorectal adenocarcinomas. Adenocarcinoma of appendix should be kept in one of the rare differential diagnosis of any unexplained haematuria when all most common indications for the conditions are ruled out by investigations.

## Conflict of Interest

Authors have no conflict of interest to disclose.

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# Obstructive Mucocele of the Maxillary Sinus in an 18 Year Old Cambodian Female

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## Abstract

**Objective:** Sinus mucoceles are true cysts that develop secondary to obstruction of sinus ostia and can be associated with significant morbidity. Study Design. We present a case of obstructive-type sinus mucocele of the maxillary sinus, including clinical, radiographic, histologic findings, as well as treatment.

**Results:** An 18 year old female presented for evaluation and management of maxillary sinus swelling. A diagnosis of sinus mucocele was rendered after clinical, radiographic, surgical and histopathologic examinations. Recurrence developed within four months of the initial surgical intervention.

**Conclusions:** Sinus mucoceles may be associated with significant morbidity and are currently managed most often by endoscopic nasal surgery.

## Introduction

Sinus mucoceles are true cysts lined by pseudostratified respiratory epithelium and have a mucous or mucopurulent content [1]. They are produced by the accumulation of mucous secretions within tissue or the sinus cavity, secondary to obstruction of the sinus ostia (obstructive type). By definition, if there is partial obstruction of ducts of seromucous glands within the sinus wall, such true cysts are called retention cysts of the maxillary sinus. While retention cysts are typically asymptomatic and incidental findings, the obstructive type sinus mucocele is capable of significant expansion and destruction [2]. Chemical mediators, such as prostaglandin E2 and collagenase, are released at the capsule of the mucocele, possibly causing bony destruction and allowing the mucocele to expand into adjacent structures [3]. They can lead to exophthalmos, limited eye movement and headaches in patients. Rarely, ethmoid sinus involvement may induce oculomotor nerve paralysis. The frontal sinus is most commonly affected, whereas involvement of sphenoid, ethmoid, and maxillary sinuses are unusual sites of involvement [4]. We present a case of obstructive type sinus mucocele of the left maxillary sinus in an 18 year old female.

## Case Report

An 18 year old Cambodian female presented to Children's Surgical Center at the National Rehabilitation Center in Phnom Penh, Cambodia for evaluation of left maxillary sinus swelling and discomfort (Figure 1). In addition to notable facial asymmetry, the enlargement was associated with elevation of the left orbit. No visual disturbances, however, were noted. A computerized tomography (CT) scan without contrast was ordered and showed a cystic process of the left maxillary sinus (Figure 2) and treatment was planned for February 2014. An 18-gauge needle was chosen for aspiration through an existing bony defect apical to teeth 12-14, returning a mucoid material. Subsequent surgical access was gained in the same area and, upon entry into the sinus, the membrane appeared normal. The lumen of the sinus was entirely filled with a gray, viscous, mucoid material. This, along with a portion of the sinus lining, was removed and submitted for histopathologic examination. An antrostomy of the sinus was completed prior to closure. Recovery and healing were uneventful.

Histologic examination of the submitted specimen showed fragments of fibrous and fibromyxoid stroma with small blood vessels and foci of chronic inflammation. Foamy histiocytes were seen in isolated portions of the specimen. While the majority of the specimen was rather paucicellular, foci of plump, angular and spindle-shaped cells were seen. Immunohistochemical stains for S100 protein were negative. The histologic findings, in combination with those of the CT imaging and surgical exploration, were consistent with a sinus mucocele, obstructive type. Within four months of surgery, the patient returned for follow-up with lesion recurrence, necessitating further intervention. A second surgical procedure was completed and follow-up is ongoing.

## Discussion

Langenbeck first described mucoceles as hydatids in 1820. Later, in 1909, Rollet coined the term mucocele. They are found most often in the frontal sinus, with those of the maxillary sinus generally considered rare [5,6]. While mucoceles are benign processes, they behave like space occupying lesions, causing erosion of surrounding bone and displacement of adjacent structures. Their proximity to vital structures can be a cause of significant morbidity if left untreated [4]. Obstructive type sinus mucoceles occur secondary to the obstruction of the natural orifices and are most often associated with chronic inflammation, allergy, surgery or trauma. They distend the bony walls of the sinuses as the intraluminal pressure increases and eventually erode the bone by

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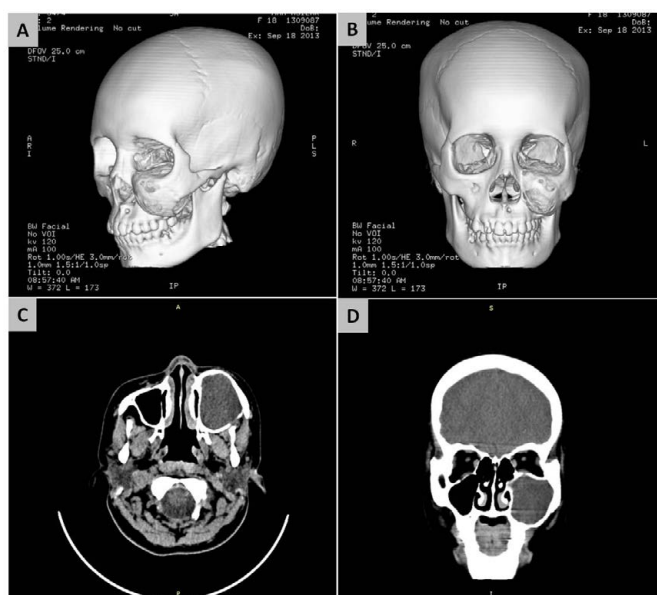
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**Figure 1:** Clinical image showing swelling of the left maxillary sinus region.



**Figure 2:** A: Three dimensional computed tomography demonstrating expansile lesion of the left maxillary sinus – lateral view; B: Frontal view; C: Computed tomography showing homogenous, expansile view of the left maxillary sinus – axial view; D: Coronal view.

pressure resorption [6]. Occasionally, bone dyscrasias, such as fibrous dysplasia or osteopetrosis, can cause obstruction of the ostia and lead to sinus mucocoeles.

Typically, sinus mucocoeles are diagnosed in adults during the 3<sup>rd</sup> and 4<sup>th</sup> decades. However, patients as young as 4 have been reported [1]. There is a slight male predilection [7]. Clinical symptoms may include headache, diplopia, visual impairment, nasal obstruction, and a variety of other symptoms related to involvement of the various cranial nerves and the pituitary gland, depending upon the location of the individual mucocoele. Primary antral mucocoeles usually occur as swellings of the cheek or mucobuccal fold, with displacement of the dentition and occasional nasal obstruction or exophthalmos. Poorly localized pain or tenderness often accompanies the swelling [6].

