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Contact
Turkish Journal of Surgery
Address: Koru Mah. Koru Sitesi, Ihlamur Cad. No: 26
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Phone: +90 (312) 241 99 90 **Fax:** +90 (312) 241 99 91
E-mail: editor@turkjsurg.com

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Contact
Bilimsel Tıp Yayınevi
Address : Bükreş Sokak No: 3/20 Kavaklıdere, Ankara, Turkey
Phone : +90 (312) 426 47 47 • +90 (312) 466 23 11
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Fax: +90 (312) 426 93 93
E-mail: bilimsel@bilimseltipyayinevi.com
Web: www.bilimseltipyayinevi.com

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Type of manuscript	Word limit	Abstract word limit	Reference limit	Table limit	Figure limit
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Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp. 1561-5.

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Address: Koru Mah. Koru Sitesi, Ihlamur Cad. No: 26
06810 Çayyolu, Ankara, Turkey

Phone: +90 (312) 241 99 90

Fax: +90 (312) 241 99 91

E-mail: editor@turkjsurg.com

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Phone: +90 (312) 426 47 47 • +90 (312) 466 23 11

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E-mail: bilimsel@bilimseltipyayinevi.com

Web: www.bilimseltipyayinevi.com

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FROM THE EDITOR'S DESK

Dear Authors of the Turkish Journal of Surgery,

It is our biggest pleasure to present you the June 2019 issue of the Turkish Journal of Surgery. This issue is once again full of remarkable papers of various fields of surgery. Furthermore, we are glad to host many articles written by foreign authors from different corners of the world. It is obvious that the Turkish Journal of Surgery is becoming a world journal day by day. As we constantly stress, we are pleased to receive your valuable manuscripts, no matter where they come from. We promise a quick and fair review. Authors of the Turkish Journal of Surgery have the advantage to publish their works in an "open access" journal, which brings more visibility and more citations.

Nowadays, the medical publishing community, especially periodicals, is under the menace of predator journals. Almost every day, we receive "strange" invitations for submission or reviewal from unknown medical journals. These newly established journals habitually charge high amount of publication or open access fees with an unclear and unethical reviewing process. Authors wish to publish their precious works but the growing number of these journals leads to an immense confusion in medical publishing. The revolution of digital publishing in the last decade has unfortunately made such journals easy to establish and promote. Each novelty brings a concomitant problem.

You have, in your hands, the 35th volume of the Turkish Journal of Surgery. It demonstrates the long history and experience of the journal. Undoubtedly, it also brings trustworthiness for the authors and readers, which is nowadays one of the most important values for a medical periodical. We can maintain our distinctive qualities with the great endorsement of by the Turkish Surgical Association. We are always dedicated to preserve our values in terms of ethics and keep on improving the Turkish Journal of Surgery together with our authors and readers. Your valuable comments and contributions are received with great pleasure. Please, feel free to share your opinions and suggestions.

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Best regards,

Kaya SARIBEYOĞLU
Professor of Surgery
Turkish Journal of Surgery
Editor

ORIGINAL ARTICLE
Turk J Surg 2019; 35 (2): 79-85

Long-term results of the patients who were applied laparoscopic adjustable gastric banding

Sabri Özden[1], Barış Saylam[1], Fatih Mehmet Avşar[1]

[1] Clinic of Surgery, Ankara Numune Training and Research Hospital, Ankara, Turkey

ABSTRACT

Objective: The most effective treatment step in morbid obesity is surgical treatment. The purpose of the present study was to investigate the long-term follow-up results and success rates in laparoscopic adjustable gastric banding.

Material and Methods: The change in body mass index, percentage of excess weight loss, comorbidities, and resulting complications were investigated in 220 patients who were morbidly obese and applied laparoscopic adjustable gastric band between April 2006 and February 2012, throughout the 6-year follow-up period. Forty-six patients who did not show up for their routine follow-ups were excluded from the study.

Results: In the present study, band removal percentage was 35.63%. The percentage of excess weight loss in patients who were followed up without removal of the band was 46.03%. Complications were observed in 46.5% of the patients. The most frequently observed complication among the major complications was band intolerance, which is also the most common cause of band removal. Band removal was considered as a failure in laparoscopic adjustable gastric band operations, and patients were referred to other surgical methods.

Conclusion: When improved patient compliance and careful and close patient follow-up are provided in the early stages of laparoscopic adjustable gastric band application, it may be possible to reach percentage of excess weight loss results that would be the nearest to those achieved by gastric bypass or sleeve gastrectomy methods. However, high complication rates and necessity to perform other bariatric surgical procedures in the majority of the patients in the long-term follow-up suggest that the laparoscopic adjustable gastric band operation is not the first choice in bariatric surgery.

Keywords: Body mass index, laparoscopic adjustable gastric band, laparoscopic sleeve gastrectomy, laparoscopic Roux-en-Y gastric bypass, percentage of excess weight loss

INTRODUCTION

Morbid obesity is a life-threatening health problem that reduces an individual's quality of life by preventing his/her sociocultural life with many comorbid diseases and complications (1). In the surgical treatment of obesity, laparoscopic adjustable gastric band (LAGB) surgery is a restrictive surgical procedure. It appears to be an advantageous surgical technique as it does not involve any anastomosis or resection, it is reversible, there are very few life-threatening complications, and it is a minimally invasive intervention.

The main purpose of the present study was to investigate success rates, complications, their incidence, and treatment and to determine improvement rates of existing comorbidities in patients who underwent LAGB operation.

MATERIAL and METHODS

The study was conducted between April 2006 and February 2012 in our clinic on 220 patients who were applied LAGB operation. Forty-six patients who did not show up for their routine follow-ups and could not be reached were excluded from the study. Data were analyzed retrospectively using hospital records, outpatient applications, routine follow-ups, and surveys. The local ethics committee approved the study (approval no. 2013-545). Informed consent was not required owing to the retrospective nature of the study.

Patients who were applied LAGB were selected according to the National Institute of Health (NIH-1991) guide (2). Surgical procedures of all patients were performed by the same surgical team. As to the surgical technique, the perigastric technique was applied to the first 82 patients, and the pars flaccida technique was applied to the other 92 patients (3,4). The bands of 82 patients were inflated 2 ccs with per-

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Corresponding Author
Sabri Özden
E-mail: drsabriozden@gmail.com

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igastric technique during the operation and readjusted during the follow-up, 4 weeks later. On the other hand, the bands of 92 patients who were operated with pars flaccida technique were inflated for the first time 4 weeks later after the operation.

Majority of the patients were discharged in 1-2 days in the postoperative period. Patients were checked in week 1 by esophagus stomach duodenum (ESD) fluoroscopy. A semi-solid diet was recommended at postoperative week 4 to the patients. If no problem existed in the ESD fluoroscopy performed in week 4, the band was inflated with Iopamiro-SF under fluoroscopy. Patients were called for control appointment every 2 weeks during the first 6 months. After the first 6 months, patients were called once in 6 weeks if the band was adjusted in a way so as to achieve 1-2 kg/week weight loss. In the second year, they were evaluated every 3 months, monitoring body mass index (BMI), ESD fluoroscopy, and blood tests. After the second year, patients have been followed up two times in 1 year. In addition to routine follow-ups, patients were followed up by a dietician.

Complications

Complications that could be treated medically or with simple surgical procedures in a relatively simpler way and have less negative effects on weight loss were classified as minor complications (port infection, port tube separation, and port slippage). Those that could be treated in a more difficult way, such as removing the band with general anesthesia, and that had more negative effects on weight loss were considered as major complications (band opening, band slippage, pouch enlargement, band erosion/migration, and band intolerance).

Slippage: The cephalic prolapse of the antrum with consequent caudal dislocation of the band is called band slippage. Dysphagia and vomiting are major symptoms of band slippage (5).

Pouch enlargement: Dilatation of the pouch, regardless of changes in the angle of the band, is called pouch enlargement. If a patient has symptoms, such as lack of satiety, regurgitation, heartburn, or chest pain, a clinician has to consider pouch enlargement (5).

Band erosion/migration: Band erosion/migration means that the band in place after adjustable gastric band surgery has grown into the stomach. In patients, one or more symptoms may be present, such as vague abdominal pain, decreased sensation regarding the procedure, decreased sensation in satiety, weight gain, or inability to lose weight. The diagnosis of this complication was made as the band was seen partially or fully in the stomach by endoscopy (6).

Band intolerance: Band intolerance is a condition where full food intolerance develops in patients. Patients complain of severe vomiting.

In these patients, in ESD fluoroscopy or even if pathology was not detected in endoscopy, proton pump inhibitors and medical treatments with antiemetics, through draining all the liquid in the band, were attempted. If persistent vomiting continued despite medical treatment more than 1 month or esophagitis was detected in endoscopy and it did not improve or symptoms reoccurred after refilling, band removal was applied.

Weight Loss

In the present study, the applied method was considered to be unsuccessful in patients whose percentage of excess weight loss (%EWL) was < 25%.

The %EWL was calculated as follows:

%EWL= [(operative weight–follow-up weight)/operative weight–ideal weight] × 100.

The ideal body weight of each patient was estimated based on a target BMI of 25 kg/m^2 (7).

Statistical Analysis

Data were screened retrospectively. For numerical data, they were analyzed by average, standard deviation, and minimum and maximum values. For qualitative data, they were analyzed according to the distribution of number and percentage variables. For non-parametric values, the comparison of numerical data with multiple groups was performed by the Kruskal-Wallis test, and the comparison with dual groups was analyzed by the Mann-Whitney U test. Percentage values were analyzed by the Chi-square test. $p< 0.05$ was considered as statistically significant.

RESULTS

Between April 2006 and February 2012, 174 out of 220 patients who were applied LAGB operation in our clinic were included in the study. The percentage of followed-up patients is 79.09%.

In the study, there were 141 women and 33 men. Average age was 35.24 (18-62) years. Postoperative average BMI was 50.07 (36-74) kg/m^2. There was no operative mortality. Postoperative average follow-up period was 45.37 months.

Complications

In the study, 66 (37.9%) major complications were observed (Table 1).

Slippage: Slippage was observed in 19 (10.91%) patients. In these patients, the average time that passed from the first operation was 24 (10-48) months. Band removal was performed in 15 out of the 19 patients. Among these patients, 4 were applied laparoscopic sleeve gastrectomy (LSG), and 7 were applied laparoscopic Roux-en-Y gastric bypass.

Pouch enlargement: Pouch enlargement was observed in 6 (3.44%) patients. For pouch enlargement, the average time that passed from the first operation was 29 (12-48) months. Only one out of 6 patients was applied rebanding. The other patients' bands were removed. Sufficient weight loss was achieved in the patient who was applied rebanding.

Table 1. Distribution of the complications

Complications	n (%)
Minor complications	30 (17.22)
Port infection	19 (10.91)
Port tube separation	4 (2.29)
Port slippage	7 (4.02)
Major complications	66 (37.9)
Band opening	5 (2.87)
Slippage	19 (10.91)
Pouch enlargement	6 (3.44)
Band erosion/migration	14 (8.04)
Band intolerance	22 (12.64)

Band erosion/migration: Band erosion was observed in 14 (8.04%) patients. For band erosion, the average time that passed from the first operation was 28 (12-60) months.

Bands of all patients with band erosion were removed. Among these patients, 2 patients were applied LSG, 1 patient was applied laparoscopic gastric bypass, and 1 patient was applied open gastric bypass.

Band intolerance: Band intolerance was the most frequently observed complication in the present study, and it was the most common cause of band removal. It was observed in 22 (12.64%) patients. The average time that passed for band intolerance was 30 (6-72) months.

In these patients, band removal was performed in 15 patients, and 7 patients responded to medical treatment. Among these patients whose band was removed, 4 patients were applied LSG, 5 patients were applied laparoscopic gastric bypass, and 1 patient was applied open gastric bypass.

Band removal: Band removal was applied to 62 (35.63%) patients. Of these patients, 33 (18.96%) underwent a different surgical procedure (Table 2). The average time from the first operation date was 28 (2-72) months.

Table 2. Causes for band removal and average time for band removal

Causes for band removal	n (%)	Average month (min-max)
Band opening	3 (1.72)	33 (3-60)
Slippage	13 (7.41)	24 (10-48)
Pouch enlargement	7 (4.02)	29 (12-48)
Band erosion/migration	14 (8.04)	28 (12-60)
Band intolerance	15 (8.62)	30 (6-72)
Inability to lose weight/ Patient's desire	10 (5.74)	31 (4-60)
Total	62 (35.63)	28 (2-72)

Weight Loss

When annual weight checks and BMI of 174 patients were analyzed, four separate groups were formed: patients who were followed up without band removal, patients who did not want another operation after band removal, patients who were applied LSG after band removal, and patients who were applied gastric bypass after band removal.

When 112 patients who were followed up without band removal were considered, the average weight dropped from 138.36 kg to 101.29 kg. On the other hand, the average BMI dropped from 48.54 kg/m^2 to 36.24 kg/m^2. Compared with the other groups with an average weight loss of 38.19 kg and an average BMI of 12.29 kg/m^2, the results were close to the gastric bypass group and better than the other groups (Table 3).

When mean %EWL was considered, it was seen that the best group was the bypass group with 48.98%, followed by the patient group who was followed up by the band. It was noteworthy that %EWL was < 25% for the patient group who did not undergo another surgery after band removal.

When the patient group who was followed up by the band was compared with the patient group who was not performed another surgery after band removal, there was a statistically significant difference between the groups in terms of the end of follow-up weight, BMI, and %EWL ($p< 0.05$). When this group was compared with the group who was performed LSG after band removal, there was a statistically significant difference between the groups in terms of the end of follow-up weight, BMI, and %EWL ($p< 0.05$). However, when this group was compared with the group who underwent gastric bypass, the difference between the groups in terms of the end of follow-up weight, BMI, and %EWL was not statistically significant ($p> 0.05$) (Table 3).

Comorbidities

Various comorbid diseases were present in 43 (24.7%) patients. These diseases were type 2 diabetes mellitus in 13 (7.4%) patients, essential hypertension in 16 (9.1%) patients, arthralgia in 8 (4.5%) patients, and sleep apnea in 6 (3.4%) patients.

In 10 out of 13 patients with diabetes, some improvements, such as removing oral antidiabetic drugs or reducing insulin dosage, were observed. Some improvements were also observed in 11 out of 16 patients with hypertension in the form of a reduction in drug dosage or complete cessation and in 5 out of 8 patients with arthralgia in the form of a reduction in non-steroid anti-inflammatory drug use or complete cessation. On the other hand, in 4 out of 6 patients who had sleep apnea and had to use a continuous positive airway pressure device, the need for the device was reduced, or it was no longer needed (Table 4).

Table 3. Average weight, BMI, EWL changes in patient groups who were applied different surgical procedures (*Kruskal-Wallis test)

	All patients	Band not removed	Band removed, No other surgery	Band removed + LSG	Band removed + Gastric bypass	p*
Number of patients	174	112	28	13	21	
Preoperative average weight (kg)	138.3	138.36	136.53	141.53	137.55	0.816
Preoperative average BMI (kg/m^2)	49.12	48.54	50.07	49.8	50.81	0.927
End of follow-up average weight (kg)	103.61	101.29	113.82	112.3	97.4	0.013
End of follow-up average BMI (kg/m^2)	37.61	36.24	41.5	39.96	36.34	0.008
End of follow-up average %EWL	41.91	46.03	24.75	32.89	48.98	0.040

BMI: Body mass index, EWL: Excess weight loss, LSG: Laparoscopic sleeve gastrectomy.

Table 4. Number of patients who have comorbidities and their improvements

Comorbidity	n (%)	Improvement in disease n (%)
Type 2 diabetes mellitus	13 (7.4)	10 (5.7)
Essential hypertension	16 (9.1)	11 (6.3)
Artralgia	8 (4.5)	5 (2.8)
Sleep apnea	6 (3.4)	4 (2.2)
Total	43 (24.7)	30 (17.2)

DISCUSSION

In the present study, we evaluated the long-term follow-up results of 174 patients who underwent LAGB operation. The study had the reliability that could be compared with the literature both in terms of the number of patients and in terms of follow-up rate. The average follow-up period of the patients was long enough to provide long-term results (8,9).

An ideal bariatric surgery method should be a method that has the highest %EWL and preferably reversible, in addition to the minimum morbidity and mortality rates. Therefore, gastric band application is a method that has been used for approximately 20 years in obesity (10).

In the literature, long-term outcomes regarding the method, a lot of complications, and reductions in percentages in the EWL were reported (3,11). Many centers in Europe made the transition to other surgical procedures, primarily gastric bypass and sleeve gastrectomy (8). In our study, band removal has been accepted as a failure for LAGB surgery, and patients were referred to revision surgery. Considering all patients, mean %EWL was 41.91%. However, since this figure includes those patients who did not undergo another surgery after band removal and those patients who underwent revision surgery after band removal, it would be more accurate to exclude these groups to assess the LAGB operation.

There is no statistically significant difference between these four groups in terms of preoperative BMI and weight values. On the other hand, there is a statistically significant difference in terms of the end of follow-up weight, BMI, and %EWL values. Especially, there is a significant difference between the group who was followed up by the band and the LSG group and the group who did not undergo another surgery. There is no statistically significant difference between the gastric bypass group and the group who was followed up by the band. This may suggest that the LAGB operation can be successful in weight loss as gastric bypass. However, considering the long-term results in our study, band removal and necessity of revision surgery have occurred in the majority of patients owing to various complications. O'Brien et al. published a systematic review in 2013 (12). The present study indicated similar long-term weight losses for LAGB and gastric bypass and also similar high rates of complications and necessity of revision surgery, such as our study (12).

When the mean %EWL was considered, the most successful group is the gastric bypass group (49.98%), followed by patients who were followed up with the band (46.03%). It is not surprising that the most unsuccessful group is the group who was not performed another surgery after band removal. This situation demonstrates how necessary it is to apply revision surgery in patients in whom complication developed and also may show that gastric bypass may be the preferred revision procedure after LAGB. In the literature, there are many studies on revision surgery after failed LAGB. In these studies, patients who underwent revision surgery, with follow-up results of %EWL values, are close to our study (13-15). Elhanas et al. published an ex-

tensive review in 2013 about revision surgery and suggested gastric bypass as revision surgery for LAGB (15).

In 112 (64.36%) patients who were followed up with the band, the mean %EWL was 46.03%, the preoperative average BMI was 48.5 kg/m^2, the end of follow-up average BMI was 36.2 kg/m^2. These rates are close to other studies in the literature (8,9,11,16-18).

In our study, the most frequent complication among the major complications is band intolerance, which is also the most common cause of band removal. A total of 22 patients showed band intolerance, and 15 out of these patients did not respond to medical treatment; therefore, these patients' bands had to be removed. Whereas Suter et al. have reported esophagitis and pathological pH scores even shortly after the LAGB application, Gutschow et al. have shown esophagitis in 30% of the patients and pathological pH scores in 43.8% of the patients in a study during an average 30-month follow-up period (19,20). In addition to the presence of studies supporting that band intolerance may be due to very tight banding, in patients where the bands were loosened but no respond was received or reoccurrence of the condition was observed, it is obvious that factors, such as psychological or psychosocial factors of the patients, also need to be taken into consideration (17).

Band slippage was observed in 19 (10.91%) patients. This rate varies between 3.6% and 6.9% in the literature (8,16,17). Frequently performed adjustments in patients who cannot achieve optimal weight loss can be thought as a cause of high slippage rates.

The pouch enlargement rate (3.44%) is lower than the literature (8,9,16,17). In the literature, one of the most important causes of pouch enlargement was reported as overly inflated bands (21). We believe that the reason that our rate is lower than the literature is owing to the fact that patients were closely followed up, and their checks were performed in a timely manner.

The band erosion rate is at the same level with many studies or even at better levels (9,11,17). Himpens et al. have associated the high erosion rate in their study to performing an endoscopic examination and use of the perigastric technique on every patient who gained weight even if there were no symptoms. On the other hand, Suter et al. believe that it is due to more than the 5-year follow-up period and performing routine endoscopy again (17). The reason that the incidence of band erosion in our study was lower than that in the literature may be due to the fact that endoscopy was performed only on those symptomatic patients, and that routine endoscopy was not performed.

The band was removed in 35.63% of our patients. The band removal rate in our study is consistent with the literature (9,18,22). The cause of high band removal rate can be considered as band intolerance, which is the most common cause, and that patients did not change their dietary habits during that time. In our study, band removal was considered as a failure in LAGB operations, and patients were referred to revision surgery. Approximately half of the patients whose band was removed underwent a new operation, such as gastric bypass or sleeve gastrectomy. Patients were followed up to prevent weight gain in this way.

Our data showed that 69.7% (n= 30) from all of the concomitant disease (n= 43) in patients with obesity healed after surgical treatment. The improvement rates of all concomitant disease based on type 2 diabetes mellitus, essential hypertension, and obstructive sleep apnea syndrome were 76.9%, 68.7%, and 66.6%, respectively. These results were consistent with the literature in patients who were morbidly obese who were treated surgically (23-25).

Twenty-one patients who were treated with gastric banding had concomitant diseases. We observed healing for comorbidities in 17 patients. The improvement rates of type 2 diabetes mellitus, hypertension, and arthralgia were statistically significant ($p< 0.05$) in patients who were treated with gastric banding. These results were superior from the literature for patients who were morbidly obese who were treated with banding (23-25).

CONCLUSION

When improved patient compliance and careful and close patient follow-up are provided in the early stages of LAGB application, it may be possible to reach %EWL results that would be the nearest to those achieved by gastric bypass or sleeve gastrectomy methods. However, high complication rates and necessity to perform other bariatric surgical procedures in the majority of the patients in the long-term follow-ups suggest that the LAGB operation is not the first choice in bariatric surgery.

In addition, it should be emphasized that it is important to apply a new bariatric surgical method to prevent weight gain after band removal.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Ankara Numune Training and Research Hospital (2013-545).

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

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Author Contributions: Consept - S.O., M.F.A.; Design - S.O., M.F.A.; Supervision - M.F.A., B.S.; Data Collection and/or Processing - S.O.; Analysis and Interpretation - S.O., M.F.A.; Literature Search - S.O.; Writing Manuscript - S.O., M.F.A.; Critical Reviews - B.S., M.F.A.

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ORİJİNAL ÇALIŞMA-ÖZET
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Laparoskopik ayarlanabilir gastrik bant uygulanan hastaların uzun dönem sonuçları

Sabri Özden[1], Barış Saylam[1], Fatih Mehmet Avşar[1]

[1] Ankara Numune Eğitim ve Araştırma Hastanesi, Cerrahi Kliniği, Ankara, Türkiye

ÖZET

Giriş ve Amaç: Morbid obezitede en etkili tedavi basamağı cerrahi tedavidir. Bu çalışmanın amacı; laparoskopik ayarlanabilir gastrik bant (LAGB) ameliyatı uygulanan hastalarda uzun dönem takip sonuçları ile başarı oranını irdelemektir.

Gereç ve Yöntem: Çalışmada Nisan 2006-Şubat 2012 arasında laparoskopik ayarlanabilir gastrik bant operasyonu yapılan 220 morbid obez hastada; 6 yıllık takip süresinde vücut kitle indeksindeki değişim, fazla kiloların kaybı (FKK) yüzdesi, ek hastalıklar ve düzelme oranı, oluşan komplikasyonlar, sıklığı ve yapılan tedaviler incelenmiştir. Rutin takiplerine gelmeyen 46 hasta çalışma dışı bırakılmıştır.

Bulgular: Çalışmamızda bant çıkarılma yüzdesi %35,63'tür. Bant çıkarılmadan takip edilen hastalarda FKK %46,03'tür. Major komplikasyonlar içinde en sık görülen komplikasyon; bant çıkarılmasının da en sık sebebi olan bant intoleransıdır. Bant çıkarılması LAGB operasyonu için başarısızlık olarak kabul edilmiş ve hastalar başka cerrahi yöntemlere yönlendirilmiştir.

Sonuç: İyi hasta uyumu, titiz ve yakın hasta takibi sağlandığında LAGB uygulaması ile erken dönemde gastrik baypas ya da sleevegastrektomi yöntemlerine yakın FKK yüzdesi sonuçlarına ulaşmak mümkün olabilir. Ancak uzun süreli takiplerde, yüksek komplikasyon oranları ve hastaların önemli bir kısmında diğer bariatrik cerrahi yöntemlere geçilmek zorunda kalınması, LAGB operasyonunun ancak seçilmiş hastalarda uygulanabileceğini düşündürmektedir.

Anahtar Kelimeler: Vücut kitle indeksi, laparoskopik ayarlanabilir gastrik bant, aşırı kiloların kaybı yüzdesi, laparoskopik sleeve gastrektomi, laparoskopik Roux-N-Y gastrik baypas

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Routine histopathological examination of gallbladder specimens after cholecystectomy: Is it time to change the current practice?

Mohamed Benkhadoura[1], Akrem Elshaikhy[2], Soad Eldruki[3], Osama Elfaedy[4]

[1] Department of General Surgery, Benghazi Medical Center, Benghazi University, Benghazi, Libya
[2] Department of General Surgery, Al-jala Hospital, Benghazi University, Benghazi, Libya
[3] Department of Pathology, Benghazi Medical Center, Benghazi, Libya
[4] Department of General Surgery, St. Luke's General Hospital, Kilkenny, Ireland

ABSTRACT

Objective: Routine histopathological examination of all gallbladder specimens, regardless of the clinical characteristics of the patient or macroscopic aspect of the gallbladder, is the current approach to detect the presence of gallbladder carcinoma. The aim of the present study was to assess whether or not it would be safe to adopt a policy of processing only gallbladder specimens with preoperative or intraoperative suspicion for malignancy without compromising patient safety.

Material and Methods: From January 2009 to June 2017, all histopathology reports of 3423 consecutive gallbladder specimens after elective and emergency cholecystectomies were retrospectively analyzed in two university hospitals.

Results: A total of 3423 gallbladder specimens submitted for histopathological examination during the study period were included into the study. The results of histopathological examination of these gallbladder specimens showed that chronic cholecystitis was found in 2792 (81.6%), acute cholecystitis in 237 (6.9%), and cholesterolosis in 223 (6.5%) patients. Dysplasia was found in 5 (0.14%) patients, and gallbladder carcinoma was detected in 4 (0.11%) patients. All patients with gallbladder carcinoma were diagnosed either preoperatively or intraoperatively, and none of the patients with gallbladder carcinoma were diagnosed from the histopathological examination.

Conclusion: A strategy of selective approach for histopathological examination of gallbladder specimens may be safe in areas with very low incidence of gallbladder carcinoma. Such selective strategy is more cost-effective, reduces the workload of pathologists, and does not appear to compromise patient outcome.

Keywords: Gallbladder cancer, gallbladder specimen, histopathological examination, incidental finding

INTRODUCTION

Cholecystectomy is one of the most common abdominal surgical procedures performed worldwide (1). It is standard practice to submit all gallbladder specimens for routine histopathological examination (HPE) postoperatively, regardless of any grossly visible abnormalities, to exclude unexpected gallbladder cancer (GBC) (2). GBC is a rare disease with a dismal prognosis (3). The incidence of GBC varies widely among different geographical regions and ethnic groups. Rates may differ even inside a region or a country. Northern India and Pakistan, East Asia, South America, and Eastern Europe are found to have the highest rates of GBC (1). Incidental GBC is found in 0.2%-2.9% of all cholecystectomies performed for gallstone disease (4,5). Patients with incidental GBC diagnosed with stages Tis and T1a can be treated by simple cholecystectomy alone. Patients with stage T1b and beyond should undergo further surgical treatment (2,5). However, several recent studies have questioned the necessity for routine HPE of all gallbladder specimens. The main debate on selective versus routine histological assessment of gallbladder specimens is based on findings of incidental GBC (6). Currently, there is an emerging trend to consider selective HPE of cholecystectomy specimens removed for benign gallbladder disease.

The aim of the present study was to assess whether or not it would be safe to adopt a policy of processing only gallbladder specimens with preoperative or intraoperative suspicion for malignancy without compromising patient safety.

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Corresponding Author
Mohamed Benkhadoura
E-mail: khdoura@yahoo.com

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MATERIAL and METHODS

From January 2009 to June 2017, all histopathology reports of 3423 consecutive gallbladder specimens after elective and emergency cholecystectomies were retrospectively analyzed in two university hospitals, Benghazi medical centre and Al-Jala hospital in Benghazi, Libya. The study was performed according to the World Medical Association Declaration of Helsinki.

Patient data on age, sex, and histopathological diagnosis were recorded. Incidental GBC is defined as GBC identified only after HPE (1,6). The term incidental GBC was not used when GBC was suspected on preoperative imaging (ultrasound and/or computed tomography), intraoperative, or opening of the gallbladder specimen.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 18.0 software (SPSS Inc., Chicago, IL, USA). Data were analyzed using the chisquare test.

Table 1. Details of histopathological findings from 3423 cholecystectomy specimens

Histopathological diagnosis	Number	Percent
Chronic cholecystitis	2792	81.6
Acute cholecystitis	237	6.9
Empyema gallbladder	47	1.4
Gangrenous gallbladder	36	1.1
Cholesterolosis	223	6.5
Gallbladder polyp	2	0.1
Gallbladder diverticulum	2	0.1
Gallbladder adenoma	2	0.1
Porcelain gallbladder	2	0.1
Adenomyomatosis	67	2.0
Xanthogranulomatous cholecystitis	4	0.1
Dysplasia	5	0.1
Carcinoma	4	0.1
Total	3423	100.0

RESULTS

Of the 3423 gallbladder specimens submitted for HPE during the study period, 486 were males (14.2%), and 2937 were females (85.8%). Median age of the patients was 40 (14-93) years. Chronic cholecystitis was found in 2792 (81.6%) patients, acute cholecystitis in 237 (6.9%), and cholesterolosis in 223 (6.5%) (Table 1). Dysplasia was observed in 5 (0.14%) patients, and GBC was detected in 4 (0.11%).

All patients with GBC were diagnosed either preoperatively or intraoperatively. Two cases were diagnosed by ultrasound and computed tomography, showing abnormalities in the gallbladder wall with suspicion of malignancy. The other two cases had intraoperative findings suggestive of GBC and were confirmed subsequently by HPE as primary GBC. All of the four malignant specimens were reported as adenocarcinomas from the HPE. Two patients were found to have T2 lesions, and 2 patients had T3 lesions (Table 2).

DISCUSSION

There has been controversy in the literature regarding routine or selective HPE of gallbladder specimens when cholecystectomy is performed for benign gallbladder diseases. The main debate by those studies that suggest selective HPE is that first, it is unlikely to have incidental GBC in a normal-looking gallbladder specimen (2,3,7-15). Second, unexpected early GBCs (stages Tis and T1a), which may look normal on gross examination, do not require further treatment as simple cholecystectomy is adequate. Third, routine HPE of all gallbladder specimens overburdens the histopathology department and hospital resources (6).

Studies recommending selective HPE observed that the possibility of missing an early cancer diagnosis is very low, and that almost all incidental GBCs are associated with findings on gross examination of the gallbladder specimen. Bazoua et al., Emmett et al., and Darmas et al. have reported incidental GBC rates of 0.17% (5/2890), 0.25% (12/4776), and 0.27% (4/1452), respectively (7-9). Tayeb et al. have noted incidental GBC in only 3 out of 426 (0.70%) cases (10). All cases of incidental GBC in these studies had a macroscopically abnormal gallbladder; hence, these studies suggest that it is safe to adopt a selective approach to

Table 2. Details of the patients with a histopathological diagnosis of gallbladder carcinoma

Patient	Age (years)	Sex	Preoperative suspicion	Intraoperative finding	Stage (T) and grade
1	47	Male	No	Thick-walled gallbladder, severe inflammation, severe adhesions	T2, WDAC
2	40	Male	No	Gallbladder growth, severe inflammation, severe adhesions	T2, WDAC
3	61	Male	Yes by US and CT	Gallbladder mass, severe inflammation, severe adhesions	T3, PDAC
4	61	Female	yes by US and CT	Gallbladder mass, severe inflammation, severe adhesions, liver metastases	T3, PDAC

US: Ultrasound; CT: Computed tomography; WDAC: Well differentiated adinocarcinoma; PDAC: Poorly differentiated adinocarcinoma.

HPE. Furthermore, Deng et al. have found 46 (0.32%) patients with GBC out of 14.369 cholecystectomy specimens, of which only 2 patients with stages Tis and T1a did not show suspicious lesions on preoperative and intraoperative findings (2).

Some studies showed that it may be justified to exclude gallbladder specimens from the HPE by using macroscopic examination. van Vliet et al. have shown that of the 1375 gallbladder specimens examined macroscopically, not one incidental GBC is found (11). Of the 185 (13.5%) specimens of all gallbladder specimens that showed macroscopic abnormalities for which they would require further HPE in case of a selective policy, GBC was found in 6 specimens.

Similarly, in the study by Mittal et al. of 1305 patients, incidental GBC has been found in 13 patients out of 610 macroscopically abnormal gallbladder specimens (12). In a macroscopically normal gallbladder specimen, no cases of GBC have been found. Our study showed that all patients with GBC were diagnosed either preoperatively or intraoperatively, and none of the patients with GBC were diagnosed from the HPE.

