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## The Fourth International Symposium of Coloproctology Proceeding



4<sup>th</sup> Constantine Day  
of Coloproctology



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# FACTA UNIVERSITATIS

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The Fourth International Symposium of Coloproctology  
Proceeding



UNIVERSITY OF NIŠ

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2. Papantchev V, Hristov S, Todorova D, et al. Some variations of the circle of Willis, important for cerebral protection in aortic surgery — a study in Eastern Europeans. *Eur J Cardiothorac Surg* 2007; 31:982–998.

3. Jovanović S, Gajić I, Mandić B, Mandić J, Radivojević V. Oral lesions in patients with psychiatric disorders. *Srp Arh Celok Lek* 2010; 138:564–569. (Serbian)

4. Valença MM, Martins C, Andrade-Valença LPA. Trigeminal neuralgia associated with persistent primitive trigeminal artery. *Migrâneas cefaléias (Brasil)* 2008; 11:30–32.

5. Belenkaya RM. Structural variants of the brain base arteries. *Vopr neurokhir* 1974; 5:23–29. (Russian)

### Abstract:

6. Tontisirin N, Muangman SL, Suz P, et al. Early childhood gender in anterior and posterior cerebral blood flow velocity and autoregulation. In *Abstract of Pediatrics* 2007. (doi:10.1542/peds. 2006-2110; published online February 5).

### Books:

7. Patten MB. *Human embryology*, 3rd edn. McGraw-Hill: New York, 1968.

8. Marinković S, Milisavljević M, Antunović V. Arterije mozga i kičmene moždine—Anatomske i kliničke karakteristike. *Bit inženjerinng: Beograd*, 2001. (Serbian)

### Chapters:

9. Lie TA. Congenital malformations of the carotid and vertebral arterial systems, including the persistent anastomoses. In: Vinken PJ, Bruyn GW (eds) *Handbook of clinical neurology*, vol. 12. North Holland: Amsterdam, 1972; pp 289–339.

### Unpublished data:

10. Reed ML. *Si-SiO<sub>2</sub> interface trap anneal kinetics*, PhD thesis. Stanford University: Stanford, 1987.

### Online document:

11. Apostolides PJ, Lawton MT, David CA, Spetzler RF. Clinical images: persistent primitive trigeminal artery with and without aneurysm. *Barrow Quarterly* 1997; 13(4).

[http://www.thebarrow.org/Education\\_And\\_Resources/Barrow\\_Quarterly/204843](http://www.thebarrow.org/Education_And_Resources/Barrow_Quarterly/204843)

12. Cerebrovascular embryology, in: power point; 2000. [http://brainavm.oci.utoronto.ca/staff/Wallace/2000\\_curriculum/index.html](http://brainavm.oci.utoronto.ca/staff/Wallace/2000_curriculum/index.html)

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**FACTA UNIVERSITATIS**

*Series: Medicine and Biology* Vol. 21, No 1, Special Issue, 2019, pp. i-i  
The Fourth International Symposium of Coloproctology • Proceeding

**Editorial**

Dear colleagues,

The Department for Colorectal Surgery, Clinic for Digestive Surgery, Clinical Center Niš in cooperation with the Society of Coloproctology of Yugoslavia, is organizing for the fourth time the International Symposium - Constantine Day of Coloproctology in Niš. Our lecturers are well known surgeons from abroad and from Serbia. Having in mind excellent experience from previous meetings and feedback from our colleagues, this year it was decided that the main focus be on proctology. The selection includes the most common proctology conditions, which practitioners encounter in everyday practice from primary to tertiary health care center. Majority of these lectures are part of this special issue giving insight into large amount of data on these subjects. We are delighted that the University of Niš and the Faculty of Medicine recognized the importance and value of this issue for education of our younger fellow colleagues, and we sincerely hope they will benefit from it.

Prof. Dr. Goran Stanojević, Guest Editor  
President of the Organizing Committee

# THE FOURTH INTERNATIONAL SYMPOSIUM OF COLOPROCTOLOGY

Niš, Serbia, May 17th, 2019

Venue: Faculty of Medicine, University of Niš

[www.constantinedayofcoloproctology.com](http://www.constantinedayofcoloproctology.com)

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## PROGRAM

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- 07:00–15:00    **Registration**
- 08:30–09:00    **OPENING CEREMONY**
- 09:00–10:30    **I LIVE SURGERY;**  
**Chair: Bela Teleky (Austria)**  
OR I Milligan-Morgan – Z. Krivokapic (Serbia)  
OR II THD – Carlo Ratto (Italy)
- ROUND TABLE:**  
Antonio Villanueva-Herrero (Mexico), Alex Moskalev (Russia),  
Valeriu Surlin (Romania), Vlada Cuk (Serbia), Goran Stanojevic (Serbia)
- 10:30–11:00    Coffee break
- 11:00–12:30    **II Session**  
**HOW TO MANAGE PILONIDAL DISEASE & NON-HEALING WOUNDS**  
*Chairs: Evangelos Xynos (Greece) Goran Barisic (Serbia), Vlada Cuk (Serbia)*  
Excision of pilonidal disease – Goran Stanojevic (Serbia) (25 min)  
vs  
Flap procedure (off-midline) – Antonio Villanueva-Herrero (Mexico) (25 min)  
Non-healing wounds after anal surgery (20 min) – Oleg Biryukov (Russia)  
Discussion: 20 min
- 12:30–14:00    **III session**  
**ANAL FISSURE**  
*Chairs: Alex Moskalev (Russia), Velimir Markovic (Serbia)*  
Anal fissure – Conservative treatment, how long? – Valeriu Surlin (Romania) (20 min)  
Sphincterotomy – Carlo Ratto (Italy) (25 min)  
vs  
Fissura excision – Antonio Villanueva-Herrero (Mexico) (25 min)  
Discussion: 20 min
- 14:00–15:00    Lunch break  
**SCPY Meeting**
- 15:00–16:30    **IV session**  
**ANAL & RECTOVAGINAL FISTULA**  
*Chairs: Antonio Villanueva-Herrero (Mexico), Krivokapic Zoran (Serbia)*  
Fistulotomy – Evangelos Xynos (Greece) (25 min)  
vs  
Sphincter preserving procedure- Bela Teleky (25 min)  
Minimal invasive procedure for rectovaginal fistula – Alex Moskalev (Russia) (20 min)  
Discussion: 20 min
- 16:30–17:00    **CLOSING REMARKS**





## Review Article

**PILONIDAL DISEASE****Milica Nestorović<sup>1,2</sup>, Vanja Pečić<sup>3</sup>, Branko Branković<sup>1,2</sup>, Dragan Mihajlović<sup>1</sup>, Dejan Petrović<sup>1</sup>, Ljiljana Jeremić<sup>1,2</sup>, Ivan Pešić<sup>1,2</sup>, Nebojša Ignjatović<sup>1,2</sup>, Marko Gmijović<sup>1</sup>, Zoran Krivokapić<sup>4</sup>, Goran Stanojević<sup>1,2</sup>**<sup>1</sup>Clinic for Digestive Surgery, Clinical Center Niš, Niš, Serbia<sup>2</sup>Faculty of Medicine, University of Niš, Niš, Serbia<sup>3</sup>Center for Minimally Invasive Surgery, Clinical Center Niš, Niš, Serbia<sup>4</sup>First Surgical Clinic, Clinical Center of Serbia. Faculty of Medicine, University of Belgrade, Serbia

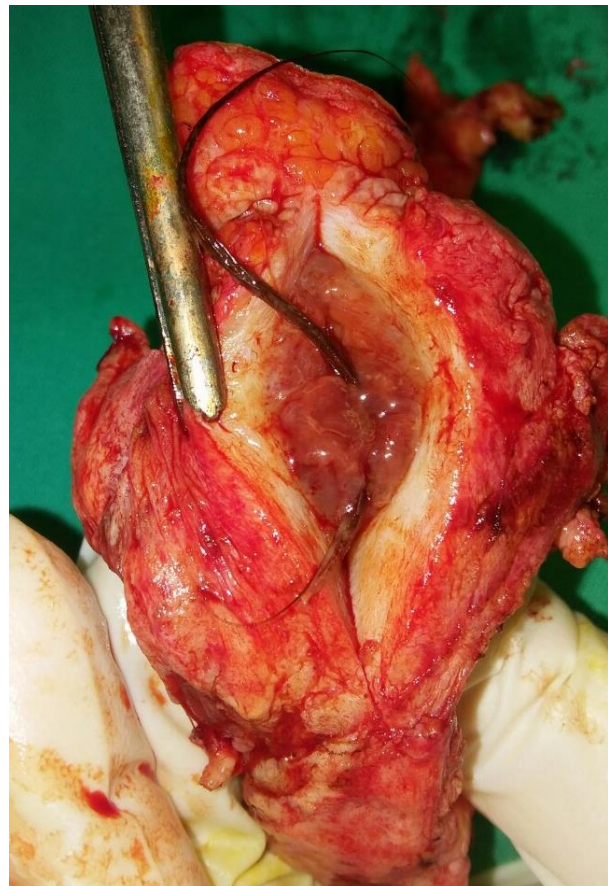
**Abstract.** *Pilonidal disease is a common and well-recognized medical condition. It affects people in reproductive age, especially men and in combination with in-patient and outpatient treatment and absence from work it causes a considerable socioeconomic loss. This fact led to a renewed interest in understanding of the disease and search for the ideal method of treatment. The purpose of this review was to provide update on therapeutic options for patients with pilonidal disease. In case of chronic or recurrent pilonidal disease various treatment options exist, addressing different measures of surgical outcome. Like for many conditions, there is increase in the use of minimally invasive techniques in the treatment, which could be alternative to surgical excisions for pilonidal disease. Procedures for treatment of pilonidal disease can be divided in two large groups: minimally invasive treatment and excisional procedures. Although various treatment options exist nowadays, surgery is still preferred as definitive treatment. The optimal closure of the wound following an excision is still under debate since outcome measures depend mostly on type of closure selected. Most of the procedures fail to achieve the goals altogether. The final decision on treatment should be made based on surgeon and the patient' preference.*

**Key words:** *Pilonidal disease, pilonidal sinus excision, pilonidal surgery.*

**Introduction**

Pilonidal disease is a common and well-recognized medical condition. Its first description dates back to 1833, when Herbert Mayo described a sinus containing hair. In 1880, Hodge suggested the term “pilonidal”, from the Latin word pilus, which means hair and nidus for nest (Fig. 1). Pilonidal disease (PD) affects people in reproductive age, especially men, which is in combination with in-patient and outpatient treatment and absence from work a considerable socioeconomic loss. This fact led to a renewed interest in understanding the disease and search for an ideal method of treatment [1].

The purpose of this review is to provide update on therapeutic options for patients with PD. Authors searched Medline using PubMed for articles in English language not older than ten years using search terms “pilonidal disease”, “pilonidal sinus”, “excision of pilonidal disease”, “pilonidal disease guidelines”. Older publications were hand searched and selected if considered relevant for the subject.



**Fig. 1** Nest of piles (pilonidal disease)

## Incidence and risk factors

Incidence of pilonidal disease differs between continents. It's rare in Asia and Africa and high in Caucasians, highest recorded in Mediterranean area. Its incidence is rising due to reasons that are yet to be established. For example in Germany in 2012 there was increase from 29 patients per 100.000 earlier recorded to 48 per 100.000. It is probably due to sedentary life style, since even in population with small incidence rate, like Japan, pilonidal disease is seen more often in people with jobs requiring long sitting hours [2,3]

Pilonidal disease is more common in dark-skinned and dark-haired persons with excess body hair. Obesity is also recorded as risk factor [3,4]. Apart from these, male gender, poor body hygiene and excessive sweating are also described as risk factors. In the lack of prospective studies Harlak et al. published a prospective case control study in 2010 conducted among 587 patients and 2,780 healthy control subjects investigating risk factors for development of PD. According to their findings there are three most predictive risk factors: body hair rate, bathing habits and sitting time. Using logistic regression analysis there was 219-fold higher risk for hairy people who shower or bathe two or less times per week and sit more than six hours per day compared with hairless people who shower or bathe three or more times per week and sit less than six hours a day to develop disease. The adjusted risk of PD was 6.33-fold greater for those who bathe two or less times per week than the risk for those people who take three or more baths per week, while the adjusted risk was 4.3-fold higher for individuals who were sitting more than six hours in a day. BMI was found to be a less important risk factor, but results might be different in investigation of community-based population, since this study included only active soldiers [5]. Later study also found irregular bathing as a risk factor for PD [4].

From its first description to the middle of 20th century PD is thought to be congenital. Probably the most cited theory of PD development is one by Gorge. E. Karydakis from General Army Hospital in Greece, who published his work in *Lancet* in 1973, after he examined 4670 previously operated Army candidates (with nearly 50% recurrence rate), and operated on 1687 patients using his new method [6]. He developed further the theory on hair insertions, which was first mentioned by Patey and Scarff in 1946. According to Karydakis PD is acquired and causative process that can be defined precisely using equation. The equation consists of three main factors which play a role in the hair insertion process: Hair (H) x Force (F) x Vulnerability (V). It can be used to calculate the possibility of PD. If these three main factors occur, then hair insertion and pilonidal sinus result. It is possible to list many secondary factors which together make up the three main factors, such as for example for H: number of loose hair, type or shape of hair, or for F: depth of natal cleft and friction; for V: wide pores, presence of wounds or scars at the natal cleft. All these factors not only explain all the known

variations of the incidence PD, and the variation of its incidence in the same population over time, but also provide an answer to presence or absence of disease in some cases, for example, the presence of pilonidal sinus in some 'hairless' individuals, and its absence in others with hirsutism [7].

Experimental case matched study by Doll et al., compared mechanical strength of hair in occipital, lumbar, and intergluteal region and its relation to development of PD. The study has shown that vertical strength of occipital, lumbar, and intergluteal hair (along dorsal crest) from patients suffering from pilonidal disease was significantly greater than hair from their matched pairs. Cut hair fragments from occipital region were found in pilonidal nest which suggests that disease is related to this particular region as source. In concordance to their study authors are suggesting reduction in production of hair fragments in occipital (for example by shaving), removing cut hair along dorsal crest, reducing contact with hair within intergluteal fold such as with promptly showers after a hair cut in persons at risk [8].

## Diagnosis and management

The diagnosis of PD is mostly established based on patient's history and clinical findings. Clinical finding are almost always visible characteristic pits in the intergluteal cleft, sometimes with hair extruding from their openings (Fig. 2). In recurrent disease or in chronic phase, sinus tract opening is visible (Fig. 3). According to Task force of the American Society of Colon and Rectal Surgeons from 2013, presacral mass should be



**Fig. 2** Pits in intergluteal cleft



**Fig. 3** Recurrent pilonidal disease

ruled out by digitorectal examination. Laboratory or imaging methods are not routinely used. It is important to distinguish PD from other conditions, such as perianal fistula, Crohn' disease or some infectious diseases (TBC, Syphilis or actinomycosis) [9]. Pilonidal disease can sometimes be mistaken for solitary hidradenitis suppurativa but unlike PD, hidradenitis affects more women than man. Their sonographic characteristics are also similar and accordingly PD might be a variant of localized form of hidradenitis suppurativa. Their histology is somewhat different, although histology finding cannot be always helpful in distinguishing PD from hidradenitis suppurativa [10].

Pilonidal disease can initially present as sacrococcygeal abscess. It is widely accepted that in this case incision and drainage are preferred method of treatment. Disease recurrence following this episode is reported to be 20% after 20 years, and there is no justification for wide excisions in this case since 80% of patients will be over treated and with substantial morbidity and doubled average time to return to work [11]. According to retrospective study from Australia on 134 patients with lateral longitudinal incision and 74 with midline incision, abscess with incision away from midline healed faster ( $p=0.02$ ). Although admitting limitations of the study they concluded that pilonidal abscess should be drained away from the midline [12].

In case of chronic or recurrent disease various treatment options exist, addressing different measures of surgical outcome.

Like for many conditions there is increase in the use of minimally-invasive techniques in the treatment of PD, which could be alternative to surgical excisions for PD. Nowadays the treatment options could be divided in two large groups: minimally-invasive treatment or excisional procedures.

### Minimally-invasive treatment of PD

Pit picking procedure was first described in 1965 by Lord and Millar who excised in local anesthesia affected pits using small elliptical excision, removed the hair and showed resolution in 32 out of 33 patients. Bascom was also one of the surgeons who recognized the importance of pit excision with addition of lateral incision for debridement of the sinus cavity [13]. In a recent study with adolescent patients, disease resolved in 92% of cases using this technique, although follow up period was limited to 5 months. According to authors advantages of this procedure is ease of performance in outpatient setting, it is well tolerated, requires minimal postoperative care and offers rapid recovery [14]. Reported recurrence rates with this procedure range from 10–20% [15].