While diagnosis is often by rhinoscopy, CT scans of the paranasal sinuses or magnetic resonance imaging (MRI) with gadolinium contrast

may be helpful [8]. MRI may be particularly useful in differentiating mucocoeles from neoplastic processes [4]. CT scans of maxillary sinus lesions typically show a uniformly expansile mass within the antrum and thinning of the bone, mostly of the anterior wall [9].

Infection of sinus mucocoeles (mucopyocoele) with pyogenic bacteria may result in the accumulation of pus within the lumen and increased morbidity. The most frequent organisms include staph aureus, alpha-hemolytic streptococci (six isolates), *Hemophilus* spp. (five isolates), and Gram-negative bacilli (six isolates). The predominant anaerobes are *Peptostreptococcus* sp., *Prevotella* sp., *Fusobacterium* sp., and *Propionibacterium acnes*.

On microscopic examination, obstructive type mucocoeles within paranasal sinuses are lined by pseudostratified ciliated columnar epithelium. Squamous metaplasia and reactive bone formation can appear in areas adjacent to cystic epithelium. Occasionally, there is activation of T<sub>H2</sub> lymphocytes due to increased expression of IL-12 and IL-2 which can lead to an increased inflammatory response [7].

The treatment can be either radical or conservative. Conservative surgical care involves marsupialization of the mucocoele with maintenance of adequate sinus drainage, which relieves the symptoms and prevents recurrence. This is now done most often by endoscopy using medial maxillectomy with mucosal flap [7,10,11]. With Endonasal sinus surgery, Bockmuhl and colleagues [5] reported that 98.4% of 185 patients were long-term disease free. Previously, mucocoeles have been removed through external approaches, such as a Lynch-Howarth incision, Caldwell-Luc approach, or an osteoplastic flap. Surgical excision is the treatment of choice and early intervention is indicated to prevent visual compromise or the development of a mucopyocoele.

## Conclusion

Sinus mucocoeles are characterized by the potential for significant morbidity when not treated promptly or adequately. We have presented a case involving the maxillary sinus in an 18 year old female, which recurred after the initial surgical procedure.

## Conflict of interest

Authors have no conflict of interests to declare

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# Surgical Planning in Pan Facial Trauma Using Additive Manufacturing Medical Model-A Case Study

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## Abstract

Additive Manufacturing (AM) technology is an engineering technology which has a wide scope in medical field. Of various medical fields, craniofacial and maxillofacial surgery adapted this technology and is making use of it to overcome the shortcomings of traditional procedures. Medical application of AM or Rapid prototyping was started two decades ago and is expanding its frontiers with the advancement in technology and technical expertise by the medical professionals. AM technology is widely being used in maxillofacial surgery for hassle free planning, patient education and execution of the surgical procedure and for precision using medical models. The Current case is of pan facial trauma with multiple facial bones fracture treated by surgical planning on AM medical model to adapt the mini plates to be prior to the surgery. This paper also deals with the importance of AM medical models in complex surgeries for better outcome.

**Keywords:** Additive manufacturing; 3D printing; Rapid prototyping; Maxillofacial surgery; Pan facial trauma; Adaptation on mini plates

## Introduction

Additive Manufacturing is a process that creates parts in an additive by adding layer-by-layer. This technology produces models or prototype parts from source such as Computed Tomography (CT scan), Magnetic Resonance Imaging (MRI), Cone Beam Computed Tomography (CBCT), Computer Aided Designs (CAD) or from any Reverse Engineering techniques [1]. AM technology is used for building physical models and prototype parts from 3D CAD data in various industries such as Automobile, Aerospace, Mechanical, Medical, dental and so on [2,3]. AM applications have generated increased interest in recent years, and many countries are trying to apply AM technique to various fields round the globe. Among which medical field is one of the most benefited industries with this technology? As the medical field requires patient specific medical model, which is unique for each patient and easy to get it using AM technology, it allows user for the mass customization, i.e. X number of parts in a single batch can be produced as X unique parts. In the early stages of AM, it is used in the medical industry for pre planning of complex surgeries [4,5]. The first application of stereolithography in Maxillofacial Surgery was performed by Brix and Lambrecht in 1985 for craniofacial surgery planning, here after the technological advances in hardware and software of AM has been refined and incorporated in craniofacial surgery in recent years [6]. AM medical models are considered an interesting appliance for diagnosis in congenital malformations, craniomaxillofacial defects, pathologies, reconstruction, maxillofacial trauma, orthognathic surgery, facial asymmetry, surgical planning, and in designing custom made prosthesis which helps in professional-patient communication for its ease of availability [7,8]. The virtual image is made into a physical medical model by a technical process called AM. This technique was originally emerged as Rapid Prototyping in mechanical engineering and has found applications in medicine. The word prototyping was first used to describe the act of producing a prototype i.e., a unique product, the first product, or a reference model. In the past, prototypes were handmade by sculpting or casting and their fabrication demanded a long time. With the development of information technology, three-dimensional models can be devised and built based on virtual prototypes. Computers can now be used to create accurately detailed projects that can be accessed from different perspectives in a process known as computer-aided design (CAD). To materialize virtual

objects using CAD, a computer-aided manufactory (CAM) process has been developed. To transform a virtual file into a real object, CAM operates using a machine connected to a computer, similar to a printer or peripheral device [9]. In the present day as per ASTM latest classification there are seven processes available for fabrication of AM medical model [10]. Classification based on the process and raw material used to fabricate the processes, among the seven processes the Material Extrusion process is available easily throughout the globe and it's easy to maintain. The operating and initial cost for these machines are also very less. Due to its ease of availability and cost factor Material Extrusion process is used for fabricating medical models widely. Fused Deposition Modeling falls under the category of Material Extrusion. Models made out of this technique have good strength and these models can be used for functional purpose and this technique also provides the flexibility of printing models with multiple colors, but in most cases each color at a time [11]. The 3D CAD patient data is converted in to Stereo Lithography (stl) file format to accept globally for any AM machine to fabricate physical model [12]. The current case is of pan facial trauma which was treated by AM medical model in mock surgery to finalize sequence of steps to adopt in actual surgery and also to optimize surgery procedure.

