Morbidity and Efficiency of Transobturator Polypropylene Mesh in Treatment of Urinary Incontinence

A 12 years experience

IOAN SCARNECIU^{1,2*}, ADRIAN BRINZA², IONUT-ALEXANDRU BANUTA², CAMELIA CORNELIA SCARNECIU^{1,2}, ALEXANDRU GEORGIAN LACULICEANU^{1,2}, DANIEL PORAV HODADE^{3,4}, CIPRIAN TODEA MOGA^{3, 4}, VERONICA GHIRCA^{3,4}, MARTHA ORSOLYA^{3,4}, LAURIAN MAXIM^{1,2}

¹University of Transilvania Faculty of Medicine, 56 Nicolae Balcescu Str., 500019, Brasov, Romania

²Clinical Emergency County Hospital, 25-27 Bucuresti Road, 500326, Brasov, Romania

³University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, 38 Gheorghe Marinescu Str., 540139, Targu Mures, Romania

⁴Clinical Emergency County Hospital, 1st Gheorghe Marinescu St., 540103, Targu Mures, Romania

Urinary incontinence is a socio-economic problem with a major impact on quality of life. Although there are multiple non-surgical and drug solutions, surgical treatment remains the most effective method for stress urinary incontinence. Placement of transobturator polypropylene tape is a safe method with minimal intraoperative and postoperative complications. This study had a minimal rate of complications at a one-year follow-up; the biggest problem is represented by de novo overactive bladder (20.26%) that responded successfully to conservative treatment in most cases. The surgical treatment cure rate was 97.8%. TOT is a safer method with less intraoperative complications than TVT, at the same time the success rate is comparable to TVT.

Keywords: urinary stress incontinence, transobturator tape, overactive bladder

Urinary incontinence is defined as involuntary loss of urine that occurs in both sexes, predominantly in females [1,2]. Urinary incontinence in men may have multiple causes [3-7]. One of the most common causes is an obstacle located in the lower urinary tract, as result the bladder will overfill which will lead to urinary loss. The most common obstacle encountered is benign prostate hyperplasia [8-10], although other rare pathologies should not be forgotten [11-14].

There are two major categories: stress urinary incontinence and urgency urinary incontinence. Stress urinary incontinence is defined by the leakage of urine as result of physical exercise, sneezing or cough; while urinary urgency incontinence is the loss of urine associated with the urge to urinate [1,2]. Urinary incontinence is a socioeconomic problem with a major impact on quality of life [11-19]. In the absence of specialized treatment, it can affect the quality of life through repeated urinary infections [20,21]. The association of urinary incontinence with a ureteral stent mounted for other reasons can cause reflux pyelonephritis [22-27]. Severe urinary incontinence has a prevalence between 6-10% in Europe and the USA [28-30].

Urinary incontinence treatment:

a.Non-surgical: fluid intake optimization, weight loss [31,32], pelvic floor muscle training (PFMT) [29], incontinence pessaries and intravaginal devices [33].

b.Medicinal products: vaginal estrogens [34], anticholinergics [35], β_3 adrenergic agonists [36], serotonin-noradrenaline reuptake inhibitors [37], and others [38-43].

c.Invasive treatment: stress incontinence surgery, neuromodulation and intravesical onaboutulinumtoxinA [44].

The placement of a synthetic mid-urethral sling is the first-line surgical treatment with a success rate more than 80% [45] and a very good tolerance [46]. There are currently two widely used techniques: transobturator tape (TOT) and tension-free vaginal tape (TVT) that are based on

mounting a strip of polypropylene mesh [47-48]. TOT was first described in the Netherlands in 1998, subsequently introduced in France in 2001 and in the USA in 2003 [49].

The main objective of this study is to evaluate the efficiency and morbidity associated with surgical intervention *out-in* TOT for stress urinary incontinence and mixed urinary incontinence in County Emergency Clinical Hospital Brasov, Romania, Department of Urology.

Experimental part

Methods

This is a prospective study on female patients with stress urinary incontinence and mixed urinary incontinence, who underwent surgical treatment in *out-in* TOT between January 2006 and January 2018.

All patients underwent a complete preoperative examination that includes: urology and obstetric history, complete clinical examination, usual laboratory tests, cistoscopy with Marshall or Ulmsteen maneuvers, abdominal ultrasound.

Inclusion criteria: pure urinary stress incontinence, mixed urinary incontinence, vaginal prolapse \leq than stage 1. Exclusion criteria: vaginal prolapse higher than stage 1, gynecological associated pathology [50-52], patients suffering from psychiatric or neurological disorders.

Surgery in the TOT maneuver was performed by a single urologist under spinal anesthesia.