There has been a concern about the presence of early GBC in a normal-looking gallbladder specimen. However, simple cholecystectomy is considered adequate in these patients, and no further therapy is required (8,11-13).

Recent studies have recommended patients' age as an additional factor for selecting specimens for HPE of gallbladder specimens. Elshaer et al. have suggested that age should also be used to select gallbladder specimens that should be submitted to HPE as all patients with cancer in their study are above 51 years (13). This could aid in combination with the intraoperative appearance of the gallbladder to identify those specimens requiring histopathological analysis, especially in an area with a lower incidence of incidental GBCs. Similarly, Romero-González et al. have considered the age of ≥ 60 years as one of the risk factors for GBC (14). In their study, the surgeon first identified the risk factors for GBC and then performed a macroscopic analysis of the gallbladder specimen just after surgery. All three histopathologically confirmed GBCs in their study were suspected by the surgeon following macroscopic analysis. Furthermore, Wrenn et al. have concluded that selective screening based on risk factors (including older patients), intraoperative findings, and on-table examination of the specimen may be a feasible and more cost-effective alternative to universal screening (15).

On the other hand, studies that recommend routine HPE of gallbladder specimens are based mainly on the identification of high rates of incidental GBCs and also need additional treatment (16-21). Siddiqui et al. have identified incidental GBC in 6 specimens out of 220 cholecystectomy specimens, of which 3 patients with advanced stages (T2 and T3) underwent revision surgery (16). Shrestha et al. have reported 1 stage T2 disease and 3 stage T3 disease out of 9 incidental GBCs in 668 cholecystectomy specimens (17). Ul Haq et al. have shown 2 patients with stage T2 disease out of 5 incidental GBCs in a series of 107 specimens, and Ghimire et al. have found 2 patients with stage T2 disease out of 10 incidental GBCs in a series of 783 specimens (18,19).

It is noted that almost all of these studies suggesting routine HPE are from geographical areas with a relatively high incidence of GBC (Table 3). Moreover, most of the studies that recommend submitting all gallbladder specimens for routine HPE regardless of its gross appearance report a definitive gross abnormality in the cases diagnosed with incidental GBC. For example, Kalita et al. have found 18 unsuspected incidental GBC cases in a study of 4115 patients (20). However, gross examination of these 18 cases showed localized growth in 10 cases and diffuse thickening of the gallbladder wall in 8 cases. In the study by Hamdani et al., 7 cases of incidental GBC have been observed (21). After reviewing gross findings of these incidental GBCs, 3 cases had a polypoidal mass, 2 cases had wall thickenings, and 2 cases had mucosal irregularity. Similarly, Shreshtha et al. have reported 9 incidental GBCs out of 668 cases of cholecystectomy specimens (17). However, on gross features of the incidental GBC cases, 5 cases had growth (2 fungating mass and 3 solid gray white mass), 2 cases had an irregular mucosa, 1 case had a contracted gallbladder, and 1 case had a thick fibrosed wall.

We recommend that in all patients undergoing cholecystectomy for gallstone disease, the gallbladder specimen should be opened and examined for macroscopic abnormalities before deciding to submit the specimen for HPE. Based on patient characteristics and macroscopic appearance of the gallbladder, it appears safe to adopt a selective approach for those specimens with preoperative or intraoperative suspicion for malignancy, especially in areas with very low incidence of GBC.

Our study has some limitations. First, this is a retrospective study. Second, the patient population is associated with a single region in Libya, which may not reflect the demographics of other regions and other medical centers throughout the country. Hence, a prospective, multicenter study is required in order to safely modify the existing guideline.

CONCLUSION

A policy of selective approach for HPE of gallbladder specimens may be safe in areas with very low incidence of GBC. Such selective approach is more cost-effective, decreases the workload of the histopathology department, and does not appear to compromise patient outcome.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects".

Table 3. Studies recommending routine or selective histopathological examination of gallbladder specimens in different countries

Country	Study	Year	Recommendation
China	Deng et al. (2)	2015	Selective
Pakistan	Tayeb et al. (10)	2015	Selective
	Siddiqui et al. (16)	2013	Routine
	Ul Haq et al. (18)	2011	Routine
UK	Emmett et al. (8)	2015	Selective
	Elshaer et al. (13)	2014	Selective
	Bazoua et al. (7)	2007	Selective
	Darmas et al. (9)	2007	Selective
Netherlands	van Vliet et al. (11)	2014	Selective
India	Kalita et al. (20)	2013	Routine
	Hamdani et al. (21)	2012	Routine
	Behari et al. (1)	2010	Routine
	Mittal et al. (12)	2010	Selective
Mexico	Romero-González et al. (14)	2012	Selective
Nepal	Ghimire et al. (19)	2011	Routine
	Shrestha et al. (17)	2010	Routine
Sri lanka	De Zoysa et al. (3)	2010	Selective

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2019; 35 (2): 86-90

Kolesistektomi sonrası safra kesesi örneklerinin rutin histopatolojik incelemesi: Mevcut uygulamayı artık değiştirmeli miyiz?

Mohamed Benkhadoura[1], Akrem Elshaikhy[2], Soad Eldruki[3], Osama Elfaedy[4]

[1] Bingazi Üniversitesi Bingazi Tıp Merkezi, Genel Cerrahi Bölümü, Bingazi, Libya
[2] Bingazi Üniversitesi Al-jala Hastanesi, Genel Cerrahi Bölümü, Bingazi, Libya
[3] Bingazi Tıp Merkezi, Patoloji Bölümü, Bingazi, Libya
[4] St. Luke's Genel Hastanesi, Genel Cerrahi Bölümü, Kilkenny, İrlanda

ÖZET

Giriş ve Amaç: Safra kesesinin makroskopik görünüşü ve hastanın klinik özelliklerine bakılmaksızın safra kesesi örneklerinin rutin histopatolojik incelemesi safra kesesi karsinomunu tespit etmek üzere yürütülen mevcut yaklaşımdır. Bu çalışmanın amacı, hasta güvenliğini tehlikeye atmadan sadece preoperatif ve intraoperatif malignite şüphesi bulunan safra kesesi örneklerini işlemden geçirme politikasını benimsemenin güvenli olup olmayacağını ortaya koymaktır.

Gereç ve Yöntem: Ocak 2009 ve Haziran 2017 arasında elektif ve acil kolesistektomi sonrası 3423 ardışık safra kesesi örneklerinin histopatoloji raporları iki üniversite hastanesinde retrospektif olarak incelendi.

Bulgular: Çalışma dönemi boyunca histopatolojik incelemeye tabi tutulan toplam 3423 safra kesesi örneği çalışmaya dahil edildi. Bu safra kesesi örneklerinin histopatolojik incelemesi sonucunda 2792 (%81,6) kronik kolesistit, 237 (%6,9) akut kolesistit ve 223 (%6,5) kolesterolüz bulundu. Displazi 5 (%0,14) hastada ve safra kesesi karsinomu 4 (%0,11) hastada tespit edildi. Safra kesesi karsinomu bulunan tüm hastalar preoperatif veya intraoperatif olarak tanı aldı ve bu hastaların hiçbiri histopatolojik inceleme sonucunda safra kesesi karsinomu tanısı almadı.

Sonuç: Safra kesesi karsinomu insidansının çok düşük olduğu bölgelerde safra kesesi örneklerinin histopatolojik incelemesi için selektif bir yaklaşım stratejisinin geliştirilmesi güvenli olabilir. Bu tür bir selektif strateji daha uygun maliyetli olup patologların iş yükünü azaltmakta ve hasta sonuçlarını etkilediği görülmemektedir.

Anahtar Kelimeler: Safra kesesi kanseri, safra kesesi örneği, histopatolojik inceleme, insidental bulgu

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ORIGINAL ARTICLE
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Short term outcome of laparoscopic ventral mesh rectopexy for rectal and complex pelvic organ prolapse: case series

Fatma Ayça Gültekin[1]

[1] Department of General Surgery, Zonguldak Bulent Ecevit University School of Medicine, Zonguldak, Turkey

ABSTRACT

Objective: Laparoscopic ventral mesh rectopexy (LVMR) is a technique gaining more recognition for the management of pelvic floor disorders, such as external rectal prolapse (ERP), high grade internal rectal prolapse (IRP) and rectocele. LVMR also allows correction of coexisted pelvic organ prolapse. This study aimed to evaluate the safety, efficacy and functional outcome of LVMR for rectal and complex pelvic organ prolapse.

Material and Methods: All patients who underwent LVMR from February 2014 to October 2017 were included into the study. The patients were evaluated preoperatively and three months postoperatively. Surgical complications and functional results in terms of fecal incontinence (measured with the Wexner Incontinence Score= WIS) and constipation (measured with the Wexner Constipation Score= WCS) were analyzed.

Results: Thirty (4 males) patients underwent LVMR. Seventeen (56.6%) patients had complex pelvic organ prolapse according to MRI findings. Median operative time and postoperative stay were 110 minutes and 4 days, respectively. No mesh-related complication and recurrence were observed. Before surgery, 21 (70%) patients had complained about symptoms of obstructed defecation. WCS decreased significantly from median 19 to 6 ($p< 0.001$). Preoperative median WIS of 9 patients was 14 and went down to 6 postoperatively ($p= 0.008$). WCS significantly improved after LVMR in patients with symptomatic rectocele combined with enterocele or sigmoidocele ($p= 0.005$), and significant improvement was also observed in patients with symptomatic rectocele combined with gynecologic organ prolapse, preoperative median WCS was 18 and the postoperative value fell to 8 ($p= 0.005$).

Conclusion: LVMR is an effective surgical option for rectal and complex pelvic organ prolapse with short-term follow-up.

Keywords: Rectal prolapse, pelvic organ prolapse, laparoscopic ventral rectopexy

INTRODUCTION

Since laparoscopic ventral mesh rectopexy (LVMR) was reported by D'Hoore in 2004, it has become the most common surgical procedure for external rectal prolapse (ERP) in Europe (1). Currently, LVMR is not only performed for ERP but also increasingly performed for internal rectal prolapse (IRP) and obstructive defecation syndrome (ODS) (2-7). During LVMR, the rectum is mobilized ventrally and the rectovaginal septum is dissected to the lowest part of the pelvic floor. The anterior wall of the rectum is fixed to the sacral promontory with mesh. Ventral position of the mesh also helps to perform colpopexy. Suturing of the posterior vaginal fornix (or posterior vaginal vault) to the same mesh provides some degree of correction, and any associated vaginal vault prolapse and obliteration of the Douglas pouch prevent enterocele, too (8). Main advantages of the technique are nerve sparing limited anterior dissection of the rectum and reinforcement of the rectovaginal septum with mesh, which gives support to both posterior and middle pelvic compartment. Long term results of LVMR have shown that LVMR is safe and effective for the treatment of ERP, IRP and rectocele with low recurrence rate, good functional results and rare mesh related complications (3). Although LVMR is being progressively performed in Europe and United States of America, few studies come from non-western countries (9-11). This study aimed to evaluate our surgical and functional short-term results of LVMR in a small consecutive series of patients from Turkey. To the best of our knowledge, this series seems to be the first and largest case series of patients that underwent LVMR in Turkey.

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Corresponding Author
Fatma Ayça Gültekin
E-mail: faycagultekin@yahoo.com

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MATERIAL and METHODS

Study Design

This observational cohort study is a retrospective analysis conducted in a tertiary referral center in Turkey. Between February 2014 and October 2017, LVMR was performed in 30 consecutive patients with ERP, IRP or symptomatic rectocele by one EBSQ-Coloproctology (European Board of Surgical Qualification in Coloproctolgy) certified colorectal surgeon. The study received ethical approval from the Hospital Ethics Committee. Informed consent was obtained from all of the patients.

Patients and Evaluation

Indications for LVMR were ERP, high grade IRP and/or rectocele associated with fecal incontinence or obstructed defecation. In addition, vaginal vault prolapse or uterovaginal prolapse could be present. All rectocele patients had failed in at least 3 months maximal conservative treatment (dietary modifications, laxatives and biofeedback therapy). Preoperative work-up comprised a complete history and physical examination and a flexible sigmoidoscopy/colonoscopy. Patients with ERP did not undergo any further investigations. A dynamic MR-defecography was performed to confirm diagnosis of IRP, rectocele and/or enterocele. Descending perineum (DP)> 3 cm was also a recorded pelvic structural abnormality during dynamic MR-defecography. IRP was classified into high grade and low grade using the Oxford rectal prolapse grading system (12).

Patient characteristics, previous surgery, perioperative data, length of hospital stay and complications (30 day postoperative complications) were obtained from the electronic medical database.

Functional outcomes were assed preoperatively and three months after LVMR by Wexner incontinence score (WIC) and Wexner constipation score (WCS) (13,14).

Surgical Technique

The surgical technique for LVMR was adopted from the technique described by D'Hoore et al., with a few modifications as previously reported (1,15,16). In brief, the patients were placed in steep Lloyd-Davies position using special stirrups (Yellofin; Allen Medical, Massachusetts, USA). A 30-degree scope was placed in the sub-umbilical position with Hasson Technique, followed by the placement of 12-mm working port in the right iliac fossa and 5-mm ports each in the left lower quadrant and the right lateral abdominal wall. A very superficial peritoneal incision was created on the right side of the sacral promontory and continued on the right pararectal plane down to deepest part of the pouch of Douglas with a small extension onto the left side. The rectovaginal septum was dissected down to the level of the pelvic floor muscles. The lateral stalks were kept intact (Figure 1). L-shaped polypropylene mesh (Figure 2) was fixed to the pelvic-floor musculature on both sides of the rectum with absorbable tacks (Figure 3). The mesh was laid along the right side of the rectum with

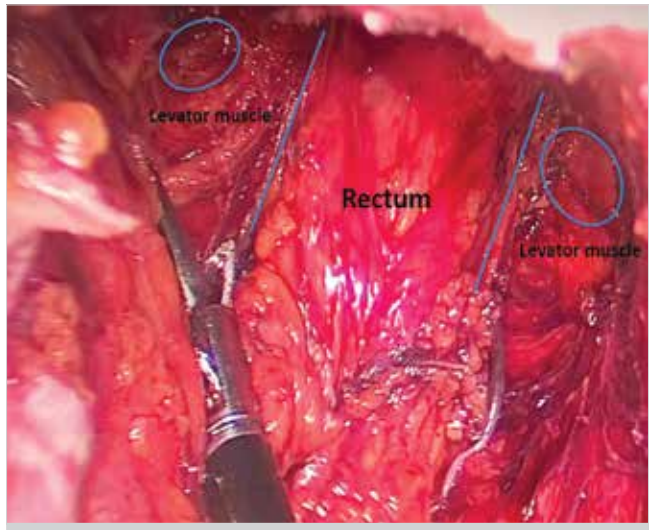

Figure 1. Dissection of the recto-vaginal septum and pelvic-musculature.

Figure 2. Preparation of the polypropylene mesh, which was trimmed to an L-shaped configuration.

the proximal end fixed to the sacral promontory with nonabsorbable tacks (Figure 4). If middle compartment prolapse was present, vaginal fornix (or posterior vaginal vault) was suspended and sutured to the same mesh. The peritoneum was then closed over the mesh with 2/0 absorbable vicryl suture.

Statistical Analysis

Statistical analyses were performed with SPSS 19.0 software (SPSS Inc., Chicago, IL, USA). Variables were expressed as mean ± std. deviation and categorical variables as frequency and percent. Continuous variables were compared with Mann-Whitney

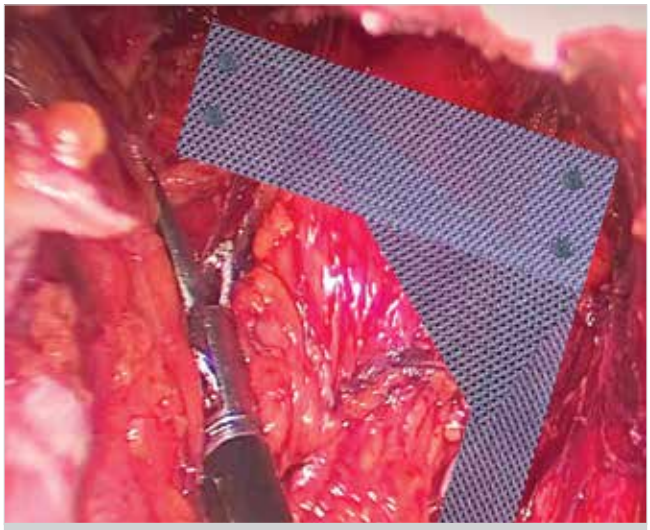

Figure 3. The polypropylene mesh was secured onto the pelvic-floor musculature on either side of the rectum with absorbable tacks.

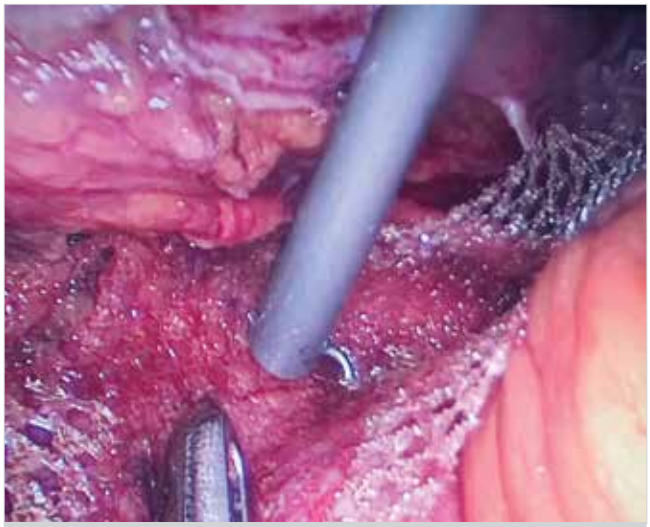

Figure 4. Proximal end of the polypropylene mesh fixed to the sacral promontory with nonabsorbable tacks.

U test. Repeated measures were evaluated with Wilcoxon Signed Rank test. P value of less than 0.05 was considered statistically significant for all tests.

RESULTS

A total of 30 patients (26 females) had LVMR between February 2014 and December 2017. Median follow-up time after LVMR was 23.9 months (range: 4-42.1). Patient characteristics and operative data are listed in Table 1. Mean age was 54.3 (± 13.6) (median = 53; range: 19-82) and mean BMI was 29.8 kg/m^2 (± 5.9). A history of previous abdominal or pelvic surgery was assessed in 30% of the patients. Patients were classified as ASA I (10%), ASA II (53%), ASA III (27%) and ASA IV (10%). At physical examination, nine patients had an ERP and 20 a rectocele. Three patients had a concurrent descending perineum, vaginal vault and uterovaginal prolapse. Preoperative imaging results are summarized in Table 2. Dynamic MR-defecography was performed in 21 patients. Enterocele and sigmoidocele were identified on dynamic MR-defecography in 7 patients. In six patients, descending perineum in combination with rectocele was found on dynamic MR-defecography. In a patient with symptoms of ODS and normal physical examination, dynamic MR-defecography showed grade III IRP. On imaging studies, 56.6% (17/30) patients showed at least two different forms of co-existing abnormalities.

Table 1. Patient characteristics and operative data

Variable	Value
Female/male	26/4
Age (years) (mean ± SD)	54.3 (± 13.6)
BMI (kg/m^2) (mean ± SD)	29.8 (± 5.9)
Previous abdominal surgery, n (%)	9 (30%)
Physical examination	
Rectal prolapse	9
Rectocele	16
Rectocele + vaginal vault prolapse	1
Rectocele + uterovaginal prolapse	1
Rectocele + perineal descensus	2
Normal	1
ASA* Score, n (%)	
ASA I	3 (10%)
ASA II	16 (53%)
ASA III	8 (27%)
ASA IV	3 (10%)
Operation time, (minute) (median, range)	110 (80-300)
Length of hospital stay, days (median, range)	4 (3-8)
Postoperative 30 day complications, n (%)	-
Follow-up (months) (median, range)	23.9 (4-42.1)

* ASA: American society of anaesthesiologists.

Surgery was performed laparoscopically in all patients. Median total operating time was 110 minutes (range: 80-300 minutes). Extensive endometriosis resulted in a perforation of the vagina in one patient. The defect was closed laparoscopically with sutures, and the procedure was completed with placement of the mesh. No postoperative early (< 30 days) complication was observed. Median hospital stay was 4 days (range: 3- 8 days). Preoperatively, nine patients reported fecal incontinence. WIS preoperatively varied from 10 to 20 (median: 14) and went down to 6 (range: 4-8), postoperatively. The difference was statistically significant (p= 0.008) (Figure 5). Twenty-one patients had symptoms of ODS with median WCS 19 (range: 14-26) and

Table 2. Dynamic magnetic resonance (MR)-defecography findings patients with rectocele		
Physical examination	**Dynamic MR*-defecography findings**	**n**
Rectocele	Rectocele	3
Rectocele	Rectocele + enterocele	5
Rectocele	Rectocele + sigmoidocele	2
Rectocele	Rectocele + perineal descensus	6
Rectocele + vaginal vault prolapse	Rectocele + vaginal vault prolapse	1
Rectocele + uterovaginal prolapse	Rectocele + uterovaginal prolapse	1
Rectocele + perineal descensus	Rectocele + perineal descensus	2
* MR: Magnetic resonance.		

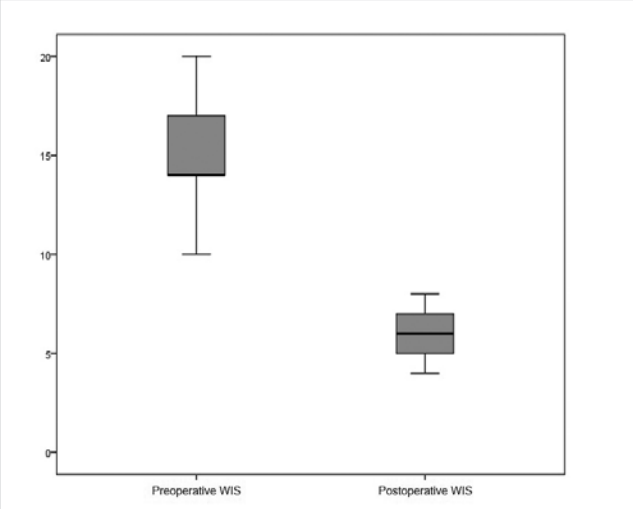

Figure 5. Preoperative and postoperative Wexner Incontinence Score (WIS) for patients with external rectal prolapse.

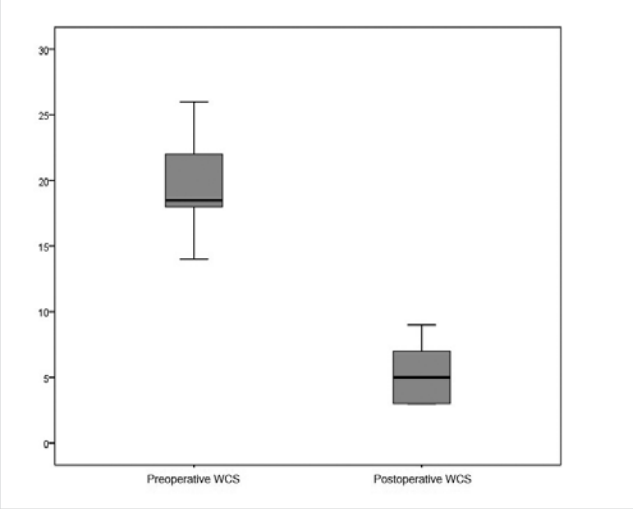

Figure 6. Preoperative and postoperative Wexner Constipation Score (WCS) for patients with symptomatic rectocele combined with enterocele or sigmoidocele.

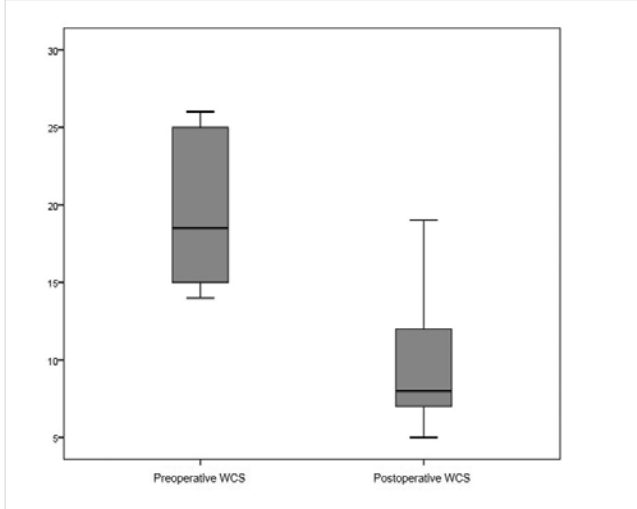

Figure 7. Preoperative and postoperative Wexner Constipation Score (WCS) for patients with symptomatic rectocele combined with gynecologic organ prolapse (descending perineum, vaginal vault and uterovaginal prolapse).

the postoperative value fell to 6 (range: 3-19). The difference was statistically significant (p< 0.000). Functional outcome evaluated separately in patients with symptomatic rectocele combined with enterocele or sigmoidocele and gynecologic organ prolapse (descending perineum, vaginal vault and uterovaginal prolapse). WCS significantly improved after LVMR in both patient groups. WCS before surgery was 10 (median, range 14-26), decreasing to 5 (range 3-9) postoperatively in patients with symptomatic rectocele combined with enterocele or sigmoidocele; this difference was statistically significant (p= 0.005) (Figure 6). Statistically significant improvement in WCS was noted in patients with symptomatic rectocele combined with gynecologic organ prolapse (descending perineum, vaginal vault and uterovaginal prolapse), the preoperative score was 18 (median, range: 14-26) and the postoperative value fell to 8 (median, range: 5-19) (p= 0.005) (Figure 7). In a patient with grade III IRP, WCS decreased from 22 to 7.

DISCUSSION

This study reports the outcome of 30 patients undergoing LVMR for ERP, IRP and symptomatic rectocele. To the best of our knowledge, our 30-case series of LVMR represents the largest case series from Turkey to date. Among Turkish surgeons transanal techniques (Altemeire or Delorme procedure) are used for frail patients with ERP, but for surgically fit patients, Frykman-Goldberg procedure (Resection rectopexy) or suture rectopexy are preferred for the treatment of ERP. Various transanal (Stapled transanal rectum resection (STARR)) and transperineal (Transperieneal mesh repair) techniques are adopted for the treatment of IRP and symptomatic rectocele according to surgeon experience in Turkey.

LMVR is currently adopted by many colorectal surgeons from Europe and North America as the established procedure for the treatment of ERP, IRP and symptomatic rectocele (1,3-7,17). Despite supporting data about the advantages and long-term outcome of LVMR worldwide, this procedure has gained very low acceptance among Turkish surgeons. First advantage of LVMR is preserving rectal ampulla, which is very important for restoring the continence. Secondly, as the ventral position of the mesh reinforces vaginal septum and prevents descent of the pelvic floor, LVMR corrects both posterior and middle compartments prolapse. Moreover, limited anterior dissection and avoiding division of the lateral rectal stalk prevent postoperative new-onset constipation or worsening pre-existing constipation (1,8). Long-term outcome of LVMR has shown that LVMR is a safe and effective procedure with good patient satisfaction and low rates of recurrence. The rates of complications and mesh-related problems are limited, and the number of de-novo symptoms is acceptable (3,16,18).

This series is primarily a learning experience, documenting the introduction of LVMR into a tertiary health care center of Turkey. Although follow-up is short, it does demonstrate the feasibility of performing LVMR. The procedure can be introduced successfully without requiring excessive operating time, length of hospital stay or resulting in increased morbidity. No mesh related complication was observed in our series. However, the data in the US Food and Drug Administration report emphasizes that mesh erosions tend to occur within 12 months after surgery, therefore in the current study, long-term follow-up was necessary for identified mesh related complications (19). Previous multicenter studies have reported 1.3% to 2.0% mesh erosion rates (3,18). Type of mesh is another important consideration about mesh related complication of LVMR. In our series, we preferred to use polypropylene mesh. In an international collaboration of surgeons reporting 2203 ventral rectopexy patients, it has been stated that synthetic mesh was used in 1764 (80.1%) and biological graft in 439 (19.9%). A total of 45 (2%) patients had mesh erosions, and at time of analysis, 2.4% (42/1764) and 0.7% (3/439) mesh erosion rates were identified in patients with synthetic mesh and biological graft, respectively (18). However, when recurrence rate is considered, there is no circumstantial evidence to support the use of one type of mesh over the other (20). In our series, no recurrence was observed since follow-up was short, and for evaluation of real recurrence rate after LVMR, a longer follow-up time of at least 5 years is necessary. However, we believe that in order to prevent early technical failure, a firm fixation of the mesh to the sacral promontory and rectum/pelvic-floor musculature has a vital importance.

A recent consensus report, by a panel of international experts, considers ERP as a definitive indication for ventral mesh rectopexy (2). In an observational study of long-term outcome of 919 consecutive patients after ventral mesh rectopexy, 242 ERP patients showed a decrease of fecal incontinence complaints from 40.5% to 14.8% during 33.9 months (range 0.4-143.6) median follow-up (3). For ERP, a similar result in the reduction of incontinence was observed in the current study as in previous studies in the literature (3,16,18). However, we did not observe worsening of the constipation as none of the patients with ERP had constipation symptoms before surgery. Also, no new onset constipation was observed during short-term follow-up in our study.

In this series, complex pelvic organ prolapse was present in 70% of the patients and for the diagnosis of complex pelvic organ prolapse, we chose to use dynamic MR defecography, which provides excellent morphological and functional information on the pelvic floor. In our study, at physical examination, 20 patients had rectocele and on dynamic MR defecography 17 patients showed at least two different forms of co-existing abnormalities. The current findings are consistent with a previous report by Mellgren et al., which suggested that rectocele, as a solitary finding, is rare and the frequency of associated pelvic abnormalities in patients with anorectal disorders is high (21). Therefore, the assessment of associated pelvic abnormalities is essential before planning surgery. Several studies have shown that surgical correction of single compartment could worsen or even trigger the symptoms of the untreated compartment (22-24). Therefore, a standard multicompartment procedure is necessary for the treatment of multicompartment pelvic organ prolapse, and LVMR helps to correct posterior and middle pelvic organ prolapse by the position of mesh since the anterior rectal fixation of mesh reinforces rectovaginal septum and provides some degree of suspension to the middle pelvic compartment (1). While follow-up did not exceed 3 months, the complex pelvic organ prolapse patients in our study showed significant improvement in constipation in the short-term. Although LVMR is increasingly being used in the treatment of such complex pelvic organ prolapse, there is a discrepancy in the literature about long-term functional outcome of the technique in patients with multicompartment pelvic organ prolapse. van den Esschert has reported that during short-term follow-up, LVMR improved defecation problems of all patients

with ODS, whereas at late follow-up, one third of the patients described aggravation of ODS symptoms (25). Similarly, the long-term degradation of typical and associated symptoms after enterocele treatment by ventral rectopexy has been observed in various studies (26,27). In a recently published article of D'Hoore, the author has argued that patients who could benefit from LVMR for ODS must be more carefully selected because LVMR in patients with ODS and IRP may not provide significant improvement in terms of functional outcome (28). However, Oxford grading system helps to subclassify IRP, and the research of the Oxford Group has shown LVMR provide good functional outcome in patients with high-grade IRP and concomitant enterocele (12,29). In our series, WCS of a patient with high grade IRP improved from 22 to 7. In the same article, D'Hoore has also suggested that patients with significant perineal descent and a denervated pelvic floor do not respond to LVMR (28). In our series, we observed various degrees of perineal descensus in patients with rectocele. Although statistically significant improvement was found in short-term functional outcome following LVMR in rectocele patients with gynecologic organ prolapse (descending perineum, vaginal vault and uterovaginal prolapse), ODS symptoms did not improve after LVMR in 2 patients with severe perineal descensus on physical examination.

Several limitations about the study should be taken into account. The study includes a case series with a small sample size and single surgeon experience in a heterogeneous group of patients. The length of follow-up of this study is too short in order to assess the durability and complications of LVMR. Finally, this series is limited by its retrospective character.

CONCLUSION

Laparoscopic ventral mesh rectopexy appears a safe and effective procedure to correct ERP, high grade IRP and symptomatic rectocele with low morbidity rate and significant reduction of incontinence and constipation. Complex pelvic organ prolapse treatment by LVMR is also effective and is associated with a short-term good functional outcome, but we think that careful patient selection is mandatory for complex pelvic organ prolapse treatment by LVMR in order to prevent long-term degradation of the symptoms.

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ORİJİNAL ÇALIŞMA-ÖZET
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Rektal ve kompleks pelvik organ prolapsuslarında laparoskopik ventral mesh rektopeksinin kısa dönem sonuçları

Fatma Ayça Gültekin[1]

[1] Zonguldak Bülent Ecevit Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Zonguldak, Türkiye

ÖZET

Giriş ve Amaç: Laparoskopik ventral mesh rektopeksi (LVMR), eksternal rektal prolapsus (ERP), yüksek derece internal rektal prolapsus (İRP) ve rektosel gibi pelvik taban hastalıklarının tedavisinde daha çok kullanılır hale gelmiştir. LVMR ayrıca pelvik organ prolapsuslarının da tedavisine olanak sağlamaktadır. Bu çalışmada LVMR'nin, rektal ve kompleks pelvik organ prolapsuslarında güvenlik etkinlik ve kısa dönem fonksiyonel sonuçları incelenmiştir.