## Case Report

This is a case of 25 year old male, who sustained injuries due to road traffic accident. He was reported with bleeding from mouth and nose and loose teeth in the anterior region of the lower jaw. On clinical examination, the patient was conscious coherent and responding to

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verbal commands. The Glasgow coma scale was 15 on 15. Head injury was clinically ruled out. On examination of face, there was peri-orbital ecchymosis, flattening of nasal bridge, subconjunctival hemorrhage, deranged occlusion, sublingual hemorrhage and avulsed maxillary and mandibular anterior teeth. A provisional diagnosis of pan facial trauma was made and computed tomographic scan (CT scan) was advised. The 3D reconstructed computed tomographic scan Figure 1 revealed, fracture of the fronto-nasal region, fractures on anterior and lateral walls of maxillary sinus on both sides, mandibular parasymphysis fracture on left side, dento alveolar fracture on maxillary and mandibular anterior region. Thus the diagnosis of pan facial trauma was confirmed. The DICOM (Digital Imaging and Communication in Medicine) images obtained from CT scan were processed through MIMICS software. This software converts DICOM data to 3D CAD (Computer Aided Design) data [13]. The CT scan consists of patient complete information i.e. exposed to the scan area. From the complete information the bony information is segregated in the MIMICS software in the initial stage using Hounsfield Units. In the later stage only required region of interest is separated using the edit mask, cut, split tools etc. For the current case injuries or fractures are observed on the region of mandible, maxilla and the nasal regions. After analyzing the fractures data from MIMICS the intensity of the fracture is clearly identified and for the ease of identification each fracture portion is colored differently as shown in (Figure 2). The STL file is processed through the CURA software, which is open source preprocessing software for Fused Deposition Modelling technique AM machine. In this software the layer height, orientation of the medical model, fill density of the medical model and temperature to operate can be defined for fabrication of AM medical model. For the current case Maker Pi M14 machine is used for the fabrication of medical model. The material used is PolyLactic Acid (PLA) with additives is used as a filament. The basic principle of FDM technique is to extrude the filament from the nozzle at desired temperature with required diameter to form the required shape or model. AM medical model was made in different colors and parts according to the displacement of fractures and reduction was done on the model. Proper occlusion was achieved. Once the reduction was satisfactory, necessary miniplates were bent according to the contour of the anatomical structure. Complete planning was done on the medical model and to finalize the size and shape of the mini plate as shown in (Figure 3). The case was operated under general anesthesia and nasotracheal intubation. Standard surgical procedures were followed and the fractures were fixed at fronto-nasal region, naso-maxillary buttress, zygomatico-maxillary buttress on left and right sides with 2.0 mm plates and necessary screws. Mandible was fixed with 2.5 mm and 2.0 mm plates and necessary screws as shown in (Figure 4). The whole procedure took about 2 hours. There was precession in the surgery and the time required has drastically minimized. As the plates were adapted in prior, the reduction was easy and proper. This helped in minimizing the operating time thereby the complications due to prolonged general anesthesia. The patient recovered with no complications. The postoperative radiographs were taken to confirm the placement of the plates and reduction of bones. Figure 5 represents the postoperative Orthopantomogram and Figure 6 is postoperative Para nasal Sinus View.

## Discussion

Since many years, surgeons depended on plain X radiographs for the diagnosis and treatment planning. The older diagnostic aids provided a two dimensional image of a three dimensional object. Thus for proper orientation, another radiograph was advised perpendicular to the first radiograph. With the advancements in diagnostic aids, a third dimension was added to the existing radiography [3 dimensional CT Scan]. This was of a great use to the surgeons for both planning and patient education. Thus far, 3-dimensional (3D) reconstructed

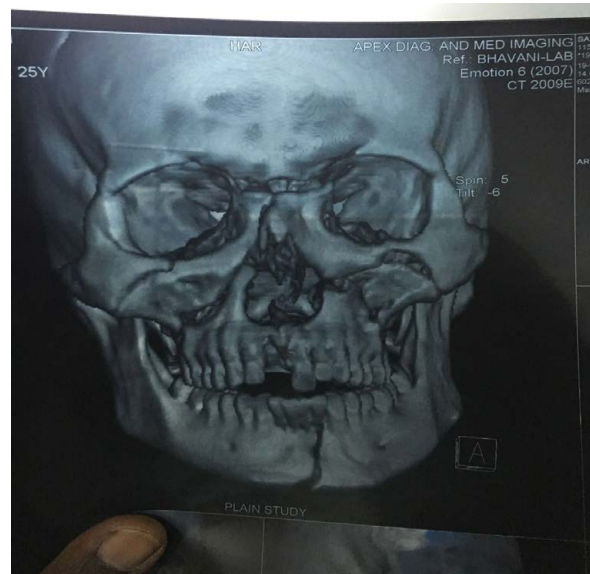


Figure 1: X-ray of the patient.

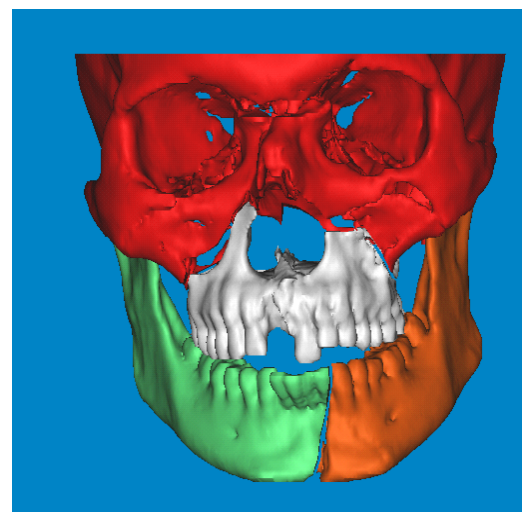


Figure 2: 3D CAD model of the patient.

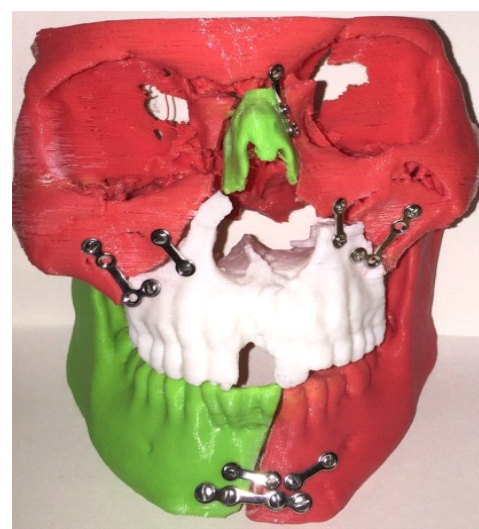


Figure 3: AM medical model of the patient.