Fibrin glue is often used in surgical practice. Its use in treatment of PD started in 2000. In 2018, results from single center study were published on 146 patients with PD of which 13% previously already had some kind of treatment. Procedures were done as one day surgery under general anesthesia (apart from one patient). After insertion of blunt probe for tract identification, sinuses were curetted and then flush with saline solution. Afterward the fibrin glue was inserted. No additional dressings were needed. Median operating time was 9 min. There were 27% of recurrences after the first glue application. Twenty four patients with recurrence decided for repeated treatment. Cumulative healing after 2 rounds was 96.9%. This procedure does not require technical equipment and can be easily thought and performed [16]. According to Cohran review current evidence is uncertain regarding the benefits associated with fibrin glue as monotherapy in PD or as adjunct to surgery. There is small number of low quality trials on the subject. RCT are needed to enroll larger number of patients measuring clinically relevant outcomes.

Phenol is also used in minimally- invasive treatment for many decades. It is a necrotizing material which causes burns on mucosa and skin. The preferred phenol is liquid (pure or 80%) or crystallized which turns into liquid form quickly at body temperature. Application tool is different according to the entrance technique. In the incision techniques, usually cotton swab with phenol is moved in the cavity. In the techniques without incision, one of the sinus openings are cannulated with a venous catheter or a blunt-ended metal trocar and phenol is injected into the sinus without pressure and left for 1–3 minutes. The injected volume of phenol is mean  $1.7\pm 1.9$  ml. The sinus is then washed out with normal saline to prevent phenol leakage. The patients treated under local anesthesia are able to leave the hospital immediately after the procedure. Recurrence is regarded as occurrence of the same complaints after asymptomatic period and a second cause of treatment failure. Most studies mentioned that repeated applications were done if necessary (continuation of purulent discharge). Time interval between the repeated applications was variable among the studies (from 1–6 weeks). Wound healed long but there was immediate return to activities. Satis-

factory results with no evidence of recurrence or prolonged discharge were obtained in 60–100% of the patients [18]. Up to date there is only one RCT trail that compared effect of phenol injection with excision and open healing. Study included 140 patients equally distributed in both arms. Time to complete wound healing ( $16.2 \pm 8.7$  versus  $40.1 \pm 9.7$  days) was significantly in favor of the phenol injection group ( $p < 0.001$ ). The median operation time was significantly shorter ( $p < 0.001$ ). Pain score after surgery as well as painkiller intake were also in favor of phenol group. At the mean follow-up of  $39.2 \pm 9.0$  months no difference was seen in the recurrence rate between the two arms. Authors of the study concluded that phenol injection is as effective as the excision with open healing in the PD treatment [19]. Phenol therapy can be combined with other methods of treatment such as video-assisted diathermy ablation of the sinus cavity, with achievement of good results after 22 months of follow up in terms of fast wound healing and low recurrence [20].

Endoscopic treatment of PD implies ablation of sinus tract using video assisted guidance. In the literature it is found under the name of EPSiT (endoscopic pilonidal sinus treatment) or VAAPS (video-assisted ablation of pilonidal sinus). View through the endoscope allows identification of lateral tracts [21]. A recent systematic review and meta-analysis of endoscopic treatment of PD with nine studies and 497 patients was published. The mean operating time was  $34.7 \pm 17.7$  min. Procedure was performed as day-case surgery in all. Seven studies reported the pain VAS (measured from 0–10) within the first week after the procedure, the mean VAS was  $1.35 \pm 0.8$  (range, 0.5–2), while 36 (8.6%) patients required intravenous analgesics in the first postoperative day. Failure of the technique was recorded in 40 (8.04%) patients, 20 (4.02%) had persistent (non-healing) pilonidal sinus, and 20 (4.02%) developed recurrence of SPD after complete initial healing of the primary wound. The weighted mean failure rate of the technique was 6.3% (95% CI 3.6–9.1). Failure of the technique was managed with redo of endoscopic treatment in 24 patients. Complication rate across the study ranged between 0 and 11.1%. Complications included hematoma, infection, persistent discharge, and failure of healing. The mean weighted complication rate was 1.1% (95% CI 0.3–2.4). The mean time to complete healing after the procedure was  $32.9 \pm 23$  days. The mean time to return to work and normal activities was  $2.9 \pm 1.8$  day. Ninety five percent were completely satisfied with the procedure. Authors conclude that endoscopic treatment of PD is a novel and promising method whose main advantage over conventional surgery are mild postoperative pain, quick healing, and short time to return to work and daily activities. The long-term outcome of the procedure is still unclear and longer follow-up is needed [22].

After good initial results Georgiou published data on Pilonidal disease Laser Treatment (PiLaT) in patients with primary disease. Patients with disease recurrence were excluded. In local anesthesia and in prone position after debridement and flushing with saline solution of

pits and sinus tracts, a 1–2 mm metallic probe was inserted into sinus. Energy was delivered through a tip of the probe in circumferential manner in order to shrink and obliterate tract. Primary end point of the study was healing at 8 weeks, and preservation of these results up to 12 months. After one year out of 60 patients enrolled, overall success rate was 92%. All of patients who failed the first time except for one, agreed to undergo again PiLaT procedure. With this results success rate reached 98% [23]. Similar results were earlier published in Belgium with reported recurrence of 2.9% and success rate of 87.5% [24]. Both studies conclude that it is safe, highly effective, almost painless and easy to learn and to perform and should be offered to all patients. Drawback of this procedure is its cost (around 600 euro), which could be balanced with earlier return to work. These studies included small number of patients (60 and 40), and promising results should be evaluated through longer follow up and in RCT.

## Excisional procedures

Open excision is the approach most frequently implemented globally. Complete resection of the sinus is followed by thorough curettage of the cavity. The wound is left to heal by secondary intention or wound edges can be marsupialized. The disadvantage of this procedure is long healing time with delayed return to work. Reported recurrence rates vary greatly from 2% to 35% [25]. Meta-analysis on 26 RCT and 2530 patients compared open wound to primary closure. Wound with primary closure did heal faster. On the other hand recurrence rates were lower for open wounds (RR 0.60, 95% CI 0.42 to 0.87). This meta-analysis did not show difference in rates of SSI between two groups [26]. Randomized control trial compared Limberg flap procedure to secondary wound healing following excision (Fig. 4). Limber flap procedure took longer 60 (30–80) vs. 30 (10–75) minutes ( $p < 0.001$ ) and had higher



**Fig. 4** Limberg flap procedure

complication rate (49% vs. 12%,  $p < 0.001$ ). Limberg flap procedure failed to show advantage over open wound mainly due to high complication rate [27]. One of the conclusions of the previously mentioned meta-analysis was that there was advantage of off-midline over midline wound closure, although in some studies midline suturing is of no importance if it is done in tension free manner [26]. Sevinc et al., conducted a RCT comparing midline and off-midline closure. Patients with primary PD were randomly assigned into 3 groups (two different flap procedures and tension free primary closure), 50 each. Main outcome measures were complications and recurrence. The groups were similar in terms of infection rate and development of seroma. The mean painless sitting time was significantly shorter in primary group. The median follow up time of the study was 24.2 months and the recurrence rates were similar ( $p=0.876$ ). According to the authors of the study release of subcutaneous tissue enabling tension free suture line eased wound healing [28].

Off-midline procedures, such as Karydakias flap or Limberg rotation flap are oriented towards flattening of the natal cleft. Low recurrence rate after originally described Karydakias procedure, is due to simple objective "no raphe, no wound and scar at the depth". The intact skin put at the depth seems not to inherit the vulnerability of the raphe. The natural depth of the intergluteal fold, the raphe, is invaded by the hair and scar in the midline can easily become new entry point [6].

Meta-analysis from 2018 tried to give an answer to the question, which off-midline procedure is most appropriate. Eight studies involving 1121 patients were included. Patients were operated with either Karydakias flap (KF) or using Limber flap reconstruction. All of the studies were conducted between year 2004 and 2013. Long time follow up rate ranged from mean 15.5 to 33.3 months. In some studies modified Limberg flap technique was used, by performing excision with the lower border of the rhomboid 2 cm lateral from to the cleft. In subgroup analysis there was no difference between modified Limberg flap (LF) and conventional LF in all outcome measures including recurrence, except for postoperative rate of seroma. No statistically significant difference in recurrence rate between LF and KF was noted (OR=1.07; 95%CI[0.59-1.92];  $p=0.83$ ). There was significant difference in terms of seroma favoring LF [OR=2.03; 95%CI[1.15-3.95];  $p=0.01$ ). There were no differences in wound rupture nor in wound infection rate. Data on overall morbidity could not be pooled due to high statistical heterogeneity. In two studies statistically significant difference were found favoring LF, while in remaining six morbidity was comparable. KF required shorter operating time in all studies. Most of the studies report similar time to return to work in both arms [29].

The recurrence rate is the most important variable for the comparative assessment of different treatment modalities, although in most publications recurrence is not defined. In some cases surgical treatment is followed by a non-healing wound that sometimes requires second operation. From the academic perspective, absence of wound healing is not correctly designated as a recurrence,

but from the patient's point of view, the only relevant fact is that repeat surgery must be done. For that reason the term "treatment failure" would be preferable [15].

When it comes to long term patient satisfaction recurrence is most important. Study on 583 male patients from military cohort with long follow up (7-22 years) investigated patient satisfaction with surgical treatment in terms of in-hospital time, outpatient treatment, pain, aesthetic impression and long term recurrence rate. According to the results patients are dissatisfied with the results of any surgical technique, if they experience recurrent disease. Pain during wound treatment and cosmesis has no influence on patient satisfaction in the long term, as long as they are recurrence-free over the next 20 years [2].

Recurrence rate following surgery for PD depend on follow-up time. This was pointed out in the meta-analysis and merge analysis from 2018, on combined RCT/non-RCT studies with 89,583 patients available from 1833 to 2017. This dependence, i.e. the steepness of increase of recurrence with longer follow-up times, is specific to a surgical procedure. According to these data primary midline closure should be abandoned, while older therapies (such as marsupialization) may be reconsidered. Flap procedures (Karydakias, Bascom, Limberg) and asymmetric procedures are superior, as proven by RCT and combined RCT/non-RCT trials. Follow-up of PSD patients should always be planned long term, i.e., five or ten years for reliable conclusion [30].

Currently there are three guidelines for the treatment of PD available, all made by relevant surgical societies, from Italy, USA and Germany [31-33]. In Germany despite the increasing number of novel procedures most surgeons still prefer traditional methods. The level of evidence on most topics is moderate or low, while most of RCT are lacking a power calculation and do not describe allocation concealing. Most trials have been performed in Middle East and Southern Europe, which questions the applicability of the obtained results [31]. Patient needs to be adequately informed about all aspects of treatment, from possible complications, cosmetic effects, postoperative course, to risk for recurrence [32]. Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons published the latest guideline for PD treatment in 2019 [33]. Based on low quality evidence there is weak recommendation for elimination of hair from the intergluteal cleft and surroundings in both, acute and chronic pilonidal disease, in the absence of abscess as a primary or adjunct treatment measure. Based on moderate quality evidence in patients with acute or chronic pilonidal disease without abscess, phenol application is an effective treatment that may result in rapid and durable healing (strong recommendation). Fibrin glue may be effective as a primary or adjunctive treatment of PD (weak recommendation based on moderate-quality evidence). Patients who require surgery for chronic PD may undergo excision and primary repair (with consideration for off-midline closure), excision with healing by secondary intention, or excision with marsupialization. Flap-based procedures may be performed, especially in the setting of complex and recurrent chronic PD when other techniques have failed (strong recommendation

based on moderate-quality evidence). Minimally invasive approaches to acute and chronic PD that use endoscopic or video assistance may be used but require specialized equipment and expertise (weak recommendation based on moderate-quality evidence). It is emphasized, that these guidelines should not be inclusive of all proper methods of care nor exclusive of other methods [33]. The final decision on treatment has to be individualized for every patient taking into consideration also surgeon experience and confidence in performing different techniques [32,33].

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## Conclusion

Although various treatment options exist nowadays surgery is still preferred as definitive treatment. The optimal closure of the wound following an excision is still under debate since outcome measures depend mostly on type of closure selected. Most of the procedures fail to achieve the goals altogether. The final decision should be made based on surgeon and patients' preference.

## Review Article

**CONSERVATIVE TREATMENT FOR ANAL FISSURE – FOR HOW LONG?  
– REVIEW OF THE LITERATURE AND PERSONAL EXPERIENCE**Valeriu Șurlin<sup>1,2</sup>, Sorin Scurtu<sup>2</sup><sup>1</sup>1st Clinic of Surgery, Clinical County Emergency Hospital of Craiova, Craiova, Romania<sup>2</sup>PROCTOLINE Clinic Craiova, Craiova, Romania

**Abstract.** *Anal fissure (AF) is a common proctologic disease and health problem, with potential for chronicity, causing the patient a debilitating suffering. The pathogenesis, in most of the cases consists in a vicious circle of pain-internal anal sphincter (IAS) spasm-decrease blood irrigation of mucosa-delay of healing. Treatment should aim to break this mechanism by cutting or relaxing the IAS and restoring adequate blood flow to promote healing. If anal stretch is becoming history, surgical sphincterotomy has the highest rate of healing and the least percentage of recurrence, but incontinence for flatus and stool may occur so “medical or “chemical” sphincterotomy using calcium channel blockers (CCB), nitric oxide donors, botulinum toxin injection are used with success rates from 50% to over 90%, also in combination with other conservative measures like warm sitz baths, stool softeners, high fiber and more liquid daily ingestion. All of those therapeutic measures are also stated in current guidelines. The question we tried to answer in this paper is for how long we can prolong the conservative, non-operative treatment in AF. Based upon literature research and our personal experience we may state that the earlier institution of medical specific treatment (CCB, nitric oxide donors, botulinum toxin) has more chances to heal the patient and avoid surgery. Success is also dependent on the good communication with the patient, detailed explanation of the purpose of the treatment, how to assess himself the evolution, and employ botulinum toxin earlier if patient is less compliant to topic treatment. Conservative non-operative management should be pushed as long as it is correctly applied and progression is made both from subjective and objective point of view and patient is compliant and content.*

**Key words:** *anal fissure, conservative treatment, internal anal sphincter, chronic anal fissure.*

**Introduction**

The definition of an anal fissure according to the Manual of Coloproctology, second edition is a painful tear in the epithelial lining of anoderma anterior or posterior, distal to the dentate line [1].

The etiology is considered to be multifactorial, including passage of hard stools, forceful and bulky defecation, diarrhea, trauma and other causes.

From the objective point of view, we encounter 2 types of anal fissures in our practice, as every other proctologist does. The recent fissures, usually less than 2 weeks, which are linear in shape, sharp, clean edges, bleeding during the examination that we may call acute anal fissures (AAF).

The other aspect is an anal fissure, triangular in shape, with apex at the dentate line, base at the anal verge, a “sentinel pile” on the outside, a hypertrophic papilla at the apex, edges may be sclerous, the base of the fissure may exhibit fibers of the internal sphincter, without any objective sign of granulation tissue. In the old books, this was the classical description of an anal fissure, nowadays we consider this a chronic fissure (CAF).

**Pathogenesis of the Chronic Anal Fissure**

The pathogenesis of the CAF is surely a complex one, there is no single mechanism involved.

The most consistent findings in anal fissures are the hypertonicity of the internal sphincter with an elevated resting tone. This is an objective sign that we note immediately when we try to examine the patient by digital tact, that is mostly impossible, requiring sedation, local anesthesia by topic of injection, loco-regional or general anesthesia to complete the proctologic examination. Manometric studies of the resting anal tone support this objective finding [2].

Internal sphincter spasm is generated by the presence of the fissure, deep enough to expose the sensitive nerve endings and it is reflex and it is decreasing the blood flow that crosses it to reach anoderma, contributing to a delayed or no healing progression. This has been demonstrated in several studies assessing the blood perfusion using Doppler laser flowmetry [3, 4].

In most of the cases this chronic aspects of AF are located at the posterior and anterior commissures, only 10% of the patients having fissures at the anterior midline and in 1% both commissures being involved [5]. Anterior location is more frequent in women [6]. There is a postulate that fissures occurring on other places than anterior and posterior commissures should raise the suspicion of other diseases like Crohn disease, sexually

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transmitted disease or even AIDS [7]. Explanation of this predilection may come in the majority of cases, from the anatomy, blood supply coming from inferior rectal arteries, on both sides, crossing the internal anal sphincter to reach anal anoderma, do not have any or minimal contact in the posterior commissure in 85% of cases. This fact was demonstrated by Klosterhafen et al in a post-mortem angiographic study [8].

A personal observation is that cicatrization may be delayed also in patients suffering from chronic diseases as diabetes mellitus or renal insufficiency, due to the alteration of small blood vessels as a result of a systemic disease. All of those features suggest that the anal fissure behaves like a chronic ischemic wound, due to a vicious circle of “pain - IAS spasm - decreased blood flow - no healing - pain”. Some studies found consisting evidence for small blood vessels alterations similar to a vasculopathy. Maria et al. identified in the peripheral blood of patients with chronic anal fissures circulating antibodies against intimal endothelial cells and deposits of antigen-antibody complexes in the small branches of the rectal arteries [9].