Gereç ve Yöntem: Şubat 2014-Ekim 2017 tarihleri arasında LVMR yapılan tüm hastalar çalışmaya dahil edilmiştir. Hastalar preoperatif ve postoperatif 3. ayda değerlendirilmişlerdir. Cerrahi komplikasyonlar ve fonksiyonel sonuçlar; fekal inkontinans, Wexner İnkontinans Skoru (WİS) ve konstipasyon, Wexner Konstipasyon Skoru (WKS) ile değerlendirilmiştir.

Bulgular: Otuz hastaya (4'ü erkek) LVMR yapılmıştır. On yedi (56,6%) hastada dinamik-Mr defekografi bulgularına göre kompleks pelvik organ prolapsusunun olduğu tespit edilmiştir. Ortalama operasyon ve hastanede kalış süreleri 110 dakika ve 4 gündür. Mesh komplikasyonu veya rekürrens izlenmemiştir. Preoperatif 21 (%70) hastada obstrüktif defekasyon yakınmaları olduğu tespit edilmiş olup, WKS'nin median 19'dan postoperatif 3. ayda 6'ya düştüğü görülmüştür (p< 0,001). Preoperatif WİS'in hesaplandığı ve median 14 olduğu 9 hastada postoperatif 3. ayda 6'ya düştüğü saptanmıştır (p= 0,008). Semptomatik rektosel ile birlikte enterosel ve sigmoidoseli olan hastalarda da WKS LVMR sonrası anlamlı derecede düzeldiği görülmüş (p= 0,005) ve ayrıca anlamlı düzelme semptomatik rektosel ve beraberinde jinekolojik organ prolapsusu olan hastalarda da izlenmiş; preoperatif median WKS'nin 18'den postoperatif 8'e gerilemiştir (p= 0,005).

Sonuç: Serimizdeki hastalarda kısa dönem takiplerde LVMR'nin, etkili bir cerrahi seçenek olduğu tespit edilmiştir.

Anahtar Kelimeler: Rektal prolaps, pelvik organ prolaps, laparoskopik ventral rektopeksi

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Endoscopic and histopathological features of the upper gastrointestinal system polyps: evaluation of 12.563 procedures

Hüseyin Çiyiltepe[1], Durmuş Ali Çetin[1], Ebubekir Gündeş[1], Ulaş Aday[1], Aziz Serkan Senger[1], Selçuk Gülmez[1], Sabiye Akbulut[2], Mustafa Duman[1]

[1] Clinic of Gastroenterological Surgery, Kartal Kosuyolu High Specialization Health Application and Research Center, Istanbul, Turkey
[2] Clinic of Gastroenterology, Kartal Kosuyolu High Specialization Health Application and Research Center, Istanbul, Turkey

ABSTRACT

Objective: With the widespread use of esophagogastroduodenoscopy (EGD) in recent years, upper gastrointestinal system polyps have started to be encountered more often. Although most patients with gastric polyps are asymptomatic, these are important due to their malign potential, and gastric cancer may develop if left untreated.

Material and Methods: Records of 12.563 patients who underwent EGD at Kartal Kosuyolu High Specialization Health Application and Research Center for any reason between January 2013 and June 2016 were reviewed retrospectively. Patients with at least 1 histopathologically proven polyp were included in this study.

Results: A total of 12.563 endoscopic procedures of the upper gastrointestinal system were investigated and 353 (2.8%) polypoid lesions were detected. Mean age of these patients was 56.3 years and 241 (68.3%) of the patients were female. Gastric polyps were found most commonly in the antrum (50.1%) and of all gastric polyps, 245 (69.5%) were less than 1 cm. Histopathological evaluation showed that hyperplastic polyp (HP) (n= 151, 42.8%) was the most common polyp type, followed by fundic gastric polyp (FGP) (n= 51, 14.4%). Non-polyp gastric mucosa evaluation of 298 patients revealed that 34.9% of the cases were *Helicobacter pylori* positive, 19.4% had intestinal metaplasia, and 11.4% had atrophic gastritis.

Conclusion: Polyps of the upper gastrointestinal system are generally detected coincidentally as they have no specific symptoms. Polypectomy is required for gastric polyps because of their potential for malign transformation according to medical evidence.

Keywords: Upper gastrointestinal system, polyp, endoscopy, hiperplastic polyp, fundic gastric polyp

INTRODUCTION

In recent years, gastric polyps have started to be encountered more often with the widespread use of esophagogastroduodenoscopy (EGD) (1). Any abnormal growths projecting above the plane of the mucosa into the lumen of the stomach are defined as ˝gastric polyps˝. Gastric polyps most frequently originate in the mucosa, which may even be submucosal or extrinsic (2,3).

Incidence rate of gastric polyps ranges from 2% to 6% during upper endoscopy and less than 1% in the general population; however, it has begun to gradually increase due to the high amount endoscopic procedures (4,5).

The British Society of Gastroenterology has classified gastric polyps into 2 different groups (6) (Table 1). The first group is epithelial polyps, such as fundic gland polyps (FGP), hyperplastic polyps (HP), adenomatous polyps (AP), hamartomatous polyps and non-hamartomatous-polyposis syndromes. The second group is non-mucosal intramural polyps, such as the gastrointestinal stromal tumor, leiomyoma, inflammatory fibroid polyp, fibroma and fibromyoma, lipoma, ectopic pancreas, neurogenic and vascular tumors, and neuroendocrine tumors (carcinoids).

It has been reported that hyperplastic polyps are the most common type especially at the areas where *Helicobacter pylori* infection is common. With the chronic use of proton pomp inhibitors (PPI) and eradication of *H. pylori*, FGP has become more common (7,8).

Most patients with gastric polyps are asymptomatic, which can be found during routine EGD. Larger polyps can cause bleeding, abdominal pain and even gastric outlet obstruction. They are important because they have malign potential and gastric cancer may develop if they are untreated (9).

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Corresponding Author
Hüseyin Çiyiltepe
E-mail: drciyiltepe@hotmail.com

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Table 1. Classification of gastric polyps (The British Society of Gastroenterology, 2009)

Epithelial Polyps	Non-mucosal Intramural Polyps
Fundic gland polyp	Gastrointestinal stromal tumor
Hyperplastic polyp	Leiomyoma
Adenomatous polyp	Inflamatoryfibroid polyp
Hamartomatous polyp	Fibromaand fibromyoma
• Juvenile polyp • Peutz-Jeghers' syndrome • Cowden's syndrome Polyposis syndromes (non-hamartomatous) • Juvenile polyposis • Familial adenomatous polyposis	Lipoma Ectopic pancreas Neurogenic and vascular tumours Neuroendocrine tumours (carcinoids)

This study aimed to present demographic, clinical, endoscopic and pathological characteristics of patients with gastric polyps and the frequency of these lesions.

MATERIAL and METHODS

Study Design

After receiving approval from the review board (Kartal Dr. Lutfi Kirdar Educational and Research Hospital Ethics Comittee, Date of Approval: 27/10/2016; Reference number: 2016.4/3-14), we retrospectively reviewed the patients who had undergone elective EGDs at Kartal Kosuyolu High Specialization Health Application and Research Center for any reason between January 2013 and June 2016. All endoscopic procedures were performed by gastroenterologists or gastroenterology surgeons. All patients had signed informed consents before EGDs. Patients with previous history of gastric resection and on whom we had performed therapeutic procedures such as sclerotherapy, endoscopic variceal ligation, percutaneous endoscopic gastrostomy or stent placement were excluded.

Patients with gastric polypoid lesions other than those with endoscopically suspected GIST or ectopic pancreas underwent polyp sampling and/or polypectomy. Endoscopic ultrasonography was performed to diagnose GIST.

Information about patients' age, gender and polyp location, size, number, histological classification and gastric mucosal changes were obtained from endoscopic and pathological reports. Histological classification of the polyps was carried out according to the guidelines of the British Society of Gastroenterology. The samples taken from normal stomach tissue surrounding polyps were evaluated in terms of *H. pylori*, chronic atrophic gastritis and intestinal metaplasia. No biopsy was done for the diagnosis of endoscopic GIST or ectopic pancreas.

Statistical Analysis

All statistical analyses were performed using SPSS (version 15, Chicago, IL ,USA). Quantitative variables were described using mean ± SD and categorical variables were described using frequency and proportion. Comparison of the categorical data between the two groups was analyzed by Chi-square test and p values < 0.05 were considered statistically significant. One-way ANOVA test was used to compare the relationship between *H. pylori*, IM and AG and three subgroup of polyps.

RESULTS

We investigated a total of 12.563 endoscopic procedures of the upper gastrointestinal system performed at our clinic within the last 3.5 years and detected 353 (2.8%) polypoid lesions. Mean age of these patients was 56.3 ± 12.8 (18-85) years and 241 (68.3%) of the patients were female, while 112 (31.7%) were male (Table 2).

While a single polyp was seen in 298 (84.5%) patients, multiple polyps were detected in 55 (15.5%). Endoscopic evaluation showed that 177 (50.1%) of the polyps were located in the antrum, 71 (20.1%) in the corpus, 43 (12.2%) in the fundus, 27 (7.6%) in the cardia, 14 (4%) in multiple areas of the stomach, and 21 (5.9%) were located either in the distal esophagus or the duodenum.

When polyp sizes, which were endoscopically measured, were classified into 3 different groups, it was seen that the number of polyps smaller than 5 mm was 120 (33.9%), the number of the ones sized between 5 to 10 mm was 125 (35.4%), and the number of the ones larger than 10 mm was 108 (30.5%).

Pathological evaluation of the endoscopic polypectomies can be seen in Table 2. Pathological investigation demonstrated that HP (n= 151, 42.8%) was the most frequently detected one followed by FGP (n= 51, 14.4%), gastrointestinal stromal tumor (n= 48, 13.6%), and polypoidfoveolar hyperplasia (n= 44, 12.5%). While 7 (2%) patients were diagnosed with adenomatous polyps, two were diagnosed with low grade dysplasia. According to the pathology results of the group referred to as "other," which had a total of 21 (5.9%) patients, 9 patients had squamous papilloma, 3 had neuroendocrine tumor, 1 had lymphangiectasis, 1 had blood-fibrin mass, and 7 had foreign-body reaction granulation tissue.

Non-polyp gastric mucosa evaluation of 298 patients revealed that 34.9% of the cases were *H. pylori* positive, 19.4% had intestinal metaplasia, and 11.4% had atrophic gastritis. When *H. pylori* positivity was investigated separately in HP, FGP, and polypoidfoveolar hyperplasia cases, it was seen that positivity was significantly higher in cases with HP (Table 3). Moreover, *H. pylori* positivity was separately evaluated according to HP sizes. There was a statistically significant relationship between polyp sizes and *H. pylori* positivity (Table 4).

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Table 2. General features of the polyps and patients with polyps as detected by endoscopy

	General	Hyperplastic Polyp	Fundic Gland Polyp	Adenoma	Polypoid Foveolar Hyperplasia	Inflamatory Fibroid Polyp	Xanthoma	GIST	Ectopic Pancreas	Other
Polyp										
n	353/12.563	151/353	51/353	7/353	44/353	11/353	4/353	48/353	16/353	21/353
%	2.8	42.8	14.4	2.0	12.5	3.1	1.1	13.6	4.5	5.9
Age	56.3 ± 12.8	58.5 ± 12.6	55.0 ± 11.9	56.7 ± 15.1	56.0 ± 9.9	51.0 ± 18.1	54.7 ± 13.3	57.3 ± 12.3	48.3 ± 14.1	51.6 ± 15.3
Gender										
Female/Male	241/112	103/48	41/10	4/3	29/15	7/4	2/2	28/20	11/5	16/5
%	68.3/31.7	31.8/68.2	80.4/19.6	57.1/42.9	65.9/34.1	63.6/36.4	50/50	58.3/41.7	68.8/31.3	76.2/23.8
No. of polyps										
Single	298 (84.5%)	144	18	5	37	9	1	48	16	20
Multiple	55 (15.5%)	7	33	2	7	2	3	-	-	1
Polyp Size										
< 5 mm	120 (33.9%)	52	27	1	26	4	2	-	4	4
5-10 mm	125 (35.4%)	50	23	4	16	6	2	-	12	12
> 10 mm	108 (30.5%)	49	1	2	2	1	-	48	-	5
Location										
Antrum	177 (50.1%)	99	1	2	32	7	3	16	12	4
Corpus	71 (20.1%)	23	21	2	2	-	1	16	3	3
Cardia	27 (7.6%)	12	4	2	3	-	-	6	-	-
Fundus	43 (12.2%)	6	24	-	6	1	-	5	-	1
Multiple gastric	14 (4.0%)	11	1	-	1	-	-	-	-	-
Other	21 (5.9%)	-	-	-	-	3	-	5	-	13
Helicobacter pylori										
Positive	101 (34.9%)	64	7	6	11	3	1	ND	ND	9
Negative	188 (65.1%)	87	44	1	33	8	3	ND	ND	12
Intestinal metaplasia	56/289 (19.4%)	35/151	3/51	6/7	7/44	2/11	1/4	ND	ND	2/21
Atrophic gastritis	33/289 (11.4%)	23/151	1/51	5/7	3/44	-	-	ND	ND	1/21

GIST: Gastrointestinal stromal tumor, ND: Non diagnosed.

Table 3. Relationship between *Helicobacter pylori*, IM and AG and three types of polyps

	Hyperplastic polyp	Fundic gland polyp	Polypoid foveolar hyperplasia	p
Helicobacter pylori				
- Positive	64	7	11	< 0.05*
- Negative	87	44	33	
Intestinal metaplasia (IM)	35/151	3/51	7/44	-
Atrophic gastritis (AG)	23/151	1/51	3/44	-
* Statistically significant.				

Table 4. Relationship between *Helicobacter pylori* and size of hyperplastic polyps

Polyp size	Hyperplastic polyp *H. pylori* +	Hyperplastic polyp *H. pylori* –	p
< 5 mm	16	36	0.001*
5-10 mm	17	33	
> 10 mm	31	18	
Total	64	87	
* Statistically significant.			

DISCUSSION

As polyps of the upper gastrointestinal system are generally small and asymptomatic, they are coincidentally detected by EGDs performed for other purposes. Although the incidence of polyps and their histopathological features vary according to different geographical areas, it is seen in about 0.8-2.4% of the general population. While the rate of polyps randomly detected in upper endoscopy procedures performed for other purposes was stated to be 2.2% in a large series conducted in our country, the same rate was reported to be 2.6% in Far Eastern countries, and 6% in the US (8,10,11). The main reason of the differences seen among geographical areas pertains to *H. pylori* prevalence and PPI use. The rate of polyps detected by endoscopies in our study was 2.8% and this result was in line with the literature data.

Mean age of the patients detected to have polyps was 56.3, and mean age figures among the groups were similar. Other studies in the literature have also reported that patients of a similar age group frequently had gastric polyps.

A great majority of the patients diagnosed to have polyps within the scope of the study was female (68%). Many studies conducted in our country reported that polyps were seen more frequently in the female population and this rate varied between 58 and 67% (12,13). It was suggested that this rate was higher in our study as the number of female patients was higher as well. No statistically significant relationship, however, was found between the histopathological features of polyps and gender ($p< 0.05$).

Data offered by studies in the literature suggest that gastric polyps are generally singular, located in the antrum, and are smaller than 1 cm (14). The results of our study also revealed that they were singular in 84% of the patients, located in the antrum in about half of them, and a great majority (70%) was smaller than 1 cm.

Although there is no consensus on the ways in which asymptomatic polyps should be approached in the general literature, the general approach of endoscopists is to take biopsy samples from the polyp and perform polypectomy depending on the pathology results. The preferred mode of treatment in our own clinic is to excise or sample all polyps especially larger than 5 mm accompanied by snare or with hot biopsy forceps. Muehldorfer et al. have found out remarkable differences only between the pathology results of polyp biopsies and polypectomy specimens when they were compared and suggested polypectomy be performed on polyps larger than 5 mm (15).

HPs are the kind of polyps seen most frequently among all benign gastric polyps and are generally smaller than 2 cm, singular, sessile or pedicled, frequently located in the antrum but can be seen in all gastric localizations (6). Chronic atrophic gastritis and *H. pylori* positivity and association are often seen in gastric mucosa samples accompanying HP (16). The results of our study did not only reveal a statistically significant relationship between HP and *H. pylori* positivity but also a significant relationship between polyp size and *H. pylori* positivity (Tables 3,4).

Though rare, there can be malign transformations in HPs, which proves to be significant as there can be a possible increase in the risk of associated synchronous cancer development. Some sources cite the rate of malign transformation to be between 1.9 and 19% (17). It has been reported by some investigators that increased size of the polyp (> 1 cm) increases the risk of

malignant transformation and p53 genetic mutation is effective in this transformation (18). Similarly, some researchers have reported that the risk of cancer development in the surrounding gastric mucosa is higher than the polyp itself in HP cases and multiple biopsies should definitely be taken from the surrounding mucosa (6). In our study group, adenomatous changes were seen in 6 patients (3.9%) but no malign transformations were detected in the pathological evaluation of the surrounding gastric mucosa.

FGPs, on the other hand, are polyps which account for 16-51% of epithelial polyps and can be associated with sporadic or familial adenomatous polyposis (FAP) syndrome, are mostly smaller than 1 cm and located in the gastric corpus and fundus (19). In a study by Weston et al., the authors have stated that correct diagnosis can be established with a high probability through observation by a single endoscopist (20). Its pathogenesis is not known clearly. Dysplasia development is lower than 1% in sporadic fundic gland polyps and there is no relationship between atrophic gastritis and *H. pylori* (21).

There is adenomatous polyposis coli (APC) genetic mutation in FAP-related FGP cases and multiple polyps covering the whole gastric corpus are seen in these cases. The risk of malign transformation is quite high in FAP-related FGPs (25-41%) in comparison to the sporadic form (22). Furthermore, it has been suggested that colon involvement should also be investigated in these cases. There is, however, no adequate data in the literature as to the number of gastric polyps to be suspicious of FAP. There are studies which recommend sigmoidoscopy especially for patients under the age of 40 with multiple FGPs and for cases whose pathology results indicate dysplasia existence (6,23).

When the studies published in Turkey were taken into consideration, it was seen that the number of HPs in our study was lower than other studies, whereas the number of FGPs was higher (Table 5). We think that the reason for this discordance is related to the fact that the patients in our hospital were on antiaggregant therapy for their cardiac comorbidities alongside with regular use of PPI and the gradual yearly increase in PPI administration in the general population. Although previous studies have reported that *H. pylori* positivity in patients with gastric polyps was about 50-70% in Turkey, we found *H. pylori* positivity to be 34.9% in our study probably because of the same reason (12,24).

While there is a relationship between FGP formation and chronic PPI administration according to some authors, there is no such relationship according to many others. The inverse relationship between FGP and *H. pylori*, however, is clearly known (25-27). The subgroup evaluation conducted within the scope of our study revealed that there was a statistically significant high rate of *H. pylori* positivity in HPs, whereas there was no relationship between the two in FGPs (Table 3).

APs are true neoplasms which are the precursors of gastric cancers. They account for 3-26% of benign epithelial gastric polyps and are mostly singular, smaller than 2 cm, can be seen in all areas of the stomach but are more often localized in the antrum (28). When the surrounding gastric mucosa is scrutinized it is seen that most of it is associated with atrophic gastritis and intestinal metaplasia. It has no proven relationship to *H. pylori*. Although various studies have reported that the neoplastic transformation is between 6 and 47%, this rate is higher in polyps larger than 2 cm (29,30). In our study group, 2 out of 7 patients (28.5%) had low grade dysplasia. It has been suggested that all parts of the stomach should be carefully investigated for mucosal anomalies in cases with adenomatous polyps and a control EGD should be conducted after 6 months if incomplete polypectomy was performed (6).

Table 5. Comparison with other studies in the literature

Author	Country	Year	Number of polyps (%)	Hyperplastic polyp	Fundic gastric polyp	Adenomas	*Helicobacter pylori*	Atrophic gastritis	Intestinal metaplasia
Carmack et al. (8)	USA	2009	7.877/12.564 (6.5%)	17%	77%	0.7%	2.2%	22%	4.9%
Sonnenberg et al. (7)	USA	2015	71.575/812.926 (8.8%)	18.5%	79.9%	0.9%	1.34%	0.7%	2.1%
Cao et al. (1)	China	2012	254/24.121 (1%)	28.3%	50.6%	0.05%	42.2%	-	-
Fan NN et al. (11)	China	2015	4.043/157.902 (2.5%)	25%	65%	1.8%	4.6%	-	-
Gencosmaoglu et al. (12)	Turkey	2003	91/2.630 (3.4%)	46%	14%	2.7%	49%	-	36%
Sezikli et al. (14)	Turkey	2014	123/6.607 (1.8%)	65.9%	0.8%	10.6%	32.5%	-	-
Büyükaşık et al. (24)	Turkey	2015	59/55.987 (0.1%)	69%	3.3%	6.7%	68.2%	56%	39%
Atalay et al. (13)	Turkey	2015	174/14.240 (1.2%)	83.9%	6.1%	7.4%	-	-	-
Vatansever et al. (10)	Turkey	2015	666/29.940 (2.2%)	36.2%	8.3%	1.9%	-	-	-
Present study	Turkey	2016	353/12.563 (2.8%)	42.8%	14.4%	2.0%	34.9%	11.4%	19.4%

When the malign transformation potential of polyps and their similarities during endoscopic procedures are taken into consideration, the British Society of Gastroenterology suggests that all polyps larger than 5 mm should be completely excised or sampled if possible. The British Society of Gastroenterology also suggests that at least 2 biopsies should be conducted for polyps smaller than 1 cm, while 4 or more biopsies should be done for polyps larger than 1 cm in cases where total polypectomy is not viable. It has been proposed that endoscopic control should be carried out following 1 year after total polypectomy in HPs, and it has been reported that no follow-ups are necessary in patients diagnosed with HP but were seen to have no polyps at the end of the first year and in FGP cases (6).

Study Limitations

The limitations of this study include its retrospective design, single center and the absence of stomach mucosa specimens around the polyp in some patients.

CONCLUSION

Polyps of the upper gastrointestinal system are generally detected coincidentally as they have no specific symptoms and prove to be significant because of their potential for malign transformation. Although their endoscopic images vary, they do not provide physicians with clear information on their pathology. Polypectomy should be performed for the ones which can be excised when they are detected, and follow-up should be carried out following the performance of biopsies with an adequate number and depth for polyps which cannot be removed.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Kartal Dr. Lutfi Kirdar Training and Research Hospital (2016.4/3-14).

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

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ORİJİNAL ÇALIŞMA-ÖZET
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Üst gastrointestinal sistem endoskopisinde saptanan poliplerin endoskopik ve histopatolojik özellikleri: 12.563 işlemin değerlendirilmesi

Hüseyin Çiyiltepe[1], Durmuş Ali Çetin[1], Ebubekir Gündeş[1], Ulaş Aday[1], Aziz Serkan Senger[1], Selçuk Gülmez[1], Sabiye Akbulut[2], Mustafa Duman[1]

[1] Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Merkezi, Gastroenteroloji Cerrahi Kliniği, İstanbul, Türkiye
[2] Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Merkezi, Gastroloji Kliniği, İstanbul, Türkiye

ÖZET

Giriş ve Amaç: Son yıllarda özefagogastroduodenoskopi (ÖGD)'nin yaygın olarak kullanılması ile birlikte üst gastrointestinal sistem poliplerine daha sık rastlanmaktadır. Gastrik poliplerin çoğu asemptomatik olmakla birlikte, malignite potansiyeli taşıdıkları için önemlidir ve tedavi edilmezse gastrik kanser gelişebilir.

Gereç ve Yöntem: Ocak 2013-Haziran 2016 tarihleri arasında herhangi bir nedenle Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesinde ÖGD yapılan 12,563 hasta retrospektif olarak kayıt edildi. Histopatolojik olarak kanıtlanmış en az bir polibi bulunan hastalar çalışmaya dahil edildi.

Bulgular: Kliniğimizde son 3,5 yılda yapılan 12,563 üst gastrointestinal sistem endoskopisi incelenmiş olup 353 (%2,8)'ünde polipoid lezyon saptanmıştır. Ortalama yaş 56,3 ± 12,8 18-85 yaş) idi ve hastaların 241(%68,3)'i kadın, 112 (%31,7)'si erkekti. Endoskopik incelemede poliplerin çoğu antrumda (%50,1) ve 1 cm'nin altında (69,5%) idi. Patoloji değerlendirmesinde en sık hiperplastik polip (HP) (n= 151, %42,8) ve fundik gastrik polip (FGP) (n= 51, %14,4) saptandı. 298 hastada polip dışı gastrik mukoza değerlendirilmesinde olguların %34,9 unda *H. pylori* pozitifliği, %19,4'ünde intestinal metaplazi ve %11,4'ünde ise atrofik gastrik saptandı.

Sonuç: Üst gastrointestinal sistem poliplerine özgü bir semptom olmaması nedeniyle genellikle tesadüfi olarak saptanırlar. Malign dönüşüm potansiyeli var olduğundan saptandıkları zaman polipektomi yapılması gerekmektedir.

Anahtar Kelimeler: Üst gastrointestinal sistem, polip, endoskopi, hiperplastik polip, fundik gastrik polibi

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ORIGINAL ARTICLE
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Changing pattern of perforated PUD: Are NSAIDs to be blamed?

Ochonma Egwuonwu[1], Okoli Chinedu[1], Gabriel Chianakwana[1], Stanley Anyanwu[1], Chiemelu Emegoakor[1], Henry Nzeako[1]

[1] Department of Surgery, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria

ABSTRACT

Objective: This study aimed to determine if there is association between gastric perforation and non-steroidal anti-inflammatory drugs (NSAIDs) abuse in patients presenting with perforated peptic ulcer disease (PPUD).

Material and Methods: The data were collected retrospectively from May 2011 to May 2015 and then prospectively until December 2017. Sixty patients diagnosed with PPUD on exploratory laparotomy were evaluated. Data were analyzed using SPSS (version 21.0). P value ≤ 0.05 was considered significant.

Results: A total of 60 patients were operated on for PPUD during the study period. Forty-five (75.0%) patients gave significant history of NSAIDs use, of which nine (20.0%) had medical prescription, while others were over the counter medications. None of the patients was on ulcer prophylaxis including those who were on long term use and with prior dyspeptic symptoms. Five patients (11.1%) were on the recommended dose of the NSAIDs, thus patients in this series showed irrational use of NSAIDs. Forty-two (93.3%) patients had gastric perforation, while only three of the patients had duodenal perforation. The association between significant NSAIDs use and gastric perforation was found to be significant (p= 0.002). There was no difference in the site of perforation when patients who were on long term NSAIDs were compared with short term NSAIDs use (10.0 vs. 35.0) (p= 0.061). In addition, long term NSAIDs use (p= 0.041), ignorance of proper dose of the medication (p= 0.003), and gastric ulcer perforations (p= 0.011) were independent causes of mortality in the studied patients when age and duration of the presentations were matched.

Conclusion: NSAIDs use, including both long- and short-term use, was significant among patients with gastric perforation.

Keywords: Perforated peptic ulcer, Gastric ulcer, NSAIDs

INTRODUCTION

Globally, 4 million people suffer from peptic ulcer diseases (PUD) annually. Ten - twenty percent of these cases are complicated and 2-10% of these ulcers perforate (1). Though uncomplicated PUD can be generally managed medically, perforated peptic ulcer disease (PPUD) is a life-threatening condition which requires emergency intervention. Though conservative approach to management has been described by Taylor, most of these patients are treated surgically using open repair or laparoscopic repair depending on expertise (2,3). With progressive negative decline of definite acid reducing surgeries, most of these patients have primary repair with or without omental patch and triple therapy. Biopsy is added in case of stomach perforations.

Alhough duodenal perforations are more commonly reported, it appears that the dynamics of the socio-demographics of patients with PPUD depends on the region studied (4,5). In the West, duodenal perforation is more common and generally confined in the elderly population who are on ulcerogenic drugs, 1 while among the Orientals in Japan, gastric perforations are more due to increased incidence of gastric malignancy (6). Most reports from our environment suggest that perforated duodenal ulcer is more common than gastric perforations and that patients with former pathology are generally younger than the latter (4,5). Exposure to *Helicobacter pylori* infection and use of non-steroidal anti-inflammatory drugs (NSAIDS) are the most common risk factors predisposing to PPUD, other factors include alcohol, smoking, stress and use of crack cocaine (7). However, it is difficult to blame

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Corresponding Author
Okoli Chinedu
E-mail: eduokoli@yahoo.com

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one risk factor as the cause of PPUD in a patient because most patients have more than one risk factors. In our environment, abuse of NSAIDs among different age groups is increasingly being recognized. These medications are readily available without prescription for various indications. These medications are commonly used for relieve of body aches, arthritic pains, and as part of medications for cardiovascular diseases. Patients on NSAIDs including aspirin are at increased risk of having adverse gastrointestinal events (7,8).

Based on the observation of unusual upsurge in the number of gastric perforations in our practice in contrast to other reports from other centers in Nigeria, the authors decided to investigate if there is any association between the increased incidence of gastric perforation in our patients with NSAIDs use (4,5,9).

MATERIAL and METHODS

The data were collected retrospectively from 2011 to May 2015 and then prospectively until December 2017. Adults with clinical suspicion of perforated peptic ulcer diseases were referred from nearby primary and secondary health facilities. On presentation at the accident and emergency department of the hospital, the patients were evaluated and resuscitated with intravenous fluid, electrolytes, and blood transfusion as appropriate. They were sent for chest radiograph for the presence of air under the diaphragm.

The patients were then counseled for both surgery as well as inclusion into the study. All patients who consented to surgery were moved to the theatre. All of the patients underwent emergency exploratory laparotomy through a midline incision, with primary repair of the perforation and addition of omental patch in cases of duodenal perforation. Peritoneal lavage was usually done with a minimum of 5 liters of warm normal saline. The ulcer edges were biopsied in all patients with gastric perforations. The following data were entered into a structured proforma; age, sex, initial site of pain, mode of onset of pain, previous history of PUD, use of NSAIDs, smoking, alcohol intake, site of ulcer, type of repair, suture used, post-operative complications, length of hospital stay, and outcome of treatment. Patients in the retrospective group who did not have intra-operative diagnosis or incomplete data were excluded. Only 60 patients who had intra-operative finding of perforated gastric or duodenal ulcer were included into this study. Patients were initially managed at the intensive care unit (ICU) before being moved to the ward. Patients were grouped into different categories based on

I. Recent use of NSAIDs and no recent use.

II. Long term NSAID use (more than 4 weeks) and Thos who had recent significant intake of NSAIDS (daily consumption of NSAIDs in past 3 weeks) .

II. Patients took NSAIDs based on medical prescriptio and those who did not have any prescription (uknown dose).

IV. Patients who were on recommended dose of NSAIDs and patients who did not.

The study was carried out at no extra cost to the eligible patients who gave their informed consent. There was strict observation of the patients' confidentialities by using codes in place of names for reference, analysis and presentation of the results of this study. This study adhered to the tenets of the declaration of Helsinki for research in humans.

Data were analyzed using Statistical Package for Social Sciences (IBM SPSS statistics for Windows version 21.0. Armonk, NY: IBM Corp). Results of categorical variables were expressed using tables and charts where appropriate while continuous data were expressed using mean and standard deviations, where appropriate. Associations between categorical data were determined using the Pearson Chi square test or Fishers Exact test were appropriate. Independent T test was used to determine the mean difference between continuous data. Statistical significance was inferred at p value of < 0.05.

RESULTS

A total of 60 patients had intra-operative diagnosis of PPUD during the study period. Forty-one males and nine females made up the study population giving a ratio of 5.2:1 . Mean age (standard deviation) of the study population was 47.74 (16.08) years; age ranged from 21-80 years. The duration of symptoms before presentation ranged from 2 hours to 2 months. The first symptom in all patients was abdominal pain. Most of the patients felt pain at the epigastrium and described the onset of the pain as sudden (66.0) (Table 1). Fifty percent of the patients agreed to previous history of dyspepsia while 10.0 % of the patients could not remember such symptoms, while 40% of the patients denied any prior history of dyspepsia. None of these patients had undergone upper gastrointestinal endoscopy before presentation but 9 patients had had PUD diagnosis by a clinician.

The sites and sizes of the perforations were noted (as shown in Table 2). None of the patients had definitive acid reducing surgery. Only 14.0 % of the patients had drain inserted. Thirty-four percent of the patients died while 51.5% of the remaining patients developed complications which were treated, and the patients were later discharged (see Table 2 for details).