**Figure 4:** Actual surgery photos after fixing mini plates to patient.



**Figure 5:** Postoperative orthopantomogram.



**Figure 6:** Para nasal sinus view.

image derived from computed tomography (CT) data was the best option available for evaluation and treatment of surgical problems in dental and craniomaxillofacial surgery and various other specialties. The major drawback of this modality is that the reconstructed images could not be analyzed comprehensively on various planes and sections as it is only represented as pictures on a screen [14]. In 1987, Brix and Lambrecht used, for the first time, a physical medical model in health care. It was a three-dimensional model manufactured using a computer numerical control (CNC) device, a type of machine that was

the predecessor of rapid prototyping [15]. Medical applications for AM are expanding rapidly and are expected to revolutionize health care [16]. The application of AM medical model in medicine can provide many benefits, including: the customization and personalization of medical products, drugs, and equipment; cost-effectiveness; increased productivity; the democratization of design and manufacturing; and enhanced collaboration [17- 20].

Intraoperative bending of plates can be time consuming. Bending the plates on the medical models fabricated using additive manufacturing technologies prior to the surgery reduces operating times. Lethaus et al. [21] have found saving of an average of 40 percent of the reduction of operating time in cases of mandibular reconstruction. Ideal positioning of mandibular segments, time saving by no intraoperative repeated bending and adapting of plates, use of the original surface of the cortical bone as a template for adapting the recon plate, facilitating the preoperative surgical simulation and restoration of centric occlusion of the patient were some of the benefits of virtual surgical planning and construction [22,23]. The authors found similar advantage by using AM medical models. The operating time was reduced significantly and the adaptation of the mini plates was accurate. The pre-determined position also aided in good reduction of the bony segments and reduced the chance of postoperative plate breakage.

## Conclusion

The current case of pan facial trauma consists of multiple fractures in the facial region. This kind of multiple fractures is relatively rare. Since there are multiple fractures, the surgery becomes complicated and time taking. As multiple mini plates are to be fixed, the adaptation of mini plate to the patient anatomy is not so easy using conventional CT or X-ray technique, which decreases the outcome. As in this case, multiple fractures and multiple mobile bony fragments make it complicated and time taking. With help of AM medical model, these mini plates are adapted to the patients near normal anatomy before the surgery, which aided in proper manipulation and reduction of fracture fragments and also saved significant amount of surgical time. Comparing with total surgery time of 2 hours 50% of time (1 hour) of surgery time is reduced using AM medical model. The authors suggest that this technique is quite handy and can be applied to other scenarios. The authors conclude that, Additive manufacturing or 3D printing is a good aid in the field of medicine. There is multitude of trends for the usage of 3D printing in the field of Oral and Maxillofacial Surgery. By using these models, the diagnosis, patient education and treatment planning becomes easy while minimizing the operative time and complications. The only drawback of this technology is its cost. With the advancements in technology, we hope that when the cost comes down, the usage could become widespread in the field of Maxillofacial Surgery and medicine.

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# Abdominal Wall Endometriosis: Four Cases Presentation and Literature Review

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## Abstract

Abdominal wall endometriosis is a very rare site for extragenital endometriosis. We present 4 cases diagnosed and treated in two gynecological services of Iasi, Romania, and we review the literature data on this topic. The endometriotic implant in our cases occurred in the post-cesarean section scar, and was diagnosed after 1-4 years from the intervention. The main symptom was local pain (in 2 cases with a cyclical pattern). The initial diagnostic was endometriosis in 3 cases, and granuloma in one case. The ultrasound adequately described the situation and the consistency of the tumor in 2 cases. The treatment was surgical excision, and the post-operative evolution was favorable. In conclusion, although a rare disease, endometriosis is accessible for the diagnostic and treatment, being a pathology that both surgeons and gynecological should consider.

**Keywords:** Endometriosis; Extragenital endometriosis; Abdominal wall endometriosis

## Introducere

Endometrioza de perete abdominal este o formă rară de endometrioză, estimată la 0,03-1,08% din cicatricile postcezariene [1]. și 0,5-1% din formele de endometrioză extragenitală [2-4]. Diagnosticul este dificil și trebuie diferențiat de alte patologii de perete abdominal : granulom de fir, lipom, abces, chist sau hernie, motiv pentru care majoritatea cazurilor se adresează inițial chirurgilor. Poate deveni clinic evidentă la un interval foarte variat, endometrioza parietală se diagnostichează la 3 luni - 10 ani după intervenție [5,6]. Prezentăm 4 cazuri de endometrioză parietală abdominală (EPA) diagnosticate și tratate în 2 servicii de specialitate din Iași.

## Prezentarea cazurilor

- 1) Pacienta CF, în vârstă de 31 ani, internată la 12 luni post cezariană, pentru formațiune dureroasă, cu dureri ciclice, fenomene inflamatorii la nivelul cicatricii de cezariană Figura 1. Diagnosticul inițial a fost granulom de fir ; se practică excizia formațiunii iar rezultatul anatomopatologic evidențiază aspect de endometrioză : glande de aspect endometrial înconjurat de un endometru subțire (Figura 2).
- 2) Pacienta MA, de 34 ani, cu antecedente de endometrioză pelvină, se prezintă la 4 ani după cezariană, cu o formațiune tumorală dureroasă de 20 × 10 mm la nivelul cicatricii de cezariană. Se intervine chirurgical ; explorarea per operatorie evidențiază o tumoră parietală aderentă la toate straturile parietale (țesut celular subcutanat, aponevroză și mușchi, peritoneul parietal și cel pre vezical). Se practică excizia formațiunii. Examenul histopatologic evidențiază endometrioză parietală : celule și glande endometriale, înconjurat de fibroză (Figura 3).
- 3) Pacienta TPE, 29 ani, se prezintă la 2 ani după cezariană, pentru o formațiune tumorală dureroasă, de 2,5 cm de diametru, situată la nivelul cicatricei mediane subombilicale. Se practică excizia tumorii de 2,5 cm, iar rezultat anatomopatologic confirmă endometrioza parietală (Figura 4).
- 4) Pacienta TC, în vârstă de 36 ani, se prezintă la 22 luni postcezariană (a doua cezariană) pentru dureri intermitente la extremitatea stângă a cicatricei; examenul clinic evidențiază o formațiune

tumorală de 10 × 10 mm, mobilă pe planurile profunde. Explorarea ecografică Figura 5 confirmă prezența formațiunii, și subliniază aspectul său hipocogen relativ omogen. Se practică excizia chirurgicală iar examenul histopatologic confirmă endometrioza: glande endometriale înconjurat cu stroma endometrială și focare hemoragice (Figura 6).

## Discuții

Endometrioza este o afecțiune care afectează 10-15% din femeile de vârstă reproductivă. În general, localizarea afecțiunii privește pelvisul, organele genitale și cele învecinate acestora. Există însă și forme cu localizare extrapelvină. Dintre acestea, un tip particular, cu diagnostic diferentiat dificil și care deseori este văzută de chirurgii generaliști este endometrioza parietală. Deși au fost descrise și cazuri cu alte localizări - pe cicatricea de epiziotomie sau pe porturi de laparoscopie -, cea mai frecventă formă este cea pe cicatricea post-cezariană.

