

IL15 RESULTS OF CONSERVATIVE TREATMENT OF BENIGN STRICTURES OF THE ESOPHAGUS WITH BOUGIENAGE: CROSS SECTIONAL STUDY REPRESENTING FIRST EXPERIENCES IN REPUBLIC OF MACEDONIA

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BACKGROUND: Benign esophageal strictures are complications that result from various causes. They can be structurally categorized into two groups: simple and complex. Treatment is similar in most of cases that require dilatation and means use of three general types of dilators that are currently in use. However, despite the last guidelines on esophageal dilatation, the therapeutic response, optimal timing of treatment and interval between sessions can vary and there is no strong consensus in the literature regarding this fact.

OBJECTIVE: To analyze, the first 3 year experience of Digestive Endoscopy Unit of the University Clinic of Gastroenterohepatology of the Medical Faculty, Skopje, Republic of Macedonia, in treating benign esophageal strictures, since the Savary-Gilliard technique of 'bougienage' was introduced for the first time in Republic of Macedonia, at our Institution in December 2013, by assessing etiology, length of stricture, number of dilations required to achieve satisfactory therapeutic response, as well as the relationship between the type, extent of stenosis and therapeutic response. **METHODS:** One hundred and forty seven dilations were analyzed during a period from 20-th December 2013, until March 2016 were analyzed in 56 patients. **RESULTS:** The caustic strictures were the most prevalent, occurring in 12 (48%) of patients, followed by peptic stenosis presenting 28% of patients. The long and corrosive strictures needed more sessions to the absence of dysphagia. Peptic and short stenoses best answered on treatment and need fewer dilatation sessions per patient.

CONCLUSION: caustic stricture is the most common type of benign esophageal stenosis and the most refractory to treatment, especially the long stretch. Peptic stenosis is the second one cause of benign esophageal strictures and responded well to endoscopic therapy. The higher the extent of stenosis, the greater the number of sessions required. Short strictures have good prognoses in most cases. The number of dilations depended directly on the cause and extent of stenosis. Bougienage, irrespective of type and extent of esophageal stenosis is safe and grateful procedure.

KEY WORDS: esophageal stenosis, bougienage.

INTRODUCTION: Benign esophageal strictures are complications that result from various causes, like gastroesophageal reflux disease, accidental or deliberate ingestion of corrosive substances, congenital rings and esophageal membranes, radiation therapy,

eosinophilic esophagitis etc. They can be structurally categorized into two groups: simple and complex (1). Simple strictures are symmetric or concentric, usually short with a diameter of 12 mm or more or easily allow passage of a diagnostic upper endoscope. Complex strictures have one or more of the following features: asymmetry, diameter <12 mm or inability to pass an endoscope. Regardless of the cause, dysphagia as symptom is a main indication for dilation of benign strictures (2). Treatment is similar in most of cases that require dilatation and means use of three general types of dilators that are currently in use. These are: (1) mercury or tungsten-filled bougies (Maloney or Hurst), (2) wire-guided polyvinyl dilators (Savary-Gilliard or American type), and (3) “through-the-scope” balloon dilators. The technic using Maloney/Hurst or Savary-Gilliard dilators is known well as ‘bougienage’. The degree of dilation within a session should be based on the severity of the stricture. The “rule of 3” has been accepted and applied to bougie dilation of esophageal strictures (3). Specifically, the initial dilator chosen, should be based on the estimated stricture diameter. Serial increases in diameter are then performed. However, despite the last ASGE guideline on esophageal dilatation from 2006 (4), the therapeutic response, optimal timing of treatment and interval between dilatation sessions can vary and there is no strong consensus in the literature regarding this fact. Dilatation of esophageal strictures in Republic of Macedonia and University Clinic of Gastroenterohepatology is not new. The use of olive dilators was introduced at our Clinic few decades ago. The University Clinic of otorhinolaryngology has long experience using mercury or tungsten-filled bougies (Maloney/Hurst), meaning the same for the Clinic of Pediatric Surgery. In this retrospective study, we present the first 3 year experience of Digestive Endoscopy Unit of the University Clinic of Gastroenterohepatology of the Medical Faculty, Skopje, Republic of Macedonia, in treating benign esophageal strictures, since the Savary-Gilliard technique of ‘bougienage’ was introduced for the first time in Republic of Macedonia, at our Institution in December 2013.