Significant NSAIDs use was common among the 45 (75.0%) patients who were studied, only nine patients (20.0%) had NSAIDs prescribed by medical personnel, while the rest got the medications from patent medicine dealers. None of the former was on either proton pump inhibitor nor Histamine type 2 blockers. Only five patients (11.1%) were on the recommended dose of the NSAIDs, thus patients in this series showed irrational use of NSAIDs. Forty two (93.3%) patients had gastric perforation, while only three of the patients had duodenal perforation. The association with significant NSAIDs use and gastric perforation

Table 1. Patient characteristics

Patient characteristics	Gastric	Duodenum		
Age distribution (in years)				
21-30	9	3	20.0	
31-40	7	2	15.0	
41-50	8	1	15.0	
51-60	15	5	33.330	
61-70	6	1	11.67	
71-80	3	0	5.0	
Mean age	47.90 ± 16.34	46.88 ± 15.67		0.870
Mode of onset				
Sudden	31	12	66	0.001
Insidious	16	1	34	
Prior history of dyspepsia (n= 25)	21	4		1.000
Previous diagnosis of PUD (n= 9)	7	2		0.631
Site of initial pain (n= 50)				
Epigastric	38	11		
Right lower quadrant	6	1		
Central	2	1		
Generalized	1	-		
Sex (n= 50)				
Male	37	10	84	1.000
Female	9	3	16	
Smoking (n= 8)	5	3	2	0.120
Alcohol	29	4	27	0.376
NSAIDs (n= 45)	42	3	13	0.002
Mean duration of symptoms	47.84 ± 18.34*	43.71 ± 14.39		0.540

* One patient presented after 2 months of onset of symptoms and was excluded being an outlier.
PUD: Peptic ulcer diseases.
NSAIDs: Non-steroidal anti-inflammatory drugs.

was found to be significant (p= 0.002) (Table 3). There was no difference in the site of perforation when patients who were on long term NSAIDs were compared with short term NSAIDs use (10.0 vs. 35.0) (p= 0.061). In addition, long term NSAIDs use (p= 0.041), ignorance of proper dose of the medication (p= 0.003), and gastric ulcer perforations (p= 0.011) were independent causes of mortality in the studied patients when age and duration of the presentations where matched. Furthermore, mean age of the patients that died was significantly more than the mean age of the surviving patients (p= 0.019). Smoking and alcohol abuse were not significantly associated with death (p= 0.438 and p= 0.100) respectively.

DISCUSSION

PPUD is a common cause of peritonitis in our center with an average of 10 cases undergoing operative treatment per year. In our study, more males were affected, which concurred with other reports in the literature (1,4,5,9,10). Some of the speculated reasons for the high incidence of PPUD amongst males in our environment may be due to smoking and excessive alcohol consumption prevalent amongst this gender. Though the average age of patients in our series was similar to the mean age reported by other authors in other centers in Nigeria (4-5,9) it was generally lower than the mean age seen in western clime where the majority of the patients are above 60 years of age and the incidence of perforated PUD is found to be higher in females taking ulcerogenic drugs (1,11).

Most of our patients presented with acute onset epigastric pain which later became generalized while only few patients reported insidious onset pain. The former is so classical of PPUD, such that Edward Crisp who was the first to report 50 cases of PPUD

Table 2. Operative characteristics of the patients

Operation characteristics			**p**
	Gastric perforation	**Duodenum perforation**	
Intra-operative findings Site of perforation (n= 60)			
Antrum	32	-	
Body of stomach	15	-	
First part of duodenum	-	13	
Size of perforation			
Mean size of perforation	2.03 ± 1.67	1.50 ± 1.22	0.573**
Suture for closure (n= 48)			
Silk	6	1	
Delayed absorbable (polyglycolic acid)	34	7	
Post-operative findings			
Mean hospital stay	12.39 ± 2.61	8.1 ± 2.87	0.998**
Complications* (n= 38)			-
Surgical Site Infection	7	2	
Entero-Cutaneous fistula	1	1	
Peritoneal abscess	2	-	
Burst abdomen	1	-	
Acute kidney injury	1	-	
Intestinal obstruction	1	-	
Death (n= 22)	17	3	

* Excluding death.
** T- test otherwise Fishers Exact tests.

Table 3. Categorization of patients on NSAIDs

Type of perforation	**Use of NSAIDs**	**No recent history of NSAIDs**	**p***
Gastric	42 (70.0)	5 (8.33)	0.002
Duodenal	3 (5.0)	10 (16.67)	
	Significant use in the last 2 weeks	Long term	
Gastric	34 (75.56)	8 (17.8)	0.061
Duodenal	1 (2.22)	2 (4.44)	
	Medically prescribed	Over the counter prescription	
Gastric	7	35	0.041
Duodenal	2	1	
	Recommended dose	Takes it based on personal discretion	
Gastric	4	38	0.032
Duodenal	1	2	

* Fishers Exact tests.
NSAIDs: Non-steroidal anti-inflammatory drugs.

and accurately summarized the clinical aspects of perforation, concluded that: 'The symptoms are so typical, I hardly believe it is possible that anyone can fail to make the correct diagnosis' (12).

In our series, there was more gastric perforations than duodenal perforation, which is a reverse in the trend documented in the literature in our environment (4,5). though a rising incidence of gastric ulcers has been reported by Ndububa et al., at Ile-ife, Osun state in which there was similar incidence of duodenal and gastric ulcers (9). Our series showed similar trend found among the orientals with high incidence of malignant gastric ulcers, however, all histology reports in our series were benign (6). Furthermore, it was observed that 75.0% (45) of the patients in our series had recent history of ingestion of NSAIDS, a common over the counter medications. Seventy percent (42) of the patients with PPUD had gastric perforation while only 3 (5%) had duodenal perforations. Of the 42 patients who had gastric perforation, 35 (77.8) patients had significant intake in the last 2 weeks. Most of the patients on NSAIDs (80.0%) bought the medication over the counter without prescription. It was difficult for us to compare our findings with other studies in our environment on PPUD because of the peculiar high prevalence of perforated benign gastric ulcers in our series. However, one can deduce that irrational use of NSAIDs was common among our studied subjects. NSAIDs are one of the etiological factors of PUD, they act by inhibiting the COX II enzyme there by limiting the gastro-protective effective of this enzyme (7). This observation of high intake of NSAIDs in our study suggests the need for further systematic research to determine the exact role of these medications in causing gastric perforations. Only 10.0% (6) and 6.0% (4) of the patients agreed to taking alcohol above the recommended limits of 14 units, and smoking respectively. Studies have shown that the deleterious effect of NSAIDs on gastric mucosa has synergistic effect in the presence of Helicobacter pylori infection, alcohol and smoking (1,13). interestingly, duodenal perforations in our series were exclusively found in females. No particular reason could be suggested for this finding.

Furthermore, our series showed high mortality rate particularly in patients who presented with gastric perforations with no recorded case of mortality in patients with duodenal perforation. Post-operative complications were also higher in patients in the gastric perforation group. Only 20.0% (10) of the patients in our study presented within 12 hours of onset of symptoms. Some authors have suggested that delaying the time point of operation beyond 12 h after the onset of clinical symptoms would worsen the outcome in PPUD (2,14). Though delayed presentation is one of the factors blamed for high mortality rate, there was no significant difference in the time for presentation and size of perforation both group of patients (gastric or duodenal perforation) however, patients with gastric perforation were more likely to die if they presented after 12 hours of onset of symptoms (15). Besides delayed perforation, our study showed that older age,and use of NSAIDs were significantly associated with mortality while duodenal perforations were not. Smoking and alcohol abuse were also not significantly associated with mortality in our study. Our mortality rate was higher than that reported by Ugochukwu et al. and Nuhu et al (4,5). There was no case of gastric perforation in both studies. No reason could be suggested for the high mortality rate of gastric perforations more than duodenal perforations. Probably the degree of inflammatory response due to the acidic content and volume of fluid produced in the stomach and following gastric perforation cause extensive irritation of the peritoneal cavity hence exaggerated systemic inflammatory response.

Finally, we recorded 2 cases of spontaneous closure of PPUD and one case of failed conservative management after 2 months of treatment in a private hospital in a patient who had gastric perforations. All three patients were explored because of persistent fever, abdominal pain and ileus. This further strengthens the role of surgery in management of patients with PPUD. Taylor had described non operative management of PPUD in selected group of patients, these findings in our study suggest that this may not be readily applicable in our setting where most of the patients present late (2).

This study had some limitations including the inability to determine the exact dose of NSAIDs and the brand consumed by the patients because most of the patients could not recollect this information during the pre-operative evaluation.

In conclusion, gastric perforations were more common in our series with both high mortality and post-operative complication rates more than duodenal perforations. Significant use of NSAIDs was associated with gastric perforations which were less common in other studies in our environment. NSAIDs use or prescription should be guided and administered with proton pump inhibitors or Histamine type 2 blockers.

Ethics Committee Approval: This study was approved by the ethical board of Nnamdi Azikiwe University Teaching Hospital.

Informed Consent: Written informed consent was obtained from patients who participated in the prospective part of the study. The data from the retrospective patients were de-identified so no consent was needed.

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ORİJİNAL ÇALIŞMA-ÖZET
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Perfore peptik ülser hastalığında değişen durum: NSAİİ suçlanabilir mi?

Ochonma Egwuonwu[1], Okoli Chinedu[1], Gabriel Chianakwana[1], Stanley Anyanwu[1], Chiemelu Emegoakor[1], Henry Nzeako[1]

[1] Nnamdi Azikiwe Üniversitesi Eğitim Hastanesi, Cerrahi Bölümü, Nnewi, Nijerya

ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, perfore peptik ülser hastalığı (PPÜH) sebebiyle başvuran hastalarda gastrik perforasyon ve nonsteroid antiinflamatuvar ilaç (NSAİİ) kötüye kullanımı ile arasında bir ilişki olup olmadığını belirlemekti.

Gereç ve Yöntem: Veriler, Mayıs 2011 ve Mayıs 2015 tarihleri arasında retrospektif ve Aralık 2017'ye kadar da prospektif olarak toplandı. Eksploratoris laparotomi ile PPÜH tanısı alan 60 hasta çalışmaya dahil edildi. Veriler SPSS 21.0 kullanılarak analiz edildi ve p değeri ≤ 0,05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışma dönemi içerisinde toplam 60 hasta PPÜH için opere edildi. Kırk beş (%75) hasta NSAİİ kullanım öyküsü belirtti. Bu hastalardan dokuzunun tıbbi reçetesi varken, diğerleri reçetesiz satılan ilaçlardan oluşmaktaydı. Uzun dönem kullananlar ve daha önce dispeptik belirtiler gösterenler dahil olmak üzere hastaların hiçbiri ülser profilaksisi kullanmamaktaydı. Beş (%11,1) hasta NSAİİ'nin tavsiye edilen kullanım dozunu aşmamıştı, bu yüzden bu serideki hastalar NSAİİ irrasyonel kullanımı ile ilişkiliydi. Kırk iki (%93,3) hastada mide delinmesi varken sadece üç hastada duodenal delinme mevcuttu. Büyük ölçüde NSAİİ kullanımı ile mide delinmesi arasındaki ilişki anlamıydı (p= 0,002). Uzun dönem ve kısa dönem NSAİİ kullanımı karşılaştırıldığında, delinme yeri açısından anlamlı bir fark bulunmadı (10,0 vs. 35,0) (p= 0,061). Ayrıca, yaş ve başvuruların süresi eşleştiğinde uzun dönem NSAİİ kullanımı (p= 0,041), ilacın doğru dozu hakkındaki bilgi eksikliği (p= 0,003) ve gastrik ülser delinmesi (p= 0,011) çalışılan hastalarda bağımsız mortalite sebepleri arasındaydı.

Sonuç: Hem uzun hem kısa dönem kullanımı dahil NSAİİ kullanımı mide delinmesi olan hastalarda anlamlıydı.

Anahtar Kelimeler: Perfore peptik ülser, gastrik ülser, NSAİİ

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ORIGINAL ARTICLE
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Analysis of the surgical treatment of the patients operated on by using laparoscopic and classic splenectomy due to benign disorders of the spleen

Vladimir Milosavljevic[1], Boris Tadic[1], Nikola Grubor[1], Dragan Eric[1], Milorad Reljic[1], Slavko Matic[2]

[1] Department of Hepatobiliary and Pancreatic Surgery, Clinic of Digestive Surgery, Clinical Centre of Serbia, Belgrade, Serbia
[2] Department of Surgery , Belgrade University School of Medicine, Belgrade, Serbia

ABSTRACT

Objective: Laparoscopic splenectomy became the standard surgical procedure in the 1990s. The goal of this study was to analyze the outcome of the patients who underwent laparoscopic splenectomy for the benign hematologic diseases of the spleen and compare its results with open splenectomy.

Material and Methods: The study was conducted as a retrospective cohort study analyzing and comparing the data obtained from 196 patients' case records in the Clinic for Digestive Surgery, Clinical Center of Serbia, for the benign disorders of the spleen, divided into two groups: patients operated with laparoscopic technique and patients in whom classic splenectomy was performed. The analyzed parameters were divided into three groups as preoperative, intraoperative and postoperative.

Results: In the laparoscopic splenectomy group, less intraoperative blood loss, lower incidental intraoperative complications and a shorter duration of surgery were recorded. The incidence of postoperative complications and reoperations was higher in the group of classically operated patients. Postoperative recovery, expressed by the duration of postoperative abdominal drainage, recovery of intestinal peristalsis and length of postoperative hospitalization, was significantly shorter in the laparoscopic group.

Conclusion: Laparoscopic splenectomy is an effective and safe surgical procedure in the treatment of many benign diseases of the spleen. Improvement of the laparoscopic technique of surgical teams and technical improvement of the laparoscopic equipment can lead to even wider application of laparoscopic splenectomy as standard operative procedure, and thus to safer and better quality treatment of patients with wider spectrum diseases of the spleen.

Keywords: Laparoscopy, spleen, laparoscopic splenectomy, benign disorders of the spleen

INTRODUCTION

The first laparoscopic splenectomy in the world was done by Delaitre and Maignien in 1991 (1). For the past decade, laparoscopic splenectomy has become widely accepted and applicable in the treatment of many diseases of the spleen. The most common benign hematologic diseases of the spleen in which splenectomy is indicated are immune thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura, hereditary spherocytosis, autoimmune hemolytic anemia, benign tumors, and splenic cysts (2).

Indications for laparoscopic splenectomy are the same as for open (classic) splenectomy, except in cases of trauma, where the role of laparoscopy is still the subject of consideration.

The goal of this study was to analyze the outcome of the patients undergoing laparoscopic splenectomy due to benign hematologic diseases of the spleen and compare the surgical treatment results with an open splenectomy and the present the importance of laparoscopic approach in the treatment of benign disorders of the spleen.

MATERIAL and METHODS

The study was conducted as a retrospective cohort study. The data obtained from the history of the disease was analyzed and compared, with the aim of getting

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Corresponding Author
Boris Tadic
E-mail: tadicboris@yahoo.com

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insight into certain parameters. The study covered a total of 196 patients operated on due to benign diseases of the spleen at the Clinic for Digestive Surgery - the First Surgical Clinic of the Clinical Center of Serbia. Informed consent was not received due to the retrospective nature of the study. Ethics committee approval was received for this study from the local ethics committee of the Clinical Centre of Serbia.

Patients were divided into two groups. The first group consisted of 93 patients who were operated on by using the laparoscopic technique (LS) in the period from 2007 to 2017 and the second group consisted of 103 patients operated on by using the classic approach (CS) in the period from 2001 to 2017.

The choice of surgical technique or approach was based on certain characteristics of the patient: type of the disease (e.g. in the case of a tumor of the spleen, the classic approach had the advantage, so that the preparation for the pathohistological analysis would be comprehensive, the size of the spleen also had an important role in the choice of the approach, larger spleens were operated on using the classic approach, as well as patients with comorbidities which presented a contraindication for laparoscopic surgery).

Laparoscopic splenectomy began its application at the First Surgical Clinic in 2007, since then and until 2017, patients from this group have been monitored. A group of patients operated on using the classic approach has been monitored since 2001 in order to have similar groups for comparison, because since 2007 there has been a significantly greater number of laparoscopic surgeries; however, after the introduction of a laparoscopic procedure and due to expressed contraindications with this approach or due to technical reasons, classic splenectomy was performed.

For patients operated on due to benign hematological diseases, diagnosis and primary drug therapy were performed by a hematologist. Platelets were analyzed daily in the preoperative period, as well as from the first postoperative day until the release of the patient, in order to have an insight into the therapeutic effects of the patients operated on.

Patients were treated with low molecular weight heparin (Fraxiparine, Aspen Notre Dame de Bondeville, France), with the addition of anticoagulation therapy in cases of a platelet count increase at > 500 x 10^9/L. Corticosteroid therapy was gradually reduced until complete suspension.

For patients who were operated on due to benign, non-hematological diseases of the spleen (benign tumors and cysts), the diagnosis was made by means of ultrasound examination, computerized tomography, and magnetic resonance imaging of the abdomen.

Parameters that were compared and monitored in both groups of the patients were: 1. Preoperative, which included: gender, age, body mass index, diagnosis of the disease, and size of the spleen (measured within the preoperative diagnosis); however, for hematological patients, preoperative number of platelets and length of hematologic treatment were also recorded. 2. Intraoperative, which included: intraoperative blood loss (amount of blood from the operative section aspirated through the suction system and then measured with the help of burettes), duration of the operation (measured in minutes), intraoperative complications (bleeding, injuries of other organs etc.), and for LS groups, conversion into open procedure and detection of accessory spleen. 3. Postoperative, which included: the time period in which the drain and the nasogastric tube were taken out (measured in days). Reintervention, most commonly due to infection, surgical wound disruption, intra-abdominal collection, abscess, pancreatic fistula etc., the length of postoperative hospitalization, and for benign hematological diseases, the postoperative number of platelets in order to gain insight into the therapeutic effect of the surgical treatment.

In all postoperative patients, prophylactic antibiotic therapy (Amoxycillin, Hemofarm Stada, Serbia) was administered during the postoperative course according to all current guides (3,4). Furthermore, all patients were postoperatively vaccinated according to current vaccination protocols (5). Dindo-Clavien scale was used to evaluate postoperative complications (6).

The study did not include patients with malignant hematological disorders and patients with associated cardiovascular comorbidities, as well as patients in whom the surgical procedure was contraindicated.

Statistical Package for the Social Sciences version 21.0 (IBM Corp.; Armonk, NY, USA) program was used for data analysis. If they met the criteria of normal distribution, the results were presented in the form of an arithmetic mean and standard deviation. Otherwise, they were represented by the median and the range of values. Categorical data are presented with absolute and percentage values. T-test was applied to compare continuous variables subjected to normal distribution, otherwise the Mann-Whitney test was used. The X2 test was used to analyze categorical type data. All statistical methods were considered significant if p (p) value ≤ 0.05.

RESULTS

Out of a total of 196 patients who were involved in the study, 93 of them were in the laparoscopic group, while the classic group included 103 subjects.

The groups tested did not differ much when it came to gender distribution, genders were equally represented (p= 0.461), the LS group had 38 (40.4%) male and 56 (59.6%) female patients, while the classic group had 47 (45.6%) male and 56 (54.4%) female patients.

Average age of these two groups was the same (p= 0.096). Patients in the LS group were on average 38.24 ± 13.6 years old, while CS group patients were 41.68 ± 15.02 years old. Average nutrition value in the LS group was 25.62 ± 2.73 kg/m^2, while the CS group patients amounted to 26.43 ± 2.43 kg/m^2.

Different types of disease (AIHA, benign tumors, cystic, ITP and spherocytosis) were equally represented in both groups (p= 0.184). The representation of various diseases in the groups tested is shown in Table 1.

The difference in spleen size was as follows: LS group (13.24 ± 1.82cm) and CS group (14.34 ± 3.21 cm). Larger spleen was the case in the classic group.

There was no significant difference in preoperative platelet counts between the groups tested (p= 0.164). In the LS group, the value was 71.78 ± 14.52, while in the CS group, it was 68.29 ± 14.81. Additionally, the length of hematological treatment of these two groups was not different as well (p= 0.474). The laparoscopic group was treated with preoperative medication for 23 months (10-120), and those that in the classic group for 30 months (10-120).

The presence of accessory spleens in the LS group was 19 (20.2%) and 11 (10.7%) in the CS group. A percentage difference in the presence of accessory spleen was noticed.

Intraoperative bleeding was significantly more extensive during classic splenectomy, rather than during laparoscopic splenectomy (p< 0.001). In the LS group, it resulted in 32 mL (5-225) and 56 mL (10-310) in the CS group.

Intraoperative complications of the patients were noticed in 4 (4.3%) patients of the LS group, and in 7 (7.4%) patients of the classic group. The need for reintervention was significantly more frequent in the classic group (7.8%), while the laparoscopic group had no need for reintervention. There was a single fatal outcome in the laparoscopic group, while the classic group had two fatal outcomes. There were no statistically significant differences in the frequency of fatal outcomes between these two treatments.

The laparoscopic technique surgery was significantly shorter when compared to the classic surgery, 83.46 ± 14.40 compared to 91.80 ± 15.32 minutes, respectively. A statistically significant difference in the duration of these two interventions was proven in favor of the laparoscopic surgery (p< 0.001).

Abdominal drain and nasogastric tube were placed significantly longer during classic surgery than during laparoscopic surgery (p< 0.001 and p< 0.001). Average duration of abdominal drain retention after laparoscopic surgery was 2 days, a minimum of 1 and a maximum of 3, while the average duration in the classic surgery group was 3 days, with a minimum of 1 and a maximum of 15 days. The nasogastric tube was retained on average for 2 days (1-3) in the LS group and 3 (2-7) days in the CS group.

Average postoperative hospitalization for the LS group lasted for 4 days, with a minimum of 2 and a maximum of 12, while for the CS group it was significantly longer, on average 9 days, with a minimum of 7 days and a maximum of 22 days.

Different incidence and severity of postoperative complications according to Dindo-Clavien Classification (DC) were shown, with I, then II and class III that were significantly represented in the classic group (p= 0.006; p= 0.002; p= 0.005).

In the LS group, there were 9 subjects of gradus I according to Dindo-Clavien Classification. These patients required additional, postoperative drug therapy in the form of antibiotics, antiemetics and antipyretics. Six patients belonged to gradus II according to DC classification and required additional antibiotic therapy. One patient had percutaneous drainage of the collection from a loge that was surgically removed from the spleen (grade III). A single myocardial infarction (grade IV) was recorded in one patient, and finally one deadly outcome was noted due to fulminant sepsis, after a series of non-surgical complications (gradus V).

In the CS group, these numbers were significantly higher. 25 patients were gradus I and 23 cases were gradus II. Eleven patients were in gradus III, followed by 5 patients in gradus IV. Two of the patients died after a series of complications (grade V). The representation of DC classification in the groups tested is shown in Table 2.

Table 1. Representation of various diseases in the group

	Group		
Diseases of the spleen	**Laparoscopic splenectomy n (%)**	**Classic slenectomy n (%)**	**p**
AIHA	2 (2.1)	4 (3.9)	0.1841
Benign tumors	5 (5.3)	15 (14.6)	
Cysts	19 (20.2)	14 (13.6)	
ITP	58 (61.7)	58 (56.3)	
Spherocytosis	10 (10.6)	12 (11.7)	

AIHA: Autoimmune hemolytic anemia, ITP: Idiopathic thrombocytopenic purpura.

Table 2. Representation of DC classification in the groups

	Group		
(DC) gradus	**Laparoscopic Splenectomy n (%)**	**Classic splenectomy n (%)**	**p**
I	9 (9.6)	25 (24.3)	0.006
II	6 (6.4)	23 (22.3)	0.002
III	1 (1.1)	11 (10.7)	0.005
IV	1 (1.1)	5 (4.9)	0.122
V	1 (1.1)	2 (1.9)	0.615

DC: Dindo-Clavien classification.

DISCUSSION

The first laparoscopic splenectomy was done 27 years ago in Paris by Delaitrea and Maignien. Shortly after, the initial objectives of laparoscopic splenectomy were defined, and they meant the following: that the results were identical to the classic splenectomy in terms of efficiency and safety, followed by reduced abdominal wall trauma, easier postoperative period and shorter hospitalization (1).

A special advantage is given to laparoscopic splenectomy when it comes to hematological disorders. These patients generally take corticosteroid therapy, which can have an impact on the development of infections and dehiscence of the surgical wound, and taking into account all the benefits achieved by the laparoscopic technique, laparoscopic splenectomy is the gold standard when it comes to these diseases (7,8).

The age of the patients who were laparoscopically operated on was 38.24 ± 13.6 years, while those that were subjected to classic surgery were 41.68 ± 15.02 years old.

The most common indication for splenectomy among benign hematological diseases is immune thrombocytopenic purpura (ITP). The frequency of this disease is ranging, according to some authors, from 60-80% (2). According to the results of our study in the LS group of patients, 61.7% of them were operated on due to ITP, while that only happened to 56.3% of those in the CS group. According to percentage representation, our data does not deviate from the data in the literature.

Average treatment time by the hematologist in the LS group was on average 23 (10-120) months while this number amounted to 30 (10-120) months in the classic group. Preoperative platelet counts in the LS group amounted to 71.78 ± 14.52 x 10^9/L while the same value went as high as 68.29 ± 14.81 x 10^9/L in the classic group, meaning there was no significant statistical difference between the groups regarding the duration of the preoperative treatment, as well as the platelet count preoperatively.

Accessory spleens are found in about 10-15% of the adults. Usually, they are between 1 and 2 cm. An accessory spleen in our study was present in 19 (20.2%) patients in the laparoscopic group of patients and in 11 (10.7%) patients in the classic group.

According to our study, intraoperative blood loss was 32 mL (5-225) in the LS group of patients, while it went as high as 56 mL (10-310) in the classic group. In a study by Rozario et al., the average intraoperative bleeding in the LS group of patients was 40 ml (0-150) (2). Italian authors Nobili et al. have published a study in which intraoperative bleeding during laparoscopic splenectomy was 60 mL (30-500) (9).

In our study, in patients who underwent laparoscopic splenectomy, a conversion was performed into an open procedure in four cases. In all four cases, the conversion was due to intraoperative bleeding. The bleeding was due to instrumental rupture of the spleen in one patient, due to poorly placed endovascular stapler in two patients, due to arterial injury to the lower half of the spleen in one patient.

In the US National Register, between 2005 and 2010, 37006 splenectomies were recorded, showing a worrying percentage of conversions of 22.5-33.99%, with very few patients being treated with laparoscopic technique at around 13.3% (10). Some authors point to a small conversion rate into an open procedure with a percentage of around 0-4% depending on the type of intraoperative complication when it comes to increased intraoperative bleeding and when splenomegaly is present (9,11). In our study, the percentage of intraoperative complications in the LS group amounted to 4.3%, and those were the cases were intraoperative bleeding and conversion took place, while in the classic group, it was 7.4%, where besides intraoperative bleeding, there were also injuries of the tail of the pancreas and damages to the stomach wall.

Average duration of the surgery according to the data from our study in the LS group was 83.46 ± 14.40 minutes, while the average duration of surgery in the CS group was 91.80 ± 15.32 minutes.

According to many studies, the percentage of reintervention ranges between 0-6.7% (11-13). In our study, there were no reinterventions in the laparoscopic group, whereas there were eight in the classic group. Reinterventions in the CS group of patients were due to bleeding, fistula, intra-abdominal collections/abscesses and surgical wound disruptions.

Literature data indicates a significantly lower percentage of postoperative complications in patients operated on laparoscopically. Winslow et al. have performed a meta-analysis of 51 series out of a total of 2940 patients, out of whom 2119 were laparoscopically operated on and 821 underwent the classic surgery, and demonstrated a statistically lower percentage of complications in the group of patients under laparoscopic treatment, which was 15.5% compared to 26.6% for the classic treatment (14).

Postoperative hospitalization, according to the results of the majority of authors, ranges from 1 to 25 days and is mainly dependent on the performance or simultaneous additional surgeries, most often laparoscopic cholecystectomies, then the age of patients, where a longer stay in the hospital is related to their older age, as well as postoperative complications (9,12).

Average postoperative hospitalization according to the results of our study was 4 (2-12) days for the LS group, whereas for the CS group, the average postoperative hospitalization amounted to 9 (7-22) days.

Some authors advocate that after each splenectomy, it should be mandatory to place the drain in the left subphrenic space, sometimes even two drains in cases of the classic group, although there are authors who complain that the drain should not be placed routinely, but only in cases of pancreatic injury (15-17). In addition to the above mentioned postoperative parameters in our study, we also dealt with a time period in which, after splenectomy, the drain and nasogastric suction were removed. In our study, after each splenectomy, we placed the drains, and the average time that elapsed until the elimination of the drain and after the surgery in the LS group was 2 days (1-3 days), while in the CS group this time was on average 3 days (1-15 days). As for the average time that elapsed until the removal of the nasogastric tube, in the LS group, it was 2 days (1-3 days), while in the CS group, it was 3 days (2-7) days.

Gonzales et al. have published 89% good response after laparoscopic and open splenectomy in their study (18). Zheng et al. have published a ten-year long experience in laparoscopic splenectomy in treating ITP in which they have reported the results of the success of the treatment, with percentages ranging between 80.3-89% retrospectively (19).

In our study, the best therapeutic response was most represented, and the worst one was least represented. In one patient within the LS group and two patients in the CS group, therapeutic outcomes were unknown due to fatal outcomes. In the laparoscopic group, complete therapeutic response was the case in 83.8% of patients, while the same value went as high as 80% in the classic group.

CONCLUSION

The official position of most European and World guides on surgical practice today is that LS is indicated for most benign and malignant diseases of the spleen, where an indication for surgical treatment exists, regardless of the age or body weight of the patient. Our study has confirmed the fact that laparoscopic splenectomy is an effective and safe surgical procedure in the treatment of many benign and malignant diseases of the spleen. The results speak strongly in favor of better detection of accessory spleens in the group of patients in whom laparoscopic splenectomy has been performed. Speaking of proven advantage of the laparoscopic approach in relation to preoperative diagnostics, we can conclude that laparoscopic splenectomy, both in terms of diagnostics and therapeutic effect, has advantages over classical surgery. Further sophistication of laparoscopic surgical techniques technical improvements of laparoscopic equipment can lead to even wider application of LS as a standard surgical procedure, and thus to a safer and better treatment of patients with a wide spectrum of spleen diseases.

Ethics Committee Approval: Ethics committee approval was received for this study from the local ethics committee of the Clinical Centre of Serbia.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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ORİJİNAL ÇALIŞMA-ÖZET
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Dalağın iyi seyirli hastalıkları sebebiyle laparoskopik ve klasik splenektomi kullanılarak opere edilen hastaların cerrahi tedavi analizi

Vladimir Milosavljevic[1], Boris Tadic[1], Nikola Grubor[1], Dragan Eric[1], Milorad Reljic[1], Slavko Matic[2]

[1] Sırbistan Klinik Merkezi, Sindirim Cerrahisi Kliniği, Hepatobiliyer ve Pankreas Cerrahisi Bölümü, Belgrad, Sırbistan
[2] Belgrad Üniversitesi Tıp Fakültesi, Cerrahi Anabilim Dalı, Belgrad, Sırbistan

ÖZET

Giriş ve Amaç: Laparoskopik splenektomi, 1990'lı yıllarda standart cerrahi ameliyat haline gelmiştir. Bu çalışmanın amacı, dalağın iyi huylu hematolojik hastalıkları için laparoskopik splenektomi olan hastaların sonuçlarını analiz etmek ve bunları açık splenektomi ile karşılaştırmaktı.

Gereç ve Yöntem: Bu çalışma, laparoskopik teknik ile opere edilen hastalar ve klasik splenektomi uygulanan hastalar olarak iki gruba ayrılan dalağın iyi seyirli hastalıkları sebebiyle Sırbistan Klinik Merkezi, Sindirim Cerrahisi Kliniğine başvuran toplam 196 hastanın verilerini analiz eden ve karşılaştıran bir retrospektif kohort çalışma olarak yürütüldü. Analiz edilen parametreler preoperatif, intraoperatif ve postoperatif olarak üç gruba ayrıldı.

Bulgular: Laparoskopik splenektomi grubunda daha az intraoperatif kan kaybı, daha düşük intraoperatif insidental komplikasyon ve daha kısa ameliyat süresi not edildi. Klasik splenektomi grubunda postoperatif komplikasyonlar ve re-operasyon insidansı daha yüksek bulundu. Postoperatif abdominal drenaj süresi, intestinal peristalside iyileşme ve postoperatif hastanede kalış süresi ile ifade edilen postoperatif iyileşme laparoskopik grupta anlamlı derecede daha kısaydı.

Sonuç: Laparoskopik splenektomi, dalağın birçok iyi seyirli hastalığının tedavisinde efektif ve güvenilir bir cerrahi işlemdir. Cerrahi takımların laparoskopik tekniklerindeki gelişme ve laparoskopik ekipmanlardaki teknik gelişim laparoskopik splenektominin standart cerrahi müdahale olarak daha geniş çapta kullanılmasına ve böylelikle dalağın daha geniş hastalık spektrumlarında hastaların daha kaliteli ve güvenilir tedavilerine sebep olabilir.