Mandatory visits for urological re-evaluation were performed at 6 and 12 months. In case the patient had postoperative complications, she came for re-evaluation outside of the pre-established schedule. Each visit included: abdominal ultrasound and bladder residual volume, objective and subjective presence of postoperative urinary incontinence.

We also analyzed the incidence of intraoperative complications, early and late postoperative complications.

The statistical analysis was performed using EpiInfo Build 7.2.2.16 11/02/2018, with a confidence interval set at 95%.

Results and discussions

From January 2006 till January 2018 in the Emergency County Hospital Brasov 301 patients underwent surgical treatment for UI with transobturator tape. All procedures were performed under spinal anesthesia. In 86.38% (260) surgery was performed for pure urinary stress incontinence and in 13.62% for mixed urinary incontinence. The average length of hospitalization was 4.7 days with a minimum of 4 days and a maximum of 9 days. No other simultaneous surgery was performed.

Baseline characteristics

Table 1 summarizes the general characteristics. The mean age of the patients was 57.9 ± 10.4 years, with a range between 42 and 73 years. The average height was 158 cm with a standard deviation of 7 cm. The average patient weight was $65.4 \text{ kg} \pm 10.8 \text{ kg}$ with an average body mass index of 26.5 + -3.8. A total of 46 patients had a body mass index greater or equal to 30 kg/m². The hormonal status determined that 70.43% of the patients were in the menopause period, of which substitution hormone therapy was evidenced in 53 patients (17.6%). Affirmative 210 patients said were sexually active.

The obstetrical anamnestic reveals that 293 patients had at least one birth of which: 81 patients specified a natural birth of a macrosome fetus, 48 had a caesarean section, and 15 needed additional maneuvers such as fetal extraction by forceps. Hysterectomy for a cervix neoplasm was observed in 27 (8.97%) patients. A total of 108 patients were smokers. About a third of patients suffer from other associated conditions such as Hypertension (29.23%), Type 2 diabetes (5.98%) (table 1).

1		Total N=301	1
		100010001	
	Average age (years and SD)	57.9 +- 10.4	
	Average height (cm and SD)	158 +-7	
	Average weight (kg and SD)	65.4 +-10.8	
	Average BMI (kg/m² and SD)	26.5+-3.8	
	Menopausal n (%)	212 (70.43)	Table 1
	Hormonoterapy n (%)	53 (17.6)	BASELINE CHARACTERISTICS
	Urinary stress incontinence n (%)	260 (64.45)	
	Urinary mixt incontinence n (%)	41 (35.55)	
	Sexually active n (%)	210 (69.67)	
	Deliveries		
	Macrosome n (%)	81 (26.91)	
	Caesarean section n (%)	48 (15.94)	
	Forceps/Vacuum n (%)	15 (4.98)	
	Hypertension	88 (29.23)	
	Type 2 diabetes	18 (5.98)	
	Previous hysterectomy	27 (8.97)	
	Smoking	108 (35.88)	

Intraoperative and early postoperative complications

Intraoperative haemorrhage greater than 150 mL was detected in 15 (4.98%) patients. Neither one of the patients required blood transfusion. No vaginal or bladder perforation occurred during the surgery. In the postoperative period, 17 patients experienced urine retention after removal of the Foley catheter. A Foley catheter was mounted for additional 5-7 days and no tape removal was required. Three of the patients had a massive hematoma that has reduced after conservative treatment and did not require evacuation. No septic complication have been determined.

Late postoperative complications

A patient experienced vaginal erosion, the patient did not follow recommendation of sexual abstinence. At 1year examination, a patient experienced *de novo* dyspareunia for which estrogen treatment was prescribed.

De novo OAB (overactive bladder) was reported at 70 (23.25%) patients at 1 month. At 12 months, symptomatology of overactive bladder decreased to 61 (20.26%). These patients received antimuscarinic treatment with improvement of symptomatology in 40 cases at 6 months. The rest of the patients were recommended for intravesical onaboutulinum toxin A.

Inguinal pain was found in 32 (10.63%) cases starting 24 hours postoperatively. At the one-month visit, only 9 (2.99%) patients experienced pain. Only 1 patient had pain at 1 year follow-up (table 2).