## Treatment

Not all acute anal fissures go into this vicious circle leading to a non-healing, ischemic wound. Normally, a wound in this area should heal spontaneously like any other wound in the human body, in a period of maximum 2 weeks. A part of them may indeed do so, as in the anamnesis of the patients, they report episodes of constipation, with pain after one strenuous, difficult defecation, after an episode of constipation, bleeding on paper, pain that reappears after several stools with minor bleeding, symptoms typically related to an anal fissure, but they gradually resolve and, when seen in consultation, the examination reveals normal anoderma.

Some of the patients performed by themselves sitz baths, take stool softeners or laxatives, eat more fibers and drink more liquids to soften the stools, a fact that reduces the pain after defecation and improves symptoms. Some of them consult their pharmacist or family doctor, in the best case, and are advised to use ointments, suppositories, jelly containing substances that promote local contact anesthesia, have anti-inflammatory, siccative effect, and promote cicatrization, made either from natural plants or synthetic. These products are plenty on the market, and are advertised for hemorrhoids and/or anal fissures, consisting in fact in a purely symptomatic treatment. This treatment is considered as conservative one and is used by many specialists in proctology as a first line therapy and is also included in guidelines. Treatment of CAF anal fissure should not aim to the wound itself but to the breaking of this vicious circle by any means, by addressing the internal anal sphincter spasm and improving blood flow.

From its first description in 1829 by Recamier, we have the first therapeutic measure indicated as anal stretching, a technique that will weaken the thin internal

anal sphincter by overstretch, but without any control in preventing damages to the external anal sphincter, therefore it is considered historic.

The most successful treatment of the AF was surgical sphincterotomy, initially performed in the AF's bed, cutting only through the fibers of the anal sphincter that are visible, or going up to the dentate line, excising wound edges, papilla and sentinel pile a so called fissurectomy, that will rejuvenate the wound and help healing.

This operation was successful in almost all cases but left a deformity of a keyhole appearance or a groove responsible for a period of time of minor leakage of liquid drops of stools or staining the underwear. In some patients this could be permanent, in others may be present for a determined period of time.

To avoid this, recently a lateral sphincterotomy is indicated, involving the distal part of the internal sphincter. An anterior internal sphincterotomy is prohibited by the fact that external anal sphincter is weaker in this region. The success of the surgical sphincterotomy is related to the amount of internal sphincter that is cut. A complete sphincterotomy, up to the dentate line will be mostly effective in healing almost all fissures but may increase the percentage of the incontinence symptoms. Risk of incontinence may be as high as 10%, especially for flatus [10, 11]. A postal survey of patients operated for anal fissure revealed a higher rate of incontinence: 28.7% for stool and 31.5% for gas. Risk for incontinence may increase over the years because of the weakening of the anal sphincter with age [12]. If a lateral sphincterotomy is performed, a part of 25% up to 50% of sphincter maybe cut with good results in healing and risk of incontinence [1] the recurrence maybe higher or healing incomplete in worst cases, but it can be extended by a second intervention.

Another possibility is to tailor the sphincterotomy only for the fibers of internal sphincter seen in the fissure bed. Both techniques are credited with lower rate of incontinence.

The way of doing it: open or closed sphincterotomy is a matter of choice depending upon the expertise of the proctologist, we prefer to lay it open to avoid formation of abscesses, the patient will be taught to performed regular sitz baths, perform self anal dilation with ointments that include local anesthetics and even local antibiotics, but this is low grade recommendation, based upon personal expertise and not on high grade evidence.

## Medical Treatment

The necessity of avoiding those side-effects pushed specialist in seeking a “Medical Sphincterotomy” or a “reversible sphincterotomy” or a “chemical sphincterotomy” in decreasing the internal sphincter tone by oral, topic medication, or botox injections.

*Calcium channel blockers* (CCB) Oral Nifedipine, Nifedipine gel 0.2–0.5%, Diltiazem cream 4%, were employed with success in treatment of AF based on the



effect of relaxing the smooth muscle, inducing vasodilatation and reducing anal spasm. The side effect is hypotension and headache. Topic application has more local direct effect and less systemic side-effects [13, 14]

*Nitric oxide donors.* Nitric oxide is a neurotransmitter that induces smooth muscle relaxation and therefore, internal sphincter relaxation. The mostly employed are glyceryl-trinitrate (GTN) and nitro glyceryn (NTG). GTN is used in concentrations of 0.2% to 0.4%. Although demonstrated effective in treating AF [15], contrary to what we might have expected higher concentrations do not offer higher rates of healing [16]. NTG is used in concentrations from 0.1–0.6%. Healing takes place usually after 6–8 weeks but sometimes it requires 12 weeks to heal. Side-effects, more often encountered if the dosage is increased, are headaches, making a part of the patients non-compliant to the treatment. The phenomenon of tachyphylaxia is also possible making necessary to increase dosage [17].

#### *Botulinum toxin (Botox)*

The role is to induce a local paralysis of the IAS for a period of 3–4 months, that should be enough for a complete healing. The effects are reversible and so are any incontinence symptoms during the treatment. Indicated for AF is the botulinum toxin type A [18]. The dosage found to be effective is 20–25 units injected in the anal sphincter. Studies regarding the dosage showed a surprising evidence of an efficiency in healing and incontinence non influenced by the dosage, formulation and type of toxin. Also the site and number of injections per session didn't influence the healing rate [19]. Lower doses of botox reduce the risk of incontinence and recurrence in the long term. The optimum injection site could not be determined [20]. For example, in our experience, we use to inject a total amount of 25 units (toxine type A), 12.5% on each side of the CAF.

### **Comparison between Different Treatments**

A systematic review and meta-analysis of all published treatments for anal fissure that have been studied in randomized controlled trials was performed by Nelson et al. relatively recent in 2017. The conclusions are very clear supporting calcium channel blockers over GTN, with less risk for headache as side effects, a feature important for long-term treatments. The rate of healing is lesser that of lateral surgical sphincterotomy that is credited with a rather lower rate of incontinence of 3.4–4.4%. This is probably due to performing a distal internal sphincterotomy rather than a complete one. Open LIS and closed LIS were equal in regards of efficiency [21].

Botox injections have a risk of anal incontinence, but fewer side-effects compared to nitric oxide donors [22].

### **The Sequence of Treatment Indicated in the Guidelines**

The 2014 American College of Gastroenterology clinical guideline on the management of benign anorectal disorders made the following recommendations for anal fissure [11]:

*Acute anal fissure* – Providers should use nonoperative treatments (e.g., sitz baths, psyllium fiber, and bulking agents) as the first step in therapy (strong recommendation, moderate-quality evidence)

*Chronic anal fissure* – Providers should treat chronic anal fissure with topical pharmacologic agents (eg, calcium channel blockers or nitrates) (strong recommendation, moderate-quality evidence)

*Chronic anal fissure* – Providers should refer patients who do not respond to conservative or pharmacologic treatment for local injections of botulinum toxin (strong recommendation, low-quality evidence) or internal anal sphincterotomy (strong recommendation, high-quality evidence) [23].

*The question to be answered is for how long should we keep the patient on medical or conservative (non-surgical) treatment before referring him to surgery?*

If it is an acute anal fissure the dietary changes, sitz baths, local symptomatic ointments heal the fissure in the majority of cases [24]. Rates of healing may be up to 50–80%. If a fissure has a chronic aspect, the response to such dietary and habits changes is rather low. In those cases this will remain as an “adjuvant” to the medical treatment [25]. We should not prolong this kind of treatment beyond 2–3 weeks at maximum, because this simply mostly symptomatic treatment, because after this period the AF is entered probably in the vicious circle mechanism that doesn't allow further healing.

In a study performed by Sileri et al, in which the patients were submitted gradually to medical treatment first, botox injection and as a last resource IS, we may find some orientating results. Beside dietary adjustment, sitz baths, initially, the patients with CAF were submitted to NTG 0.2% twice a day, applied to the fissure and to the internal sphincter for a period of 8 weeks with a rate of healing of 54%. If the patient was still symptomatic after 8 weeks, Botox injections were proposed or prolongation of treatment with NTG. After 12 weeks the rate of healing was 64% for NTG. Rate of healing after Botox was 84%. Patient showing an incomplete healing were submitted to either another injection of Botox or surgical sphincterotomy. LIS had a cure rate of 98.7% with no definitive incontinence on long-term follow up [26].

Personal observation come from a series of 567 patients seen in the last 4 years in consultation in our clinic as outpatient, their observation files were retrieved and data within reexamined and analyzed. There was a slight male predominance of 307/267 (1,15 x higher). Most of the patients were in the 30–50 years of age - 252 (44.44%), 20% under 30 years, and 35% over 50 years of age. So, nearly 80% of patients were over 30 years old. Co-morbidities of arterial hypertension were

met in 69 patients, diabetes mellitus in 31 and irritable bowel syndrome in 56.

Beside the basic recommendations as stool softeners, sitz baths, dietary fibers, laxatives etc. the patients were treated with topical medical ointments to relax the anal sphincter and were advised to apply it at least 4 times per day and seen regularly every 2 weeks. 207 patients healed after 2 weeks (36.5%), 147 after 1 month (26%), 90 (16%) between 4–12 weeks and 72 (12.7%) patients needed treatment for longer than 12 weeks. 10 patients were treated by botox and registered complete healing and 25 patients (4.4%) required an internal sphincterotomy for complete healing that was performed in the fissure bed involving only the sphincter up to the apex of the fissure.

We have noticed a direct relationship between the duration of fissure symptoms and the period of healing.

The most important thing during the period of treatment is good communication with the patient, detailed explanations of different methods of treatment, advantages and disadvantages, risk of side-effects, incontinence and adapt to the symptoms and psychology of each patient. The patient should be instructed to continue performing sitz baths, taking fibers, drinking plenty liquids, using laxatives, glycerin suppositories, small enemas to unblock the stools, and apply rigorously and very correctly the topical treatment. Generally, even in patients with the worst symptoms there is a clear consistent improvement after 5-6 days in intensity and duration of pain. The patient should be given an orientation for the progression of treatment to follow those 2 aspects and report them at each visit. Also video documentation should be used to monitor healing and motivate the patient (Figs. 1 and 2).

Even after the healing the patient should remain on a rich fiber diet, with plenty of liquids, avoid constipation by glycerin suppositories, small enemas or soft laxatives to avoid hard stools. In our experience, constipation was the main cause for the recurrence of the fissure. The medical



**Fig. 1** Anterior CAF with clean edges, some granulation tissue visible in the fissure bed, triangular shape – aspect in evolution under medical treatment



**Fig. 2** Posterior chronic anal fissure with fibroses in the fissure's bed, granulation tissue on the edges, under medical treatment

treatments as NTG, CCB are useful and cheaper but necessitate administration in at least two times/daily, best 4–5 times for a period of time from 2 weeks to 12 weeks, the median is 6-8 weeks. We noticed a linear relationship between the period of anal fissure and the time of healing, the longer the history of fissure, more time is taking to complete healing. The disadvantage is the necessity of multiple applications, necessitating some minimal conditions of privacy and hygiene during the day, or in the working place, some minor degree of tachyphylaxis. The patient should be seen every two weeks to be sure that the applications is correct, the diet is correct and adjust treatments by changing topical treatments

Botox is a very good option and could be recommended after 6–8 weeks of topic treatment. The disadvantage is the cost. Otherwise, the botox therapy could be very well proposed to the patients from the first place. In patients that are not compliant from any reason for topical treatment this could be recommended from the first place

The choice between medical treatments of botox, the sequence, the decision to inject botox should always comply with the patient. Remember that we treat patients and not disease. Detailed discussion with the patient, good communication, details about habits, diet, style of life, job at least should be obtained, the advantages and disadvantages of every type of treatment should be exposed and the decision taken after considering at least all those factors and the choice of patient.

In conclusion, the conservative, non-operative treatment should be pushed as much as possible, and surgery avoided as much as possible, as long as the pain and compliance of the patient otherwise passage to surgery is the most reliable and sure thing to heal.

The conservative treatment involves a great deal of work and communication with the patient, but it may be rewarding at the end, and even if a recurrence take place this is due to mainly to patient lack of adherence to the principles of diet. Of course, each recurrence may be treated with success again by medical non-surgical therapy and again the decision should be taken together with the patient and if necessary surgery will be performed when compliance of the patient is obtained.

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## Review Article

**SURGICAL TREATMENT OF ADVANCED GASTRIC CANCER****Nebojša Ignjatović<sup>1,2</sup>, Goran Stanojević<sup>1,2</sup>, Miroslav Stojanović<sup>1,2</sup>, Ljiljana Jeremić<sup>1,2</sup>, Milica Nestorović<sup>1,2</sup>, Vesna Brzački<sup>1,2</sup>, Daniela Benedeto Stojanov<sup>1,2</sup>, Miodrag Djordjević<sup>2,3</sup>, Mirjana Marinković<sup>2</sup>**<sup>1</sup>Clinic of Digestive Surgery, Clinical Center Niš, Niš, Serbia<sup>2</sup>University of Niš, Faculty of Medicine, Niš, Serbia<sup>3</sup>Clinic for Endocrine and Breast Surgery, Clinical Center Niš, Niš, Serbia

**Abstract.** *Patients with advanced gastric cancer generally have poor overall prognosis as well as survival rate. Unfortunately, in the West, gastric cancer typically occurs at an advanced stage and many of these patients have tumor invasion into adjacent structures (International Union Against Cancer [UICC]/American Joint Committee on Cancer [AJCC] Stage T4). Although T4 gastric cancer patients often have peritoneal dissemination or distant metastasis, many do not have M1 disease and are therefore candidates for surgery with the curative intent. A multivisceral resection (MVR) or gastrectomy with resection of adjacent organs is needed in T4 gastric cancer patients to achieve an R0 resection that is one of the most powerful forecasters of gastric cancer surgery results. Spleen, distal pancreas, liver, and large intestine (mostly transverse colon) were the most commonly resected organs. The therapeutic choice with acceptable postoperative morbidity and mortality rates in locally advanced patients with gastric cancer should be gastrectomy with MVR, where complete resection could be realistically obtained and where metastatic involvement of the lymph node is not evident. MVR is done with a curative R0 resection to provide advanced gastric cancer patients with the best survival chance. It was found that resections involving the pancreas, transverse colon and liver were associated with increased survival rate in comparison to MVR with resection of other structures. It was shown that survival rate significantly decreased in patients who had undergone MVR without complete resection compared to those who had an R0 resection. Nevertheless, the extent of the surgical resection required and further advantages of MVR are disputable.*

**Key words:** *advanced gastric cancer, gastrectomy, multivisceral resection.*

**Introduction**

Gastric cancer remains the world's second-largest cause of cancer-related death [1,2], including 10% of newly diagnosed cancers [2]. While gastric cancer pathogenesis and etiology are a prevailing research topic with no proven definitive mechanism to this day, many well described risk factors exist. Intestinal metaplasia, gastric adenomatous polyps, helicobacter pylori, pernicious anemia, giant hypertrophic gastritis (Ménétrier disease) and chronic atrophic gastritis are known to be associated with gastric cancer [3]. Unlike Western patients, Asian gastric cancer patients have a better prognosis due to earlier detection of the disease through frequent screening programs. The overall disease survival rate in Japan is over 70%. On the other hand, over two thirds of gastric cancers in the United States as well as in Europe are usually discovered with a locally advanced resectable disease in advanced stages, since routine gastric cancer screening is not recommended due to its cost. Consequently, a 5-year survival rate of merely 25% for locally advanced disease is recorded in these countries [4].

**Histopathology Classification**

Two major types of gastric cancer, intestinal and diffuse, were characterized by Laurèn in 1965. Metastasis patterns differ from the two types of gastric cancer. The diffuse tumors show a wider spread than intestine tumors. Furthermore, in diffuse cases, lymphatic permeation of the lungs, tumors of Krukenberg and peritoneal metastases are more common. However, the liver is more commonly involved in the intestinal cancer type. Gastric adenocarcinoma rarely reports intestinal metastases. Primary stomach tumors with intestinal metastases are generally poorly differentiated with or without ring-cell differentiation of the signet and most often belong to the scirrhous type. These metastases rarely include the liver and are often associated with peritoneal seeding. There were three reported cases of multiple colonic metastases of poorly differentiated gastric adenocarcinoma presenting as colonic polyposis. In one case, multiple flat elevated lesions appeared in a rare form of gastric signet ring-cell cancer with metastases to the colon [5].

In research in determining tumor stage in gastric cancer, representing the most important independent prognostic factor, as well as for clinical practice, the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) tumor, node, metastasis (TNM) staging system has been used [4].

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Determining the prognosis is highly influenced by the final pathological stage that follows the curative surgery. In patients with pathological stages II, III and IV, survival rate is significantly lower [6].