Mecanismul formării și persistenței acestor focare endometrioizice nu este bine cunoscut, discutându-se de metaplasie, diseminare venoasă sau limfatică, sau contaminare mecanică în cursul laparotomiei [2]. Ca factori de risc asociați elementului obstetrical care ar explica apariția EPA ar fi: mica cezariană (<22 săptămâni), consumul de alcool, menstruații abundente [7]. Incidența depinde mai puțin de numărul de cezariene, sau de leziuni endometrioizice viscerale asociate (prezente în 25% din cazuri pe seria lui Leite) [7].

Ecker AM și colab [8] identifică unii factori de risc asociați endometriozei parietale: index de masă corporală superior a 25 kg/m<sup>2</sup> -

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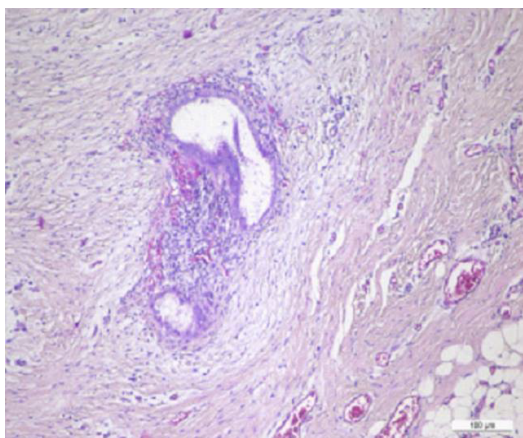
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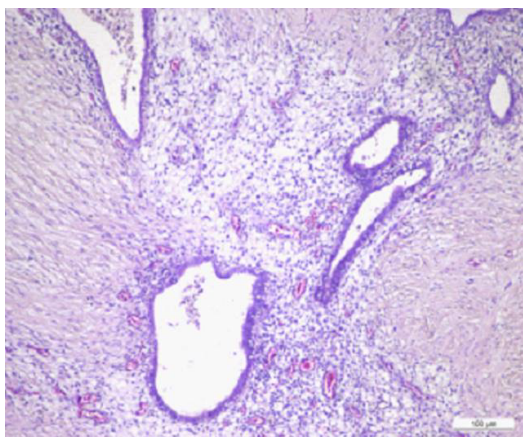
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**Figura 1:** Aspectul exterior al formațiunii tumorale situate la nivelul cicatricei postcezariană.



**Figura 2 :** Aspect de endometrioză: glande de aspect endometrial înconjurate de un endometru subțire (HE x 100).



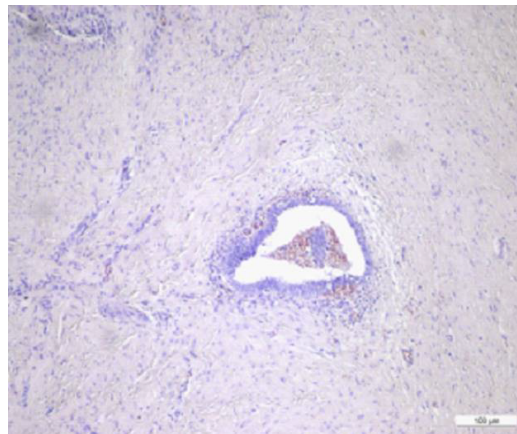
**Figura 3 :** Aspect de endometrioză parietală cu extensie la țesutul adipos (HE x 100).

70% dintre pacienți, rasa albă - 75%, multiparitatea - 87% și intervenția cezariană - 87%.

Simptomele devin manifeste la o perioadă variabilă, în medie de 5 ani [9], la cazurile noastre fiind 1-4 ani. Tabloul tipic cuprinde dureri ritmate de ciclu (66% din cele 33 pacienți din seria lui Gunes [9]) la cazurile noastre jumătate precizând acest aspect. Alte simptome includ: hemoragii disfuncționale, semne inflamatorii superficiale, alte localizări ale endometriozei. Clinic, se descrie formațiunea tumorală parietală abdominală, cu mobilitate variabilă și consistență semidură, dureroasă, cu fenomene inflamatorii asociate.

Diagnosticul paraclinic a fost pus la cazurile noastre prin ecografie (la 2 cazuri din 4). În literatură se mai citează ca metode complementare de explorare examenul RMN, elastografia [10] sau puncția aspirație cu ac fin [11].

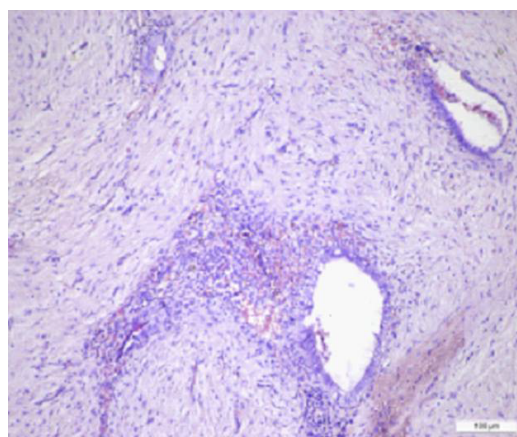
Evoluția poate fi variată: formele limitate pot avea evoluții îndelungate, până când devin simptomatice. Francica [12] într-o serie de 30 cazuri, comparând caracteristicile EPA arată că pentru leziunile mai mari de 30 mm folosirea unor metode imagistice neconcludente poate duce la întârzierea diagnosticului cu evoluție spre fistulizare.



**Figura 4 :** Aspect de endometrioză parietală cu un număr redus de celule endometriale (HE x 100).



**Figura 5:** Aspect ecografic al EPA.



**Figura 6:** Aspect anatopatologic de EPA: glande endometriale asociate unor focare hemoragice.



În ceea ce privește complicațiile posibile, sunt citate în literatură : extensia subaponevrotică, la peritoneu și alte viscere, transformare malignă [13,14].

Tratamentul este chirurgical și se recomandă excizia chirurgicală completă ; refacerea peretelui abdominal poate necesita folosirea unui material protetic.

#### Alte metode citate de unii autori sunt:

- scleroterapie cu injecție de etanol sub control ecografic, Bozkurt și colab [15].
- crioablație percutană a leziunilor, Cornelis și colab [16].
- tratament hormonal (analogi, danazol, progestative) pentru a facilita intervenția chirurgicală sau în recidive [17].