Anahtar Kelimeler: Laparoskopi, dalak, laparoskopik splenektomi, dalağın iyi seyirli hastalıkları

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A study on initial outcome of selective non-operative management in penetrating abdominal injury in a tertiary care hospital in Bangladesh

Md Sumon Rahman[1], Kamrul Hasan[2], Hasal Ul Banna[1], Akm Maruf Raza[3], Tarafder Habibullah[4]

[1] Department of Surgery, Jahurul Islam Medical College and Hospital, Kishoregonj, Bangladesh
[2] Department of Surgery, Cumilla General Hospital, Cumilla, Bangladesh
[3] Department of Pathology, Jahurul Islam Medical College and Hospital, Kishoregonji, Bangladesh
[4] Department of Surgery, Enam Medical College Hospital, Savar, Dhaka, Bangladesh

ABSTRACT

Objective: The aim of this study was to assess the initial outcome of non-operative, conservative management in selective penetrating abdominal injury in a tertiary care hospital.

Material and Methods: This was a cross sectional study done on purposively selected 36 patients with penetrating abdominal injuries of all ages admitted within 6 hours of the incident. All patients confirmed peritoneal breach and standard algorithm of management was followed. Closed monitoring was ensured with repeated investigations at regular intervals. Outcome parameters included surgical site infection (SSI), fever, hypothermia, wound dehiscence, fecal fistula, length of stay, pulmonary complication and death.

Results: A total of 36 patients with a mean age of 30 years (SD= 6.7), consisting all males, mostly (58%) from rural areas and 73% from low socioeconomic condition. Site of injury was noted in the epigastrium (42%) and right iliac region (22%). Among them, 33 (92%) patients were successfully managed with non-operative management and 3 (8%) patients needed laparotomy. Routine imaging and clinical observation could detect hollow viscus injury within 36 hours in 3 patients. Hospital stay was significantly lower (< 7 days) in conservative management.

Conclusion: Clinical examination alone and/or together with different diagnostic methods could reduce the number of negative laparotomies and associated morbidities. Single surgeon must closely monitor a patient of penetrating abdominal injury and take vital decisions from the time of admission until discharge.

Keywords: Penetrating abdominal injury, non-operative management, conservative management

INTRODUCTION

Penetrating abdominal trauma is an important public health problem accounting for a substantial proportion of all trauma admissions at tertiary care hospitals, and it continues to be a major cause of homicidal injury in Bangladesh, and even in the United States. Among penetrating abdominal injuries (PAI) stab wounds (SW) are about three times more often than gunshot wounds (GSW). It is mentioned in many literatures that PAI was being managed conservatively until the early 1900s (1-3). Laparotomy became the standard practice during "World War I" with evidence of a better chance of survival than conservative management. But in 1960, Shaftan, reported a high rate of negative laparotomies and managed 125 of 180 patients with PAI without surgery, with a mortality rate less than 1% (4). Since then, pendulum started to shift towards selective non-operative management (SNOM) for PAI. Nowadays, with the advent of minimal access surgery and modern imaging tools such as high resolution ultrasonogram, computed tomography (CT) scan laparotomy is almost avoidable because of its improved diagnostic facility, great therapeutic role and least surgical stress as well.

Current guideline allows to delay laparotomy with close observation for hemodynamically stable patients with no signs of peritonitis for PAIs even GSWs (5-6). In the United States, SNOM has become the standard care in abdominal SWs, and up to 55% of anterior abdominal SWs could be managed conservatively (7). Even with

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Corresponding Author
Sumon Rahman
E-mail: drsumon@live.com

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peritoneal breach, a considerable number of patients might have no other major intra-abdominal injury that necessitates operative management (3).

Among all trauma patients, many of them with penetrating abdominal injuries are admitted in Dhaka Medical College Hospital from all over the country every day. Most of them are transported from very far and get delayed. Majority of those patients do not have any primary management or resuscitation on the way. After admission, many of them cannot afford treatment cost. After negative exploratory laparotomy, patients might become the victims of anesthetic hazard, followed by wound infection, longer stay, increased treatment cost, higher morbidity and even death. These morbidity and mortality could be reduced by choosing selective criteria for conservative management when possible. Our observational study evaluated the outcome of non-operative management in selective PAIs with close monitoring.

MATERIAL and METHODS

This cross-sectional study was performed at the casualty unit of Dhaka Medical College Hospital Bangladesh over a period of one year (February 2011 to January 2012) in the accident center of a hospital. The study included a total of 36 penetrating abdominal injury patients of all ages, presented within 6 hours of the incident according to our selection criteria (Table 1). Institutional ethical committee clearance for collection of data and informed written consent was taken from the selected patients for conservative management.

The selected patients were evaluated by standard ATLS protocol and side by side resuscitated and then routine hematological, biochemical, focused assessment with sonography for trauma (FAST) and other common radiological imaging studies were performed. We didn't routinely practice computed tomography (CT) scan in our study because CT is generally a poor predictor of intestinal injury and pneumoperitoneum is often missed. Moreover, contrast material is not safe because of the risk of aspiration, hypersensitivity, nephrotoxicity and delay of the procedure. All patients underwent surgical toileting of the penetrating wound under local anesthesia and peritoneal breach was confirmed and repaired with or without drain. Standard algorithm of management was followed (Figure 1) (3).

Table 1. Inclusion and exclusion criteria for conservative approach in our study

Inclusion criteria
• Penetrating injury in anterior abdominal wall. • Hemodynamically stable patients. • Patients not developed the signs of peritonitis. • Patient admitted to hospital within 6 hours of injury
Exclusion criteria
• Poly trauma patients (head injury, limb fractures and perineal injuries. • Presence of peritoneal collection detected by FAST • Patient's with previous history of major abdominal surgery. • Patients with gunshot injury. • Patient's with known case diabetes mellitus, chronic liver, renal, & cardiovascular disease.

FAST: Focused assessment with sonography for trauma.

All patients were managed initially by nothing per oral (NPO) with continued nasogastric suction, urinary bladder catheterization, maintenance intravenous fluids, tetanus prophylaxis, prophylactic broad-spectrum antibiotics with metronidazole, adequate analgesics and regular motoring of hemodynamic status and vital signs with date and time were recorded and complete physical examination was done to see the associated injuries and neurological status. Plain abdominal radiograph in erect posture was done 12 hourly and abdominal ultrasonogram (USG) daily for the first 48 hours. Routine hematological and biochemical studies were repeated if needed. Oral feeding was resumed on the 3rd day in responding patients. Non-responding patients, developing any feature of peritonitis including abdominal rigidity, tenderness, fever, unresolved and progressive pneumoperitoneum or peritoneal collection or significant drop of hematocrit requiring blood transfusion were explored surgically

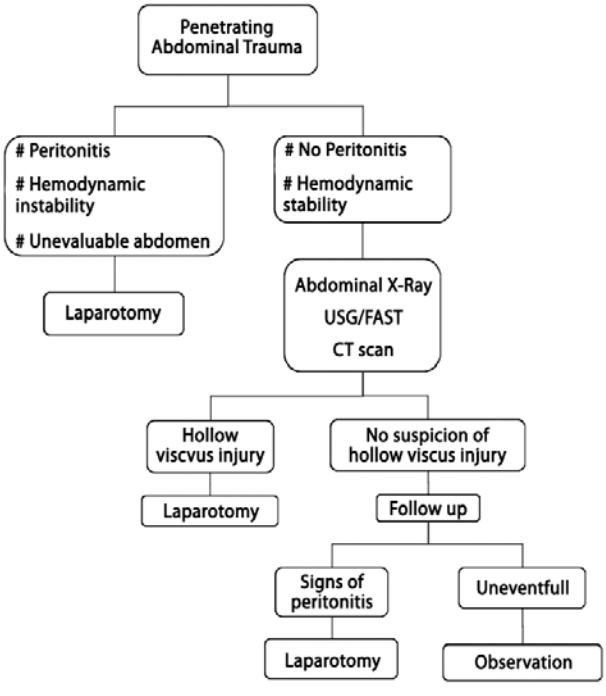

Figure 1. Algorithm for management of penetrating abdominal trauma.

immediately. Otherwise, the patients were discharged from the 3rd day onwards unless further inpatient care required.

Outcome parameters included number of patients managed conservatively and the rate of surgical site infection (SSI), fever, hypothermia, wound dehiscence, fecal fistula, length of stay, pulmonary complication and death. Other multivariables were studied as age, sex, occupation, socioeconomic condition, types of weapon, mode of injury and time interval between incident and admission.

Statistical Analysis

No software program was used for statistical analysis. Continuous variables were analyzed using median and range. All the data were expressed in frequency and percentage. Collected data were tabulated in numerical tables. Some are expressed in graph and Pie chart.

RESULTS

Thirty-six patients of PAI were selected with mild or no signs of hemodynamic instability for our study in Casualty Unit, Dhaka Medical College Hospital from February 2011 to January 2012 and managed as per designed algorithm.

Multivariable Analysis

In our series, we noted that the age incidence ranged from 19 to 62 years and the highest incidence was in between 21-40 years. Mean age was 30 years (SD= 6.7), all patients were males, mostly (58%) from rural areas and 73% from lower socioeconomic conditions. No patient could arrive within the first 2 hours and, we found maximum 33 patients arriving within 4-6 hours. Cause of injury was mostly homicidal 91.7% and sharp metallic weapons were mostly used 89%. Site of injury was most commonly noted over the epigastrium (42%) and then the right iliac region (22%) (Table 2). Among them, thirty-three patients (92%) were successfully managed with non-operative management and 3 patients (8%) needed laparotomy.

Evaluation of the Patients

Following the incident of penetrating trauma, the patients were presented with various symptoms as active bleeding from wound site, abdominal pain, evisceration of the omentum and gut, respectively (Figure 2). Then we proceeded with our management algorithm (Figure 3). Routine imaging studies including FAST and abdominal X-Ray revealed 5 patients with peritoneal free gas (pneumoperitoneum) which could be due to entry of environmental air or leaked from hallow viscus, but no evidence of peritoneal collection or solid organ damage was suspected. Within 36 hours of follow-up, three patients developed features of peritonitis and explorative laparotomy were performed immediately and rest of the patients (33) were managed with conservative treatment (Figure 4).

Outcome Analysis

Table 2. Multivariable analysis in our study

Category	Value	Percentage
Age	Mean (30 years) SD= 6.7	
Sex		
Male	36	100%
Female	0	0%
Occupation		
Farmer	6	16.7%
Businessman	4	11%
Service holder	5	14%
Rickshaw puller	8	22.3%
Day laborer	13	36%
Habitat		
Urban	15	42%
Rural	21	58%
Socioeconomic condition		
Lower	26	72.2%
Middle	10	27.8%
Higher	0	0%
Time of arrival after injury (hours)		
1-2	0	0%
2-4	3	8.3%
4-6	33	91.7%
Cause of injury		
Accidental	2	5.5%
Homicidal	33	91.7%
RTA	1	2.8%
Type of weapon		
Sharp metallic	32	89%
Nonmetallic (glass, bamboo)	4	11%
Fire arms	0	
Site of injury		
Epigastrium	15	42%
Umbilical	4	11%
Right hypochondrium	5	14%
Right iliac	8	22%
Multiple areas	4	11%

SD: Standard deviation, RTA: Road traffic accident.

Among the 36 patients, thirty-three (91.7%) patients were managed with SNOM and 3 patients needed laparotomy. On laparotomy, jejunal perforation in two cases and ileal perforation in one case were noted (Table 3). Gut wounds were trimmed, and primary repair was done with placing abdominal drain tube. We

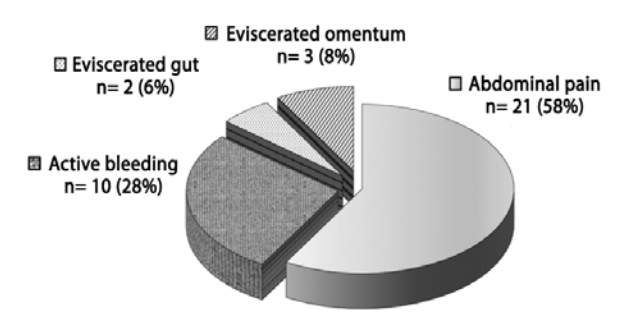

Figure 2. Presentation of patients in our series.

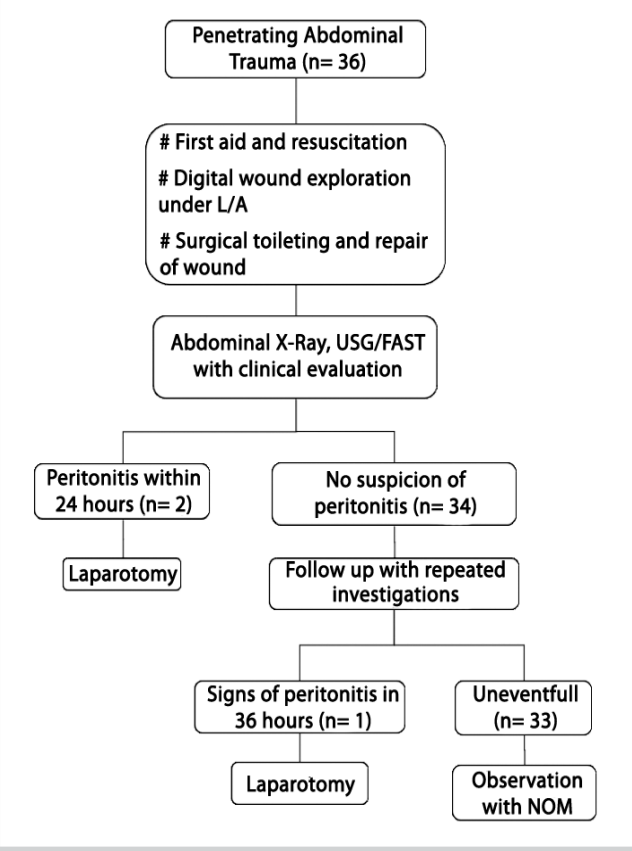

Figure 3. Algorithm for the management of penetrating abdominal trauma in our series.

didn't find any negative laparotomy and no death in our study.

In our study, among the conservatively treated patients, four developed wound infection, 3 developed fever, and two needed secondary wound closure. In the operative group, all three patients developed respiratory tract infection (RTI), anesthetic hazards, required more oxygen support, frequent nebulization and blood transfusion (Table 4). All conservatively managed 33 patients were discharged within 4-7 days.

DISCUSSION

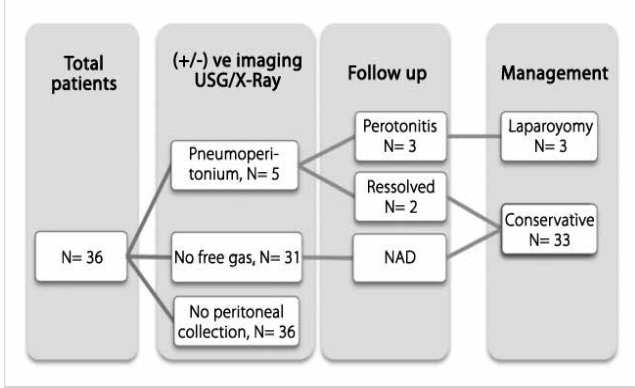

Figure 4. Imaging results in PAI patients. Pneumoperitoneum in 5 cases but all did not developed peritonitis.

Table 3. Laparotomy incidence and findings

Management	Patients (n= 36)	Percentages
Conservative	33	91.7%
Laparotomy	3	8.3%
Findings	Patients (n= 3)	Percentages
Hollow viscus injury	3	100%
Solid organ injury	0	0
Negative	0	0

The aim of this study was to observe the outcome of selective non-operative management (SNOM) of penetrating abdominal injuries by clinical evaluation and diagnostic methods and the effects of timing of the operation. Stab injury or other penetrating abdominal injury with minimal or no symptom always poses a management challenge for trauma surgeons in the casualty department. It always warrants immediate laparotomy in case of hemodynamic instability or any signs of peritonitis. However, the major challenge nowadays is to make the right decision with the help of diagnostic modalities available. Unfortunately, a single evaluation test will never provide adequate diagnosis in all cases of penetrating abdominal trauma.

Injury occurred most commonly among young persons (21-40 years) and the incidence declined rapidly with advancing age. In our study, all of the patients were males because of their mobile lifestyle, use of high-speed vehicles and involvement in civil violence and crime. In various large group studies, it has been reported that mean age ranges from 26-30 years for such trauma incidence (2,8,9).

Fifty eight percent of all PAI patients were rural dwellers in our study, which suggests that the injuries might have happened due to increased aggressiveness and arrogance among themselves for protecting their property and pride. Most of the pa-

Table 4. Complications and hospital stay in our study

Complications	No of cases		Percentages
	Conservative	Laparotomy	
Hypothermia	0	2	5.5%
Fever	3	2	14%
RTI	0	3	8.3%
Wound infection	4	2	16.7%
Secondary closure	2	2	11%
Prolong hospital stay	0	3	8.3 %
Delayed GEA recovery	0	2	5.5 %
Blood transfusion	0	3	8.3%
Duration of stay			
0-3 days	14	0	39%
4-7 days	18	0	50%
8-10 days	1	0	2.7%
11-14 days	0	2	5.6%
> 14 days	0	1	2.7%

RTI: Respiratory tract infection, GEA: General endo-tracheal anaesthesia.

tients (72.2%) were noted to come from lower class families. Probably due to active participation in high risk-taking activities, majority of the injuries was homicidal and occurred in rural areas with sharp metallic, locally-made, used in household affairs such as teta, ballam, kirich and knife etc. Most common site of external wound was noted over the epigastrium (42%) and then right iliac region. After laparotomy, jejunal perforation was most commonly noted. Lee WC at el. have reported the most common site of the external wound to be over the left upper quadrant and lower chest and small bowel (20%) followed by the liver (14%) (9). In another study, Gorge VC et al. have noticed that the most common injured organs include rectum then small bowel then liver by gunshot injury (10).

Our study included all PAI patients with peritoneal violation presented with severe abdominal pain, active bleeding from wound, eviscerated gut and omentum respectively. All of those features are not absolute indications for laparotomy and proceed with SNOM. In a study by Ertekin C et al. among 117 patients with stab wounds, 92 (79%) patients have been discharged without surgery (11). Different large group studies have also not supported the view that omental or bowel evisceration is an absolute indication for an emergency operation (8,12).

In our study, after resuscitation, FAST, chest and abdominal X-Ray were done in all patients. Throughout our study, these imaging tests were repeated as needed. We did not include CT scan routinely due to lack of availability and affordability rather than the role of CT scan being debatable in PAI. Exadaktylos et al. have described that CT may not be necessary for patients with SW. At their center in South Africa, out of 496 patients of abdominal SWs, 298 patients have been selected for SNOM. None of the patients underwent CT, and management was based on clinical examination alone (13). In a meta-analysis, CT has not been independently associated with failure or success of SNOM (14).

This study included 36 PAI patients with peritoneal violation, hemodynamically stable and arrived within 6 hours of injury. Thirty-three patients (around 92%) were successfully managed conservatively avoiding unexpected complication rates of negative laparotomy. Taviloglu K et al. have reported that when laparotomy is routine in PAI, negative and nontherapeutic laparotomy rates rise to 12% and 23%, respectively but in later periods with SNOM, these rates decline to 7% and 4% (15). Three patients in our study underwent therapeutic laparotomy based on clinical evaluation and repeated imaging studies, all of them became the victim of anesthetic hazard but there was no negative laparotomy.

Most common complication noted in our study was trauma site wound infection (16.7%) and 11% required secondary closure and 8.3% needed blood transfusion in the post-operative period. Delay of laparotomy in our study was 24 to 36 hours. Velmahos GC et al. have stated that the greatest concern related to a policy of SNOM is the complication produced by the delay of operation with unnoticed features of peritonitis. Among 80 patients with delayed laparotomy, five developed complications potentially related to delaying operation, and they believe that 24 hours' time of observation is adequate for majority of the patients (10).

Regarding hospital stay and other complications, fourteen pa-

tients (39%) were managed by SNOM, discharged within 3 days with advice to stitch off later. Eighteen (50%) patients were discharged within 7 days due to wound infection and pyrexia. Three patients underwent laparotomy and had increased morbidity not due to gut injury but for anesthetic hazard, severe wound infection, post-operative pneumonitis, fever and prolonged hospital stay, which demanded extra costly investigations and higher total treatment expense. Unnecessary laparotomies for trauma are associated with a significant complication rate, ranging from 22% to 41%, and a significantly prolonged hospital stay (12,16,17).

The ongoing dilemma for hemodynamically stable patients almost concluded with the introduction of "selective conservatism" by Shaftan (4). In a study in 1960, he suggested that clinical examination could reliably and safely predict the need for laparotomy in PAI.

CONCLUSION

Continuous clinical evaluation together with different and repeated diagnostic tools could minimize the number of non-therapeutic laparotomies and limit possible unexpected complications of negative laparotomy in penetrating abdominal injuries. Trauma surgeons who used to manage PAI may feel more comfortable dealing with a selective non-operative approach. In a developing country like Bangladesh, by adopting selective non-operative management, we could manage some of those patients with less complication and expanse safely.

Ethics Committee Approval: This study was approved by the BCPS (Bangladesh College of Physicians and Surgeons), Bangladesh ethical review committee.

Informed Consent: Informed consent was obtained from all individual patients included in our study.

Peer-review: Externally peer-reviewed.

Author Contributions: Consept - M.S.R.; Design - M.S.R.; Supervision - A.M.R., H.U.B.; Data Collection and/or Processing - M.S.R., K.H., T.H.; Analysis and Interpretation - M.S.R., A.M.R., H.U.B., K.H., T.H.; Literature Search - T.H., H.U.B.; Writing Manuscript - H.U.B., K.H.; Critical Reviews - M.S.R., A.M.R.

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2019; 35 (2): 117-123

Bangladeş'teki üçüncü basamak bakım hastanesinde penetran karın yaralanmasında seçici non-operatif yönetimin ilk çıkışı üzerine bir çalışma

Md Sumon Rahman[1], Kamrul Hasan[2], Hasal Ul Banna[1], Akm Maruf Raza[3], Tarafder Habibullah[4]

[1] Juhurul İslam Tıp Okulu ve Hastanesi, Cerrahi Bölümü, Kishoregonj, Dhaka, Bangladeş
[2] Cumilla Genel Hastanesi, Cerrahi Bölümü, Cumilla, Bangladeş
[3] Juhurul İslam Tıp Okulu ve Hastanesi, Patoloji Bölümü, Kishoregonj, Dhaka, Bangladeş
[4] Enam Tıp Okulu Hastanesi, Cerrahi Bölümü, Savar, Dhaka, Bangladeş

ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, bir üçüncü basamak bakım hastanesinde seçici penetran abdominal yaralanmalarda non-operatif, konservatif yönetimin ilk sonuçlarını değerlendirmekti.

Gereç ve Yöntem: Olay olduktan sonra ilk 6 saat içinde hastanemize başvuran 36 penetran abdominal yaralanması olan her yaştan amaca uygun seçilmiş 36 hasta üzerinde yürütülen enine kesit bir incelemeydi. Bütün hastalarda peritoneal yarık vardı ve standart yönetim algoritması uygulandı. Düzenli aralıklarla tekrarlanan incelemeler ile hastalar yakın takibe alındı. Sonuç parametrelerine, ameliyat yeri enfeksiyonu, ateş, hipotermi, yaranın açılması, fekal fistül, kalış süresi, pulmoner komplikasyon ve ölüm dahildi.

Bulgular: Hepsini erkeklerin oluşturduğu ve ortalama yaşın 30 olduğu (SS= 6,7) 36 hastanın birçoğu (%58'i) kırsal kesimden gelmekteydi ve %73'ünün sosyoekonomik durumu düşüktü. Yara bölgesini %42 ile epigastriyum ve %22 ile sağ iliyak bölge oluşturmaktaydı. Otuz altı hastanın 33 (%92)'ü non-operatif yönetim ile tedavi edildi ve geri kalan üç (%8) hastada ise laparotomi uygulandı. Otuz altı saat içinde üç hastada rutin görüntüleme ve klinik gözlem içi boş iç organ yaralanmalarını tespit edebildi. Hastanede kalış süresi, konservatif yönetimde daha düşük bulundu (< 7 gün).

Sonuç: Tek başına ve/veya farklı tanı araçlarının birlikte kullanımı ile klinik inceleme negatif laparotomi sayısını ve ilişkili morbiditeleri azaltabilir. Tek bir cerrah penetran abdominal yaralanması olan bir hastayı takip etmeli ve hastaneye başvuru esnasından taburcu olana kadar olan sürede önemli kararları vermelidir.

Anahtar Kelimeler: Penetran abdominal yaralanma, non-operatif yönetim, konservatif yönetim

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ORIGINAL ARTICLE
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The predictive power of SAPS-3 and SOFA scores and their relations with patient outcomes in the Surgical Intensive Care Unit

İbrahim Mungan[1], Şerife Bektaş[1], Mine Altınkaya Çavuş[1], Sema Sarı[1], Sema Turan[1]

[1] Intensive Care Unit, Turkiye Yuksek Ihtisas Training and Research Hospital, Ankara, Turkey

ABSTRACT

Objective: Individual risk of surgical patients is more often underestimated and there is not an absolute criterion demonstrating which patient deserves intensive care. Since a nominative assessment of these patients to quantify the intensity of critical illness is not appropriate, prognostic scores are used to assess the mortality rate and prognosis for critical patients including surgical ones. This study aimed to test the calibration power of SAPS-3 score and SOFA score of surgical patients undergoing gastrointestinal surgery, and identify any relation with patient outcomes in the department of surgical ICU.

Material and Methods: This retrospective observational study was conducted during the period between August 2017 and December 2017. It was performed at a Gastroenterological Surgical ICU, a tertiary care hospital in Ankara, Türkiye. To calculate SAPS-3 and SOFA score, physiological data and laboratory analysis on the day of ICU admission were used. Records were reviewed from hospitalization to medical discharge or hospital mortality. Statistical analysis included Mann Whitney U-test and ROC-curves to predict 30-day mortality.

Results: A total of 233 patients admitted to the Gastroenterological Surgical ICU were included into the study and the main reason for ICU admission was surgical problems. Mortality rate was 2.6 % (6 patients). Average SAPS -3 score was 32.5 and SOFA score was 30.1. A significant correlation was observed with the SAPS-3 score, but not with the SOFA score statistically in mortality as a dependent factor. The discriminative power, assessed using the AUC and the probability of death estimation, was satisfactory with the SAPS-3 scores (AUC 0.754) while it was lower with the SOFA score (AUC 0.631)

Conclusion: We found that SAPS-3 score was significantly correlated not only with mortality rate, but also with LOS in the ICU. Nonetheless, SOFA score was not related to mortality, but related to LOS in the ICU. Prognostic score systems are used to estimate mortality but they may be used to identify LOS in the ICU and postoperative complications. It can be concluded that SAPS-3 and SOFA scores may be used to prognosticate postoperative ICU requirement.

Keywords: Simplified acute physiology score, sequential organ failure assessment, surgical intensive care unit, mortality, predictive

INTRODUCTION

Surgical operations are classified as high-risk procedures and a significant proportion of intensive care unit (ICU) is composed of postoperative patients. These do not shadow the fact that the individual risk of surgical patients is more often underestimated, and less than 15% of patients who undergo those procedures have been admitted to an intensive care unit (1,2). There is not an absolute criterion or study demonstrating which patient deserves intensive care while debate is still continuing. The Society of Critical Care Medicine has published a guideline for ICU admission intending a better use of limited resources, but it has not gained popularity especially in surgical patients (3). So, risk adjustment via mortality prediction methods for this group of patients is a must.

Since a nominative assessment of these patients to quantify the intensity of critical illness is not appropriate, prognostic scores are used to assess the mortality rate and prognosis for critical patients including the surgical ones (4). Even though contradictious data are present in the literature, prognostic scoring systems (PSS) are used widely to make judgements in an objective manner (5). Among the PSSs, the Simplified Acute Physiology Score (SAPS) was investigated thoroughly and revised due to the improvements in health care (6,7). The revised version of this score system - SAPS-3 - uses 20 variables to predict hospital mortality from admission data (recorded within ± 1 h) (8). The Sequential Organ Failure Assessment (SOFA)

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Corresponding Author
İbrahim Mungan
E-mail: imungan@gmail.com

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score has primarily been proposed to assess the severity of organ dysfunction in septic patients in a sequential manner (9). Six organ systems (respiratory, cardiovascular, renal, hepatic, central nervous, coagulation) are taken into account, and the function of each is scored from 0 (normal function) to 4 (most abnormal). Serial changes in SOFA score over time are useful in predicting outcome. Its usage for mortality prediction based upon the fact that multiorgan dysfunction is commonly seen in critical situations like sepsis, chronic or acute liver failure, cancer or cardiac surgery (5,9).

Calibration and the discrimination are the two objective measures that evaluate the performance of prognostic models. Calibration -the relation of the estimated mortality with the observed mortality - is claimed to be as important as the discrimination - differentiation between survivors and nonsurvivors- in the means of the ICU eligibility of the patients and comparison of care between ICUs (7,10). Nonetheless, the calibration and discrimination power of the PSS can vary in time with the improvement in healthcare and it can vary across centers (11). As we searched in the literature, SAPS-3 and SOFA scores have not been evaluated in terms of sensitivity and specificity to predict mortality in postoperative patient population in a comparison manner. This study aimed to test the calibration power of SAPS-3 score and SOFA scores of surgical patients undergoing gastrointestinal surgery, and identify any relation with the patient outcomes in the department of surgical ICU.

MATERIAL and METHODS

This retrospective observational study was conducted during the period between August 2017 and December 2017. It was performed at a Gastroenterological Surgical ICU, a tertiary care hospital in Ankara, Türkiye. The patients included in the study were those admitted to the surgical ICU for any reason after surgery. Patients with incomplete records and length of stay of less than 24 hours were excluded from the study.

An extra formal consent other than the patients had given prior to hospitalization was not required for the current study because it was a case-control medical record review. Since our study was in the category of non-interventional clinical research with its retrospective structure, no ethics committee approval was applied.

Data Acquisition

All clinical variables of the patients were retrospectively collected from our institutional database. Patients were analyzed on the following variables: diagnosis on admission, surgery type, medical history of the patients, reason for ICU admission, laboratory findings, mortality, length of stay (LOS) in ICU and in hospital at all.

Surgery types were classified by localization of the pathology and divided mainly into four groups; biliopancreatic system (BPS), upper gastrointestinal system (GIS), lower GIS, and liver pathology. Reasons for ICU admission were classified mainly in four groups; cardiac problems like arrhythmia, respiratory problems like medical history of Chronic Obstructive Pulmonary Disease, hemodynamic problems like hypotension, and surgical problems like bleeding (bleeding from surgical site or any suspicion of bleeding, and observational admissions were classified in this category). Mortality as a variable in this study was described as death from any cause occurring within 30 days after surgery.

To calculate the SAPS-3 and SOFA score, physiological data and laboratory analysis on the day of ICU admission were used (postoperative 0). Records were reviewed from hospitalization to medical discharge or hospital mortality. Data were imported into a spreadsheet (Microsoft Excel 2013, Microsoft Corporation) for the calculation of the scores and their derived probabilities of death using the published equations and coefficients. To forestall the variability in the data collection, all values were reviewed by the authors of the study.

Statistical Analysis

Statistical analysis was performed using SPSS version 20.0 for Windows (SPSS Inc.; Chicago, IL , USA). Data were analyzed, and the continuous variables were reported as mean ± standard deviation (SD), and nominal variables were reported as total number and percentages.

Variables were first evaluated by One-Sample Kolmogorov-Smirnov test as a normality test to choose the type of statistical tests -parametric or non-parametric test-, and the results showed asymp. Sig. (2-tailed) levels ≤ 0.05, so we decided to use non-parametric tests. For statistical analysis, correlations between variables were evaluated for significance by using the Spearman's rho test. Categorical variables were evaluated by the Mann-Whitney U test of contingency. In all analyses, a 'p' value less than 0.05 was considered statistically significant and comparisons were 2-tailed.

Hosmer-Lemeshow test was used to calculate the calibration of SAPS-3 and SOFA test which express the ability of the test to determine the probability of death in accordance with the observed mortality. Discrimination was assessed using receiver operating characteristic (ROC) curves. The ROC curves were established as discrimination measurements with distributions per 10%, according to the predicted mortality and the obtained curve was appraised using the calculated area under the curve (AUC). AUC values > 0.75 was appraised as satisfactory, AUC values > 0.8 was appraised as well, and AUC values > 0.9 was appraised as very good.

RESULTS

A total of 233 patients admitted to the Gastroenterological Surgical ICU were included in the study between August 2017 and December 2017. Patients older than 18 years of age, who stayed

24 h or more in the ICU, were included. Forty-nine patients' records were excluded due to incomplete or unavailable data. Eight patients were younger than 18 years of age and excluded from the study. Patients' demographic data and operational details of the groups (survivors versus non-survivors) are presented in Table 1.

Mean age of the patients was 58.52 years, with a standard deviation of 13.94 years and the representatives of both sexes were relatively proportional (56.7% males versus 43.3% females). Main reason for ICU admission was surgical problems (66.1%), and as it was stated previously, bleeding from surgical site or any suspicion of bleeding, and observational admissions were classified in this category. Patients were operated for malignancy in 54.1% of the cases and mortality rate was 2.6 % (6 patients). Statistical analysis showed that surgery for malignancy, presence of comorbidities and reason for ICU admission were related to mortality ($p< 0.05$). The duration of surgery and being urgent had no relation with mortality. Mechanical ventilatory support was required in 7 patients and the difference between survivors and non-survivors was significant statistically ($p< 0.001$).