## Optimal Surgery Treatment

### The type of gastrectomy

The most important curability factor is surgical resection [7]. The site of the primary tumor with the resection margin of a minimum of 5cm from the edge of the tumor determines the type of gastrectomy. According to the Lauren classification, total gastrectomy is used to treat the 'diffuse' type tumors which are likely to spread laterally. It might not be necessary for distal types of tumors in case that mapping biopsies, careful radiological review, adequate staging, on-table Oesophago-Gastro-Duodenoscopy (OGD) with or without frozen section provide satisfactory results. Tumors of the gastric antrum (distal third cancers) need a subtotal (80%) gastrectomy, with the excision of regional lymphatic tissue and the division of the left gastric vein and artery. Total gastrectomy is performed when sub mucosal tumor infiltration is within 7–8 cm of GOJ or in case of a large distal third tumor. In cases of palliation or in the very elderly, only limited gastric resections are recommended. There is no oncological advantage but increased morbidity in resecting spleen and distal pancreas for a cancer in the distal two-third of stomach. Tumors of the gastric body (middle third cancers) usually need a total gastrectomy, since it depends on the proximal tumor margin. The stomach level that remains below GOJ should be at least 2cm. A 7cm margin from GOJ is required in serosa negative cancer cases, while 8cm margin from GOJ is standard in serosa positive cancer. The surgery's overall goal is appropriate lymphadenectomy (formal D2 and posterior mediastinal, periesophageal nodes), adequate local clearance, as well as low morbidity uncomplicated anastomosis. In patients with tumors of proximal stomach located on greater curvature/ posterior wall of stomach close to splenic hilum where incidence of splenic hilar nodal involvement is likely to be high, splenic and hilar node resection are considered [6].

### Extension of gastric resection

T1 disease is present at >80% of gastric cancer patients and merely 40% of early gastric cancer are related to symptoms. Overall, 85% patients have lymph node metastases, 65% patients present as advanced cancers (T3, T4), and 40% are metastatic. Since this is a locoregional disease, the primary surgical aim is to remove the primary tumor with clear longitudinal and circumferential resection margin, with resection of associated lymph nodes and combined organ resection as required (R0 resection), following the restoration of intestinal and biliary continuity to allow adequate nutritional intake [6].



**Fig. 1** Intraoperative view of advanced gastric cancer

Patients with advanced gastric cancer (Fig. 1) benefit from curative resection and an R0 resection is mainly related to improved survival rate. Some researches claim that multivisceral resection (MVR) can be done in adequately selected patients with acceptable morbidity and mortality. The most frequently resected organs were liver, distal pancreas, spleen, and large bowel (mostly transverse colon). Other frequently resected organs included gallbladder and small bowel. The organs that were less frequently resected were adrenal gland, diaphragm, pericardium, mesocolon, kidney, lung, ovary and uterus. In gastrectomy patients with MVR, the perioperative mortality rates were from 1.9 to 15.0%, with five-year survival rates of 0–40%. These researches were done with the aim to identify predictors of long-term survival, including the number of resected organs, UICC/AJCC stage, margin positivity and other factors, which may play a role in adequate patient selection for MVR. In order to provide patients with advanced gastric cancer the best chance at survival with a curative R0 resection, MVR is performed. Survival rate in MVR without a complete resection patients was shown to be significantly lower in comparison to those who underwent an R0 resection. Poor outcomes appear to be linked to both microscopic and macroscopic positive margins [8].

Despite the fact that a retrieval of a minimum of 16 lymph nodes and a surgical R0 resection are mandatory surgical principles, there is still some polemics on lymphadenectomy and the extent of surgical resection. The primary tumor removal is based on the location, extension and histologic subtype of gastric cancer [4]. R0 resection (negative microscopic and macroscopic margins) is a powerful forecaster of outcome for curative gastric cancer surgery patients. Unfortunately, gastric cancer is generally found at an advanced stage, and tumor invasion into adjacent structures (International Union Against Cancer [UICC]/American Joint Committee on Cancer [AJCC] Stage T4) is present in most of the patients in the West.

Even though T4 gastric cancer patients will often show peritoneal dissemination or distant metastases,

many of them do not have M1 disease, which makes them suitable candidates for the surgery with the curative intent. A MVR, or gastrectomy with resection of adjacent organs is needed to achieve an R0 resection in patients with T4 gastric cancer [8]. On the other hand, many patients suffer from the incurable, advanced stage gastric cancer. The primary objective of palliative resection for this type of patients is relief of symptoms such as tumor bleeding, obstruction, or perforation. Studies have shown that surgical resection for stage IV gastric cancer can be done with low operative mortality and acceptable morbidity rates. It also provides good symptomatic relief for the patient [7].

Treating patients who are at stage IV disease includes the following: systemic chemotherapy, surgical bypass procedures, palliative resection, endoscopic interventions, investigational therapies, or best supportive care. Only modest survival rates have been recorded in patients treated with best supportive care alone. Palliative resection for stage IV gastric cancer is nowadays not a standard part of care, even though it was practiced regularly in the past. Certain previous researches have shown a benefit to the stage IV gastric cancer patient in case of palliative resection. On the other hand, palliative resection also brings the risk of surgical morbidity and prolonged hospitalization. This might reduce instead of improve the quality of life and survival rate of this type of cancer patients [9].

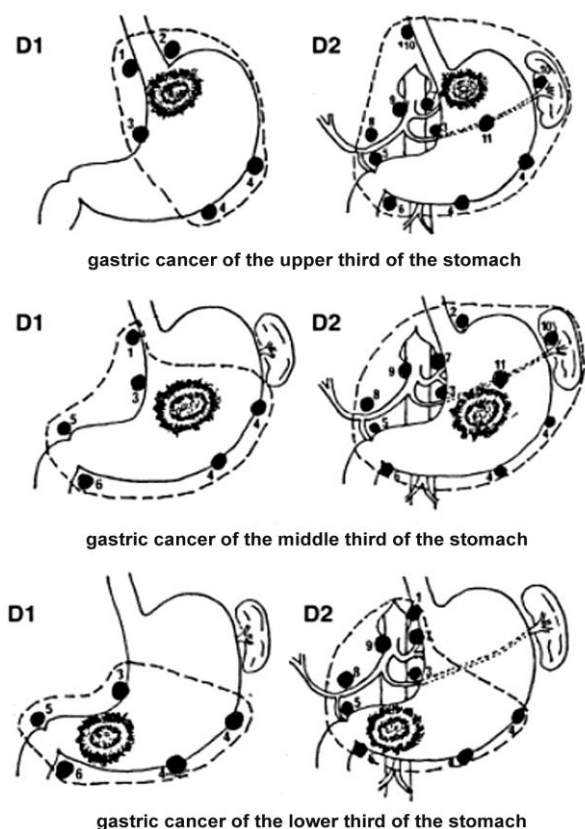
At the moment, the general opinion is that “a proximal margin of at least 3 cm is recommended for T2 or deeper tumors with an expansive growth pattern and 5 cm is recommended for those with infiltrative growth pattern”, which puts an end to a long-term dispute. However, in T4 cases, a MVR (MVR), or gastrectomy with resection of adjacent organs is sometimes needed to provide patients with advanced gastric cancer the best survival chance with a curative R0 resection, but the prognostic benefit of MVR in patients with locally advanced disease and the postoperative morbidity are still under debate [4]. Kasakura et al. [10] found a higher complication rate in MVR group in comparison to gastrectomy alone group, with no difference in survival rates. Pacelli et al. found in their Italian multicenter observational study no important differences in mortality rates and postoperative morbidity [11]. Other researches show a survival disadvantage for gastrectomy with additional organ resection. On the contrary, most researchers found an overall 5-year survival improvement (19.9%–38%) for gastrectomy with MVRs patients when compared with gastrectomy or palliative surgery patients. In patients with T4 gastric cancer undergoing curative R0 resection, the 5-year survival rate ranges from 23% to 46%. It decreases in cases of R+ resection, ranging from 17.5% to 0%. Colectomy, splenectomy, pancreatosplenectomy, or any other organ resection did not forecast poor survival. In locally advanced gastric cancer patients where a complete resection could be realistically obtained and when lymph node metastatic involvement is not evident, the gastrectomy with MVR

should be the therapeutic choice, with an acceptable postoperative morbidity and mortality rates (4). Even though radical resection has been found to be closely connected to long-term survival for gastric cancer patients, curative resection for locally advanced gastric cancer, defined as T4 in which the tumor invades adjacent structures (T4b) or perforates serosa (T4a) was related to increased postoperative morbidity and mortality. Due to early detection of gastric cancer and improved surgical technique, the gastric cancer patients' prognosis has significantly improved. On the other hand, T4 gastric carcinoma patients' prognosis remained poor. It is therefore paramount to clarify the incidence of postoperative morbidity and mortality in patients with T4 gastric cancer who opt for curative surgeries and to determine the prognostic factors in these populations [12]. Gastrectomy with D2 lymphadenectomy (resection of perigastric lymph nodes and nodes along the named branches of the celiac axis) is considered standard surgical procedure for the advanced gastric cancer and most early-stage gastric cancers [3].

### The extent of gastrectomy

The extent of gastrectomy being performed (i.e. total, subtotal/distal, or proximal gastrectomy) defines the extent of lymphadenectomy. Most commonly, a D2 dissection for a total gastrectomy would involve retrieval of lymph node stations 1-12 with a concomitant distal pancreatectomy and splenectomy. Moreover, a D1 dissection would require the perigastric nodes at stations. Lately, a modified approach to a D2 dissection by sparing the spleen and pancreas unless directly involved with the primary tumor was proposed. This technique of sparing the spleen and pancreas has shown adequate retrieval of lymph nodes without the morbidity associated with multi-visceral resection (3).

D1 lymphadenectomy happens when all N1 nodes (perigastric nodes closest to primary) are removed en bloc with the stomach (limited). D2 includes systematic removal of all N1 and N2 (distant perigastric nodes and nodes along main arteries supplying stomach) en bloc with stomach. Figure 2. Gastric cancer often remained localized to stomach and adjacent lymph node. This supports the Japanese view that radical systemic D2 lymphadenectomy has increased survival benefits. The present European description of D2 lymphadenectomy includes the removal of >15 lymph nodes, irrespective of node stations. Moreover, extended D3 lymphadenectomy represents a radical en bloc resection with N3 nodes outside normal lymphatic pathways from stomach, included in advanced stages station (hepatoduodenal ligament) or by retrograde lymphatic flow due to blockage of normal pathways [8]. The Japanese researchers have supported the claim that D2 resection should be used in all patients with invasive gastric carcinoma, including early gastric cancer patients. They also argued that a D3 lymphadenectomy should be performed in all patients with advanced gastric cancer with



**Fig. 2** Lymphadenectomy range depending on the localisation of the gastric cancer

serosal invasion [1]. Two independent factors associated with survival were total lymph node count and number of positive lymph nodes. In patients who had more than 15 N2 nodes and 20 N3 nodes examined, a significant survival benefit was recorded. The pathologic assessment of at least 15 nodes is considered standard of care. Also, D2 lymphadenectomy is recommended, even though there is no general rule on the level of dissection required (D1 vs. D2) in the U.S. Higher post-operative mortality (13% vs. 6.5%,  $P=0.04$ ) was shown in one of the Western studies and morbidity rates (46% vs. 28%,  $P<0.01$ ) in the D2 lymphadenectomy group. There was a higher chance of undergoing concomitant pancreatectomy and splenectomy. Anastomotic complications in the D2 dissection group have shown significantly higher rates, also including severe pancreatic fistula, pancreatitis, and gastric remnant necrosis. There was no difference in overall survival, gastric cancer related deaths, or recurrence-free survival in long-term results. On the other hand, recent studies from the East and West indicate improved morbidity and mortality if routine splenectomy and pancreatectomy is avoided, in comparison to traditional D2 resection [3]. Cuschieri et al. [13] evaluated 400 patients randomized to a D1 or D2 lymphadenectomy and found a significant survival difference between patients with gastrectomy and splenectomy or pancreaticosplenectomy compared to gastrectomy alone, with no regard to the extent of lymphadenectomy.

## Survival and Complication

When it comes to locally advanced gastric cancer, particularly if the adjacent organ is invaded (T4), the prognosis will be poor since a high incidence of postoperative morbidity and mortality is reported in studies, and the curative resection itself is difficult [1]. For many years, the benefits of extended organ resection for advanced gastric cancer have been discussed. This debate was recently sparked by the results of both the United Kingdom Medical Research Council and the Dutch trials evaluating the survival benefit of extended lymphadenectomy. A significant survival disadvantage in patients who have undergone gastrectomy with splenectomy or pancreaticosplenectomy was reported by both of these randomized control trials. The Medical Research Council study and the Dutch trial found that a higher complication rate, higher mortality and longer hospital stay are closely related to extended organ resection. The potential advantage of extended resection for clinical T4N0 gastric adenocarcinoma is necessary to improve the R0 resection rate of these lesions. The observed increase in the morbidity and mortality rates, with low survival benefits fuel the arguments against this approach. In patients undergoing gastrectomy alone, the complication rates of additional organ resection with gastrectomy have been reported to be high. When it comes to patients undergoing splenectomy, both overall complications and infectious complications have been reported. The increase in overall complications and infectious complications is the suggested reason for the decrease in overall survival. This is why performing additional organ resection in patients with T4 disease has been scrutinized. With minimal perioperative mortality (4%), gastrectomy with additional organ resection for gastric cancer can be realized. In this patient subset, long-term survival can be reached, with a 3-year survival rate of 47%. The biology of the primary lesion (i.e., depth of invasion and nodal stage) might forecast overall survival in this patient group. Gastrectomy with additional organ resection can be done with low mortality and acceptable morbidity if careful patient selection is implemented. In order to minimize unnecessary organ resections for early-stage disease, certain improvements should be made in preoperative evaluation to confirm T3 and T4 disease. The most powerful forecasters of survival following an R0 resection are depth of invasion and presence and extent of lymph node metastasis. With the understanding that the majority will be T3, gastrectomy with additional organ resection should be limited to clinically T4 tumors [14].

It cannot be said with certainty that gastrectomy alone, when yielding an R1 or R2 margin, is appropriate when R0 resection with MVR is feasible and safe. Just a few studies examined survival in relation to the type of organs resected. On the other hand, resections involving the transverse colon and the liver have been shown to be related to the increased survival compared to MVR with resection of other adjacent structures. The aim of R0 resection must take into account whether gastric cancer

is actually invading adjacent organs. MVR should be reserved for T4 lesions, with true histological invasion into adjacent organs, given the risk of morbidity. Adhesions secondary to desmoplastic reaction can resemble a local invasion, especially when the pancreas is involved. MVR might include resection of two or more organs in pursuit of negative margins. Four studies studied the number of organs involved or resected as a survival forecaster. Also, Martin et al. found an increase in operative complications with lower 5-year survival while comparing one-, two-, and three-organ resections in addition to gastrectomy [8].

## Conclusion

The only curative surgery for non-metastatic gastric cancer is surgical resection with extended lymph node dissection. In patients with locally advanced gastric

cancer with the goal of R0 resection, gastrectomy with MVR can be performed. The benefit of attaining an R0 resection positively influences overall patient survival, even though morbidity and mortality may be higher. Nodal status and the number of organs involved must be taken into account when it comes to patient selection for MVR and an attempt to identify true histological invasion before and during resection should be made.

In locally advanced gastric cancer patients, when a complete resection could be realistically obtained and when lymph node metastatic involvement is not evident, the gastrectomy with MVR should be the therapeutic choice with acceptable postoperative morbidity and mortality rates. Liver, pancreas and the transverse colon resections have proven to be related to increased survival in comparison to MVR with resection of other adjacent structures.

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## Review Article

**FISTULOTOMY FOR THE SURGICAL TREATMENT OF PERIANAL FISTULA OF CRYPTOGLANDULAR ORIGIN**

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**Abstract.** Perianal fistula usually results from a non-specific infection of the cryptic glands located at the anal dentate line. Identification of the exact course of a perianal fistula and the extent of anal sphincteric complex involvement are of paramount importance, in order to design the therapeutic and interventional approach and achieve the best results without impairment of the anorectal function. Several interventional methods are in use for the surgical treatment of CPF, including fistulotomy, insertion of cutting “seton”, core fistulectomy, ligation of the intersphincteric fistulous track (LIFT), rectal advancement flap, injection of fibrin glue at the fistulous track, insertion of fistulous plug, and obliteration of the fistulous track with the use of Laser. In clinical practice a combination of the aforementioned methods can be used, in particular for the complex-high or recurrent fistulae.

**Key words:** perianal fistula, fistulotomy, anal sphincter.

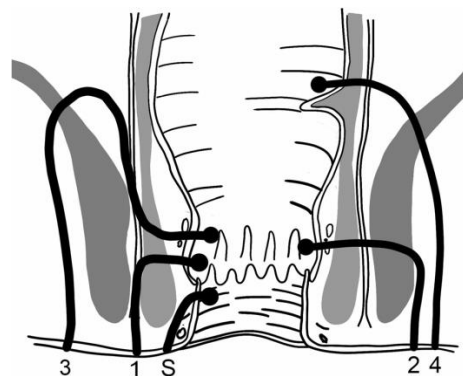
**Introduction**

Perianal fistula usually results from a non-specific infection of the cryptic glands located at the anal dentate line. Other less common causes are infection from unusual bacteria, inflammatory bowel disease – mostly Crohn’s, malignancy, trauma and radiation of the perianal area [1–4]. According to the course through the anal and perineal musculature to their origin at the dentate line, Parks et al. [5] classified perianal fistulas as subcutaneous-superficial, intersphincteric (coursing between internal and external sphincter), transsphincteric (coursing through the external sphincter and internal sphincters), suprasphincteric (coursing over the puborectalis) and extrasphincteric, the latter usually different to cryptoglandular sepsis etiology. More recently, perianal fistulae are classified as low (involvement of the distal third of the sphincteric complex) and high (involvement of the middle or/and the upper third of the sphincteric complex) (Fig. 1). In addition, low and high perianal fistulae are classified as simple and branching [6].