#### Referitor la profilaxia EPA, datele din literatură sugerează ca posibile măsuri de scădere a riscului de apariție a localizării parietale abdominale a endometriozei:

- închiderea peritoneului visceral și parietal la cezariană [18]
- nefolosirea materialului de sutură de la histerorafie la sutura peretelui abdominal [19]
- irigația abundentă cu soluție salină a planurilor peretelui abdominal înainte de închidere [20]

## Concluzii

Diagnosticul de EPA trebuie luat în considerație pentru orice tumoră parietală dureroasă apărută la distanță de o cezariană. Rezecția chirurgicală este opțiunea terapeutică recomandată ; excizia trebuie realizată în țesut sănătos.

Prevenirea EPA include inspecția și curățarea plăgilor de histerotomie și de laparotomie

#### Conflict de interese

Autorii nu declară niciun conflict de interese.

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# Distal Pancreatectomy with Spleen Preservation in Two Rare Types of Pancreatic Tumors

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## Abstract

Cystic neoplasms of the pancreas have an incidence of 10% of all cystic tumors, represented by serous cystadenomas, mucinous cystic neoplasm and solid pseudopapillary neoplasm. We present two cases with rare pancreatic tumors: two women of 18 years old and 67 years old respectively were admitted for non specific abdominal pain and dyspepsia. The CT-scans diagnosed with corporeal pancreatic of 30 × 40 mm in the first case and 98 × 66 mm in the second. Distal pancreatectomy with spleen preservation was performed in both cases with uneventful postoperative course. The pathological exam revealed pseudopapillary pancreatic tumor in the first case and mucinous cystic neoplasm, in the second case. A short review of the literature was also performed.

**Keywords:** Pancreatic neoplasms; Pseudopapillary pancreatic tumors; Mucinous pancreatic cystic neoplasm; Pancreatectomy; Left pancreatectomy; Spleen preservation pancreatectomy

## Introducere

Tumora solidă pseudopapilară de pancreas nu are o etiologie clară, se pare că este corelată cu unele tulburări endocrine, în special cu creșterea producției de estrogeni și progesteron [1].

Atât tumora pancreatică pseudopapilară cât și neoplasmul chistic mucinos sunt două forme rare de tumoră pancreatică, întâlnite predominant la femei, localizate cel mai frecvent corporeal sau caudal, cu o simptomatologie nespecifică [2].

Prezentăm în continuare două cazuri, de tumora pancreatică pseudopapilară și respectiv de neoplasm chistic mucinos.

**Cazul I:** Pacienta N.D.N de 18 ani, sex F, din mediul rural, fără antecedente semnificative, nefumatoare, se internează pentru simptomatologie nespecifică: dureri lombare (predominant stângi) cu iradiere anterioară spre fosele iliace, flanc stâng, grețuri.

Examenul clinic relevă o pacientă cu stare generală bună, normoponderală, afebrilă, orientată temporo-spațial, cu tegumente și mucoase normal colorate. Examenului clinic pe aparate și sisteme nu relevă modificări patologice. La examenul local, abdomen este suplu, mobil cu mișcările respiratorii, dureros spontan și la palpare în flancul și fosa iliacă stângă, fără semne de iritație peritoneală, cu tranzit intestinal, prezent, fiziologic și schiță de Girdano + pe partea stângă.

Biologic, nu se decelează modificări hematologice, biochimice, de coagulare și urinare.

Examenul ecografic relevă, la nivelul corpului pancreatic, o formațiune chistică de 3.5 × 3.5 cm cu septuri groase la interior care prezintă limită de demarcație cu corpul gastric (Figura 1).

Examenul RMN confirmă prezența unei formațiuni rotunde, bine delimitate de parenchimul pancreatic, localizată la nivelul corpului pancreatic de 36 mm de diametru, leziunea are contact cu mica curbura gastrică (Figura 2).

Se intervine chirurgical, explorarea intraoperatorie evidențiază o tumoră chistică cu conținut hematic de aprox 4 cm de diametru situată la nivelul corpului pancreasului, perfect încapsulată, fără adenopatii sau determinări secundare. Se disecă tumora care prezintă plan de clivaj

cu artera și vena splenică. Se continuă disecția dinspre hilul splinei cu eliberarea completă a cozii și corpului pancreasului (Figura 3). Este secționat istmul pancreatic care se suturează în surjet tip Mayo. Echografia de control, evidențiază flux prezent în vasele splenice (Figura 4). Evoluția postoperatorie este lent favorabilă: dezvoltarea unei colecții retrogastrice de 13 × 6 cm, în contact cu polul inferior al splinei, ce diminuează progresiv.

Examenul anatomopatologic relevă o proliferare tumorală cu arhitectură papilară preponderentă și monomorfism celular, delimitată de o capsulă hialinizată. Proliferarea celulară este constituită din elemente celulare poliedrice, ce mărginesc structurile papilare și conțin o stromă hialină și vase de talie mică. Nucleii celulelor rotunzi sau ovalari prezintă cromatina uniform dispersată și pleomorfism nuclear redus. Mitozele sunt reduse. Se mai remarcă prezența unor arii de necroză hemoragică și izolate focare ce infiltrează țesutul pancreatic adiacent. Imunohistochimic, citokeratina AE1/AE3 este pozitiv difuz în tumoră și țesutul pancreatic adiacent iar citokeratina 7 slab pozitiv zonal în tumoră, dar pozitivă în elementele ductale pancreatice adiacente; tumora este vimentin și enolază neuron specifică pozitivă. Aspectele morfologice sunt evocatoare pentru o tumoră solidă *pseudopapilară pancreatică* fără semne de malignitate [3].

**Cazul II:** Pacienta T.E, 67 ani, sex F, din mediu urban, hipertensivă, cu antecedente de neoplasm mamar drept operat, se internează pentru o simptomatologie nespecifică: dureri abdominale difuze în etajul superior, mai accentuate în hipocondrul stâng.

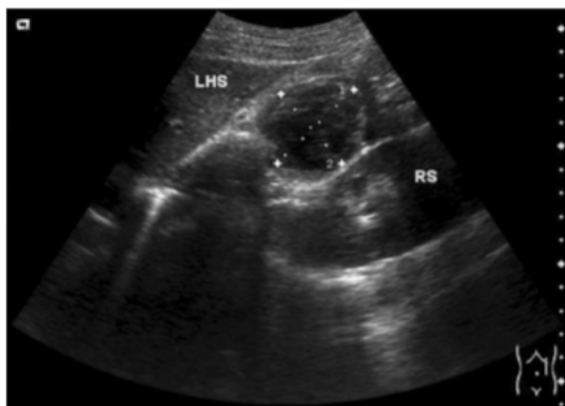
La examenul local se constată o sensibilitate la palparea profundă în etajul abdominal superior dar mai ales în hipocondrul stâng, fără semne de iritație peritoneală.