In Table 2, patients' postoperative outcomes with prognostic scores related with mortality are evaluated. The average length of stay (LOS) in hospital was 14.35 days and LOS in ICU was 5.46 days. The average SAPS-3 score was 32.5 and SOFA score was 30.1. A significant correlation was observed with the SAPS-3 score, but not with the SOFA score statistically in mortality as a dependent factor.

It is observed that 50.6 % of the patients were treated in the ICU for more than 3 days. So, further evaluation of the patients was decided on according to the length of stay in the ICU for statistical analysis in this study. In Table 3, groups were formed according to LOS in the ICU; group A represents the patients with LOS in ICU > 3 days and group B represents the patients with LOS in ICU ≤ 3 days.

Table 1. Demographic data and operational details of the groups*

	All (233)	Survivors (227)	Non-survivors (n= 6)	p+
Age (Years)	58.52 (± 13.94)	58.38 (± 14.09)	63.50 (± 3.08)	0.459
Gender (Male)	132 (56.7%)	129 (56.8%)	3 (50%)	0.74
Operation type				
BPS	92 (39.5%)	89 (39.2%)	3 (50%)	0.930
Upper GIS	83 (35.6%)	80 (35.2%)	3 (50%)	
Lower GIS	47 (20.2%)	47 (20.7%)	0	
Liver pathology	11 (4.7%)	11 (4.8%)	0	
Malignancy	126 (54.1%)	120 (52.9%)		0.022
Duration of surgery (minutes)	204.47 (± 130.4)	201.5 (± 136.5)	328 (± 182)	0.083
Medical history				
COPD	17 (7.3%)	15 (6.6%)	2 (33.33%)	0.023
Renal disease	1 (0.4%)	1 (0.4%)	0	
Hypertension	77 (33%)	77 (33.9%)	0	
CHF	20 (8.6%)	18 (7.9%)	2 (33.33%)	
DM	11 (4.7%)	11 (4.8%)	5 (3%)	
Urgent operation	16 (6.9%)	16 (7%)	0	0.501
Reason for ICU admission				
Hemodynamic problems	23 (9.9%)	22 (9.7%)	1 (16.7%)	0.043
Surgical problems	154 (66.1%)	153 (67.4%)	1 (16.7%)	
Cardiac problems	36 (15.5%)	35 (15.4%)	1 (16.7%)	
Respiratory problems	20 (8.6%)	17 (7.5%)	3 (50%)	
MVP	7 (3%)	3 (%1.3)	4 (66.7%)	< 0.001

* Values are either expressed as mean ± standard deviation or n (%).
+p-values calculated for comparison of survivors versus non-survivors group by Mann- Whitney U test.
BPS: Biliopancreatic system; GIS: Gastrointestinal system; COPD: Chronic obstructive pulmonary disease; CHF: Congestive heart failure; DM: Diabetes mellitus; ICU: Intensive care unit; MVP: Mechanical ventilatory support.

Table 2. Postoperative outcomes with prognostic scores related with mortality*

	All (233)	Survivors (n= 227)	Non-survivors (n= 6)	p+
LOS in-hospital (days)	14.35 (± 15.37)	14.03 (± 15.23)	26.67 (± 17.01)	0.035
LOS in- ICU (days)	5.46 (± 8.1)	5.11 (± 7.3)	18.83 (± 19.24)	0.011
LOS in- ICU > 3 days	118 (50.6%)	113 (49.8%)	5 (83.3%)	0.106
SAPS-3 score	32.5 (± 8.95)	32.29 (± 8.87)	40.83 (± 8.7)	0.033
SOFA score	3.01 (± 1.38)	2.98 (± 1.35)	4.17 (± 2.22)	0.249
30 day mortality	6 (2.6%)			

* Values are expressed as either mean ± standard deviation or n (%).
+p-values calculated for comparison of survivors versus nonsurvivors group by statistical analysis.
LOS: Length of stay; ICU: Intensive care unit; SAPS-3: Simplified acute physiology score; SOFA: Sequential organ failure assessment.

Table 3. Postoperative outcomes with prognostic scores and relation with LOS in the ICU*

	All (233)	Group A (n= 118)	Group B (n= 115)	p+
Age	58.52 (± 13.94)	60.66 (12.76)	56.31 (14.79)	0.026
LOS in-hospital (days)	14.35 (± 15.37)	20.46 (± 18.37)	8.09 (± 7.48)	< 0.001
LOS in- ICU (days)	5.46 (± 8.1)	9.18 (± 10.1)	1.64 (± 0.74)	< 0.001
SAPS-3 score	32.5 (± 8.95)	36.13 (± 8.52)	28.79 (± 7.82)	< 0.001
30 day mortality	6 (2.6%)	5 (4.2%)	1 (0.9%)	0.105
SOFA score	3.01 (± 1.38)	3.39 (± 1.53)	2.62 (± 1.09)	< 0.001
Malign pathology	126 (54.1%)	86 (72.9%)	40 (34.8%)	< 0.001

* Values are expressed as either mean ± standard deviation or n (%).
+p-values calculated for comparison of survivors versus nonsurvivors group by statistical analysis.
LOS: Length of stay; ICU: Intensive care unit; SAPS-3: Simplified acute physiology score; SOFA: Sequential organ failure assessment.

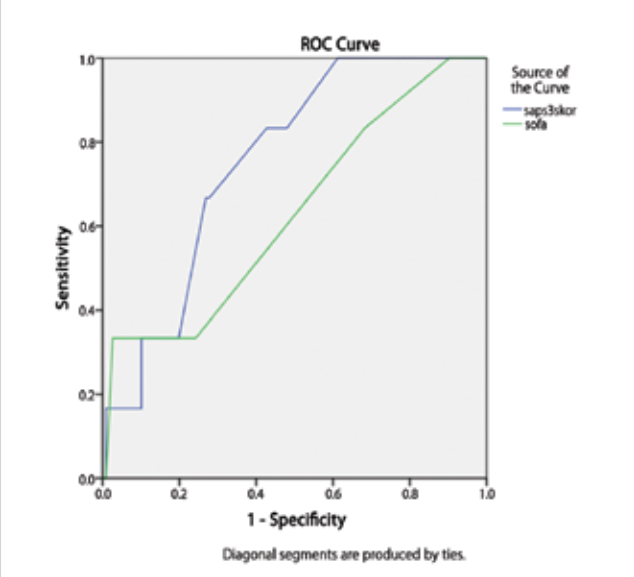

Figure 1. ROC curve for SAPS-3 and SOFA scores.

In this statistical analysis, it was clearly seen that both SOFA and SAPS-3 scores were related to LOS in ICU > 3 days (Asymp. Sig. (2-tailed) < 0.001). Age, as a variable, was also found to be related to LOS in the ICU statistically, but this was expected- as comorbidity rate increases with age- and Asymp. Sig. (2-tailed) level was higher (p= 0.026)

The discriminative power assessed using the AUC and the probability of death estimation was satisfactory with SAPS-3 scores (AUC 0.754) while it was lower with SOFA score (AUC 0.631) (Figure 1 and Table 4). The Hosmer-Lemeshow goodness-of-fit test also revealed this with the discordance of these two scores with a good calibration for the SAPS-3 global model as shown in Table 4 with sig.level 0.757 versus 0.613.

DISCUSSION

Due to the fact that surgical patients have different physiological and functional characteristics than other patients, estimation of prognosis and optimizing postsurgical care with lower misuse of ICUs are hard and complicated tasks (4). Prognostic scoring systems (PSS) like SAPS-3 and SOFA are utilized for this

Table 4. Hosmer and Lemeshow Test and Area under curve for SAPS 3 and SOFA score

	Chi-square	df	Sig	Area under curve
SAPS-3	5.009	8	0.757	0.754
SOFA	1.807	3	0.613	0.631

SAPS-3: Simplified acute physiology score-3; SOFA: Sequential organ failure assessment.

purpose in critical care medicine by disease severity assessment, comparing ICU performance and optimizing resource allocation. These systems use particular medical data to prognosticate an outcome's possibility of occurrence (10,12,13).

SAPS-3 and SOFA scoring systems are simple and require non-sophisticated data, unlike other prognostic score systems. SOFA is mainly used to evaluate the clinical course sequentially and maintain a semiquantitative estimation of mortality. Therefore, it can be concluded that SOFA has a disadvantage in failing to show actual clinic state comparing to SAPS-3 (4,13). SAPS-3 utilization is claimed to be valid for surgical patients with good discrimination and calibration power, but the SOFA score has not been evaluated in surgical patients in our country. We compare these two commonly used PSS in mortality rate and in LOS in ICU mainly.

Mortality rates in the ICU differ between centers and patient admission criteria plays a very important role in this issue. Knaus et al. have described the lowest mortality rate as 6.4% in 42 ICUs, while in our study the mortality rate was 2.6 (14). This is probably due to the fact that in our study population, the major reason for the ICU admission was basic and observational reasons- surgical reasons- and we consider mortality as death from any cause occurring within 30 days after surgery.

In our study, age factor as a variable did not affect mortality rate, but it was linked to prolonged LOS in the ICU, which was in line with the finding in the study of Leong et al. (15).

Originally, SOFA score is computed 1 day after ICU admission and every 2 days subsequently. The highest scores are claimed to be most predictive of mortality (16). In our study, SOFA and SAPS-3 scores were calculated using data derived in the ICU admission day 0 retrospectively and the average scores were significantly higher in the non-surviving group.

Discriminative power of the SAPS-3 was satisfactory and calibration was appropriate. Moreover, this model showed the relation of SAPS- 3 scores with mortality and length of stay in the ICU. AUC with SOFA score was found as 0.63,1 whereas it was found as 0.754 with SAPS-3. It is parallel to other studies that have found AUC 0.748 versus 0.810 (SOFA score versus SAPS-3 score) (16,17). Besides that, according to our findings, in this study SAPS-3 and SOFA are closely related to LOS in the ICU for more than 3 days.

In a recent study, it has been demonstrated that approximately one fourth of surgical patients in the ICU were late admission- not admitted promptly postoperatively- and developed postoperative complications. In their study, Silva et al. have claimed that clinical evaluation underestimates the risk and has low predictive value, whereas PSS usage may be helpful in ICU referral and admission as an objective criterion (4). In another study, Nassar et al. have verified the feasibility of SAPS-3 in surgical patients and recommended its use as a distinction tool in ICU eligibility (18). PSS could be customized to advance their performance in specific patient populations (13). Our findings suggest that SAPS-3 or SOFA could be used as an admission criterion after proper customization.

Some studies have compared the SOFA score with another PSS-Acute Physiology and Chronic Health Disease Classification System (APACHE) score- as a mortality prediction model to predict hospital mortality and concluded that the combination of both scores enhances prognostic value (19,20). In another study, initial SOFA score has been found comparable to APACHE 3 in the ICU mortality prediction (16).

The present study has some importance with the evaluation of different prognostic score systems in predicting mortality and relation to length of stay in ICU but it also has some limitations. First of all, one can claim that for comparison of different PSS, describing the sample size before the study is mandatory. As our study was designed in a retrospective manner this condition could not be achieved. Relatively small sample size limits the power of the analysis of goodness-of-fit Hosmer and Lemeshow Test which is poor to assess. Another potential limitation is being a single-center study with a different patients' case mix as compared to the original SAPS-3 hospital outcome cohort. Lastly, the data collector reliability could be criticized in this study. Even though this is an important topic, we are quite reliant that, in this study, bias related to inadequate data collection was limited, since collection was done by the ICU doctors.

CONCLUSION

We found that SAPS-3 score was significantly correlated not only with mortality rate, but also with LOS in ICU. Nonetheless SOFA score was not related to mortality, but related to LOS in the ICU. PSS are used to estimate mortality but they may be used to identify LOS in the ICU and postoperative complications. It can be concluded that SAPS-3 and SOFA scores may be used to prognosticate postoperative ICU requirement.

Ethics Committee Approval: Since our study was in the category of non-interventional clinical research with its retrospective structure, no ethics committee approval was applied.

Informed Consent: In extra formal consent other than the patients had given prior to hospitalization was not required for the current study since it was a case-control medical record review. No change in our current clinical practice and no randomization was performed.

Peer-review: Externally peer-reviewed.

Author Contributions: Consept - İ.M., Ş.B.; Design - İ.M., M.Ç.; Supervision - S.T., Ş.B; Resource - İ.M., S.S; Materials - İ.M., M.Ç.; Data Collection and/or Processing - İ.M., M.Ç., Ş.B., S.S; Analysis and Interpretation - İ.M., S.T., S.S.; Literature Search - İ.M., Ş.B.; Writing Manuscript - İ.M.; Critical Reviews - İ.M., S.T.

Conflict of Interest: The authors have no conflicts of interest to declare.

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2019; 35 (2): 124-130

SAPS-3 ve SOFA Skorlarının Cerrahi Yoğun Bakım Ünitesindeki hastaların sonuçları ile ilişkileri ve tahmin gücü

İbrahim Mungan[1], Şerife Bektaş[1], Mine Altınkaya Çavuş[1], Sema Sarı[1], Sema Turan[1]

[1] Türkiye Yüksek ihtisas Eğitim ve Araştırma Hastanesi, Yoğun Bakım Ünitesi, Ankara, Türkiye

ÖZET

Giriş ve Amaç: Cerrahi hastalarına yönelik bireysel risk bazen göz ardı edilmektedir ve hangi hastanın yoğun bakımda takibinin gerekliliğini gösteren mutlak bir kriter bulunmamaktadır. Bu hastaların kritik hastalığın şiddetini ölçmek için subjektif bir değerlendirme uygun olmadığından, prognoza yönelik skorlama sistemleri, cerrahi olanlar da dahil olmak üzere kritik hastalar için mortalite oranını ve prognozu değerlendirmek için kullanılır. Bu çalışmamızda, gastrointestinal cerrahi geçiren hastalarının SAPS-3 skoru ve SOFA skorunun kalibrasyon gücünü test etmeyi ve cerrahi yoğun bakım ünitesindeki hasta sonuçlarıyla ilişkisini tespit etmeyi amaçladık.

Gereç ve Yöntem: Bu retrospektif gözlemsel çalışma, Ağustos 2017 ile Aralık 2017 tarihleri arasındaki dönemde Gastroenterolojik Cerrahi Yoğun Bakım Ünitesinde gerçekleştirilmiştir. SAPS-3 ve SOFA skorunu hesaplamak için yoğun bakım ünitesine hastanın kabul edildiği gün kaydedilen fizyolojik veriler ve laboratuvar analizleri kullanıldı. Kayıtlar hastaneye yatıştan tıbbi taburculuk veya hastane mortalitesine kadar değerlendirildi. İstatistiksel analiz, 30 günlük mortaliteyi öngörmek için Mann-Whitney U testi ve ROC eğrilerini içermiştir.

Bulgular: Çalışmaya Gastroenterolojik Cerrahi Yoğun Bakım Ünitesine yatırılan toplam 233 hasta dahil edildi ve yoğun bakım ünitesinin kabul edilmesinin ana nedeni cerrahi problemlerdi. Mortalite oranı %2,6 (6 hasta) idi. Ortalama SAPS-3 skoru 32,5 ve SOFA skoru 30,1 idi. SAPS-3 skoru ile mortalite arasında anlamlı bir korelasyon gözlemlenmiştir, ancak istatistiksel olarak SOFA skoru ile anlamlı fark gözlemlenmemiştir. AUC ve ölüm tahmini olasılığı kullanılarak değerlendirilen ayırt edici güç, SAPS-3 skorları ile (AUC 0,754) tatmin edici iken, SOFA skoruyla (AUC 0,631) daha düşüktü.

Sonuç: SAPS-3 skorunun sadece mortalite oranıyla değil aynı zamanda yoğun bakım ünitesinde kalış süresi ile de anlamlı olarak ilişkili olduğunu bulduk. Bununla birlikte SOFA skoru mortalite ile ilişkili değildi, fakat yoğun bakımda kalış süresi ile ilişkiliydi. Skorlama sistemleri sadece mortaliteyi tahmin etmek için değil yoğun bakım ünitesinde kalış süresi ve ve postoperatif komplikasyonları tanımlamak için de kullanılabilir. SAPS-3 ve SOFA skorlarının postoperatif yoğun bakım ünitesi gereksinimini tahmin etmek için kullanılabileceği sonucuna varılabilir.

Anahtar Kelimeler: Basitleştirilmiş akut fizyoloji puanı, kademeli organ yetmezliği değerlendirmesi, cerrahi yoğun bakım ünitesi, mortalite, prediktif

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ORIGINAL ARTICLE
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Therapeutic effect of gastrografin and predictors of operative intervention in patients with adhesive small bowel obstruction: A randomized controlled study

Hamid Reza Khorshidi[1], Parviz Majidi[1], Azar Pirdehghan[2]

[1] Department of General Surgery, Hamadan University of Medical Sciences, Hamadan, Iran
[2] Department of Community and Preventive Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

ABSTRACT

Objective: The study aimed to investigate the therapeutic effect of gastrografin for the conservative treatment of patients with adhesive small bowel obstruction (ASBO) and to identify the predictors of failure of conservative treatment in these patients.

Material and Methods: A randomized controlled trial was conducted on 52 patients with the diagnosis of ASBO in 2016. 100 mL of Gastrografin and 100 mL of 0.9% saline solution were gavaged through the nasogastric tube in the case (n= 26) and control (n= 26) groups, respectively. Patients in the case group were subjected to plain abdominal X-Rays at 12, 24 and 48 hours after administration of gastrografin.

Results: Fifty-two patients with a mean age of 57.6 ± 11.4 years (range 37-81), including 34 (65.4%) males were enrolled into the study. The number of patients who were successfully conservatively treated in the case group was 21 (80.8%), which was significantly higher than 13 (50%) in the control group (p= 0.04). Among these patients, mean hospital stay in the case group was 37.2 ± 5.5 hours (range 28-46), which was significantly shorter than 45.8 ± 9.2 hours (range 36-61) in the control group (p= 0.004). In multivariate analysis, more than one previous laparotomy was the only predictor of failure of conservative treatment (p< 0.001).

Conclusion: Gastrografin may be associated with improvement of patients with ASBO. Lower number of previous laparotomies may be a predictor of successful conservative treatment of these patients.

Keywords: Gastrografin, adhesive small bowel obstruction, predictors

INTRODUCTION

Small bowel obstruction is one of the major causes of hospitalization which imposes significant health and economic burden (1). Adhesive small bowel obstruction (ASBO) due to prior laparotomy is the most common cause of small bowel obstruction which can be treated operatively or conservatively (2). Emergent operative intervention is performed in patients with ASBO with signs of strangulation or peritonitis which is technically difficult and is associated with bowel injuries and high postoperative morbidity (3,4). Conservative treatment including nasogastric tube decompression, intravenous fluid replacement and close monitoring may result in resolution of obstruction in most of the patients with ASBO; however, who fails conservative treatment should undergo operation (5).

Recently, utilization of water-soluble contrast agents mainly gastrografin has become more popular for the diagnosis and treatment of patients with ASBO (6). However, there is no consensus on the therapeutic effect and protocol of using these agents for conservative management of patients with ASBO. Several studies suggest that water-soluble contrast agents may be used for the diagnosis of resolution of obstruction, predicting the need for surgical intervention and simultaneously, can be used for conservative treatment of ASBO by stimulating the bowel movement due to their hyperosmolar effect and water movement into the small bowel lumen (7-11). Contrary, there are some studies showing that using water-soluble contrast agents has no therapeutic effect as a conservative treatment in patients with ASBO (12,13) .

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Corresponding Author
Hamid Reza Khorshidi
E-mail: khorshidi@umsha.ac.ir

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The present study aimed to investigate the therapeutic effect of gastrografin for the conservative treatment of patients with ASBO and to identify the predictors of failure of conservative treatment in these patients in our center.

MATERIAL and METHODS

Patient Selection

A randomized controlled trial was conducted on patients with the diagnosis of ASBO in 2016. Inclusion criteria were the patients with history of prior laparotomy presenting with obstruction related symptoms including abdominal distention and pain, vomiting, and constipation and radiological findings including air-fluid levels and small bowel distention in plain abdominal X-Ray. Patients with history of prior laparotomy within a month before the development of symptoms, signs and symptoms of strangulation or peritonitis including abdominal guarding tenderness or rebound tenderness, fever and leukocytosis of more than 10000, sepsis, septic shock, pregnancy, history of malignancy, allergy to iodine, incarcerated incisional or inguinal hernia were excluded from the study. Fifty-two patients were enrolled into the study and were randomly assigned to the case (n= 26) and control (n= 26) groups by simple randomization method using random numbers generated through computer. The CONSORT flow diagram showing the patients selection process is depicted in Figure 1.

Study Protocol

A nasogastric tube was inserted for each patient in the emergency department and stomach contents were drained for two hours. Then 100 mL of oral gastrografin solution (Bayer Schering Pharma, Germany) and 100 mL of 0.9% saline solution were gavaged through the nasogastric tube in the case and control groups, respectively. The nasogastric tube was clamped for two hours. Following clamping, all patients were continuously monitored and visited by a same surgeon. Patients in the case group were subjected to plain abdominal X-Rays at 12, 24 and 48 hours after administration of oral contrast media.

In patients in whom the oral contrast was detected in the cecum in each plain abdominal X-Ray, the nasogastric tube was removed and oral feeding with liquids was started. Conservative treatment was considered successful when improvement of patient symptoms with passage of gas or feces was occurred during the 48 hours of administration of contrast media or saline. Otherwise, conservative management was considered failed when strangulation or peritonitis was suspected during 48 hours of gavage administration, the contrast media was not reached to the cecum or no flatus or bowel movement occurred after 48 hours of gavage administration. In such cases, conservative treatment was terminated and emergent operative intervention including adhesiolysis or bowel resection through a midline incision was undertaken by the same surgeon.

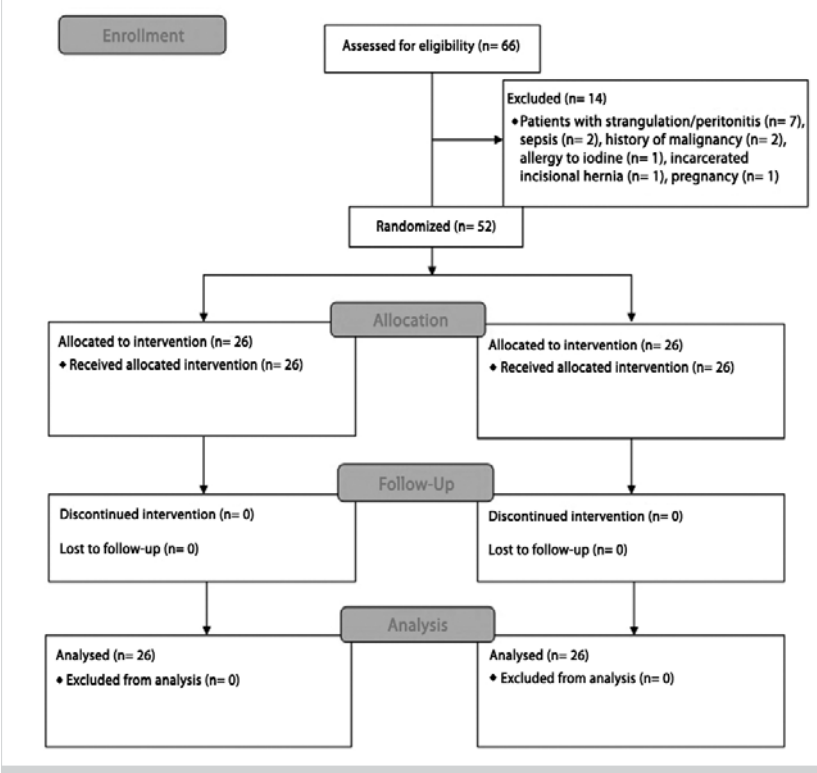

Figure 1. CONSORT flow diagram of the process of patient selection.

Ethics

This study was conducted after obtaining the approval of Ethics Committee of Hamadan University of Medical Sciences. Patients were enrolled into the study when the aims and objectives of the study were explained and a written informed consent was taken from each patient. The study has been registered in the Iranian Registry of Clinical Trials with reference number of IRCT201704259014N160.

Statistical Analyses

Data were analyzed using the SPSS statistical software (IBM SPSS Statistics for Windows, Version 23.0, IBM Corp., Armonk, NY, USA). Qualitative and quantitative data were compared using Chi-square and independent two sample-t tests, respectively. Univariate analysis and multivariate analysis using logistic regression were performed to assess predictors of failure of conservative treatment. P value less than 0.05 was considered significant.

RESULTS

Fifty-two patients with a mean age of 57.6 ± 11.4 years (range 37 - 81), including 34 (65.4%) males were enrolled into the study. As shown in Table 1, there was no significant difference between age, gender, indication and compartment of previous laparotomy, and number of previous laparotomies in the case and control groups. Duration of symptoms before admission were 33.2 ± 18.6 hours (range 5.8-91.3) and 30.8 ± 17 hours (range 9-75.3) in the case and control groups, respectively, with no significant difference (p= 0.63)

The number of patients who were successfully conservatively treated in the case group was 21 (80.8%), which was significantly higher than 13 (50%) in the control group (p= 0.04). Among these patients, mean hospital stay in the case group was 37.2 ± 5.5 hours (range 28-46), which was significantly shorter than 45.8 ± 9.2 hours (range 36-61) in the control group (p= 0.004).

In univariate analysis, longer duration of symptoms before admission and more than one previous laparotomy were the significant predictors of failure of conservative treatment in all patients with ASBO (p= 0.024 and p= 0.001, respectively). However, in multivariate analysis, more than one previous laparotomy was the only predictor of failure of conservative treatment (p< 0.001).

DISCUSSION

Our results showed that conservative therapy using Gastrografin was associated with significant improvement and substantial reduction in hospital stay of the patients with ASBO using a cut-off point of 48 hours after administration of gastrografin or saline for making decision to operate the patients with persistent symptoms.

Gastrografin is an extremely hypertonic water-soluble iodinated contrast agent having an osmolality of 1900 mOsm/L, which is six

Table 1. Demographic data of the patients and histopathology and anatomical location of the appendix in each group

	Case group (n= 26)	Control group (n= 26)	p
Gender, males %	61.5	69.2	0.77
Age (yrs/old)	56.6 ± 10.7* (range 38-75)	58.6 ± 12.2 (range 37-81)	0.52
Indication of previous abdominal operation			
Appendicitis	13	10	0.58
Perforated peptic ulcer	5	6	1
Volvulus	4	5	1
Cholecystitis	2	3	1
Hernia	0	1	1
Gynecologic	2	1	1
Number of previous abdominal operations			0.7
1	23	21	
2	3	5	
Previous operation for ASBO	2	4	0.64
Abdominal compartment of previous operation			
Infracolic	13	10	0.58
Supracolic	7	8	1
Both	6	8	0.75

* Mean ± standard deviation.

ASBO: Adhesive small bowel obstruction.

times that of plasma. Following administration of Gastrografin, the pressure gradient is increased across the lumen of the small bowel which results in absorption of fluid into the lumen of the intestine, decrease of bowel wall edema, increase of peristalsis and subsequent resolution of small bowel obstruction (10).

Therapeutic effect of water-soluble contrast agents have been investigated in many studies. In a randomized controlled trial by Haule et al., 22 out of 25 (88%) patients with ASBO have been treated successfully with gastrografin compared to 16 out of 25 (64%) patients undergoing standard conservative treatment with no significant difference. However, in this study, the use of gastrografin was attributed to a significant reduction in length of hospital stay and time for resolution of obstruction. The authors used a cut-off point of 5 days after randomization for deciding to operate (14). Another randomized controlled trial by Rahmani et al. on 84 patients with ASBO has shown that the need for surgical intervention in contrast to length of hospital stay was not significantly reduced in patients who were treated with gastrografin compared to the control ones using a cut-off point of 4 days (15). In a recent multicenter randomized controlled trial by Scotté et al., administration of gastrografin in 121 patients with ASBO has not been found to be associated with reduction in the rate of operation or length of hospital stay using cut-off point of 48 hours waiting compared to 121 patients in the control group (24% vs. 20% and 3.8 vs. 3.5 days, respectively) (11). On the other hand, similar to our data, in a multicenter observational study by Zielinski et al. a significant reduction in rates of surgical intervention and hospital stay has been reported using cut-off point 3-5 days waiting in 173 patients treated with gastrografin for ASBO compared to 143 patients conservatively managed without gastrografin (20.8% vs. 44.1% and 4 vs. 5 days, respectively) (6). Also, a recent systematic review and meta-analysis by Ceresoli et al., have supported our findings, showing that administration of water soluble contrast agents resulted in a significant reduction of need for surgical intervention and length of hospital stay (16). The observed discrepancy through various studies may be due to different study designs, sample sizes and treatment protocols including using different cut-off points for deciding to operate.

In our study, more than one previous laparotomy was the only predictor of failure of conservative treatment of ASBO. Available data vary through studies about predictors of failure of conservative treatment of ASBO. Similar to ours, in a study by Bueno-lledo et al., age and number of previous laparotomies are the predictors of failure of conservative treatment of ASBO (17). A study by Komatsu et al. have shown that in univariate analysis for predictors of failure of conservative treatment of ASBO, age and number of previous laparotomies are significant however, in multivariate analysis the number of previous laparotomies is not significant (18). In contrast to our data, in a study by Miquel et al., age over 75 years was the predictor of failure of conservative treatment of ASBO after colorectal resection surgery while number of previous laparotomies or duration of symptoms before admission were not the predictors (19). Besides, Zielinski et al. 2010 concluded that either the age or number of previous laparotomies were not predictors of failure of conservative treatment of ASBO (20).

CONCLUSION

The present study showed that administration of gastrografin may be associated with improvement of patients with ASBO, and lower number of previous laparotomies may be a predictor of successful conservative treatment of these patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Hamadan University of Medical Sciences.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Consept - H.R.K., P.M.; Design - H.R.K., P.M., A.P.; Supervision - H.R.K.; Materials - P.M.; Data Collection and/or Processing - P.M., A.P.; Analysis and Interpretation - H.R.K., P.M.; Literature Search - P.M., A.P.; Writing Manuscript - P.M., A.P.; Critical Reviews - H.R.K.

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ORİJİNAL ÇALIŞMA-ÖZET
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Adheziv ince bağırsak obstrüksiyonu olan hastalarda gastrografinin terapötik etkisi ve operatif girişim öngörücüleri: Randomize kontrollü çalışma

Hamid Reza Khorshidi[1], Parviz Majidi[1], Azar Pirdehghan[2]

[1] Hamadan Tıp Bilimleri Üniversitesi, Genel Cerrahi Anabilim Dalı, Hamadan, İran
[2] Hamadan Tıp Bilimleri Üniversitesi, Topluluk ve Önleyici Tıp Anabilim Dalı, Hamadan, İran

ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, adheziv ince bağırsak obstrüksiyonu (AİBO) olan hastaların konservatif tedavisinde gastrografinin terapötik etkisini araştırmak ve bu hastalarda konservatif tedavinin başarısızlık öngörücülerini belirlemekti.

Gereç ve Yöntem: 2016 yılında AİBO tanısı almış olan 52 hasta üzerinde randomize kontrollü bir çalışma yürütüldü. Olgu (n= 26) ve kontrol (n= 26) gruplarında ardışık olarak 100 mL gastrografin ve 100 mL %0,9'luk salin solüsyon nazogastrik tüp aracılığıyla verildi. Olgu grubundaki hastalar, gastrografin alımını takip eden 12, 24 ve 48. saatlerde direkt karın grafisi incelemesine tabi tutuldu.

Bulgular: Otuz dördü (%65,4) erkek olmak üzere toplam 52 hastanın ortalama yaşı 57,6 ± 11,4 yıl (aralık: 37-81) idi. Olgu grubunda başarılı bir şekilde konservatif olarak tedavi edilen hasta sayısı 21 (%80,8) idi ve bu sayı control grubundaki 13 (%50) hastadan anlamlı derecede yüksekti (p= 0,04). Bu hastaların içerisinde olgu grubunun ortalama hastanede kalış süresi 37,2 ± 5,5 saat (aralık: 28-46) olarak bulundu ve bu kontrol grubunun ortalama hastanede kalış süresinden [45,8 ± 9,2 saat (aralık 36-61)] anlamlı derecede daha kısaydı (p= 0,004). Çok değişkenli analizde, konservatif tedavinin başarısızlık öngörücüsü önceden geçirilmiş birden fazla laparotomi olarak bulundu (p< 0,001).

Sonuç: Gastrografin, AİBO'lu hastalarda iyileşme ile ilişkili olabilir. Daha az sayıda önceden geçirilmiş laparotomi başarılı konservatif tedavinin öngörüsü olabilir.