**Diagnostic Methods**

Identification of the exact course of a perianal fistula and the extent of anal sphincteric complex involvement are of paramount importance, in order to design the therapeutic and interventional approach and achieve the best results without impairment of the anorectal function. Magnetic resonance imaging (MRI) is considered the gold standard diagnostic tool for the assessment of cryptoglandular perianal fistulae (CPF), in particular the high ones, with

accuracy rates above 90% [7–10]. Also, valuable information for high, complex and recurrent CPF can be obtained with the use of three-dimensional endosonography. Accuracy rate of this modality ranges from 50% to 100%, depending on the examiner’s expertise [10–15]. Combination of both modalities increases accuracy [10].



**Fig. 1** Diagrammatic representation of the Park’s classification of perianal fistula. S: subcutaneous-superficial; 1: intersphincteric; 2: transsphincteric; 3: suprasphincteric; 4: extrasphincteric [5].

**Treatment**

Several interventional methods are in use for the surgical treatment of CPF, including fistulotomy [16–18], insertion of cutting “seton” [19–21] or loose “seton” [21–23], core fistulectomy [24], ligation of the intersphincteric fistulous track (LIFT) [25], rectal advancement flap [26–30], injection of fibrin glue at the fistulous track [23,31,32], insertion of fistulous plug [33,34], and obliteration of the fistulous track with the use of Laser [35–37]. In clinical practice a combination

of the aforementioned methods can be used, in particular for the complex-high or recurrent fistulae.

### Fistulotomy for the Low CPF

Despite some discrepancies in the indications among several guidelines [10], fistulotomy (FT) is the most common method for the surgical treatment of CPF. The main indications of FT are the superficial-subcutaneous, intersphincteric and low transsphincteric (involving less than 30% of the anal sphincter complex) CRF [9,10,14,38]. Relative contraindications of FT for intersphincteric and low transsphincteric CPF are i) preoperative impairment of continence, ii) multiparous female with marginal fecal continence, iii) previous surgery, iv) recurrent CRF after fistulotomy, and v) Crohn's disease. Absolute contraindications of FT as the sole treatment are high transsphincteric, suprasphincteric and extrasphincteric CPF [10,39–41].

As regards the operative technique, under general anesthesia and the guidance of preoperative imaging assessment, i) the external opening is visualized, ii) the internal opening at the dentate line is identified with the injection of methylene blue through the external opening, iii) any branching of the fistula is also sought and identified, iv) a probe is gently inserted from the external opening, through the fistulous track to the internal opening at the dentate line, and v) the FT is carried out in a lay-open fashion with the use of a scalpel or electrocautery.

FT for the simple and low CPF is associated with high success rate, ranging from 80% to 100%, at the immediate follow-up [41–44]. Garcés-Albir et al [13] report no recurrence after FT for simple and low CPF at one-year postoperatively, provided the extent of fistulotomy had been quantified preoperatively with three-dimensional endosonography. Cariati [45] reports 100% healing rate after FT for low CPF involving  $\leq 10\%$  of the distal external anal sphincter, at 6 months. Interestingly, van der Hagen et al [46] report that success rate of FT for low CRF decreases by time; from 93% at 12-month postoperatively to 74% and 61% at 48- and 72-month postoperatively. It is stated that recurrence can be either the result of treatment failure because of overlooked fistula branching or recurrent patient disease, as fistula recurrence occurs at different location in 54% of the cases. Patient predisposition may explain the latter observation, as it has been shown that there is an increased expression of pro-inflammatory cytokines and epithelial-to-mesenchymal cell transition in CPF. Therefore, molecular mechanisms may also interfere in pathogenesis and also persistence of CPF [47].

Some degree of incontinence, usually in the form of mucous discharge, is reported by more than 30% of the

patients after FT [41,43,48]. Incontinence is minimal when FT is limited to the distal anal sphincter complex, and increases in parallel to the length of the external anal sphincter division [13]. Impairment of continence after FT is also related to preoperative functional status [41,43].

### Complementary FT for High CPF

FT may be part of the surgical treatment of high and complex CRF. Chatterjee et al [49] combined partial FT (from the external opening to the level of the dentate line) with cutting “seton” passing through the deep fistulous track in 16 patients with high CPF. They observed one recurrence and incontinence to flatus in one patient. A similar surgical approach was applied by Durgun et al [50] in 10 patients with high CPF, with no recurrence and only two patients complaining of incontinence to flatus.

Fung et al [51] performed partial FT of the subcutaneous part of the fistulous track and placed a loose seton through the fistulous track involving the sphincter complex in 46 patients with high CPF. They report a healing rate of 86% and a recurrence rate of 19%, at a median follow-up of 42 months. Finally, Schultze and Ho [52], treated 75 patients with high and complex CPF with a staged approach: at the first stage they performed FT involving the subcutaneous part of the fistulous track and placed a loose “seton” through the fistulous track involving the sphincter complex and, at the second stage four months later, they performed a LIFT procedure. They observed a recurrence rate of 12%, mostly attributed to incomplete identification and drainage of the fistulous track branching, and minor incontinence in one patient.

### Conclusions

Prior to surgical intervention for the treatment of CPF, image identification of the fistulous track by MRI is mandatory. FT is the commonest procedure performed for the treatment of the low CPF, namely the subcutaneous, the intersphincteric and the low transsphincteric fistula that involves less than 30% of the external sphincter mass. Relative contraindications of the procedure are Crohn's disease and pre-existing impaired continence. Initial healing rate is very high, but there is a tendency of increased recurrence by time, as a result of either incomplete identification of fistulous track branching or patient's predisposition. Incontinence after FT is of low incidence and minor severity. Partial FT can be combined with other techniques, such as “seton” placement or LIFT for the surgical treatment of the high transsphincteric, suprasphincteric and extrasphincteric fistulae.

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## Review Article

**SPECIFIC ASPECTS OF ANESTHESIA IN PROCTOLOGY**Radmilo Janković<sup>1,2</sup>, Marija Stošić<sup>2</sup><sup>1</sup>Faculty of Medicine, University of Niš, Niš, Serbia<sup>2</sup>Clinic for Anesthesia and Intensive Therapy, Clinical Center Niš, Niš, Serbia

**Abstract.** *Proctology, as a domain of abdominal surgery, deals with the treatment of diseases affecting the end part of the large bowel, its terminal 20 cm, to which anus anatomically belongs as well. In view of the physiological role of this part of the digestive tract (stool control), all the diseases and disorders in the region cause patient discomfort and produce significant problems in everyday life. On account of that, diagnostic management should be performed promptly in order that effective treatments could be introduced as soon as possible. The most commonly used techniques of anesthesia in proctology are local anesthesia, independent or in combination with intravenous analgesedation, regional anesthesia (spinal and epidural), and general anesthesia. Local anesthesia combined with analgesedation has been the preferred approach in recent studies, since it is able to provide adequate settings for the planned surgery, patient comfort and minimization of side effects. An adequate anesthesia technique reduces metabolic response to surgical stress and length of hospitalization, which markedly affects cost-effectiveness of the treatment.*

**Key words:** *proctology, anesthesia, sedation, postoperative pain, PONV.*

**Introduction**

Proctology, as a domain of abdominal surgery, deals with the treatment of diseases affecting the end part of the large bowel – its terminal 20 cm – to which anus anatomically belongs as well. The most common symptoms and pathological signs in this region are bleeding, itching, pain, feeling of pressure, and the most common pathological conditions are hemorrhoids, anal abscesses, fistulas, fissures, condylomas and tumors. In view of the physiological role of this part of the digestive tract (stool control), all the diseases and disorders in the region cause great patient discomfort and produce significant problems in everyday life. On account of that, diagnostic management should be performed promptly in order that effective treatments could be introduced as soon as possible [1].

Hemorrhoids and other anorectal disorders occur in 4-5% of adults worldwide. Although most of these patients can be treated conservatively, in many of these cases surgical treatment is required. These surgical procedures are among the most common surgical interventions, with more than 90% of these performed in out-patient surgical settings [2]. An optimal anesthesia technique for such surgical procedures should provide an adequate surgical setting, rapid patient recovery, minimal postoperative side effects, and improve perioperative patient comfort. Furthermore, it should improve the effectiveness of work in an operating room, provide as short as possible patient hospitalization, with positive

effects on cost-effectiveness of the treatment. The principal goal of out-patient anesthesia is to provide rapid patient turnover, rapid patient discharge in absence of any side effects, minimal intrusion into patient's everyday life and reduction of the risk for infections and postoperative complications [3,4].

The most commonly used techniques of anesthesia in proctology are local anesthesia, independent or combined with intravenous analgesedation, regional anesthesia (spinal and epidural), and general anesthesia.

**Local Anesthesia and Intravenous Analgesedation**

At the beginning of 1950s, Schneider was the first to introduce a modified local anesthesia infiltration technique, which has later gained wide acceptance in proctology [5]. The technique utilizes a curved needle for the application of hyaluronidase in order to improve tissue laxity and facilitate the infiltration of perianal tissues with a solution of local anesthetics. Postoperative patient discomfort and pain associated with the technique are thus minimized. It has been shown that the use of hyaluronidase increases the effectivity of local anesthesia in all anorectal surgical procedures.

In recent years, the availability of new sedation techniques used in combination with local anesthesia increased the number of surgical interventions performed in the conditions such as these. This technique provides very satisfactory surgical settings, patient comfort, short hospitalization periods, and cost-effectiveness compared to other techniques employed in out-patient anorectal surgery.

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Possible local complications occur usually during the application of local anesthetic and injury to the anatomical structures at the application site itself. Systemic complications tend to occur if larger concentrations of the solution of local anesthetic reach systemic circulation. Out of these, syncope, toxic reactions, hypersensitivity reactions and anaphylaxis should be mentioned. Toxic reactions are the most common of these, accounting for over 90% of reactions to local anesthetics [6].

Patient satisfaction with local anesthesia combined with intravenous analgesia is in correlation with appropriate control of postoperative pain and absence of side effects, such as urine retention, nausea and vomiting. The success depends as well on the experience and operative skills of the surgeon in the provision of effective infiltration analgesia and careful manipulation with the adjacent tissues. An extensive local infiltration of the operating field may reduce spasms of the rectal sphincters and produce better postoperative analgesia [7].

The combination of intravenous analgesia using benzodiazepines and opioids, as well as propofol, etomidate and ketamine with local anesthesia is a safe and effective technique for this type of surgery. The approach may shorten patient stay in the postoperative recovery room and enables early hospital discharge, which produces significant economic benefits [8].

### Regional Anesthesia – Neuraxial Blocks

Regional anesthesia is a valid option for single-day surgery and is associated with a lower degree of postoperative nausea and vomiting (PONV) compared with general anesthesia, and provides better postoperative analgesia as well. After the introduction of atraumatic pencil-point smaller diameter needles into clinical practice, the incidence of post-puncture headache has been reduced, and spinal anesthesia has become a valuable option for out-patient anesthesia and surgery, since it is able to provide rapid, reliable and effective blocks with a simple injection of small doses of local anesthetics into the readily accessible subarachnoid space. Except for the risk for post-puncture headache, the main problems with the use of spinal anesthesia in out-patient settings are associated with the action of the spinal block on the bladder function and recovery of motor functions after the spinal block [9]. It is therefore necessary to check the motor and sensory activity before patient discharge from the hospital. Most interventions in proctology are associated with pain. It has been proposed that appropriate analgesia could additionally improve the outcome of the surgical intervention, reducing the response of the body to surgical stress and thus the length of hospitalization. Neuraxial anesthesia (spinal and epidural) has been shown to be very effective in reducing the response of the body to surgical and metabolic stress compared to other techniques of anesthesia (Figure 1). However, in recent years, investigating the concept of single-day surgery, several studies have



**Fig. 1** Regional anesthesia- spinal anesthesia

shown that multimodal approach to analgesia in such patients improves postoperative outcomes, reduces organ function disturbances and morbidity and, consequently, shortens hospitalization.

Local anesthetics administered subarachnoidally can be hyperbaric, isobaric or hypobaric, depending on the specific weight. Isobaric solutions of local anesthetics are most commonly used. The most commonly used agents are bupivacaine, levobupivacaine, ropivacaine, lidocaine, tetracaine etc [10].

Acute urinary retention is one of the well-known complications of spinal anesthesia. However, with lower doses of local anesthetics combined with opioids more rapid recovery after the sensory and motor block can be achieved. Since the fundamental cause of postoperative urinary retention after anorectal surgery is in part associated with perineal pain, lower incidence of urinary retention can be achieved with local infiltration anesthesia in order to alleviate postoperative pain. Side effects of spinal anesthesia can prolong hospitalization and to some extent reduce patient satisfaction with the surgical treatment.

### General Anesthesia

General anesthesia is used for more extensive surgical interventions. Intravenous anesthesia (total intravenous anesthesia – TIVA, or target-controlled infusion anesthesia – TCI), inhalation anesthesia and balanced anesthesia are the types most commonly used. Although with inhalation anesthesia with sevoflurane it is easier to control the depth of anesthesia compared to TIVA, it is associated with a higher rate of PONV, especially in the cases without prophylaxis. Propofol and etomidate are the agents most commonly used for intravenous anesthesia, depending on hemodynamic stability of the patient. Rocuronium bromide, atracurium, cis-atracurium



**Fig. 2** General anesthesia-monitoring

and others are used as muscle relaxants, depending on the duration of surgical intervention [11].

Preoperative patient preparation for out-patient anorectal surgical treatment does not require extensive measures. Standard monitoring for intraoperative anesthetic monitoring of these patients usually involves electrocardiography, pulse oximetry, capnography and non-invasive blood pressure measurement (Fig. 2).

The principal side effects of general anesthesia after anorectal surgery are PONV, vertigo and pain. Although the frequency of PONV may be reduced by using modern anesthetics and antiemetics, it is still a usual side effect of general anesthesia, which prolongs hospitalization after out-patient surgery [12].

### Therapy of Pain

Analgesia in the postoperative period should provide alleviation of pain and appropriate functional activity of the patient. The contemporary treatment of postoperative pain involves a multimodal approach to analgesia, which is achieved with optimal combinations of analgesics and their lower doses in order to optimize analgesia and minimize its side effects. The choice of analgesics should

be adjusted to the surgical intervention, since the effect of individual analgesics differs with different surgical interventions. For the treatment of acute postoperative pain opioid analgesics (fentanyl, alfentanil, morphine), non-opioid analgesics (paracetamol, non-steroid anti-inflammatory agents – NSAIDs) and local anesthetics are usually used. Gabapentinoids may have a favorable impact in this multimodal approach. Further, oral or intravenous use of acetaminophen or NSAIDs may be beneficial in out-patient settings. Selective inhibitors of cyclooxygenase-2 have also been administered, but their use diminishes due to their prothrombotic effects [13].

The choice and dose of analgesics should be adjusted to the general patient status, surgical intervention, presence of comorbid conditions preoperatively, administration of opioids, and all other factors which may influence pain relief.

### Treatment of Postoperative Nausea and Vomiting

One of the principal side effects of general anesthesia is, among others, PONV, which significantly prolongs patient hospitalization and may produce patient discomfort and dissatisfaction with the surgical intervention. Prevention is therefore of utmost importance, whenever possible.

The multimodal regimen of PONV prophylaxis is based on the idea that in medium- or high-risk patients it is rather unlikely that the desired effect will be produced with the administration of a single antiemetic agent – a combination of two or three medicaments is usually recommended instead. In these efforts, we should bear in mind different mechanisms of action of antiemetic agents, as well as their possible synergy. In medium-risk patients, PONV prophylaxis usually consists of dexamethasone or metoclopramide, or their combination, while for the prophylaxis in high-risk patients the combination of an 5-HT<sub>3</sub> antagonist (the drug of choice is most commonly ondansetron) with dexamethasone and/or metoclopramide is recommended [14].

### Conclusion

The aim of anesthesia in proctology is to provide adequate analgesia, adequate conditions for the surgery, and minimization of side effects. For that purpose, local anesthesia, independent or combined with intravenous analgesia, regional anesthesia, or general anesthesia can be used. Depending on the general status of the patient and surgical intervention itself, the attending anesthesiologist will decide upon the most appropriate of the available anesthesia techniques. Recent studies favor local anesthesia combined with intravenous sedation, since it provides good operative conditions, improves patient comfort and satisfaction, while reducing side effects. The multimodal approach to perioperative analgesia represents the combination of several agents, including local anesthetics, opioids and NSAIDs.