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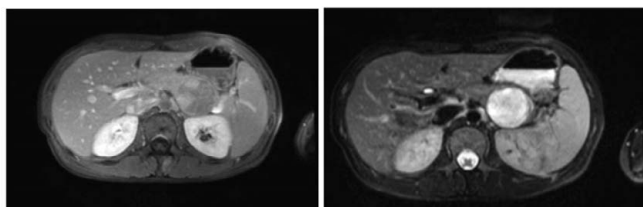
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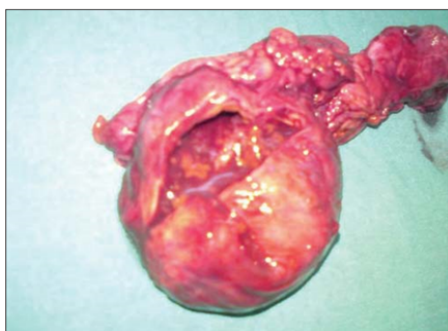
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**Figura 1:** Formațiune chistică de 3,5 x 3,5 cm cu septuri groase la interior care prezintă limită de demarcație cu corpul gastric.



**Figura 2:** Imagistică prin rezonanță magnetică: formațiune rotundă, bine delimitată localizată la nivelul corpului pancreatic (36 mm diametru) venind în contact cu mica curbură gastrică.



**Figura 3:** Piesa operatorie.

Biologic se constată o anemie normocromă normocitară (Hb = 10 g/dL, Ht = 30%), o valoare a glicemiei ușor crescută (130 mg/dL), cu valori normale ale markerilor tumorali (CA 125, CA 153, CA 19-9, alfa-fetoproteina); doar antigenul carcinoembrionar (ACE) are o valoare la limită: 3,09 ng/mL, pacienta fiind nefumătoare iar valoarea de referință fiind de maxim 2.5 ng/mL.

Pacienta a beneficiat de mai multe examene computer tomografice (3 examinări la o distanță de 6 luni, respectiv 1 an), care au evidențiat o formațiune chistică localizată la nivel caudal pancreatic, bine delimitată Figura 5 care crește progresiv în diametru (de la 79 x 55 mm la 98 x 66 mm) și amprentează posterior peretele corpului gastric.

Examenul ecografic relevă pe topografia cozii pancreasului, retrogastric, o colecție lichidiană bine delimitată, cu perete subțire, de aproximativ 75 x 70 x 105 mm, cu conținut transonic.

Endoscopia digestivă superioară, decelează la nivelul peretelui posterior gastric o amprentă extrinsecă de aproximativ 10 x 10 cm diametrul, corespunzătoare formațiunii chistice pancreatice.

Se intervine chirurgical și se evidențiază o tumoră chistică cu conținut lichidian, aparent hematic, de aprox 8 x 7 cm situată la nivelul cozii pancreasului, perfect încapsulată, fără adenopatii sau determinări secundare, în raport cu vasele splenice Figura 6. Se disecă tumora care prezintă plan de clivaj cu artera și vena splenică. Se continuă disecția pancreasului dinspre hilul splinei cu eliberarea completă a cozii și corpului pancreatic; este secționat istmul pancreatic și apoi suturat cu surjet tip Mayo (Figura 7).

Evoluția postoperatorie este favorabilă. La examenul ecografic de control în ziua 5 postoperator se evidențiază flux prezent în vasele splenice, splina cu dimensiuni normale, omogenă, fără lichid liber intraperitoneal, pacienta fiind externată la 8 zile postoperator.

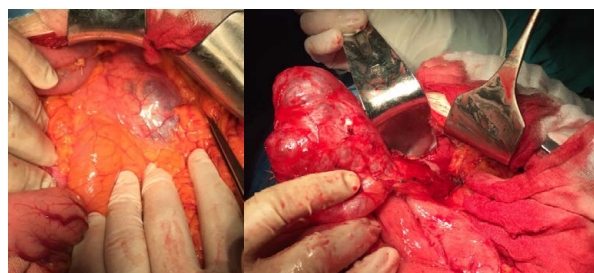
Examenul anatomopatologic relevă perete de chist multilocular de 7 x 6.5 cm, ce prezintă pereți netezi, de culoare cenușie cu vascularizație evidentă. Se mai constată atașat, parenchim glandular de 2.5 x 1 cm. Peretele intern este neted, cu resturi de conținut lichidian. Microscopic, fragmentele examinate sunt reprezentate de perete de chist multilocular Figura 8, tapetat pe versantul intern de un epiteliu simplu cilindric, mucosecretor, cu nucleu monomorf, rotund-ovalari, situați bazal sau cu un epiteliu simplu cubico-prismatic. Se mai constată focal prezența unor micropapile Figura 9 cu celule ce prezintă focal nucleu alungiți,



**Figura 4:** Control ecografic postoperator; evidențierea fluxului arterial și venos la nivelul vaselor splenice.

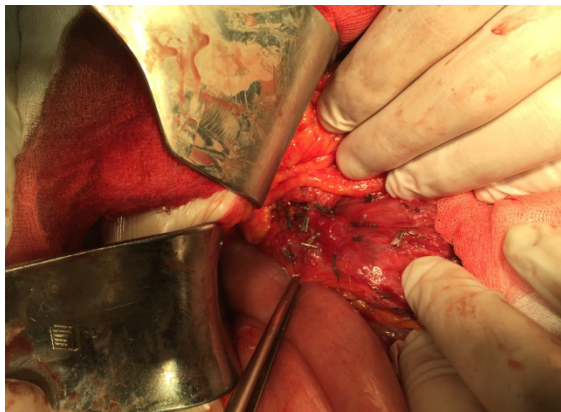


**Figura 5:** Formațiune chistică localizată la nivel caudal pancreatic.

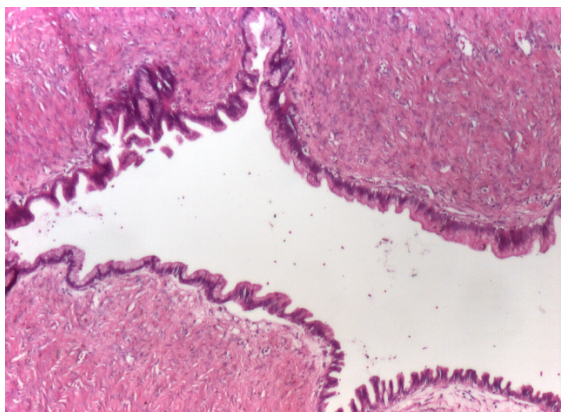


**Figura 6:** Aspect intraoperator: tumoră chistică cu conținut lichidian, aparent hematic, de aprox 8 x 7 cm la nivelul cozii pancreasului.