METHOD: All dilations, independently of their type and origin, were analyzed, during a period from December 20-th, 2013, until March 2016. The dilations performed out of technic of bouginage were excluded. The dilations were performed in an in-hospital setting, with one to two week intervals between sessions. All of the interventions were conducted by three experienced endoscopists covering the whole number of 25 patients (16, 7 and 2 patients per operator, respectively). The procedure was performed with the patient fasting for at least 12 hours, under conscious sedation using midazolam and continuous pulse-oximetry and post procedural temperature and blood pressure monitoring. Although, routine antibiotic coverage is not recommended mandatory before procedure (4), we used ceftriaxone 2g i.v. for prophylaxes of septic events. We used a flexible metal guide wire, introduced through the stricture under endoscopic vision and X-ray control, on which were passed the Savary-Gilliard type bougies [Safe Guide TM, Over the Guidewire Esophageal Dilators with 16 sizes: 15 FR to 60 FR - in 3 FR increments - equivalent values in mm – from 5 to 20 mm (Medovations inc., 102 East Keefe Avenue, Milwaukee, WI 53212 USA)]. The initial diameter of the candle is individualized according to the degree of stenosis displayed. Data were collected according to the cause, type and extent of stenosis. According type, the strictures were classified as simple and complex. The extent was used to classify them as

short - up to 3 cm, medium - between 3 and 7 cm, and long - when more than 7 cm in length. These variables were correlated with the number of dilations. The influence of etiology in the extent of stenosis was also analyzed. The ultimate goal of treatment was absence or marked reduction of dysphagia.

STATISTICAL ANALYSIS: For statistical analysis of data Pearson contingency coefficient test was used (by analyzing the influence of sex on the extent of stenosis) and ANOVA (analysis of variance of the influence of the extent and etiology on the number of dilations). The level of significance was expressed as $P < 0.05$.

RESULTS: One hundred and forty seven dilations were analyzed during a period from 20-th December 2013, until March 2016. Thirty one dilations were excluded, concerning the cases where balloon dilation technic was used. In other words 116 dilations, performed by using technic of bouginage in 25 patients (10 women and 15 men with a mean age of 52,4 years, ranging from 1-82 years), during a period of more than 3 years, were analyzed. The caustic stricture was the most prevalent cause, occurring in 12 (48%) of patients, followed by peptic stenosis presenting 28% of patients. Regarding the extent of stenosis, all individuals were evaluated of the total 25 patients included, and it was observed that 64% (16/25) had short nips, these representing the majority of peptic stenosis (6 of 16 patients). Long length stenoses were exclusively present in patients whose origin was caustic. The recurrence rate in the last, despite the high number of sessions needed to provide positive effect, was low. Forty for % of 9 patients were free from symptoms following the finish of therapy. Peptic were predominantly short stenosis - in 6 of 25 patients analyzed for extent (24%). The opposite occurred in the caustic stenosis that have predominantly long changes (7 of 12 patients with corrosive injury analyzed for extent - 58,3%). Stenoses due to esophageal surgery were also short (2 of 2 patients - 100%). Caustic injuries were those that needed more sessions, on average 6,6 dilations per patient (maximum 21 sessions in one patient), a statistically significant difference in relation to other causes ($P < 0.0005$). However, analyzing separately the postoperative cases, peptic and all other types between each other, there was no significant difference between the average number of dilations ($P = 0.175667$). Nips long segment strictures required on average 7.9 interventions per patient, while narrowing short extension stenosis, required about 2.8 dilations per patient ($P < 0.00001$). In 116 dilations performed, there were no perforations. There was minor bleeding in all patients, but not more than usual and no mortality was registered in this series.

DISCUSSION: The causal diagnosis of stenosis may be set at 80% of cases, using only the anamnesis. A barium swallow does much to define the degree of stenosis, location, determine the complexity and choose the type of dilator to be used, and usually is used as the initial examination. Upper endoscopy is essential, because it evaluates the mucosa of the affected region, excluding malignant causes and enables the performance of biopsies to be done even when the etiologic diagnosis is evident. Corrosive agents when ingested accidentally (in children mostly) or intentionally (adults in suicide attempts) can cause esophageal strictures, which bring the higher risk of perforation and more expressed rate