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## Original Article

## PATIENTS' CONTENTMENT WITH TRANSANAL HEMORRHOIDAL DEARTERIALISATION

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**Abstract.** Hemorrhoidectomy was the method of choice for treating grade 3 and 4 hemorrhoids. Due to a large number of complications, a new surgical treatment called transanal hemorrhoidal dearterialization (THD) was introduced. The aim of the study was to evaluate the effect of treatment with THD in patients with hemorrhoids. This study included 70 patients, 48 males and 22 females, who were hospitalized at the Clinical Center Nis in the period from September 2016 to September 2018. Fifteen patients had grade 4 hemorrhoids, 54 were with grade 3, one patient with grade 2. The average duration of the operation was 33.33 minutes, and patients were hospitalized for 1–2 days. We recorded: sex, age, stage, type of anesthesia, duration of surgery, length of stay, patient satisfaction, combinations of THD with other procedures, and surgical complications. In 46 patients, surgery was performed under general anesthesia, in 18 patients in spinal and in 6 patients in local anesthesia with analgesia. In 37 subjects we used THD only, and in 33 we used THD in combination with other methods. We observed the development of complications in 9 patients. Bleeding occurred in 2 patients, pain in 2, and urinary retention in 4, and abscess in 1. The majority of the patients (62.9%) were satisfied with this method, 27.1% were partially satisfied and 10% were unsatisfied. This method provides a shorter stay in the hospital, low complications rate and is a safe, fast and simple initial surgical option.

**Key words:** hemorrhoids, transanal hemorrhoidal dearterialization, patients' satisfaction, complications.

### Introduction

Hemorrhoidal disease is the most common anorectal pathology and it represents a great socioeconomic and medical problem. It is estimated that 90% of general population suffers from hemorrhoidal symptoms at least once in their life [1–3]. The rectal bleeding incidence in human population related to hemorrhoidal bleeding is around 20% per year, compared to all kinds of rectal bleeding [4], while the prevalence of hemorrhoidal disease, according to different studies, varies between 4.4% and 86% [5–7].

According to the degree of prolapse, hemorrhoids can be categorized in four groups. Grade I hemorrhoids do not prolapse; grade II prolapses during straining but reduces spontaneously; grade III requires manual reduction; grade IV hemorrhoids reduce rarely or do not at all [8]. A wide range of treatment options for hemorrhoidal diseases is available. The early stages of the disease can usually be treated conservatively with success, while advanced stages require a surgical approach. At present, surgical treatment generally involves the resection of hemorrhoidal cushions, as in conventional hemorrhoidectomy (CH), or prolapse reduction, as in stapled hemorrhoidopexy (SH) [9].

Hemorrhoidectomy is considered the standard treatment for symptomatic hemorrhoids, especially for grade III and IV [10]. For years, hemorrhoidectomy, according to Milligan-Morgan and Ferguson, was the golden standard in treating high-grade hemorrhoids [11]. However, open hemorrhoidectomy is connected with postoperative complications like pain, anal stenosis, bleeding, incontinence and even sepsis [12]. Therefore, it was imperative to develop a new, as efficient but less invasive method of treatment [13]. In 1995 a new technique called transanal hemorrhoidal dearterialization (THD), was developed. This procedure aims to reduce arterial blood flow to hemorrhoids [15,16]. This technique eliminates hemorrhoidal symptoms by the dearterialization of the terminal hemorrhoid branches of the superior rectal artery. For this procedure an instrument consisting of the proctoscope is used in combination with the Doppler probe for arterial location and ligation. The ligation of blood vessels leads to the decongestion of the hemorrhoidal tissue. Reduced tension enables the regeneration of the connective tissue inside the hemorrhoidal cushion, which results in a lower occurrence of prolapse and relief of the symptoms [17].

The goal of this study was to evaluate the effect of the treatment with transanal hemorrhoidal dearterialization in patients with grade II–IV hemorrhoids and the patients' satisfaction with the procedure.

### Material and Methods

A retrospective study was conducted, which included 70 patients treated at the Department for Colorectal Sur-

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gery of the Clinic for Digestive Surgery, Clinical Centre Nis, Serbia, during the period from September 2016 to September 2018. This study included patients with grade III and IV hemorrhoids, as well as grade II hemorrhoids, in whom the conservative treatment failed. The original technique of THD with or without mucopexy described by Carlo Ratto was used [18].

The patients were contacted by phone 6 months after the surgery. In the course of this study we recorded the following parameters: gender, age, grade of hemorrhoids, duration of hospitalization, type of anesthesia, duration of the surgery, patient satisfaction, the combination of THD with other procedures and surgical complications. A questionnaire prepared in Microsoft Word (Version 14.6.6, 2011, Microsoft Corporation, Redmond, Washington, USA) was used. The collected data were entered into an Excel data base (Version 14.6.6 2011, Microsoft Corporation, Redmond, Washington, USA). The data were analyzed in the statistical package Jandel SigmaStat (Version 2). Chi-square and Fisher's exact test were used for the analysis. The values from  $p < 0.05$  to  $p < 0.01$  were considered statistically significant.

## Results

There were 48 male (68.6%) and 22 female (31.4%) patients, aging 48.33 on average (32–82). Of the 70 patients, 15 were with grade IV, 54 with grade III and only 1 patient with grade II hemorrhoids (Table 1).

**Table 1** Demographical data of the patients

Data		N (%)
Sex	Total	70 (100%)
	Male	48 (68.6%)
	Female	22 (31.4%)
Age	Average (range)	48.33 (32–82) (years)
Grade	I	0
	II	1
	III	54
	IV	15

The average duration of the surgery was 33.33 minutes, while the patients were hospitalized for 1–2 days. This procedure was conducted under anesthesia, i.e. in 46 patients under general endotracheal anesthesia, in 18 patients spinal anesthesia was used, while in 6 patients local anesthesia with analgesedation was used. In 37 patients only THD was used, while in the other 33 patients THD was combined with other surgical methods (the Milligan-Morgan hemorrhoidectomy, the Ferguson hemorrhoidectomy etc.) (Table 2). Complications were recorded in 9 patients: bleeding occurred in 2 patients, pain in 2, urinary retention in 4, and abscess in 1 patient (Table 3).

Postoperative complications are presented in Table 3. Except for 3 patients, all the others were discharged within 24 hours with no major complaints. Three patients were readmitted for complications (abscess and

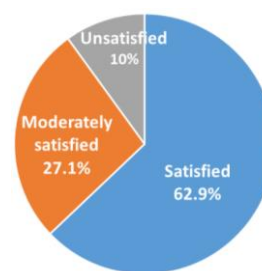
bleeding). Two patients had postoperative pain and 4 had urinary retention. Six months postoperatively, the majority of the patients (62.9%) were highly satisfied with this method, 27.1% were moderately satisfied, and 10% were unsatisfied. More than 80% of the patients would recommend this method to others.

**Table 2** Data regarding surgery

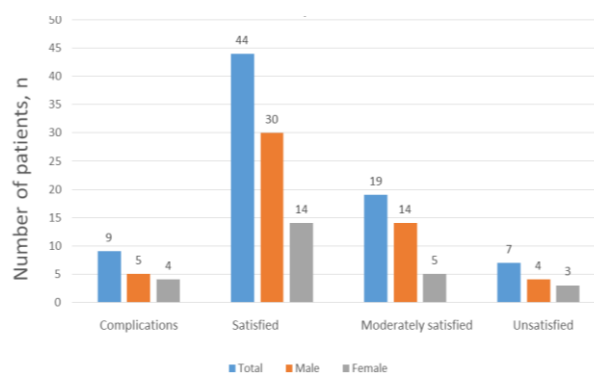
Data		N (%)
Duration of the surgery	Average	33.33 (min)
Period of hospitalization	Average (range)	1.07 (1–2) (day)
Type of anesthesia	General endotracheal	46
	Spinal	18
	Local + analgesedation	6
Procedure	THD	37
	THD + other (lateral sphincterotomy, skin tag removal, fistulotomy, excision of anal warts, removal of piles)	33
Complications		9 (12.86%)

**Table 3** Postoperative complications following THD

Complications	Number of patients
Bleeding	2
Pain	2
Urinary retention	4
Abscess	1



**Graph 1** Patients' satisfaction with the procedure in terms of symptom relief



**Graph 2** Categorizing patients in terms of complications and satisfaction with the procedure

**Table 4** Review of complications and the applied method in relation to the hemorrhoidal grade (I–IV)

Hemorrhoids	Grade	Grade	Grade	p-value
	II	III	IV	
Complications, n	0	8	1	n.s.
No complications, n	1	45	15	n.s.
THD, n	0	28	9	n.s.
THD in combination, n	1	26	6	n.s.

The percentage of observations in different categories which define the table of contingency was not significantly different from what is expected in random occurrence (Chi-square, Fisher's exact test).

## Discussion

The surgical treatment of hemorrhoids is taken into consideration when the conservative treatment fails or patients have grade III or IV hemorrhoids and symptomatic hemorrhoidal disease respectively. The methods of conventional hemorrhoidectomy sometimes results in complications, such as urinary retention (2–36%), bleeding (0.03–6%), anal stenosis (0–6%), infection (0.5–5.5%) and incontinence (2–12%), as well as postoperative pain [5, 9, 10]. To reduce pain following surgery, techniques of excision have undergone multiple modifications (including diathermia, scissors, laser, Harmonic or Ligasure hemorrhoidectomy). These modifications have not only increased surgical expenses, but have also given poorer results in comparison with usual measures. However, with transanal hemorrhoidal dearterialization not only is postoperative pain reduced but also it rarely has significant complications, such as anal stenosis or incontinence [11].

Besides being minimally invasive, THD is not an excisional procedure. This enables the regeneration of the normal anorectal anatomy; in addition, it or other surgical procedures can be done again in case of recurrence. According to our results, THD can be successfully used in combination with other proctological procedures not influencing the success of the intervention or the satisfaction of patients. In other excisional procedures, a significant resection of the mucous membrane is required; for that reason, the anal canal becomes sensitive to complications, while a combination with other interventions on the anal canal becomes unsuitable.

In this study, complications occurred in 12.85% of the participants, mostly in the form of urinary retention, pain, bleeding and abscess. Similar rates and types of complications are described in other five large studies which included 388 individuals (Bursics A, et al. 2004, Hungary; Festen S, et al. 2009, Netherlands; Gupta PJ, et al. 2011, India; Infantino A, et al. 2012, Italy; Shuurman JP, et al. 2012, Netherlands) [19]. The results of these studies are encouraging, since these complications are less fre-

quent in THD than in conventional hemorrhoidectomies [20–23]. Complications, such as urinary retention, are not really significant since they can be treated with catheterization and efficiently removed on the same day. In our study none of the complications required surgical intervention.

There have been a number of studies on THD which show its early efficacy and safety for all grades of hemorrhoids, and recently THD has been acknowledged by the National Institute for Health and Care Excellence (NICE) as a safe and efficient alternative to conventional hemorrhoidectomies in Great Britain [24]. The recent study on THD for the treatment of grade IV hemorrhoid conducted by Ratto and al. [25] showed the disappearance of symptoms in 94% of the patients, while only 6% required additional surgeries. Similar results were obtained in our study as well. This method was successful in 60% of the patients with grade IV hemorrhoids.

Due to promising results and considerably low rate of recurrence, THD meets all criteria for coming up with patients' expectations. In the studies conducted to evaluate the success of the THD procedure, patients' satisfaction has had a great role [26]. In 2010, Tempel and al. [27] carried out a study on patients' satisfaction after THD and found out that 91.5% of the patients were satisfied with the procedure because it had helped with the disappearance of the symptoms. It has been equally well evaluated by surgeons [28]. In our study 62.9% of the participants were satisfied with this procedure.

The presence of complications after THD could be considered as failure of this method. Taking into consideration this failure, we can conclude that the success of this procedure was 87.14%. A high rate of success of THD can be attributed to the fact that in all patients a technique of distal dearterialization, the DDD (Doppler-guided distal dearterialization) modification, has been used [18]. It is important to point out that the procedure can be successfully repeated several times, and that the adequate choice of patients is crucial for its success.

A drawback of this study is its retrospective character since it was not possible to establish with a certainty in which patients mucopexy was performed, so it was not possible to conclude if the success rate of THD was additionally increased.

## Conclusion

It is suggested that THD has fewer postoperative complications and shorter recovery due to reduction of postoperative pain than other conventional surgery. Patients treated with THD experience faster recovery. High satisfaction rate, tolerable rate of complications, shorter leave of absence and reduced level of postoperative pain suggest that this is a safe, fast and simple surgical option.

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## Original Article

**ESTIMATION OF RISK FACTORS OF EARLY POSTOPERATIVE MORTALITY  
IN ELDERLY PATIENTS WHO ARE SUBJECTED TO GASTRIC SURGICAL  
PROCEDURES****Ivan Pešić<sup>1,2</sup>, Milica Nestorović<sup>1,2</sup>, Vanja Pecić<sup>3</sup>, Milan Radojković<sup>1,2</sup>, Lidija Đorđević<sup>4</sup>, Miodrag Đorđević<sup>4</sup>,  
Toplica Bojić<sup>4</sup>**<sup>1</sup>Clinic for Digestive Surgery, Clinical Center Niš, Niš, Serbia<sup>2</sup>Faculty of Medicine, University of Niš, Niš, Serbia<sup>3</sup>Center for Minimally Invasive Surgery, Clinical Center Niš, Niš, Serbia<sup>4</sup>Clinic for Endocrine and Breast Surgery, Clinical Center Niš, Niš, Serbia

**Abstract.** *The use of screening programs in elderly population (age  $\geq 65$  years) comprises an increasing proportion of patients undergoing emergency general surgery (EGS) procedures nowadays. The aim was to determine the intra-hospital mortality rate in elderly patients undergoing gastric surgical procedures. 108 elderly patients ( $\geq 65$  years old) were examined, divided into two groups: deceased and surviving surgical patients, treated for diseases (benign and malignant) of the stomach. The patients were divided into four age groups and five ASA groups, taking into account the presence of chronic diseases, the values of some laboratory parameters, administered transfusion and the occurrence of surgical complications during hospitalization. The mortality rate among elderly patients was 28.7%. The significant risk factors for mortality were: emergency surgery ( $p < 0.001$ ), bleeding gastric ulcer operations ( $p = 0.042$ ), lung ( $p = 0.003$ ), kidney ( $p < 0.001$ ), heart ( $p = 0.025$ ) diseases, ASA score of 4 or higher ( $p < 0.001$ ), serum levels (higher after two times measurement) of creatinine, haemoglobin, CRP, PCT and glycemia ( $p < 0.001$ ). In order to improve medical treatment, the determination of independent validated risk indicators for mortality in elderly patients might lead to developing a dedicated scoring system.*

**Key words:** *elderly, gastric surgery, mortality.*

**Introduction**

In people aged 65 or older, the patient's risk of requiring surgical procedures is three times higher than in the younger population, especially in the case of emergency conditions [1]. Surgeons are still generally reluctant to treat elderly patients, considering them more sensitive to surgical treatments, having lower physiological reserves inside themselves, as well as more concealed diseases [1,2]. The aim of the research was to determine the overall rate of early postoperative mortality of elderly patients undergoing gastric surgical interventions, with an overview of the impact of the ASA score, malignant diseases, septic conditions, associated chronic diseases, surgical complications and some laboratory parameters to the occurrence of the mentioned.

**Materials and Methods**

The study includes the examination of 108 elderly patients ( $\geq 65$  years of age) in the period from 1<sup>st</sup> January 2013 to 31<sup>st</sup> December 2014 at the Clinic for General

Surgery of the Clinical Center in Nis, divided into two groups: deceased and surviving surgical patients. Patients were surgically treated for diseases (benign and malignant) of the stomach, with attention to the type of operation (emergency, elective), associated chronic diseases (heart and kidney diseases, pulmonary function disorder, neurological diseases of the CNS, diabetes), number of transmitted red blood cell (RBC) concentrates units and frozen fresh plasma (FFP) units. Four age groups of patients were examined: the 1<sup>st</sup> group of patients aged 65 to 69; 2<sup>nd</sup> group of patients from 70 to 75 years of age; 3<sup>rd</sup> group of patients between 76 and 80; 4<sup>th</sup> group of patients aged over 80. In the study, patients were also included in the ASA classification, and divided into five categories [3]. The study also included monitoring some laboratory parameters (serum creatinine, serum albumin, total serum proteins, erythrocyte values, leukocytes, serum hemoglobin, serum sodium and potassium values, C-reactive protein-CRP, procalcitonin-PCT, glycaemia) with their measurement on two occasions during patient hospitalization: before the surgery itself and just before the end of the clinical treatment or before the fatal outcome. The tables show the average values of the tested parameters. Following surgical complications were observed: laparotomy dehiscence, dehiscence of the primarily performed gastrointestinal anastomosis, postoperative bleeding. The data

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are presented in the form of an arithmetic mean and a standard deviation, or in the form of absolute and relative numbers. Frequency comparisons were done with the Chi-squared test. The comparison of the continuous variables was done with the Mann-Whitney test. The hypothesis was tested with a significance threshold of  $p < 0.05$ . The data analysis was performed with the SPSS 16.0 software package.