**Figura 7:** Disecția și eliberarea completă a corpului și cozii pancreasului cu ligatura tuturor colateralelor arteriale spre pancreas ale arterei splenice precum și ligatura colateralelor venoase ce provin de pe fața posterioară a pancreasului la vena splenică.



**Figura 8:** Peretele tumorii pancreatice: perete de chist multilocular, tapetat pe versantul intern de un epiteliu simplu cilindric, mucosecretor, cu nuclei monomorfi, rotund-ovalari, situați bazal sau cu un epiteliu simplu cubico-prismatic (aspect microscopic HE x 100).

suprapuși, unii ascensionați. Subiacent epiteliului, se evidențiază fibroză, izolat stromă de tip ovarian Figura 10 și structuri glandulare de tip gastric.

Aspectele morfologice identificate sunt compatibile cu un neoplasm chistic mucinos de pancreas cu displazie de grad intermediar.

## Discuții

Tumora solidă pseudopapilară de pancreas sau tumora Franz este o tumoră pancreatică rară ce apare ca o masă solitară, rotundă, adesea fluctuantă cu suprafața lobulată, zone hemoragice și necroză.

Franz este primul care a descris-o în 1959 ca tumoră papilară de pancreas benignă sau malignă” [4].

Criteriile de malignitate includ: invazia perineurală, angioinvasia și invazia profundă a țesuturilor adiacente. Un studiu efectuat la Memorial Sloan-Kettering Cancer Center New York în 2000 indică [5] prin studii anatomopatologice și de microscopie electronică faptul că imunofenotipul celulelor tumorale nu este specific și nu definește nici o linie diferențiată a vreunui tip celular pancreatic.

Tumora papilară poate fi localizată pe orice segment pancreatic și când are dimensiuni superioare a 3 cm are indicație operatorie; rezecțiile pancreatice corespund localizării tumorii. Astfel, într-un studiu din 2000, pe un număr de 14 cazuri analizate, 13 au beneficiat de intervenție

chirurgicală ce au constatat în DPC, și pancreatectomii corporeocaudale cu splenectomie și un singur caz cu preservarea splinei. Alți autori comunică rezultate similare [6,7].

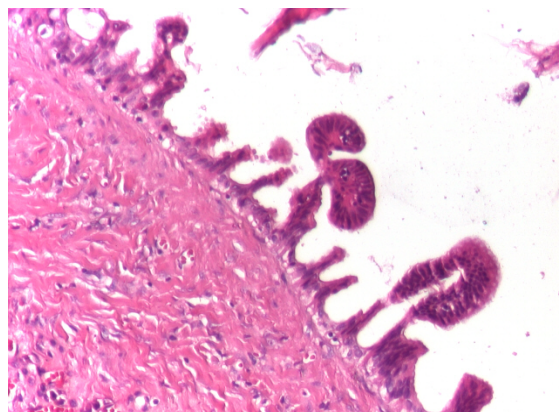
Tumora pseudopapilară solidă de pancreas este tipic pozitivă pentru vimentin, enolază neuron specifică,  $\alpha 1$  antitripsină și  $\alpha 1$  antichimotripsină [8,9]. Aceste rezultate imunohistochimice o pot diferenția de o tumoră neuroendocrină de pancreas [2,10].

Neoplasmul chistic mucinos de pancreas este o neoplazie pancreatică chistică rară, formată dintr-un epiteliu producător de mucină asociat cu stroma de tip ovarian. Localizarea este preponderent la nivelul corpului și cozii pancreatice. Apare cu o frecvență mai mare la femei față de bărbați, sex ratio de 20 la 1, vârsta medie de diagnostic fiind 40-50 de ani (pacienta noastră având 67 ani, ușor peste medie) [1,11].

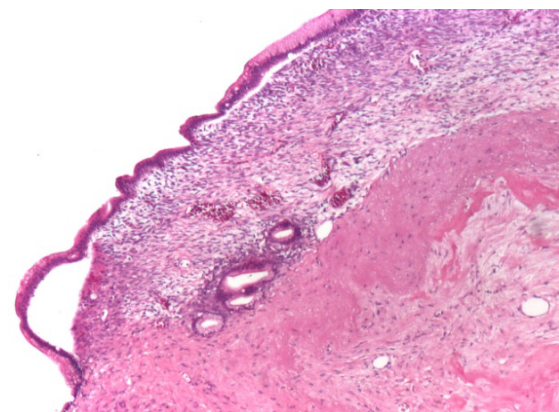
Clinic se prezintă ca o formațiune chistică cu dimensiuni variabile, uni sau multiloculară, cu conținut mucos ce poate asocia material necrotic. Gradul de atipie poate fi variabil, doar o treime pot fi maligne. Rezecția chirurgicală este curativă pentru aproape toate cazurile.

În 2004, la Sendai, Asociația Internațională de Pancreatologie stabilește ca și criteriu definitoriu pentru diagnosticul de neoplasm chistic mucinos, prezența stomei unice de tip ovarian, care nu mai apare în nicio altă formă de neoplasm pancreatic [1,11].

Fiind localizat cel mai frecvent la nivelul corpului și cozii pancreatice pancreatectomia distală, este cel mai frecvent tratament [1,11].



**Figura 9:** Peretele tumorii pancreatice: aspect micropapilar cu celule ce prezintă focal nuclei alungiți, suprapuși, unii ascensionați (aspect microscopic HE x 100).



**Figura 10:** Peretele tumorii pancreatice: subiacent epiteliului, se evidențiază fibroză, și stromă de tip ovarian multilocular (aspect microscopic HE x 100).



Tehnica pancreatectomiei distale a fost descrisă de Mayo, în 1913, iar adițional, în 1943, Mallet-Guy susține prezervarea splinei. Prezervarea splinei se poate realiza fără sau cu (Warshaw, 1988) ligatura vaselor splenice [1]. Tehnica fără prezervarea arterei și venei splenice, are o rată mai mare de complicații postoperatorii (infarcte splenice, durere, abces splenic) [1]. Tehnica poate fi realizată pe cale clasică sau laparoscopică.

## Concluzii

Pancreatectomia distală corporeocaudală cu prezervarea splinei și a vaselor splenice pare a fi indicația de elecție pentru tumorile pseudopapilare pancreatice și neoplasmele chistice mucinoase localizate la nivelul corpului și cozii pancreasului care sunt benigne sau border-line.

## Conflict de interese

Autorii nu declară niciun conflict de interese.

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