of recurrence after dilation compared to other types (5, 6). Endoscopic examination in the acute phase may indicate the prognosis. Tiryaki et al. (7) observed a better therapeutic response when dilation was initiated in the acute phase, seven days after ingestion of corrosive. In this study we started bouginage in caustic cases at least 3 months after the accident, and the success rate was pretty high - 44% without additional need for treatment, and most of the others with de novo symptoms 6 months after initial session. The affected segment extension is also a prognostic factor. In this series, we observe that the more extensive was the stenosis; the needed number of dilations was greater. After the disappearance of the symptoms, the need for retreatment was usually in the period of 3-6 months in the first year. Temir et al. (8) defend the opinion that implementation of new dilations should only be done when reappearance of dysphagia is registered. An estimated 7% to 23% of patients with longstanding gastroesophageal reflux disease (GERD) evolve with esophageal stenosis (9). As shown in this study, they are generally annular stenosis (shorter than <3 cm), typically located on the distal segment of the esophagus. This type of stenosis responds very well to dilation therapy with successful rate greater than 80% (5). The therapy with proton pump inhibitors (PPIs) in full dose and anti-reflux measures should always be carried out. Patients undergoing esophageal surgery, especially esophagectomies and even hernia repair surgeries, may develop stenosis, either due to developing local ischemia, use of "stapler" technic or by the scar processing. The success rate of endoscopic dilations in these patients is around 75% to 92%, usually requiring about three to five sessions for resolution of symptoms (13). In this sample, it was found that two patients with postoperative stenosis required on average 3 sessions for good response. According to our opinion it is safe and recommended to start the expansion immediately after appearance of dysphagia, which is opposite to other experts recommendations, taking cut of value of 2 weeks after surgery as relevant one. In addition, the ideal period is not still determined (13). It is known that only 24 hours of use of a nasogastric tube, it can be seen intraepithelial and sub mucosal edema and hemorrhage of the esophagus and if the probe remains in situ for more than 5 days, hyperemia as well as presence of ulcerations can be detected. This occurs either by direct local irritation by the probe, as well as a result of facilitation of gastroesophageal reflux. There was no patient in this series presented with stenosis resulting from the use of nasogastric tube. Radiotherapy may cause stenosis by direct damage to DNA and producing free radicals which stimulate cell death. The incidence is around 25% to 67% in the irradiated patient to primary tumor and from 1% to 20% for irradiation of tumors arising from adjacent organs (breast, lung, thyroid) (13). In this study, the post-radiotherapy stenosis was uncommon, occurring in only 3 patients (12%) who required on average 1 dilation session to achieve therapeutic response. Eosinophilic esophagitis, predominant entity in children, in which there is chronic inflammation of the esophagus, characterized by infiltration of more than 20-24 eosinophils per high-power field, detected by histopathology, is still underdiagnosed cause in adults with esophageal stenosis. The treatment includes endoscopic dilation, removal of the triggering factor (usually airborne allergens and food allergens) and topical steroids. In the present study we assessed only one patient with this diagnosis, requiring, one expansion sessions adjacent to topical steroid therapy, for dysphagia remission. Esophagitis caused by ingestion of drugs in pill form is because infrequent stenosis. Medications such as

tetracycline, nonsteroidal antiinflammatory drugs, potassium chloride and bondronates can cause stenosis by direct injury to the mucosa due to prolonged contact, decreased motor activity and decreased esophageal clearance. This study can't confirm the use of drugs to cause stenosis. Membranes and rings are causes of stenoses that respond very well to endoscopic dilatation. In the case of Schatzki's rings, 68% of patients remain without dysphagia for a period of 1 year after the first expansion, but many need new dilations throughout life (10). In the present study evaluated one patient with Schatzki ring, shows good response to endoscopic treatment. Length of stricture best correlates with its cause, and it was found that according to the causes, strictures have their own behavior. Thus, caustic strictures are generally long, opposite to peptic strictures that are short. When comparing the number of dilations undertaken with the cause and extent of the stenosis, it has been found that short lesions or annular, such as peptic and postoperative can be treated by the smaller number of dilations. Already caustic stenoses, usually long, required quite a large number of sessions. The decision on the type of dilator to be used depends on the availability of the material and experience of each service and it's endoscopists. In our service where this study was conducted, we used Savary-Gilliard dilators, consisting of flexible polyvinyl material, and progressed through the stenosis, guided by the passage of a guide wire. The use of fluoroscopy during the procedure, which has been released in the last period in most other services, can be useful in cases of tortuous and complex strictures and provides greater security to the procedure, allowing full control of the dilator and guidewire positioning and minimizing the risk of perforation. Thus the complication rate is lower, we suppose. There is no consensus on the follow-up of these patients. Moura et al. (11) suggest that the expansion should be weekly at 1 month, biweekly in 2 of 21 in 21 days in 3 and 4 months and monthly in 5, 6 and 7 months. The patient would then be instructed to return if still recounting the symptoms or if there was return of dysphagia, being considered the case as refractory if these complaints occurred in less than 3 months after the last expansion. Some authors (12) recommended that the patient must be kept in expansion program at short intervals (weekly or biweekly) at the start of therapy until the ultimate goal is reached, the absence of dysphagia; others (13), however, argue the progression to higher candle (45Fr or more), even if the patient is already asymptomatic (14). In our study in most cases, the patients were kept under one to two weekly dilation program until the absence of dysphagia. Most of the patients didn't need to reach the maximum size of dilators (60Fr - 20mm) for absence of symptoms. Immediate and postponed complications, after dilation occur in 0.5% to 1.2% (2, 21) and excess bleeding may occur in less than 0.5% of the cases (15) and bacteremia 20% - 45%. In this study, there were no cases of perforation and bacteremia, proving that the procedure is very safe. The use of corticosteroid (triamcinolone) at the site of stenosis or intralesional (in tears after expansion) is used in some centers because it is believed that by inhibiting the synthesis of collagen, can reduce the number of sessions (16, 17, 18). No patient in this study underwent intralesional corticosteroid injections.

CONCLUSION: In this study, caustic stricture is the most common type of benign esophageal stenosis and the most refractory to treatment, especially the long stretch. Peptic stenosis is the second one cause of benign esophageal strictures and responded

well to endoscopic therapy in accordance with the literature. The higher the extent of stenosis, the greater the number of sessions required. Short strictures have good prognoses in most cases. The number of dilations depended directly on the cause and extent of stenosis. Bouginage, irrespective of type and extent of esophageal stenosis is safe and grateful procedure, especially in the setting of lack of referent thoracic surgery.

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