## Results

In this study of 108 patients with gastric surgical diseases, there were 77 (71.30%) surviving and 31 (28.70%) deceased patients. None of the age groups represented significant risk factors in early postoperative mortality ( $p = 0.922$ ). Emergency surgical procedures, ASA score 4 or higher were statistically significantly more common in group of deceased gastric surgical patients ( $p < 0.001$ ). Malignant diseases were more common in group of surviving gastric surgical patients (55.80% vs. 48.40%).

Bleeding / perforation of gastric ulcer or gastric tumor were statistically significantly more common in deceased gastric surgical patients ( $p = 0.024$ ;  $p = 0.027$ ). Respiratory disorders and renal diseases were statistically significantly more common in deceased gastric surgical patients ( $p = 0.003$ ;  $p < 0.001$ ). Heart diseases were more common in surviving gastric surgical patients ( $p = 0.025$ ). The average number of transmitted FFP units was statistically significantly more common in surviving gastric surgical patients ( $p = 0.005$ ) (Table 1). The bleeding gastric ulcer surgical operations were more common in deceased gastric surgical patients regarding to surviving patients (25.80% vs 10.40%,  $p = 0.042$ ) (Table 2). There were statistical difference referring to higher serum concentration of the following values in deceased gastric surgical patients: serum creatinine, hemoglobin, erythrocyte count, leukocyte count, CRP, PCT and glycaemia ( $p < 0.001$ ) (Table 3). Gastro-intestinal anastomosis dehiscence was determined in 5 deceased surgical gastric patients (16.10%) (Fisher's test:  $p = 0.002$ ).

**Table 1** Risk factors of fatal outcome of the examined population

Risk factors	Surviving N=77 (71.30%)	Deceased N=31 (28.70%)	$\chi^2$	P
<b>Pat. characteristics (age)</b>				
65–69 year	21 (27.30%)	7 (22.60%)	0.488	0.922
70–74 year	17 (22.10%)	7 (22.60%)		
75–79 year	18 (23.40%)	9 (29.00%)		
<80 year	21 (27.30%)	8 (25.80%)		
<b>Clinical characteristics</b>				
Emergency op.	20 (26.00%)	21 (67.70%) †	16.37	<0.001
Elective op.	57 (74.00%)	10 (32.30%)		
Malignant disease	43 (55.80%)	15 (48.40%)	0.240	0.624
Benignant disease	34 (44.20%)	16 (51.60%)		
Ulcer/tumor bleeding	9 (11.70%)	10 (32.30%)	5.109	0.024
Ulcer/tumor perforation	11 (14.30%)	11 (35.50%)	4.885	0.027
Respiratory diseases	6 (7.80%)	10 (32.30%)	8.634	0.003
Heart diseases	74 (96.10%)	25 (80.60%)	5.039	0.025
Kidney diseases	0	6 (19.40%)		<0.001
Neurological disorders	11 (14.30%)	4 (12.90%)	0.035	0.851
Diabetes mellitus	0	2 (6.50%)		0.080
ASA 2	66 (85.70%)	3 (9.70%)		
ASA 3	11 (14.30%)	9 (29.00%)		
ASA 4	0	18 (58.10%)		<0.001
ASA 5	0	1 (3.20%)		
RBC concentrate units	3.52±2.23	5.74±4.42	2.2492	0.025
FFP units	6.38±4.31	4.39±2.98	2.824	0.005

† - number (%),  $\chi^2$  - Chi-squared test

**Table 2** Type of operation in the examined population

Type of operation	Surviving	Deceased	$\chi^2$	P
Perf. gastric ulcer oper.	11 (14.30%)	6 (19.40%) †	0.13	0.717
Bleeding gastric ulcer oper.	8 (10.40%)	8 (25.80%)	4.12	0.042
Gastric malignant tumor oper.	44 (57.10%)	15 (48.40%)	0.38	0.540
Gastric benignant tumor oper.	14 (18.20%)	2 (6.40%)	1.57	0.210

† - number (%),  $\chi^2$  - Chi-squared test, # Fisher's test

**Table 3** Biochemical parameters of fatal outcome in examined population

Biochem. marker†	Surviving		Deceased		F/z*	p
	1st measure.	2 <sup>nd</sup> measure.	1st measure.	2nd measure.		
Ser. creatinine	94.17 ± 56.13	84.74 ± 44.06	140.13 ± 70.72	193.39 ± 138.13	16.696	<0.001
Total proteins	58.70 ± 10.80	53.48 ± 5.53	47.31 ± 7.62	42.87 ± 7.74	0.167	0.684
Ser. albumin	33.31 ± 6.68	29.88 ± 4.28	24.65 ± 5.38	23.77 ± 4.05	5.237	0.024
Er. count	3.76 ± 0.75	3.48 ± 0.26	3.02 ± 0.78	3.44 ± 0.72	20.924	<0.001
Le. count	5.92 ± 1.76	9.69 ± 1.91	12.25 ± 6.00	12.99 ± 5.46	18.288	<0.001
Ser. Hgb	113.23 ± 23.50	108.39 ± 9.39	89.39 ± 25.22	103.29 ± 21.81	17.242	<0.001
Serum Na	136.51 ± 4.84	139.73 ± 3.05	133.90 ± 5.93	136.97 ± 4.79	0.019	0.889
Serum K	4.61 ± 0.37	3.71 ± 0.96	4.29 ± 0.99	3.60 ± 0.48	1.002	0.319
CRP	92.60 ± 56.13	–	215.09 ± 74.584	–	6.238*	<0.001
PCT	0.027 ± 0.015	–	4.817 ± 15.14	–	3.322*	<0.001
Glycaemia	0.19 ± 0.89	–	1.23 ± 3.51	–	5.231*	<0.001

† - Mean±SD, F- Anova for repeated measurements, \* - Mann-Whitney test

## Discussion

In people aged 65 years and older, the risk of death to the patient from the required surgical procedures is three times higher than to the younger population, especially in the case of emergency conditions [1]. In our study none of the age groups represented significant risk factors in early postoperative mortality ( $p=0.922$ ). Emergency surgery is a well-known risk factor [4]. It increases the operative mortality rate from 3 to as many as 10 times [5]. We determined that emergency surgery was the significant risk factor of death outcome in our patients ( $p<0.001$ ). Patients with higher ASA score have more chance of death outcome [6], as it was shown in our survey ( $p<0.001$ ). The chronic diseases presence is tightly connected with death outcome [7]. Some studies indicate that the primary preoperative factor for a poor surgical outcome in the elderly was the comorbidity itself rather than age [8]. Respiratory and renal diseases were statistically significantly more common in deceased gastric surgical patients ( $p=0.003$ ;  $p<0.001$ ). Our research showed that serum creatinine values were statistically significantly higher in deceased gastric surgical patients ( $p<0.001$ ), which was in correlation with other authors [9]. Hypoalbuminemia is a common laboratory abnormality in the elderly, which can lead to high morbidity and mortality [10]. Our research showed that hypoalbuminemia was independent risk factor of fatal outcome ( $p=0.024$ ). The serum hemoglobin concentration was higher in surviving gastric surgically treated patients, compared to the deceased ones, at the level of statistical significance, which was in correlation

with previous studies [10]. In sepsis, the underlying problem is the high rate of mortality, which is even higher than in patients at the moment of myocardial infarction [11]. The incidence of sepsis is 2% of all hospitalizations, and 6-30% in intensive care units [12]. We determined that the CRP and Le count values were statistically significantly higher in deceased gastric surgical patients ( $p<0.001$ ), correlating with published data [10]. Anastomosis dehiscence leads to greater pain and distress of the patient than any other surgical complication [13]. Dehiscence of gastro-intestinal anastomosis was determined in 5 deceased gastric surgical patients, representing statistical significance risk factor of death outcome (Fisher's test:  $p=0.002$ ). The surgical outcome of patients who need transfusion is poor, and it is not clear whether this is due to bleeding, anemia, or the transfusion itself [14]. In our study, surviving gastric surgical patients had less transmitted RBC concentrate units ( $p=0.025$ ) and more transmitted FFP units ( $p=0.005$ ).

## Conclusion

Total mortality rate was 28.7%. In gastric surgical patients, death outcome was more statistically common in: emergency surgical patients, patients with anastomosis dehiscence, respiratory and kidney comorbidities, higher ASA score patients and patients with higher serum values of creatinine, glycemia, CRP and PCT. Surviving gastric surgical patients had less transmitted counts of RBC concentrate units and more transmitted counts FFP units referring to deceased patients.

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## Original Article

## MOLECULAR MECHANISMS OF ISCHEMIC-REPERFUSION INJURY DURING LIVER RESECTION FOR COLORECTAL CANCER METASTASES- STUDY PROTOCOL

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**Abstract.** *Bleeding during liver resection is a significant threat to the clinical outcome. Portal triad occlusion with complete ischemia of the liver flow of hepatoduodenal ligament is a well-documented, safe and useful way to reduce this problem. Although the technique is efficient in limiting blood loss, there is still controversy concerning potential disadvantages and subsequent reperfusion liver injury. A prospective analysis will include at least 30 patients 18-75 years old, who are undergoing liver resection due to metastases of the colorectal carcinoma. After signing the informed consent, the parameters will be analyzed in three phases, pre-, intra- and postoperatively. During surgery (indicated by a surgical/oncological team of doctors not related to our study) liver tissue samples will be taken of the "healthy liver" (not involved in the tumor process) in which after tissue homogenization, analysis of parameters will be done responsible for the development of liver injury. This research will not affect the clinical practice, course and outcome of the treatment in patients who are included. The study may be useful for future patients who will undergo liver resections. The application of modern research methods with scientific validity of statistical processing of data and the use of appropriate literature, significant data will be obtained about the character, i.e. intensity of damage of the liver tissue in patients undergoing liver resections.*

**Key words:** *liver resection, ischemia-reperfusion injury, colorectal carcinoma metastases, apoptosis, vascular isolation of liver.*

### Research Objective

The latest achievements in liver resection surgery and significant progress in preoperative estimation, preparation and postoperative monitoring and patient care expanded the indications and range of liver resection procedures. The most important problem during hepatectomy is mandatory control of bleeding from the liver parenchyma. Uncontrolled intra- and postoperative bleeding from the resected liver is still the most severe negative prognostic factor which is in direct correlation with immediate postoperative morbidity and mortality [1,2,3]. Besides the immediate metabolic and cardiocirculatory consequences of hypovolemia of different degree, secondary negative effects of excessive bleeding during liver resection are increased need for postoperative transfusion of fresh blood, i.e. blood components and derivatives which are proven to be linked to critical coagulopathies and immunity decrease and shorter postoperative disease-free interval in liver malignancies

[4,5]. The intent to overcome this key problem resulted during the last three decades of the last century in the development of a range of different methods of *vascular control*, or *vascular liver isolation*, which depend on the location of the lesion in the liver. The condition of the liver parenchyma and the general condition of the patient may cause a complete or partial *vascular isolation* or *transitory liver ischemia* by *occlusion* of inflowing and/or outflowing liver blood vessels. Temporary disruption of only the inflow, or of both inflow and outflow of the circulation (*vascular exclusion*) of the part or the whole liver aim to quickly (but not hastily) conduct anatomically precise and technically correct liver resections in bloodless conditions. Thanks to its advantages, first of all relatively quick and easy application and satisfactory hemostatic results, the most significant and most often used method of vascular isolation of the liver is the Pringle maneuver. The method was inaugurated in 1908 [6] and it includes a complete interruption of the inflowing liver circulation by clamping of portal vein and hepatic artery, i.e. of the whole hepatoduodenal ligament by a vascular clamp, setting the tourniquet or in urgent situations with fingers. However, the disadvantage of all the methods of vascular isolation of the liver, including the Pringle maneuver, is imminent *ischemic* and then subsequent

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*reperfusion parenchymal liver damage.* Although the Pringle maneuver is efficient in reducing the blood loss from the resected liver parenchyma, critical hepatic ischemia that this maneuver causes represents a serious limiting problem that must be taken care of, particularly when there is a previous liver disease with significant vulnerability and sensitivity of the organ to hypoxia. Such transitory inflow occlusion causes parenchymal damage which is defined as ischemia-reperfusion injury (IRI). Etiological basis of this injury is a decrease in the level of intracellular ATP due to cellular anoxia which leads to an increase in intracellular  $\text{Ca}^{2+}$  ion concentration [7]. Namely, decreased ATP causes a decrease in active transport of  $\text{Ca}^{2+}$ ATPase and opening of  $\text{Ca}^{2+}$ voltage-dependent canals during depolarization of the cellular membrane which develops due to reduced activity of  $\text{Na}^+ \text{K}^+$ ATPase because of which there is an increase in the exit of  $\text{K}^+$  ions from cells and the entrance of  $\text{Na}^+$  ions in the cells. As a result, the concentration of intracellular  $\text{Ca}^{2+}$  increases significantly and leads to the destruction of the cytoskeleton [8–12]. In order to prevent critical ischemic damage, a timely reoxygenation is necessary. At the same time, however, this reperfusion causes reperfusion injury [13–16]. Namely, xanthine-dehydrogenase is converted into xanthine-oxidase and hypoxanthine, obtained from the degradation of adenine-nucleotides, is accumulated in the ischemic organ. With the beginning of the reperfusion of previously ischemic organ great amounts of superoxides are created from previously accumulated hypoxanthine by xanthinoxidase action which leads to the damage of the cytoplasm, proteins and DNA and prevents the reduction of oxygen in the mitochondria [10]. Then, peroxidation of the cytoplasmic membrane lipids takes place which is composed of two-layered lipids which causes its damage. Considering literature data which show that ischemia reperfusion injury may affect the course and outcome of the treatment in terms of intraoperative bleeding, prolonged hospitalization, increased morbidity and mortality, the study is directed at identifying the molecular mechanisms of apoptosis which are initiated during ischemia and reperfusion in liver tissue of humans.

## Ethical Standards

During the research, standard methods of preoperative preparation, operative treatment and postoperative monitoring were used. The participants may not have any direct benefit from participating in the study apart from more systematic monitoring and recording the research parameters. The study may be useful to future patients who will undergo liver resection. Since the research does not disrupt the planned liver resection protocol the participants will not be exposed to risks related to the research. The research does not include the use of untested or new medications or the testing of new surgical interventions. The mode of patient treatment included in the research is identical to the treatment of other patients with the same symptoms who were not included in this research and completely the same as the treatment applied with patients operated on at the Digestive Surgery Clinic of the Clinical Center Niš. The patients were chosen as potential participants because of the planned resection of the liver. The patients may freely accept or reject participation in the research. The participation decision will not influence the mode of operative treatment.

We emphasize that participation is voluntary and that at any given moment, at any stage, the consent may be withdrawn by the patient. The data obtained in the research will be available only to the research team because they are confidential. After informing the patients and obtaining signed consent, every patient is given a code number which will be used for storing all the information related to treatment. The conclusions obtained during the research will be published and available to public. Confidential data will not be published.

## Material and Methods

Prospective analysis will include at least 30 patients aged 18–75 who are undergoing liver resection due to metastases of the colorectal carcinoma. The patients included in the research has resectable metastases and were not undergoing neoadjuvant chemotherapy. After signing the informed consent, the parameters will be analyzed in three stages, pre-, intra- and postoperatively. Including and excluding criteria are shown in Table 1. During surgery (indicated by surgical/oncological team

**Table 1** Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> <li>▪ Confirmed diagnosis of adenocarcinoma of the colorectum after curative surgery</li> <li>▪ Resectable CRC liver metastasis</li> <li>▪ No evidence of distant metastases</li> <li>▪ No prior chemotherapy for metastatic disease</li> <li>▪ Age &gt; 18 years &lt;75</li> <li>▪ No infections requiring systemic antibiotic treatment</li> </ul>	<ul style="list-style-type: none"> <li>▪ Local recurrence of colorectal cancer</li> <li>▪ Patients with previous liver injury</li> <li>▪ Patients with prior liver surgery</li> <li>▪ Patients who in previous surgery underwent portal vein ligation</li> <li>▪ HCV or HBV infection</li> <li>▪ liver cirrhosis</li> <li>▪ Patients with a history of any arterial thrombotic event within the past 6 months, including angina (stable or unstable), MI, or CVA</li> </ul>

independent of our research) samples of liver tissue of healthy liver (not involved in tumor process) will be taken in which, after tissue homogenization, an analysis of parameters responsible for the development of ischemia reperfusion injury will be done.

**Preoperative parameters:** demographic data (age and sex), standard preoperative investigations which examine liver function in all patients included in the research (alkaline phosphatase, AST, ALT,  $\gamma$ GT, bilirubin, LDH, albumin, alpha-fetoprotein), as well as the presence of metabolic syndrome (glucose  $\geq$  6.1 mmol/L; serum triglycerides  $\geq$  1.7 mmol/L; serum HDL cholesterol  $<$ 1.04 mmol/L; blood pressure  $\geq$  130/85 mm Hg).