Anahtar Kelimeler: Gastrografin, adheziv ince bağırsak obstrüksiyonu, öngörücüler

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CASE SERIES
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Postoperative hemorrhage complications following the Whipple procedure

Osman Nuri Dilek[1], Oğuzhan Özşay[2], Turan Acar[2], Emine Özlem Gür[1], Salih Can Çelik[2], Fevzi Cengiz[2], Nejat Cin[2], Mehmet Haciyanlı[1]

[1] Department of General Surgery, Izmir Katip Celebi University School of Medicine, Izmir, Turkey
[2] Clinic of General Surgery, Ataturk Training and Research Hospital, Izmir, Turkey

ABSTRACT

Objective: Although the Whipple operation is an essential surgical technique, its high morbidity (30% to 60%) and mortality (5%) are problems to be addressed. The incidence of postoperative hemorrhage has been reported between 5% and 16% in the literature. In this study, the data and results regarding postoperative hemorrhage complications from our clinic were evaluated.

Material and Methods: The files of 185 patients who had undergone Whipple operation in our hospital in the last five years were evaluated retrospectively, and the causes of hemorrhage were attempted to be determined.

Results: It was found that 6 out of the 13 (7%) patients who had hemorrhage died. In six of there 13 cases, hemorrhage occurred due to fistulas from the portal vein, gastroduodenal artery, and pancreatic arteries at variable periods. Two cases were found to have developed disseminated intravascular coagulation as a result of sepsis. Early intervention was performed in two cases who bled from the meso veins and in one case who bled from the portal vein. Laparotomy and hemostasis were performed in a patient who bled from the gastric anastomosis line. In a patient who had been taking low molecular weight heparin, bleeding from the drains and nasogastric tube stopped following the cessation of the drug.

Conclusion: Preventive procedures such as connection of the vascular structures, use of vascular sealants, omental patching during surgery, and reducing the risk of complications by using somatostatin analogs were performed to prevent hemorrhages after Whipple operations. In addition to standard methods, angiography and embolization have emerged as effective methods in the diagnosis and treatment of hemorrhages. Furthermore, determination and elimination of independent risk factors, such as jaundice, affecting fistula formation and bleeding in the perioperative period, is important for prevention.

Keywords: Complication, hemorrhage, pancreas, treatment, whipple operation

INTRODUCTION

Although the Whipple operation is an essential surgical technique for periampullary tumors, its high morbidity (30% to 60%) and mortality (5%) rates are problems to be addressed (1-3). Pancreatic fistulas (2% to 62%) are among the most common complications after Whipple procedure (1,4). The incidence of postoperative hemorrhage has been reported as 5% to 20.2% in the literature and mortality due to hemorrhage as 15% to 58% (1,5-7). Hemorrhages may arise from the suture lines in the early period, and this study aimed to evaluate the data and results regarding postoperative hemorrhage problems in cases who developed infections and fistula in the days following surgery in our clinic.

MATERIAL and METHODS

The files of 185 patients who had undergone Whipple operation in our hospital in the last five years (2011 to 2015) were evaluated retrospectively, and the causes of hemorrhage were attempted to be identified. As a routine procedure, all patients signed consent forms containing information about the procedures and complications. Cases who had hemorrhoids, anal fissure, and etc. were excluded from the study. Our patients were classified as A, B, or C on the basis of postoperative pancreatic hemorrhage (PPH) consensus classification by the International Study Group of Pancreatic Surgery in 2007 as onset of hemorrhage (early or late), localization (extraluminal or intraluminal), and intensity (mild or severe) (Table 1) (5,6). Hemorrhages seen in the first 24 hours were identified as early hemorrhage. Leaking hemorrhages originating from drains or nasogastric tubes in the early postoperative period, those that stopped spontaneously, and those that did not alter the patient's hemodynamic stability were not taken into consideration. Mild hemorrhage

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Corresponding Author
Osman Nuri Dilek
E-mail: osmannuridilek@gmail.com

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Table 1. Patient characteristics

Patient no	Age/Sex	Indication for Whipple /PD	Etiology	Bleeding site	ISPG group	Onset of bleeding	Procedure	Outcome
1.	58/M	Bile duct tumor	PO Arrest-CPR-Sepsis	DIC	C	Day 5	ICU	Died
2.	65/M	Pancreatic carcinoma	PJ Haematoma	Pancreatic artery?	B	Day 4	Primary suture	Died
3.	66/M	Pancreatic carcinoma	Fistula	GDA	B	Day 35	Laparotomy + Primary suture + Angiography + Embolization	Survived
4.	60/M	Ampullary cancer	LMW Heparin	Drain + Nasogastric sond	A	Day 14	Stop LMW Heparin	Survived
5.	69/M	Ampullary cancer	Pancreatic fistula, sepsis	DIC	C	Day 11	ICU	Died
6.	42/F	Pancreatic carcinoma	Inadvertent surgery?	GJ Anastomosis	A	Day 1	Laparotomy + Gastrotomy + Primary suture	Died
7.	65/F	Ampullary cancer	Pancreatic fistula	Portal vein		Day 8	Laparotomy + Primary suture	Survived
8.	74/M	Pancreatic carcinoma	Pancreatic fistula	Portal vein	C	Day 27	Angiography + Laparotomy + Primary suture	Died
9.	67/F	Pancreatic carcinoma	Pancreatic fistula, PJ leakage + GJ leakage	Traumatic Portal vein laceration?	C	Day 15	Laparotomy + Primary suture	Died
10.	65/M	Bile duct tumor	Pancreatic Fistula	GDA	B	Day 7	Angiography + Laparotomy + Primary suture	Survived
11.	58/M	Pancreatic carcinoma	Inadvertent surgery?	Mesenteric vein branches	B	Day 2	Laparotomy + Primary suture	Survived
12.	67/M	Ampullary cancer	Pancreatic fistula	Mesenteric vein	C	Day 7	Laparotomy + Primary suture	Died
13.	45/M	Pancreatic carcinoma	Inadvertent surgery?	Mesenteric artery and vein branches	B	Day 1	Laparotomy + Primary suture	Survived

ISPG: International Study Group of Pancreatectomy; GDA: Gastroduodenal artery; PJ: Pancreaticojejunostomy; GJ: Gastrojejunostomy; PO: Postoperative; DIC: Disseminated intravascular coagulation; ICU: Intensive care unit; PD: Pancreaticoduodenectomy.

was identified as the condition where the patient was hemodynamically stabilized or where no need for any interventional or surgical procedures was identified during the follow-up of the patient. Severe hemorrhage was identified as hemorrhage with a high flow rate, originating from the drains or lumens, which altered the hemodynamic stability of the patient. Deaths seen within the postoperative 30 days were accepted as postoperative death. In our hospital, low molecular weight heparin (LMWH) is routinely administered 12 hours after surgery and is stopped if any hemorrhage is suspected. Angiography and embolization can be performed in daytime cases.

RESULTS

A total of 185 pancreticoduodenectomy, including 165 classical Whipple procedures and 20 pylorus-preserving pancreatoduodenectomy, were performed in our hospital in the last five years (2011 to 2015) due to tumors of the periampullary region. Three of the patients were females, and 10 were males. Mean age was 61.6 years (range, 42 to 72).

It was found in 13 (7%) of the patients who had undergone whipple operations that, a procedure was performed due to hemorrhage. Among the patients who had follow-ups due to hemorrhage, 9 (77%) underwent surgeries and 6 (46%) died in the early period (Table 1). In our series, pancreatic fistula was detected in 46 (24.8%) patients, and 6 (13%) of these patients had complications of hemorrhage due to fistulas. It was also found that endoscopic retrograde cholangiopancreaticography (ERCP) was performed diagnostically in nine patients, a stent was placed to lower billirubin levels in six patients, and a drain was placed with percutaneous transhepatic cholangiography in two patients.

In seven patients in our series, there was a combination of wide duct (4 to 7 mm) and soft pancreatic texture; the presence of fistula was detected in three of these patients as the cause of hemorrhage. In three of our cases, soft pancreatic texture and the presence of a 2 mm duct were determined. In three of our cases, normal pancreatic tissue was observed with duct widths

ranging from 2 to 5 mm (Table 1). Among our patients with hemorrhage, three of the five patients whose billirubin levels were high (direct bilirubin, range: 10.6 to 21.6 mg/dL) died as a result of hemorrhage complications. Another result we found in our patients was that serum protein levels were normal in three patients and below normal in the remaining. Platelet count was higher than normal in five of our patients and was normal in the remaining. In cases who did not develop fistulas, C-reactive protein (CRP) levels were within normal limits in the preoperative period, increased in the postoperative early period, and decreased progressively. In all cases that developed fistula and anastomotic leakage, CRP levels continued to increase until clinical recovery was obtained. In general, it was found that in our patients who developed fistulas and had high CRP levels, blood calcium levels decreased and remained below normal.

Of our two cases who developed hemorrhage in the early postoperative period, one underwent surgery due to hemorrhage from the gastric anastomosis (nasogastric tube) and the other underwent surgery due to hemorrhage from the branches of the mesenteric vein (drain), both of whom discharged with complete healing. Six of our patients were found to have bled from the portal vein (three cases), gastroduodenal artery (two cases), meso veins, and pancreatic artery (one case) due to fistulas at variable periods. Hemorrhage from the portal vein after fistula was seen on the postoperative 8th, 15th, and 27th days, and two of these patients died after surgery (Table 1). In one of the cases that was on follow-up due to fistula and bleeding from the nasogastric tube, anastomotic leakage was detected by endoscopy. The patient was taken into surgery on the postoperative 15th day; however, the patient died from hemorrhage found to have originated from erosion of the portal vein. In another patient who had blood coming out of the drain on the postoperative 7th day, hepaticojejunostomy and pancreaticojejunostomy were found to be opened, and hemorrhage from the pancreatic artery and branches of the mesenteric vein were seen. In two cases, laparotomy was performed on the 2nd and 4th days due to bleeding from the drains; hemorrhages arising from the pancreatic artery and branches of the portal vein were repaired.

Two cases were found to have developed disseminated intravascular coagulation (DIC), and these patients died as a result of sepsis. In a patient who had been taking LMWH, bleeding from the drains and nasogastric tube stopped following the cessation of the drug.

DISCUSSION

Hemorrhage after Whipple surgery is a rare but serious complication that increases mortality. In the early period, hemorrhage may develop from technical problems, bleeding/clotting disorders, and factors related to the patient; however, in the latter periods, hemorrhage emerges as a serious problem during the course of fistula and anastomosis-related problems (1,2). Hemorrhage incidence in the postoperative period reported in the literature (5% to 16%) was similar to the results of our series (7%). However, some publications report that hemorrhage risk is higher (16% to 45%) in cases who develop fistulas (1,4). Our mortality in these series was 8.5%, whereas that in our patients with hemorrhage was 46%.

A medical approach is preferred for the treatment of hemorrhages. In Grade A patients, a conservative approach is more frequently performed in the foreground, whereas in Grade B and C patients, additional processes are required to identify the localization of the hemorrhage. Nasogastric tube (35%), decrease in hemoglobin level (17%), hemodynamic instability (15%), blood coming out of the drains (11%), and the presence of melena (9%) may be helpful to make a diagnosis and determine the source of bleeding (8). Which can be determined by computerized tomography (CT) angiography in half of these cases (8). In cases where hemodynamic stability is preserved, first actions are monitoring the patient's hemodynamic levels and drains. Darnis et al. have stated that in their series of 285 cases with hemorrhage, the hemorrhages were stopped with a medical approach in 32% of cases; yet in 68% of cases, intervention (surgical, endoscopic, or embolization) was needed (8,9). In our series, CT angiography was performed in seven cases which revealed; hemorrhage from the portal vein in two cases, from the gastroduodenal artery in one case, and from the pancreatic artery in one case. The hemorrhage was stopped by embolization in one of these patients, and the rest underwent surgery. In a Grade A patient in our series, the hemorrhage stopped after conservative treatment and cessation of LMWH.

Hemorrhages into the lumen are seen in earlier periods. The most common type is hemorrhage arising from pancreaticojejunal anastomosis. In hemorrhages arising from gastrojejunal anastomosis, both diagnostic and therapeutic procedures may be performed by endoscopists. In a series by Eckardt et al., the authors have stated that the source of bleeding may be detected and treated endoscopically in one third of hemorrhages arising from gastrojejunostomy (10). Variable approaches are used for this purpose, such as injection, sclerotherapy, and clip application.

It is expressed that the routine use of somatostatin analogs in the postoperative period to both suppress pancreatic secretion and prevent complications due to fistula, particularly bleeding in cases where fistulas have developed, reduces morbidity; however, these analogs have no positive effects on mortality (11). However, in some cases, protective effects have been reported (3). It was found in our series that the risk of hemorrhage was higher (13%) in patients who developed fistulas. We also use somatostatin analogs routinely in our patients with fistulas. Soft pancreatic texture, thinness of the pancreatic duct, and the presence of fistulas are defined as major risk factors for hemorrhage (8). Tani et al. have defined the male gender, prolonged surgery,

and blood transfusion as independent risk factors (12). Some studies report that parameters such as prolonged hospital stay, ERCP and stenting, the presence of preoperative jaundice, trauma/resection of the splenic vessels, additional surgical procedures, older age, the presence of intraabdominal infection, and nutritional risk index are factors that increase the risk of hemorrhage (2,7-9,12-14). Most of the factors mentioned above were present in our series (Table 1). It is to our belief that even though ERCP and stenting provide an advantage in reducing the bilirubin levels of the patient, it may cause new problems, such as technical difficulties and increasing the risk of infection by reducing the diameters of the ducts. It was detected that the duct was thin and the texture of the pancreas tissue was soft in cases with continued pancreatic secretion from the duct, whereas the duct was wide and the texture of the pancreas tissue was hard in cases in which the duct of Wirsung was invaded by the tumor.

Elevated CRP levels in the early postoperative period is an expected condition; however, continued elevation on the postoperative third day may be a precursor of fistulas and additional complications. In our series, the continuation of elevated CRP levels was evaluated as a precursor of fistula rather than hemorrhage. In the clinical study by Ansorge et al., it has been stated that elevated CRP levels may be an important precursor of fistula development (15,16).

In cases with hemorrhage, the first preferred methods for locating the hemorrhage site are contrast-enhanced CT, CT angiography, and interventional angiographic embolization (Figure 1). The hemorrhage site can be localized by contrast-enhanced CT in half of these cases (8). It is shown in studies that the most important causes are hemorrhages arising from the stump of the gastroduodenal artery or pancreatic vessels and rupture or erosion of pseudoaneurysms of the splenic vessels. It is stated that hemorrhages can be stopped in 50% to 80% of cases who undergo embolization (1,8). Darnis et al. recommend performing routine splenic artery embolization in cases with hemorrhage who undergo pancreaticoenteric anastomosis (8). Roulin et al. state that angiography and embolization can be performed easily in all vessels except for the hepatic artery and mesenteric artery and that these procedures are at least as effective as surgery (1). In our series, foci of hemorrhages that arose from the portal vein (three patients), gastroduodenal artery (two patients), pancreatic artery, and mesenteric veins were detected in six of the Grade B and C cases. Hemorrhage from the gastroduodenal artery was successfully stopped by inserting an angiographic coil in only one of these cases. In three of the 13 patients who underwent angiography, the bleeding site could be localized. However, in two of these patients, interventional coiling was not feasible due to the direct vicinity of the bleeding source to the portal vein. These methods were performed during the day because our hospital does not have 24-hour availability of endoscopists and interventional radiologists.

Some studies suggest covering the mesenteric artery/vein and the stumps of the cut splanchnic vessels with omental or fal-

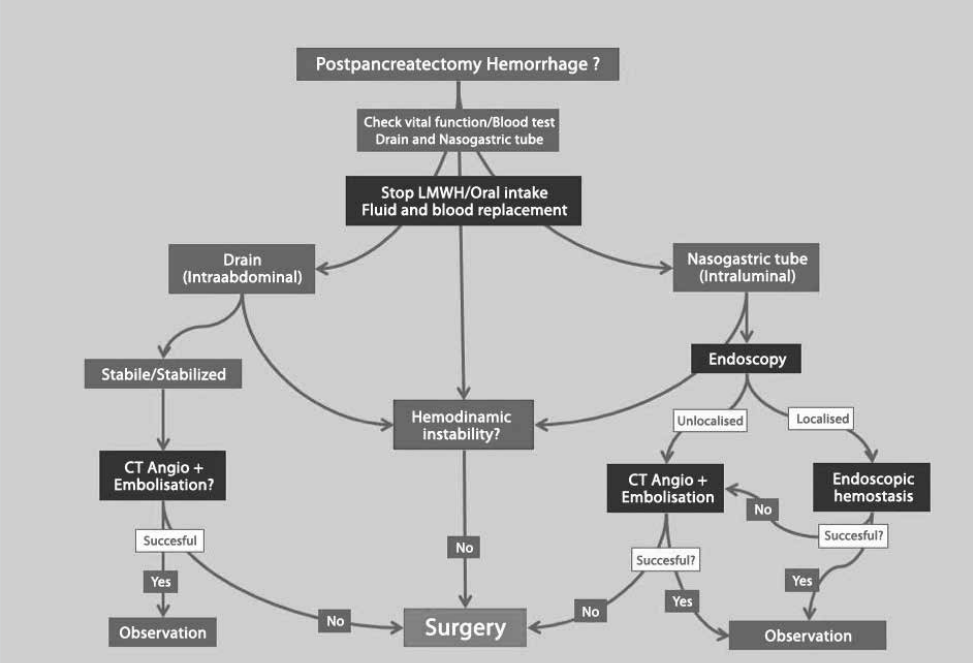

Figure 1. Algorithm for postoperative pancreatic hemorrhage.

ciform flaps to prevent hemorrhage (17-19). In a clinical study performed in Japan, it has been stated that the risk of aneurysm development due to erosion is four times higher in patients without omental flap applications and that flaps are effective in preventing the formation of aneurysms (17). However, in the literature, in a series with low numbers of cases, the use of omental flap is described as a protective and useful procedure, whereas in meta-analyses and Cochrane studies, the use of omental flap is not described as useful (12,20,21).

It is stated that hemorrhages arising from the cut pancreatic surfaces are important in etiology (22). Binding the vascular structures in pairs, using vessel sealers, and performing omental patches are suggested methods to prevent hemorrhages arising from pancreatic vessels. Adherence to the rules of surgical technique and hemostasis plays an important role in preventing hemorrhages in the early period (14,23,24). Surgery remains the only option in conditions when conservative approaches, radiologic intervention, and endoscopic procedures are insufficient (Figure 1). Surgical treatment is performed in 30% to 49% of the hemorrhages seen in patients with pancreaticoduodenectomy (1,23,25,26). In our series, this rate was found to be 77% due to lack of 24-hour availability of endoscopy and interventional radiology.

CONCLUSION

In addition to known methods, angiography and embolization have emerged as effective and promising methods in the diagnosis and treatment of hemorrhage. Furthermore, determination and elimination of independent risk factors, such as jaundice which affect fistula formation and bleeding in the perioperative period, is important for prevention.

Informed Consent: Written informed consent was obtained from all the patients who participated in this study.

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OLGU SERİSİ-ÖZET
Turk J Surg 2019; 35 (2): 136-141

Whipple ameliyatı sonrasında karşılaşılan kanama problemi

Osman Nuri Dilek[1], Oğuzhan Özşay[2], Turan Acar[2], Emine Özlem Gür[1], Salih Can Çelik[2], Fevzi Cengiz[2], Nejat Cin[2], Mehmet Haciyanlı[1]

[1] İzmir Katip Çelebi Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, İzmir, Türkiye
[2] Atatürk Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, İzmir, Türkiye

ÖZET

Giriş ve Amaç: Whipple ameliyatları, halen vazgeçilmez bir ameliyat tekniği olmasının yanında, yüksek morbiditesi (%30-60) ve mortalitesi (%5) ile cerrahinin çözüm bekleyen önemli sorunlarından biri olmaya devam etmektedir. Postoperatif hemoraji ise literatürde %5-16 sıklıkta görülmektedir. Bu çalışmada ameliyat sonrası karşılaşılan kanama problemleriyle ilgili olarak kliniğimiz verileri ve sonuçları irdelenmiştir.

Gereç ve Yöntem: Son beş yılda, hastanemizde Whipple ameliyatı yapılan 185 hastamızın dosyaları retrospektif olarak değerlendirilerek kanama nedenleri ortaya konulmaya çalışılmıştır.

Bulgular: Toplam 13 (%7) hastada kanama nedeniyle işlem yapıldığı, bunlardan altısının eksitus olduğu saptandı. Olgulardan altısında fistüle bağlı olarak değişen süreler içerisinde portal ven, gastroduodenal arter ve pankreas arterlerinden kanadığı saptandı. Sepsis sonucu iki olguda dissemine intravasküler koagülasyona bağlı kanamaların geliştiği saptandı. İki olguda mezo venlerinden, bir olguda ise portal venden gelişen kanamaya erken dönemde müdahale edilmiştir. Mide anastomoz hattından kanama gelişen bir hastamızda laparotomi ve hemostaz yapıldı. Profilaktik düşük molekül ağırlıklı heparin verilmekte olan bir hastamızda dren ve nazogastrik sondalardan olan kanamanın ilacın kesilmesini takiben durduğu saptandı.

Sonuç: Whipple ameliyatı sonrasında görülen kanamaların durdurulması amacıyla çeşitli koruyucu işlemler uygulanmaktadır. Sonuç olarak, bilinen yöntemlerin yanında, anjiyografi ve embolizasyon kanamaların tanı ve tedavisinde oldukça etkili bir yöntem olarak ortaya çıkmaktadır. Ayrıca, kanama ve fistül oluşumuna etkili sarılık gibi bağımsız risk faktörlerinin peroperatif dönemde belirlenmesi ve giderilmesi korunma için önemlidir.

Anahtar Kelimeler: Komplikasyon, kanama, pankreas, tedavi, whipple ameliyatı

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CASE SERIES
Turk J Surg 2019; 35 (2): 142-145

Approach to primary thyroid lymphoma: case series

Nihan Acar[1], Turan Acar[1], Arzu Avcı[2], Mehmet Haciyanlı[1]

[1] Clinic of General Surgery, Izmir Katip Celebi University Atatürk Training and Research Hospital, Izmir, Turkey
[2] Clinic of Pathology, Izmir Katip Celebi University Atatürk Training and Research Hospital, Izmir, Turkey

ABSTRACT

Primary thyroid lymphomas are rare thyroid neoplasms. Mucosa Associated Lymphoid tissue (MALT) lymphoma and diffuse large B-cell Non-Hodgkin lymphoma are the most common types. It is more common in the elderly, and especially in women. Patients usually present with a rapidly growing mass in the neck. This article aimed to present the epidemiological features, treatment and prognostic factors of thyroid lymphomas by retrospectively reviewing 4 patients with thyroid lymphoma. Four patients were treated for primary thyroid lymphoma, two of whom were women and two were men, with a mean age of 63.7 (51-74) years. Common complaint of those patients was the sudden swelling of the neck. Two patients were diagnosed with fine needle aspiration biopsy (FNAB) and the other two patients were diagnosed with surgical excision. Chemotherapy and radiotherapy were applied to all four patients. While one patient died in the second year of follow-up, the other three patients are still being followed. Primary thyroid lymphomas are not aggressive tumors, and the most effective treatment is radiotherapy.

Keywords: Thyroid, lymphoma, MALT, non-hodgkin

INTRODUCTION

Papillary thyroid carcinoma is the most common type of thyroid cancers. On the other hand, primary thyroid lymphomas (PTL) are rare tumors, 1-5% of all thyroid neoplasms and approximately 2% of the extranodal lymphomas (1). Male to female ratio is 1:3, and it mostly occurs after the age of 50 (age range, 50-65). Thyroid lymphomas are usually associated with Hashimoto's thyroiditis and they develop on a background of chronic thyroiditis (2).

Histologically, Hodgkin or Non-Hodgkin Lymphomas may be identified. Although B-cell Non-Hodgkin Lymphoma is the most common type, T-cell lymphoma of the thyroid has also been rarely reported (3). This study aimed to present the epidemiological features, diagnosis, treatment and prognostic factors of thyroid lymphomas by retrospectively reviewing medical records of four patients with thyroid lymphoma.

CASE REPORTS

Demographics, clinicopathologic features, diagnosis and treatment methods of the patients are given in Table 1.

Two out of four patients (50%) were female and the mean age was 63.7 (range: 51-74) years. All patients complained of suddenly growing mass of the neck. In addition, there were also systemic symptoms (75%), fever and pressure symptoms (50%) such as respiratory distress and hoarseness. Physical examination revealed diffuse cervical lymphadenopathy (LAP) in all patients, and one patient had solid palpable thyroid nodules with irregular surface. There were no palpable lymph nodes in the rest of the systemic examinations. One patient had elevated Thyrotrophin-Stimulating Hormone (TSH) level (normal range: 0.4-3.0 uIU/mL) (hyperthyroid) and one patient had low TSH level (hypothyroid). TSH levels of the other two patients and all other laboratory parameters of all patients were normal. Thyroid ultrasound (US) was performed in all patients as an initial imaging test. US showed bilaterally heterogeneous and hyperplastic thyroid gland in all patients. Besides, all patients

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Corresponding Author
Turan Acar
E-mail: drturanacar1982@gmail.com

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Table 1. Demographics, clinicopathologic features, diagnosis and treatment methods of the patients

	Case 1	Case 2	Case 3	Case 4
Sex	Male	Male	Female	Female
Age	74	68	62	51
Thyroid hormone levels	Hypothyroid	Euthyroid	Hyperthyroid	Euthyroid
Diagnostic methods	FNAB	BTT	FNAB	BTT
Pathology result	High grade lymphoma	Papillary carcinoma + diffuse large B-cell Non-Hodgkin lymphoma	Diffuse large B-cell Non-Hodgkin lymphoma	MALT lymphoma (developed in Hashimoto thyroiditis' background)
Stage	Stage 3	Stage 3	Stage 3	Stage 1
Treatment	Surgical excision + CT + RT	Surgical excision + CT + RT	CT + RT	Surgical excision + CT + RT
Mortality	Follow-up	Follow-up	Exitus	Follow-up

FNAB: Fine needle aspiration biopsy; BTT: Bilateral total thyroidectomy; MALT: Mucosa associated lenfoid tissue; CT: Chemotherapy; RT: Radiotherapy.

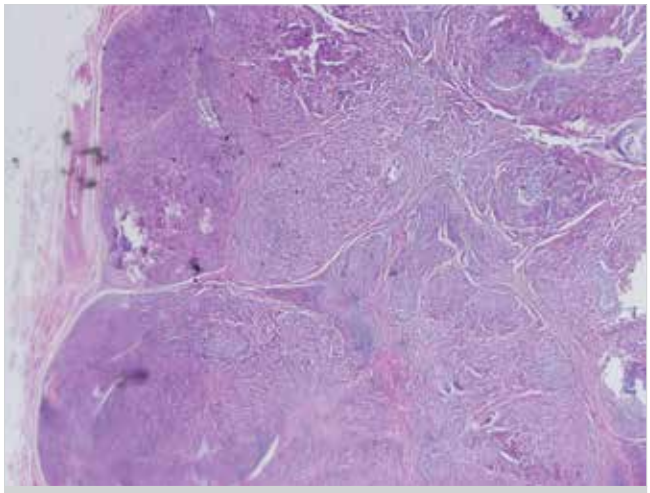

Figure 1. Diffuse atypical lymphoid infiltration and interstitial small follicles consisting of thyrocytes. X2, H&E stain.

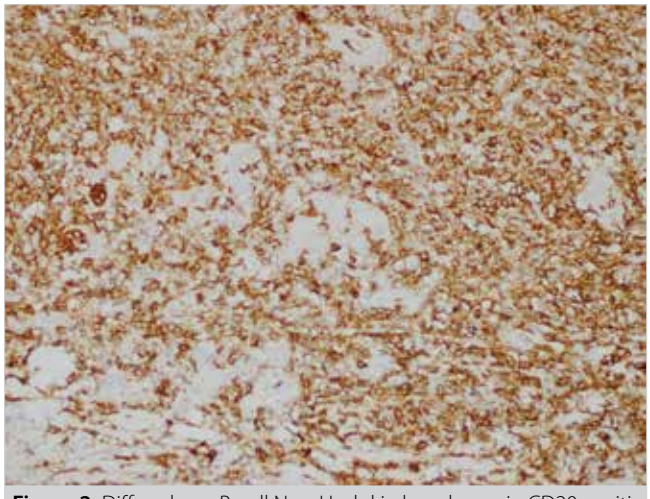

Figure 2. Diffuse large B-cell Non-Hodgkin lymphoma in CD20 positive neoplastic cells. X20.

had multiple enlarged cervical lymph nodes. Fine needle aspiration biopsy (FNAB) was performed on all patients for diagnosis. However, only two of our patients could be diagnosed as thyroid lymphoma and the other two patients were non-diagnostic with FNAB. Therefore, these two patients underwent surgical excision (total thyroidectomy) and their pathological examinations were reported as primary thyroid lymphoma (Figure 1). In addition, CD 20 was positive and CD 3, CD 45 RO, Bcl-6 and Bcl-2 were found to be negative in immunohistochemical studies in both patients (Figure 2).

Systemic cancer screening and staging were performed with computed tomography. According to Ann-Arbor Staging System, one patient was stage 1 and the other three patients were stage 3. All patients received chemotherapy (CT) and radiotherapy (RT). One patient died in the second year of follow-up. The rest of the patients who underwent total thyroidectomy and received combined therapy (CT + RT) are at the mean 46th (range: 38- 59) month of follow-up and there is no evidence of systemic or local recurrence.

Informed consent was obtained from both patients. Consents were also obtained to perform scientific studies.

DISCUSSION

PTL is a rare tumor of the thyroid and more commonly seen in middle aged-elder women. MALT lymphoma and diffuse large B-cell non-Hodgkin lymphoma are the most common types (3). In our study, the patients were also elderly, but on the contrary, gender distribution was identical.

PTL may present with rapidly growing mass, difficulty in swallowing, stridor, change in voice quality and/or pressure symptoms. With these symptoms and findings, they show some similarity to anaplastic thyroid cancers. It is detected as a solid mass that cannot be clearly distinguished with trachea or esophagus on physical examination. Salivary gland neoplasms, thyroglos-

sal duct cyst, laryngocele, teratoma, dermoid cyst, thymic cyst, paraganglioma, neurinoma and lipomas should be considered in differential diagnosis.

Lapadat et al. have shown that most primary thyroid lymphomas develop on the chronic thyroiditis/Hashimoto thyroiditis pattern (4). Thyroid lymphoma should be considered in patients with Hashimoto thyroiditis when enlargement in the thyroid gland remains, despite the thyroxine replacement therapy. Hashimoto thyroiditis was found in two of our patients who underwent thyroidectomy. Besides, 30-40% of the patients may present with hypothyroidism (5).

FNAB is sufficient for diagnosis when the samples are evaluated by an experienced cytologist. FNAB of the lesion reveals numerous large neoplastic cells with scant to moderate amount of cytoplasm, irregular nuclear contours and conspicuous nucleoli in a background of many small lymphocytes. In a study by Matsuzuka et al., among 83 patients who underwent FNAB, 65 patients (78.3%) were diagnosed accurately and 10 patients (12%) had borderline cytologic results (6). Thus, 90% of the patients with thyroid lymphoma were diagnosed or the diagnosis suspected based on fine needle aspiration biopsy. To confirm the diagnosis of lymphoma histologically and to determine the degree of malignancy, open biopsy taking 2-3 g tissue should be done for all cases. Only two of our patients could be diagnosed with fine needle aspiration biopsy (FNAB), and the other two patients were diagnosed after surgical excision.

It should not be forgotten that thyroid lymphomas may be accompanied by other primary neoplasms of the thyroid (papillary, follicular, anaplastic). For this reason, in addition to histopathological analysis, immunohistochemical staining with monoclonal antibodies should also be performed (7). One of our cases displayed a coexistence with papillary thyroid carcinoma. Immunophenotypically, neoplastic cells express CD20, CD79a, CD21 and CD35. They may be negative for CD5, CD10 and CD23 and positive or negative for CD43 and CD11c.

Due to contradictions in the surgical treatment of thyroid lymphomas, it should be differentiated from systemic lymphoma when diagnosed. According to studies from the Mayo Clinic, it is reported that disease-free survival and high cure rates are obtained with thyroidectomy and adjuvant RT (8). Today, it is stated that surgery should only be performed for histological diagnosis. Cervical-mediastinal RT should be the initial treatment choice in patients who have good prognosis and when the disease is limited to the thyroid. A study of 31 patients with primary thyroid MALT lymphoma has reported a 5-year survival rate of 90% after receiving solely RT (9). RT and CT should be added in high grade lymphomas which display extracapsular extension (5). CHOP (cyclophosphamide, adriamycin, vincristine, prednisolone) regimen with Rituximab has shown to be the best combination therapy for disease-free survival (5). It is also recommended that pathological diagnosis should be ensured by FNAB and CT should be preferred as the initial treatment when recurrence or systemic disease exists. Adding Rituximab to the treatment regimens against CD20 surface antibody results very well. In our series, one of the patients who had received combined treatment had good prognosis. CHOP- Rituximab treatment usually causes neutropenic fever and the clinicians should be careful about this clinical manifestation. In our series, one patient died from neutropenic fever. Grade of the tumor also has great importance in prognosis. Ten-year survival rate for low-grade lymphoma is 75%, and for the high-grade disease, 5-year survival rate is less than 50% (10). Besides, older age and extracapsular extension have a negative effect on the prognosis. All of our patients received CT and RT. Two patients underwent surgery for diagnosis and one patient underwent surgery due to pressure symptoms. All patients except one have been followed up without any evidence of disease.