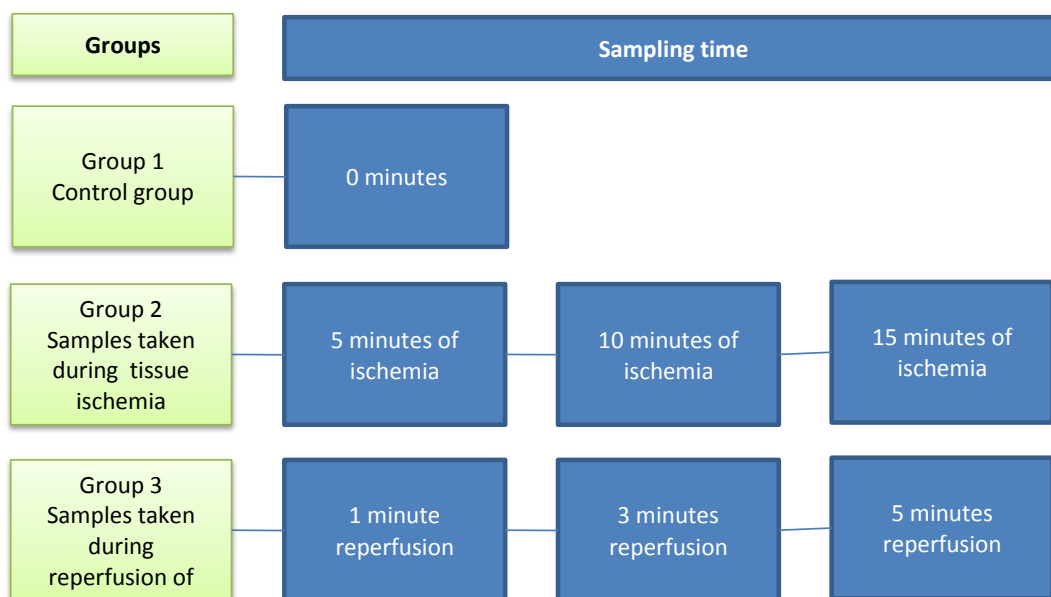
**Intraoperative parameters:** surgical approach, type and resection circumference, intraoperative blood loss, intraoperative blood compensation, liquid compensation and duration of surgery. During surgery, samples of liver tissue will be taken from the resection area. Liver tissue samples represent the tested groups. Three groups will be formed (I – control group, II – tissue samples during ischemia, III – samples after tissue reperfusion) further divided into seven subgroups based on the time the sample was taken. At zero minute, one sample is taken (control group), then after ischemia of hepatoduodenal ligament (group II) samples are taken within subgroups at 5, 10 and 15 minutes of ischemia. After ischemia, samples are taken (group III) within subgroups at 1, 3 and 5 minutes (Diagram 1). All samples will be stored in special containers and frozen at  $-80^{\circ}\text{C}$ . The tissue sample and the patient are given a code number. The research will be conducted at the Laboratory for Functional Genomics and Proteomics of the Scientific-Research Center of the Faculty of Medicine, University of Niš. In order to estimate the biochemical parameters of programmed cell death the

liver tissue was first cut into small pieces and then finely cut in ice cold water with a homogenization apparatus. The homogenate (10% v/v) will be centrifuged at 1500 rpm for 10 minutes at  $4^{\circ}\text{C}$ . The activity of *caspase -3*, acidic *DNase* and *Bax protein* concentration will be determined in the supernatant. *Caspase-3* will be determined with commercial ELISA kit (Cusabio Technology LLC, USA). The activity of acidic DNase (DNase-2) will be measured using the method of Bartholeyns et al., (1975) and the formed acid-soluble nucleotides were measured spectrophotometrically. Enzymes activity was expressed in international units in gram of protein (U/g protein). The concentration of *Bax protein* in liver homogenate will be determined with a commercial ELISA kit (Human Apoptosis regulator BAX ELISA Kit, cusabio Technology LLC, USA). The activity of the enzymes of alkaline phosphatase (AF), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT) and lactate dehydrogenase (LDH) in serum will be determined with commercial Sigma tests (St. Louis, MO, USA) using the spectrophotometric method at the Central Laboratory of the Clinical Center Niš.

**Postoperative parameters:** The postoperative liver function as well as the presence of metabolic stress will be monitored by analyzing patients' blood samples at the Central Laboratory of the Clinical Center Niš as part of control postoperative monitoring.

## The Aim of the Research

The research deals with problems accompanying the occlusion of the portal triad and tissue damage at molecular level in patients who need some of the liver resections in terms of ischemia during resection and later liver tissue reperfusion.



**Diagram 1** Intraoperative sampling of the liver tissue

End points:

1. Determine the degree of apoptosis of the liver parenchyma intraoperatively during ischemia and during tissue reperfusion in specific time intervals (the activity of *caspase-3* and deoxyribonuclease-II will be determined as well as the level of *Bax* protein in liver tissue).
2. Determine preoperatively and postoperatively the condition of liver parenchyma by determining the biochemical parameters of the liver function (the activity of the alkaline phosphatase enzyme, AST, ALT,  $\gamma$ GT, biliubin, LDH, albumin, alpha-fetoprotein, urea) and the parameters of metabolic syndrome (glucose, serum triglycerides, serum HDL cholesterol, blood pressure).
3. Determine the correlation of apoptosis parameters with functional tests of the liver during ischemia and reperfusion.

### Statistical Analysis

The estimation was done by double testing of the null hypothesis with independent t-test with accepted values of type I error  $\alpha=0,05$  and power of the study 90%. The total study sample is 30 participants. Sample size was calculated in G power program 3.1.9.2. On the basis of the gathered data, a database will be created in software package SPSS 20.0 which will be used for further statistical analysis. Statistical analysis of data will include the methods of descriptive and analytical statistics. The results will be represented in tables and graphs. All attributive characteristics of the monitoring are described in absolute and relative numbers. The description of numerical forms of monitoring we will use the measures of averages (median and arithmetic mean) and standard deviation. The choice of tests used for numeric observations depend on the nature of the distribution of the numeric markings of observation and group number. Normal distribution will be tested using Kolmogorov-Smirnov test. The testing of the hypothesis of equality of mean values in cases when two groups exist will be done by t-test for dependent or independent samples in case of normal distribution and Wicoxon test for dependent and Mann-Whitney test for independent samples when distribution is nor normal. If three groups exist, ANOVA (one-way analysis of variance) test will be used for normal distribution and Kruskal-Wallis test for other than normal distribution of data. For correlation analysis, Pearson correlation coefficient will be used with normal distribution or Spearman coefficient correlation when distribution is not normal. For determining the link between the tested parameters and the genotypes of the tested polymorphism univariate and multivariate logistic regression analysis will be used. Statistical hypothesis will be tested on the level of significance for risk of  $\alpha=0.05$ . i.e. the difference between the samples will be considered significant at  $p<0.05$ .

### Discussion

The liver is an organ which contains the most macrophages compared to other organs in the body and it has the ability to secrete oxygen radicals and tissue toxic mediators. This biological characteristic of the liver may lead to higher sensitivity. i.e. susceptibility to ischemic damage. The examination of the ischemic-reperfusion injury was done mostly on experimental models. In the last two decades of the last century the accumulated evidence has shown that the ischemic reperfusion injury of the liver is induced or potentiated by the action i.e. metabolism of several toxic chemical mediators such as reactive (free) oxygen radicals, proteases (elastase), inflammatory cytokines, thrombocyte-activating factor, vasoconstrictors endothelin and thromboxane etc., i.e. by pathophysiological events in which they participate (neutrophil infiltration and their adhesion to hepatic sinusoidal endothelial cells, elastase hyperproduction, sinusoid constriction and microcirculation damage, apoptosis, degradation of phospholipid cell membrane etc. [9,15]. On the basis of these pathophysiological mechanisms of ischemia reperfusion injury numerous strategies have been suggested for its prophylaxis and treatment the majority of which are based on the inhibition of negative effect mostly of oxygen radicals, inflammatory toxins and adhesion molecules and cascading processes in which they participate [17]. The edema of sinusoidal and Kupfer cells after ATP depletion during liver ischemia, increased production of strong endothelin vasoconstrictor and probably decreased NO production are pathophysiological mechanisms which contribute to the reduction of sinusoidal lumen [10]. Apoptosis or programmed cell death has a key role in many biological processes. Its determination is highly significant in various fields of modern medicine. In this case it represents the beginning of hepatocyte damage which leads to permanent damage. In order to determine the degree of programmed cell death, we can use markers such as caspase-3 – enzymes which initiate the apoptosis process, acidic DNase (DNase-2) which is the final stage of apoptosis – it disintegrates the nucleus material and BAX protein which points to the mitochondrial pathway of apoptosis activation. Since the effects of ischemia and reperfusion are the initiators of apoptosis which has several levels – we have chosen these parameters in order to determine the degree of programmed cell death. Based on the level of apoptosis we can conclude whether the patients should be administered apoptosis inhibitors to prevent cell death. So far, the researches in ischemia reperfusion injury mechanism were done mostly on experimental models which included working on lab animals (ex hominem) or tissue cultural (ex situ or in vitro examinations). In addition, clinical and experimental investigations are ethically unacceptable or technically undoable in the majority of conditions and diseases which cause this syndrome, except determining some parameters from systematic or local circulation, in other words-it is impossible to de-

termine them in the tissue involved with ischemia-reperfusion injury. Therefore, we believe that the most precise examination of injury mechanisms can be achieved by analyzing the listed parameters from liver tissue homogenate collected during resection intervention on the liver. Standard clinical liver resection procedure during which temporary ischemia and subsequent reperfusion are induced have enabled developing a unique experimental model during which samples are taken ‘in situ’ and ‘in vivo’ from “healthy liver” (not involved in the tumor process) in which after tissue homogenization the parameters responsible for the development of ischemia reperfusion injury is done.

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## Conclusion

The significant progress in liver resection techniques as well as new treatment methods have brought about improvement in the quality of life and longer survival of patients with liver damage who need some of the resection procedures in treatment. However, contrary to these favoring factors, resection procedures carry the risk of liver tissue damage which in many cases many jeopardize patient’s life.

Having in mind the small number of such and similar experimental studies, the application of modern research methods, with scientific validity of statistical data analysis and the use of literature, it is expected that significant data about the character i.e. the intensity of liver tissue injury in patients during resection procedures of the liver will be obtained.

**Case Report****PERINEAL HERNIA AFTER ABDOMINOPERINEAL  
LAPAROSCOPIC RESECTION – CASE REPORT****Vanja Pecić<sup>1</sup>, Milica Nestorović<sup>2,3</sup>, Ivan Pešić<sup>2,3</sup>, Dragan Mihajlović<sup>2</sup>, Ljiljana Jeremić<sup>2,3</sup>, Marko Gmijović<sup>2</sup>,  
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**Abstract.** *A perineal hernia can severely affect everyday activities. We represent a case of a sixty-five-year-old with perineal hernia after abdominoperineal resection for rectal cancer. Bulging in the perineum appeared 24 months following operation with uneventful postoperative course. She felt pain and difficulty while sitting. At physical examination the defect in perineum was approximately 3x3 cm. After cancer recurrence had been excluded, hernioplasty was planned. A 10x15 cm composite mesh was used for pelvic floor reconstruction. The mesh was sutured through urogenital diaphragm. Postoperative course was uneventful. Three years after surgery, there was no recurrence of cancer or hernia. Repair of perineal hernia is challenging, with limitation regarding guidelines in literature.*

**Key words:** *perineal hernia, abdominoperineal resection, prosthetic material.*

**Introduction**

Perineal hernia is the protrusion of intra-abdominal viscera through the pelvic floor. The etiology can be congenital, but most perineal hernias occur as an incisional hernia following pelvic surgery [1,2]. Perineal hernia after abdominoperineal resection (APR) was first reported in 1937 [3,4]. The prevalence of perineal herniation is low, ranging from 0.6% to 7%, and condition may be asymptomatic [2]. The reported incidence of perineal hernia requiring repair is <1% after APR and approximately 3% after pelvic exenteration [3]. Surgical repair is the only effective method of treatment; however, because of the complex anatomy of the pelvic floor and high abdominal pressure, the repair of these hernias is challenging. The recurrence rate is reported to be up to 37% [1]. Various approaches have been described, including abdominal, perineal and combined approaches, either simply by closing the pelvic defect or using autologous or prosthetic material [3,5]. The literature describing a successful repair technique is limited. The reported cases are rare or span over a long period in which different techniques are compared and even non mesh techniques were used. Various methods of repair have been described, but none is well established [1,2,6].

**Case report**

A sixty five year old woman came to the office complaining on painful bulging of the perineum 24 months after

abdominoperineal laparoscopic resection for rectal cancer with uneventful postoperative course (Fig.1). The size of the protrusion increased gradually. In the last three 3 months patient had felt pain and difficulty while sitting. At physical examination the defect in perineum was approximately 3x3 cm wide. The laboratory and biochemical results were within the referent range, the finding on abdominal and pelvic imaging were normal with tumor markers also within normal range. She denied other symptoms other than pain and discomfort while sitting. Apart from rectal cancer she had no previous medical history and no family history. After cancer recurrence had been excluded, hernioplasty was planned. A standard preoperative evaluation was performed. One dose of intravenous broad-spectrum antibiotic was administered 30 minutes prior to surgery. The patient was placed in a lithotomy position combined with steep Trendelenburg to allow save access to the perineum. The urethral catheter was placed to decompress the bladder. An elliptical incision was made over the hernia defect and hernia sac was dissected and opened. Intraoperative the defect measured 4x6cm (Figs. 2, 3). The pelvic defect could not be primarily sutured due to prior radical resection of the levator ani muscle. A 10x15 cm composite mesh (Parietex composite mesh) was used to reconstruct the pelvic floor (Fig. 4). The mesh was trimmed according to shape of the defect, with an overlap of at least 3cm in each direction, and was inserted through the perineal defect. The mesh was sutured through urogenital diaphragm. The perineal incision was closed with 2-0 Prolene (Fig. 5). Patient was discharged on fourth postoperative day. Postoperative course was uneventful. Three years after surgery there was no recurrence of the disease or hernia.

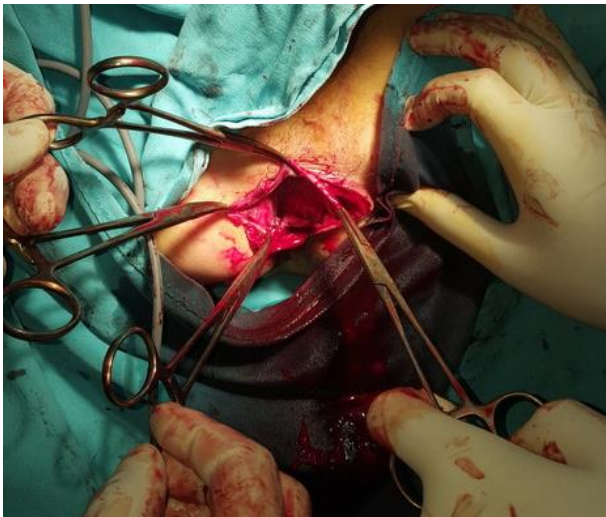
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**Fig. 1**



**Fig. 4**



**Fig. 2**



**Fig. 5**



**Fig. 3**

### Discussion

Despite evidence in the multimodality treatment, radical surgery remains the most important prognostic factor in rectal cancer [1,7]. The large pelvic wall defect after wide excision and the previously radiated tissue may induce postoperative perineal hernia. Other various factors also may facilitate the development of perineal hernia after abdominoperineal excision, including the large size of the female pelvis, previous hysterectomy, neoadjuvant treatment, excision of the levator muscles, smoking, and wound infection [3,8], although in this case none of these factors were present. During laparoscopic APR, the pelvic peritoneum is left open. In addition, laparoscopic surgery causes fewer postoperative adhesions in the abdominal cavity than conventional surgery, so the small bowel may more easily slide into the perineal area. These factors could predispose to the development of perineal hernia. The majority of perineal hernias after APR are asymptomatic and undiscovered. However, symptoms

may include bulging, discomfort, pain, small bowel obstruction, and dysuria. The diagnosis of perineal hernia can be difficult unless significant signs and symptoms become evident. The physician should have a high index of suspicion in patients presenting with perineal pain, even if no bulging mass is discovered with herniography, CT, barium enema studies and dynamic magnetic resonance imaging [9]. The indication for repair of perineal hernias is patient discomfort while sitting, skin erosion, intestinal obstruction, and dysuria. Although various approaches for perineal hernia repair have been proposed, there is no consensus on the optimal technique. Current management options include abdominal, perineal and combined approaches [9,10]. However, the reported recurrence rates after perineal repair are high, ranging from 16% [11] to 25% [12], 37% [13] and even 100% [1]. The high recurrence rate may result from the complexity of the pelvic floor anatomy and the high abdominal pressure exerted on the pelvic floor in a standing

position. Although the perineal approach is considered less invasive, it has the inherent drawbacks of poor exposure, paucity of musculofascial tissue mobilization, less durable fixation, and inability to address intra-abdominal adhesions [1,3]. The wide experience in use of absorbable or non-absorbable prostheses (mesh) to repair different types of hernia, their easy application, low complication rates and good results make them an important option in the treatment and even prevention of perineal hernia after abdominoperineal excision.

## Conclusion

Repair of perineal hernia after abdominoperineal resection represents a significant challenge for coloproctologist considering the fact there are no guidelines. The reported cases are rare or span over a long period in which different techniques are reported, but none is well established.

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