CONCLUSION

It is challenging to diagnose primary thyroid lymphomas because of their rare occurrence. For this reason, it should be kept in mind that patients with chronic lymphocytic thyroiditis should be evaluated carefully when they have a rapidly growing thyroid gland or cervical LAP. According to the literature and our clinical experience, we can state that RT is the most adequate treatment for patients especially with low grade lymphoma, and CT should be added to the treatment of the patients with high grade lymphoma.

Informed Consent: Informed consent was obtained from both patients. Consents were also obtained to perform scientific studies.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - N.A., T.A., M.H.; Design - N.A., T.A., M.H.; Supervision - N.A., T.A., M.H.; Resource - N.A., T.A., M.H.; Materials - N.A., T.A., M.H.; Data Collection and/or Processing - N.A., T.A., M.H.; Analysis and/or Interpretation - N.A., T.A., M.H.; Literature Search - N.A., T.A., M.H.; Writing Manuscript - N.A., T.A., M.H.; Critical Reviews - N.A., T.A., M.H.

Conflict of Interest: No conflict of interest was declared by the authors.

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OLGU SERİSİ-ÖZET
Turk J Surg 2019; 35 (2): 142-145

Primer tiroid lenfomasına yaklaşım: Olgu serisi

Nihan Acar[1], Turan Acar[1], Arzu Avcı[2], Mehmet Haciyanlı[1]

[1] İzmir Katip Çelebi Üniversitesi, Atatürk Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, İzmir, Türkiye
[2] İzmir Katip Çelebi Üniversitesi, Atatürk Eğitim ve Araştırma Hastanesi, Patoloji Kliniği, İzmir, Türkiye

ÖZET

Primer tiroid lenfomaları nadir görülen bir kanserdir. Sıklıkla MALT (Mucosa Associated Lenfoid Tissue) ve diffüz B hücreli non-hodgkin lenfomalar görülür. Yaşlılarda ve özellikle kadınlarda daha sık rastlanır. Boyunda aniden büyüyen kitle olarak bulgu verirler. Biz de bu yazımızda tiroid lenfoması tanısı almış dört hastamızın retrospektif olarak dosyalarını tarayarak, epidemiyolojik özelliklerini, teşhislerini, tedavi ve prognostik belirteçlerini sunmayı amaçladık. İkisi erkek ve ikisi kadın, primer tiroid lenfoma tanılı, dört hastamızın ortalama yaşı 63,75 (51-74)'tir. Hastaların ortak şikayetleri, boyunda aniden ortaya çıkan kitle. İki hastanın tanısı ince iğne aspirasyon biyopsisi (İİAB) ile diğer iki hastanın tanısı ise cerrahi eksizyon ile konuldu. Dört hastaya da kemoterapi ve radyoterapi verildi. Bir hasta takibinin ikinci yılında eksitus olurken, diğer üç hasta halen takibimizde. Primer tiroid lenfomaları agresif seyirli tümör değildirler ve en etkili tedavi radyoterapidir.

Anahtar Kelimeler: Tiroid, lenfoma, MALT, non-hodgkin

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CASE REPORT
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Alternative hepatic arterial reconstruction technique in a case of total pancreaticoduodenectomy after celiac artery resection in pancreas cancer: Iliac-hepatic bypass

Mustafa Özsoy[1], Enes Şahin[2], Mustafa Yavuz[3], Zehra Özsoy[4], Nazan Okur[5], Süleyman Şahin[1], Sezgin Yılmaz[6], Yüksel Arıkan[6]

[1] Clinic of General Surgery, Parkhayat Hospital, Afyonkarahisar, Turkey
[2] Department of General Surgery, Selcuk University School of Medicine, Konya, Turkey
[3] Clinic of General Surgery, Afyon State Hospital, Afyonkarahisar, Turkey
[4] Clinic of Internal Medicine, Afyon State Hospital, Afyonkarahisar, Turkey
[5] Department of Radiology, Süleyman Demirel University School of Medicine, Isparta, Turkey
[6] Department of General Surgery, Afyon Kocatepe University School of Medicine, Afyonkarahisar, Turkey

ABSTRACT

Surgery is the only treatment method in pancreatic cancer. Unfortunately, metastatic diseases or invasion of the main vascular structures are observed in a majority of cases at the time of diagnosis; these structures originate from the body, neck, and tail of the pancreas and are considered inoperable. The first celiac artery resection for the treatment of cancer was described by Appleby in 1953. Here, we describe our hepatic artery reconstruction technique in a case with pancreatic body cancer. A 37-year-old male patient was admitted to our emergency department due to syncope. The patient was diagnosed with acute renal failure secondary to fluid loss. Thereafter, his general condition was stable and laboratory results improved. Abdominal computed tomography was performed. Pancreatic cancer originating from the pancreatic body was detected. A pancreatic biopsy was performed and neoadjuvant gemcitabine and paclitaxel chemoradiotherapy were initiated. Surgical treatment was recommended for the identification of regression after neoadjuvant chemoradiotherapy. Following intraoperative Doppler ultrasonography, en bloc distal pancreatectomy and splenectomy involving the celiac artery trunk and total gastrectomy were performed. However, surgical margin reliability in frozen section revealed that the tumor was still present. Therefore, the surgical procedure was replaced with total pancreaticoduodenectomy. Hepatic artery reconstruction was performed from the left main iliac artery using a 4-mm ringed GORE-TEX® graft. The iliac-hepatic bypass for hepatic artery reconstruction in pancreatic cancer could be an alternative surgical technique.

Keywords: Appleby, celiac artery, iliac-hepatic bypass, pancreas

INTRODUCTION

Surgery is the only treatment method known to prolong survival in pancreatic cancer, which is one of the most lethal types of cancer. In the standard treatment of cancer originating from the body of the pancreas, splenectomy and distal pancreatectomy are involved; however, resection of the main vascular structures, such as the celiac artery and main hepatic artery, is required to achieve a curative resection (R0) in most cases (1). Unfortunately, there are limited data available on celiac artery resection in the cancer of the pancreatic body. This study aimed to describe our novel hepatic artery reconstruction technique after switching from the Appleby procedure to total pancreaticoduodenectomy in a patient with pancreatic body cancer since intraoperative frozen section revealed that the tumor had remained at the surgical margin.

CASE REPORT

A 37-year-old male patient was admitted to the emergency department due to syncope. The patient had lost about 30 kg of weight with increasingly severe abdominal pain in the 3 months before admission. Laboratory tests revealed elevated aspartate aminotransferase (100 U/L), alanine aminotransferase (80 U/L), and creatinine (2.7 mg/dL); an international normalized ratio of 1.8; and CA19-9 of 200 U/mL. In a focused assessment using sonography for trauma of the abdomen, no free fluids were detected; however, an approximately 6-cm mass of pancreatic origin

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Corresponding Author
Mustafa Özsoy
E-mail: dr.mustafaozsoy@gmail.com

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was observed in the upper abdomen. The patient was admitted to the intensive care unit due to acute renal failure secondary to fluid loss. His general condition was stable and laboratory results improved. In a dynamic upper abdominal computed tomography scan, pancreatic cancer that showed no distant organ or peritoneal spread was detected in the splenic, hepatic, and celiac artery originating from the pancreatic body (Figure 1). Additional focus was detected in a positron emission tomography scan. A pancreatic biopsy was performed under the guidance of ultrasonography (USG), and neoadjuvant gemcitabine and paclitaxel chemoradiotherapy were initiated. Surgical treatment was recommended upon the identification of regression after neoadjuvant chemoradiotherapy.

A written informed consent was obtained from the patient. No distant organ metastasis was noted in abdominal exploration. The mesenteric artery and vein were suspended through an extended Kocher maneuver. The hepatoduodenal ligament was dissected and the main hepatic artery, portal vein, and bile duct were suspended. The pancreas was transected from the retropancreatic portal vein level. The main hepatic artery was clamped, and the peak systolic velocity of the hepatic artery was measured as normal (58.60 mL/min) using intraoperative Doppler USG. Following intraoperative Doppler USG and macroscopically adequate hepatic artery pulsation, en bloc distal pancreatectomy and splenectomy, including the celiac artery trunk, and total gastrectomy, were performed. The examination of the specimen sent for surgical margin reliability revealed that the tumor was still present; therefore, we decided to perform pancreaticoduodenectomy. Conventional pancreaticoduodenectomy was completed with gastroduodenal artery connection following a choledochal dissection. Due to the presence of acute renal failure in the patient's history, hepatic artery reconstruction was performed from the left main iliac artery with the help of a 4-mm ringed GORE-TEX® (W. L. Gore & Associates, Flagstaff, Arizona, USA) graft to minimize the risk of renal ischemia due to aortic clamping. Total duration of the ischemia was 25 min. Hepatic artery flow was 60 mL/min in the repeated Doppler USG (Figure 2). Reconstruction was completed with hepaticojejunostomy and esophagojejunostomy. In the post-operative period, blood sugar level of the patient was regulated, and he was discharged on Day 15 following the operation (Figure 3). In post-operative histopathological examination, all surgical margins were found to be negative for tumors. Adjuvant therapy was completed, and the patient is cancer-free and still alive at 22 months after the operation.

Figure 1. Tumoral mass originating from the pancreatic body (star) and invading the main hepatic and celiac arteries (arrow) was detected.

Figure 2. Complete image of intraoperative iliac-hepatic bypass.

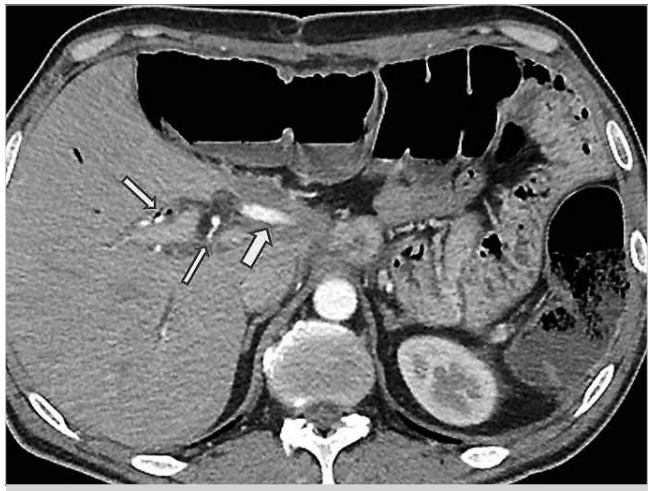

Figure 3. Presence of intrahepatic-hepatic arterial flow (thin arrow) and GORE-TEX® graft (thick arrow) in post-operative control abdominal computed tomography.

DISCUSSION

Despite the developments in surgical, adjuvant, and neoadjuvant radio-chemotherapy regimens for the treatment of pancreatic cancer, five-year survival rates are still below the desired targets. In the study by Sohn et al., only 10%-30% of pancreatic cancer patients have been reported to be eligible for the surgical treatment (2). Despite a theoretically possible curative (R0) resection due to the resection of major vascular structures and complex reconstructive surgical interventions in locally advanced diseases, severe post-operative morbidity and mortality rates are observed. Therefore, the involvement of adjacent vascular structures in pancreatic cancer is still considered inoperable by most surgeons. In recent years, publications from high-volume centers have become the basis for new discussions on the applicability of superior mesenteric and portal venous resections with acceptable complication rates (3). Although the resection of venous structures in pancreatic cancer and their impact on survival has gained acceptance, the resection of arterial structures remains the center of discussion. However, there are no studies in the literature supporting the non-resection of the arterial structures in actuality. About 30% of pancreatic cancers are located in the pancreatic body or tail, and cancer in the pancreatic body leads to early celiac and main hepatic artery invasion due to anatomic proximity (4). According to the current guidelines, in cancer cases located in the body and tail of the pancreas, the involvement of the celiac and main hepatic arteries is considered a criterion for non-resectability. However, splenic artery involvement is not included in the inoperability criteria (5).

The first celiac artery resection to treat cancer was described by Appleby in 1953 (6). Appleby identified the presence of adequate hepatic artery flow after celiac artery resection with distal pancreatectomy and splenectomy in a patient with locally advanced gastric cancer. Nimura adapted the surgical technique described by Appleby for the treatment of pancreatic cancers (7). Hepatic artery flow after celiac artery resection is achieved through the pancreaticoduodenal arc originating from the superior mesenteric artery. Although there are no comparative studies on the contribution of celiac artery resection for the survival period, promising results have been obtained in the Almano and Hartwig series in terms of post-operative complications and survival (8,9). Furthermore, the reconstruction of intraoperative hepatic arterial flow after celiac artery resection is essential. Wu et al. have reported that elevated transaminase levels, cholecystitis, and gastric ulcer incidences were detected post-operatively, despite adequate hepatic artery flow through the pancreaticoduodenal arc after celiac artery resection (10). The presence of intraoperative hepatic artery pulsation and no macroscopic discoloration in all of these complications indicate that there may be limitations in determining the adequacy of hepatic artery flow. Excessive lymphatic dissection and resection of border plexuses may cause liver ischemia in the post-operative period due to arterial vasospasm. Therefore, hepatic artery reconstruction, even in the presence of sufficient vascular flow, is thought to reduce gastric and hepatic dysfunction and prevent complications (11). Currently, hepatic artery flow can be detected using intraoperative Doppler USG and hepatic venous oxygenation rather than macroscopical evaluation by pulpability and discoloration of the liver (12). Several different techniques for hepatic artery reconstruction have been described to date. In addition to end-to-end reconstruction, the middle colic artery as well as the saphenous vein or prosthetic graft (GORE-TEX®) can be used for the reconstruction of the gastroepiploic artery (13). Machado et al. have defined the iliac-hepatic artery revascularization technique using a prosthetic (Dacron®) hepatic artery reconstruction graft (14). Complications that may be caused by celiac artery resection can be prevented through preoperative celiac artery embolization. Although collateral development in the pancreaticoduodenal arc can be achieved with celiac artery embolization, it should be performed only in patients to be resected 1-2 days prior to the surgery (15).

In our case, pancreatic cancer originating from the pancreatic body characterized by main hepatic and celiac artery invasion was detected. Upon showing response to preoperative neoadjuvant treatment, surgical treatment was recommended to ensure maximum survival time. Main hepatic artery clamping was performed before celiac artery resection. Meanwhile, as intraoperative Doppler USG scan revealed adequate hepatic artery flow, celiac artery resection and total gastrectomy were added to distal splenopancreatectomy. Due to the invasion of the posterior wall of the stomach by the mass in the pancreas, we decided that removal with total gastrectomy rather than preservation of left gastric artery by reconstruction would be more suitable for reaching the goal of R0 resection. Preoperative celiac artery embolization was not performed oin our patient, as at centers where intraoperative USG and vascular reconstruction can be performed frequently, possible complications arising from embolization can be avoided. Total pancreaticoduodenectomy was recommended based on the finding that the tumor remained in the surgical margin according to the intraoperative frozen section examination. We decided to perform iliac-hepatic bypass for hepatic artery reconstruction via ligation of the gastroduodenal artery as other reconstruction methods required total aortic clamping to achieve adequate artery flow rate. This method was preferred in our case with a history of acute renal failure owing to its ease of application and to avoid additional morbidity. Our patient completed the postoperative adjuvant therapy. He remains cancer-free and is in his 22nd post-operative month.

CONCLUSION

Vascular resections in pancreatic cancers have high rates of morbidity and mortality. However, due to advanced anesthesia and surgical techniques in high-volume centers, complex recons-

tructive techniques can be performed with acceptable morbidity and mortality rates.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

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OLGU SUNUMU-ÖZET
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Pankreas kanserinde çölyak arter rezeksiyonu (appleby) sonrasında alternatif hepatik arteryel rekonstrüksiyon tekniği

Mustafa Özsoy[1], Enes Şahin[2], Mustafa Yavuz[3], Zehra Özsoy[4], Nazan Okur[5], Süleyman Şahin[1], Sezgin Yılmaz[6], Yüksel Arıkan[6]

[1] Parkhayat Hastanesi, Genel Cerrahi Kliniği, Afyonkarahisar, Türkiye
[2] Selçuk Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Konya, Türkiye
[3] Afyon Şehir Hastanesi, Genel Cerrahi Kliniği, Afyonkarahisar, Türkiye
[4] Afyon Şehir Hastanesi, İç Hastalıkları Kliniği, Afyonkarahisar, Türkiye
[5] Süleyman Demirel Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı, Isparta, Türkiye
[6] Afyon Kocatepe Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Afyonkarahisar, Türkiye

ÖZET

Pankreas kanserlerinde yaşam süresine katkı sağlayan tek tedavi seçeneği cerrahidir. Ne yazık ki pankreas gövde, boyun ve kuyruk kesiminden köken alan kanserlerde çoğunlukla metastatik hastalığa veya komşuluk nedeniyle ana vasküler yapılara invazyon saptanarak inoperabl kabul edilmektedir. Çölyak arter rezeksiyonu ilk kez 1953 yıllında lokal ileri evre mide kanserli bir olguda Appleby tarafından uygulanmıştır. Bu makalede pankreas gövde kanserli bir hastada hepatik arteriyel rekonstrüksiyon tekniğimizi sunmayı amaçladık. Otuz yedi yaşında erkek hasta acil servise senkop nedeniyle başvurdu. Hasta sıvı kaybına sekonder akut böbrek yetmezliği tanısıyla yoğun bakım izlemine alındı. Genel durumu düzelen hastanın elde edilen dinamik üst abdomen tomografisinde pankreas gövde kısmından kaynaklanan ana vasküler yapıları içerisine alan uzak organ veya peritoneal yayılım göstermeyen pankreas kanseri saptandı. Pankreas biyopsisi sonrasında gemsitabin ve paklitakselden oluşan neoadjuvan kemoradyoterapi başlandı. Neoadjuvan kemoterapi sonrasında pankreastaki kitlede gerileme saptanması üzerine cerrahi tedavi uygulanmasına karar verildi. İntraoperatif Doppler ultrasonografi (USG) sonrasında çölyak arter ve total gastrektominin ilave edildiği unblok distal pankreatektomi ve splenektomi uygulandı. Lakin intraoperatif frozen incelemede cerrahi sınırın pozitif olması üzerine total pankreatikoduodenektomi uygulanmasına karar verildi. Hepatik arter rekonstrüksiyonu 4 mm'lik ringli goroteks greft yardımıyla sol ana iliyak arterden yapıldı. Çölyak arter rezeksiyonu sonrasında hepatik arteriyel rekonstrüksiyon için goroteks greft yardımıyla iliohepatik baypas uygulama kolaylığı nedeniyle tercih edilebilir bir yöntemdir.

Anahtar Kelimeler: İliohepatik baypas, appleby, pankreas, çölyak arter

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CASE REPORT
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Syringocystadenoma papilliferum located at the nipple: Description of an extremely rare case with review of the literature

Yaşar Subutay Peker[1], Murat Urkan[1], Salih Hamcan[2], Ali Fuat Çiçek[3], Mehmet Ali Gülçelik[1]

[1] Clinic of General Surgery, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey
[2] Clinic of Radiology, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey
[3] Clinic of Pathology, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey

ABSTRACT

Syringocystadenoma papilliferum (SCAP) is a rare, benign tumor of the apocrine sweat glands, and only two nipple-located SCAP cases have been reported. Very few cases of malignant transformation and metastasis have been reported. We share our experience with SCAP located at the nipple that recurred with intraductal papilloma (IP). A female patient aged 26 years presented to our clinic with a mass at the posterior of the left nipple. The mass was excised, and the pathology report revealed SCAP. The patient had no recurrence for 1 year, but the mass recurred later in the same location. Re-excision was planned and conducted. Diagnosis of the second excised mass according to the pathology report was florid-type ductal epithelial hyperplasia and IP. SCAP may be located in female genitals, extremities, and trunk but these are rarer than in the head and neck. This is the third case reporting SCAP at the nipple. SCAP may be related to nevus sebaceous, resulting in basal cell carcinoma or syrigocystadenocarcinoma papilliferum; however, no data have been reported about the relation of SCAP with IP. The relation may be due to microscopic characteristics of SCAP, including the presence of papillary processes between two epithelial alignments. As a conclusion of this case presentation, SCAP of the nipple must be followed up for IP transformation or recurrence. Further evaluation may be needed for this dark side of the rare and little-known pathological entity; however, because of its rareness, it seems troublesome to diagnose.

Keywords: Intraductal papilloma, syrigocystadenocarcinoma papilliferum, syringocystadenoma papilliferum

INTRODUCTION

Syringocystadenoma papilliferum (SCAP) is a rare benign tumor of the apocrine sweat glands and is usually located in the head and neck region (75% of the cases) which commonly arises at the second decade of life. More frequently, SCAP is a congenital lesion. It was first described by J. H. Stokes in 1917 (1). Breast-localized (especially nipple-localized) SCAP is extremely rare. SCAP may be classified at three forms including plaque, nodular or linear; however, there is no consensus about the classification because of the rarity of the cases (2). SCAP is characteristically described macroscopically as erythematous symmetrical lesions. It may be misdiagnosed with many lesions but more frequent with basal cell carcinoma macroscopically and intraductal papilloma (IP) microscopically. Treatment of both lesions is excision, and excisional biopsy is the best technique for diagnosing the lesion as either SCAP or IP.

This study aimed to report the clinical presentation of a female patient with SCAP of the nipple recurring with intraductal papilloma (IP), whose microscopic features are similar and create a dilemma for the pathologists in accordance with the literature.

CASE REPORT

A white female patient aged 26 years presented to our clinic with an exophytic growing mass for 3 months, located just to the right of her left nipple. The mass measured approximately 0.5 cm in diameter with palpation; it was mobile, and there was no ulceration on the lesion. Patient's laboratory tests were totally in normal range. The patient underwent excisional biopsy under local anesthesia. Final pathology of the specimen revealed SCAP with benign papillary formations.

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Corresponding Author
Yaşar Subutay Peker
E-mail: subutaypeker@gmail.com

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One year after excision, the patient presented to our clinic with recurrence of the mass in the same location, this time more deeply located and less exophytic. Physical examination showed a mobile subcutaneous mass 0.9 cm in width, without any cutaneous alternations. Ultrasound revealed a hypoechoic mass measuring 0.9 x 0.8 cm with increased vascularity. Local excision of the mass was planned and conducted. Final pathology of the second excisional biopsy revealed IP, florid hyperplasia, and fibrocystic alternations (fibrosis, periductal inflammation, apocrine metaplasia, macro-microcysts) (Figures 1-3). The patient was discharged and has been followed up for approximately a year without recurrence.

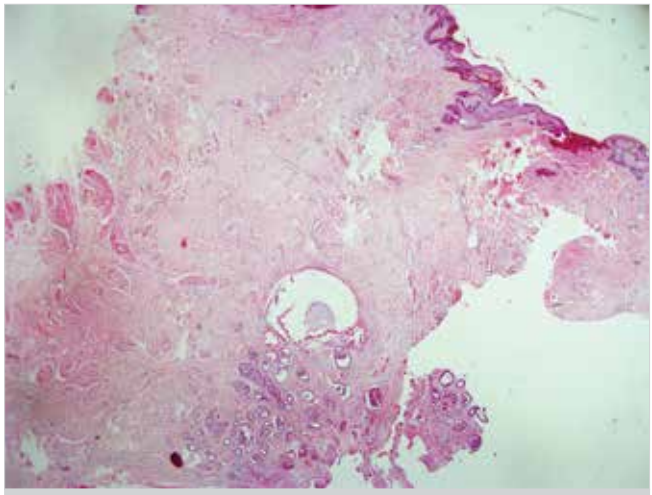

Figure 1. There are cystically dilated lactiferous ducts showing florid type intraductal proliferation. There is also another dilated duct with cystic apocrine metaplasia adjacent to the ducts with usual duct hyperplasia. (H&Ex20).

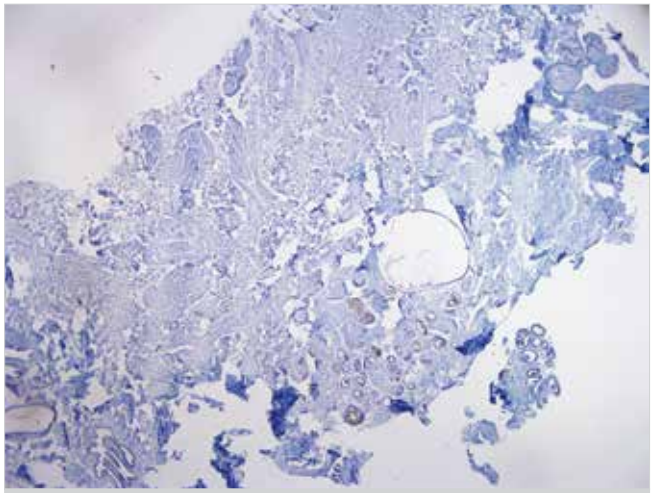

Figure 2. Focal weak ER positivity within the intraductal proliferation (ERx20).

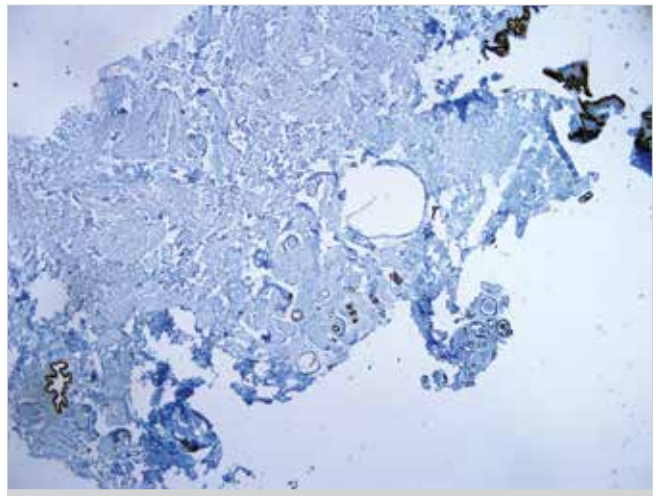

Figure 3. Patchy and focal staining with CK5/6. (CK5/6x20).

DISCUSSION

SCAP is described as a rare dermatological benign lesion. The most common localization for SCAP is the head and neck. Other locations are rare and only one case of SCAP localized at the external auditory canal has been reported (3). Only 2 other nipple-located SCAP cases have been reported, to the best of our knowledge (4,5). Although SCAP is a benign lesion, malignant metastatic lesions, known as syringocystadenocarcinoma papilliferum (SCACP), have also been described (3,6). SCACP are mild malignant tumors; only one case has been described for lymphovascular invasion, and very few cases for metastasis (6). Predisposing factors and progression of SCAP and transformation to SCACP are still uncertain. Much work has been done and debates about the malignant transformation of SCAP are ongoing. Parekh et al. have shown that SCACP lesions resulting from SCAP are related to nevus sebaceous of Jadassohn's (NSJ), in agreement with various other studies (6-8). However, SCAP is a rare entity that arises from NSJ. Kamyab-Hesari et al. have reported the rate of SCAP formation after NSJ to be 1.19%, and Hsu et al. have reported it as 2.7% (7,8). Since not all NSJ transforms to SCAP, not all SCAP lesions arise from NSJ, as was the case in our patient. Ayadi et al. have described tubuloapocrine adenoma associated with SCAP, but it is hard to identify which lesion was the precursor of the other or whether they were independent from each other (9). Sporadic SCAP lesions are also described, as in our present case.

Currently, SCAP lesions have no clinical importance except their cosmetic results. However, malignant transformation and malignancy potential for SCACP or basal cell carcinomas are being newly debated, as mentioned above. Shen et al. and Levinsohn et al. have described BRAF and RAS mutations at sporadic SCAP lesions, but none at SCAP lesions that transformed from NSJ. The study has concluded that the Ras-MAPK pathway is active only

for sporadic SCAP lesions (10,11). BRAF mutation is described for many benign and malignant (especially aggressive) human tumors; malignant melanoma is the most frequent malignant tumor having a BRAF mutation and must be emphasized. Unfortunately, because SCACP cases are very rare, the immunohistochemical and mutational properties of these cases are unknown. Thus, debates on the immunohistochemical and mutational properties of SCAP are ongoing (3,10).

The entity of SCAP being rare probably results in the rarity of SCACP. Almost no published reports exist for the management of these cases. Another reason for the rarity of publications on the management of SCAP is that diagnosis of SCAP is only made with a microscope; very few physicians are experienced enough to diagnose it with its characteristic macroscopic features. For the reasons mentioned above, we suggest that SCAP lesions must be completely excised because of the unknown potential for malignant transformation.

Microscopic features of SCAP include glandular proliferation, fibromatous - inflammatory reaction, and papillary formations lined by double-layer epithelium (3,6). Differential diagnosis for SCAP localized at the nipple is reported as IP and nipple adenoma (3). Because of the characteristic microscopic features, SCAP is a diagnostic dilemma for pathologists, as in our case. Our patient had a diagnosis of SCAP after her first excisional biopsy. The recurrent specimen excised from the same location was diagnosed as IP with other benign features because of a lack of papillary formation lined by double-layer epithelium. There are no strict rules for the diagnosis of SCAP, so we decided not to diagnose SCAP without one of its microscopic characteristics, even though other findings refer to SCAP. We think pathologists must not be too eager to diagnose SCAP to chase a rare case and must evaluate cases deeply for the diagnostic dilemma debated above.

The currently presented case may be the third case for SCAP localized at the nipple but the first case for SCAP recurrence with IP. Since there is a close relation between NSJ and SCAP, we want to draw attention to the relation between SCAP and IP because of their similar microscopic features. Unfortunately, cases are too rare for this topic to be debated.

CONCLUSION

In conclusion, our case is the third case report for nipple-originated SCAP but the first case report of SCAP recurring with IP. The etiology of SCAP and malign transformation is debated, and for this reason we suggest local resection for suspicious lesions. Finally, pathologists must keep in mind the entity of SCAP but must not misdiagnose with the differential diagnosis of SCAP.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Consept - Y.S.P.; Design - Y.S.P.; Supervision - M.A.G.; Resource - A.F.Ç.; Materials - Y.S.P.; Data Collection and/or Processing - S.H.; Analysis and Interpretation - Y.S.P.; Literature Search - M.U.; Writing Manuscript - Y.S.P.; Critical Reviews - M.A.G.

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OLGU SUNUMU-ÖZET
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Meme başının syringocystadenoma papilliferum lezyonu: Literatür ışığında nadir bir olgunun sunumu

Yaşar Subutay Peker[1], Murat Urkan[1], Salih Hamcan[2], Ali Fuat Çiçek[3], Mehmet Ali Gülçelik[1]

[1] Sağlık Bilimleri Üniversitesi, Gülhane Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, Ankara, Türkiye
[2] Sağlık Bilimleri Üniversitesi, Gülhane Eğitim ve Araştırma Hastanesi, Radyoloji Kliniği, Ankara, Türkiye
[3] Sağlık Bilimleri Üniversitesi, Gülhane Eğitim ve Araştırma Hastanesi, Patoloji Kliniği, Ankara, Türkiye

ÖZET

Syringocystadenoma papilliferum (SCAP), apokrin ter bezlerinin nadir görülen benign bir tümörüdür ve bugüne kadar sadece iki tane meme başı yerleşimli SCAP olgusu bildirilmiştir. Çok az sayıda malign transformasyon ve metastaz bildirilmiştir. Bu olgu sunumunda; intraduktal papilloma (İP) ile tekrarlayan ve meme başı yerleşimli SCAP ile alakalı deneyimlerimizi paylaşmaktayız. Yirmi altı yaşında kadın hasta kliniğimize sol meme başının arkasında kitle ile başvurdu. Kitle eksize edildi ve patoloji raporu SCAP olarak raporlandı. Hastanın bir yıl boyunca nüksü olmadı fakat kitle daha sonrasında aynı lokalizasyonda tekrarladı. Tekrar eksizyon planlandı ve yapıldı. Patoloji raporuna göre ikinci eksize edilen kitlenin tanısı florid tip duktal epitelyal hiperplazi ve İP idi. SCAP, kadınlarda genital bölgede, ekstremitelerde ve gövdede bulunabilir, ancak bunlar baş ve boyundan daha nadirdir. Olgu sunumumuz, meme başında SCAP bildirilen üçüncü olgudur. SCAP nevus sebaseus ile ilişkili olabilir, bazal hücreli karsinom veya srigosistadenokarsinoma papilliferum ile sonuçlanabilir; ancak SCAP'ın İP ile ilişkisi hakkında herhangi bir veri bulunmamaktadır. İki lezyon arasındaki ilişki, iki epitelyal taban arasındaki papiller proçeslerin varlığı da dahil olmak üzere SCAP'ın mikroskopik özelliklerine bağlı olabilir. Bu olgu sunumu sonucunda, meme başının SCAP lezyonu, İP'e dönüşümü veya İP ile tekrarlaması açısından izlenmesini önermekteyiz. Nadir ve az bilinen bu patolojik antitenin karanlık yüzünü aydınlatabilmek için ileri değerlendirmeler gerekebilir; ancak olgu azlığı nedeniyle bunun oldukça zor olduğu değerlendirilmektedir.

Anahtar Kelimeler: İntraduktal papillom, syringokistadenokarsinoma papilliferum, syringokistadenoma papilliferum

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