Table	2
COMPLICAT	FIONS

Intraoperative	
Haemorrhage >150ml (n, %)	15 (4.98%)
Early postoperative	
Hematoma (n, %)	3 (0.99)
Urinary retention (n, %)	17 (6.64)
Late postoperative	
Vaginal erosion (n, %)	1 (0.33)
De novo dyspareunia (n, %)	1 (0.33)
De novo OAB (n, %)	61 (20.26)
Inguinal /perineal pain (n, %)	1 (0.33)

Objective and subjective success rate, 1 year follow-up

Of total 301 patients, at 6 months, all patients presented at urological evaluation; 11 (3.65%) women neglected urological re-evaluation at 12 months. Subjectively, patients experienced a satisfaction rate after surgery at 95.02% (286 cases) at 6 months. The objective cure rate at 6 months was 97% (292); cystoscopy with concomitant Marshall or Ulmsteen maneuvers. Noteworthy 7 women out of the 11 who subsequently neglected urological re-evaluation at 12 months tested positive for the maneuvers.

months tested positive for the maneuvers. At 1 year follow-up 290 (96.35%) patients have shown up. Due to abandonment of urological evaluation, the objective cure rate increased to 97.8% (284/290). The subjective rate was 93.68%.

We analyzed potential factors that may be involved in the subjective and objective recurrence of UI: age, more than 2 vaginal deliveries, hormonal status (menopausal), BMI, smoking, fetus macrosomia, cesarean section. The

http://www.revistadechimie.ro

subjective recurrence of UI was associated with the quantity of vaginal delivery, with a statistically significant p=0.034 and OR=5.427 (fig. 1). Other changes that could affect the rate of recurrence were not observed in this study.

Subjective recurence





We analyzed the variables that could be involved in the development of the *de novo* OAB in patients that underwent surgery. No statistically significant data was observed.

The subjective cure rate in this study at one-year followup was 93.68% while the objective cure rate was 97.8%. This study has similar results as the studies previously described by Serrati M. et al [53], with a subjective and objective cure rate at 5 years of 90.8% and 90.3%. Similarly, Serrati M. et al, in a prospective study with a 10 years followup, has shown a 95% cure rate [54]. In the studies mentioned above, they presented multicenter studies in which the operative team was formed by several doctors, including residents. We analyzed the experience of a single physician with over 15 years experience in the treatment of urinary incontinence. The rate of intraoperative complications remains very low in this study, with no bladder or vaginal perforation. A Cohrane meta-analysis performed in 2017 demonstrated a comparable short-term cure rate of the TOT vs TVT. The TVT approach is associated with a higher rate of intraoperative complications than TOT, as result TOT sling is a safer version of TVT tapes with comparable results [45]. A high cure rate in our study is explained by a rigorous selection of patients and no cases with previous surgery for UI [54]. The only risk factor found in this study for subjective recurrence of UI was number of vaginal deliveries. A small sample size and little number of recurrences associated with a one-year follow-up period may explain our results. De novo overactive bladder observed after TOT in the literature is reported by Serrati M. et al in 24% at 1 year follow-up, 19% at 5 years and 14% at 10 years [53, 54]. This study revealed similar results to those previously described with an OAB rate of 20.26% after one-year follow-up. Antimuscarinic treatment improved symptomatology in 65.57% of these cases. Specialty literature highlights smoking as a factor that directly affects the severity of OAB symptoms [55, 56]. As a result, lifestyle changes could lead to a decrease symptomatology in *de novo* OAB installed after surgery [57]. A longer follow-up and multicenter study with larger samples could indicate the limitations of a successful surgical treatment for stress and mixed urinary incontinence.

Conclusions

This study has shown that surgical treatment of urinary stress incontinence with TOT procedure is a safe method with minimal intraoperative complication. The biggest problem seems to be the *de novo* overactive bladder installed after surgery, reducing the patient's quality of life.

References

1.HAYLEN, B.T., DE RIDDER, D., FREEMAN, R.M., SWIFT, S.E., BERGHAMS, B., LEE, J., MONGA, A., PETRI, E., RIZK, D.E., SAND, PK., SCHAER, G.N., Int Urogynecol J, **21**, no. 1, 2010, p. 5-26

2.BUMBU, A., PASCA, B., TIT, D. M., BUNGAU, S., BUMBU, G., Farmacia, **64**, no. 3, 2016, p. 419.

3.RADAVOI, G.D., PRICOP, C., JINGA, V., MATES, D., RADOI, V.E., JINGA, M., URSU, R.I., BRATU, O.G., MISCHIANU, D.L., IORDACHE, P., Rom J Morphol Embryol., **57**, no. 2, 2016, p. 467-475.

4.MARCU, D., SPINU, D., MISCHIANU, D., SOCEA, B., OPREA, I., BRATU, O. Romanian Journal of Military Medicine, **120**, no. 3, 2017, p. 39-42.

5.POPESCU, R., BRATU, O., SPINU, D., MARCU, D., FARCAS, C., DINU, M., MISCHIANU, D. Romanian Journal of Military Medicine, **118**, no. 3, 2015, p. 16-19.

6.CIUCA, G.A., BRATU, O., SPINU, D., DINU, M., FARCAS, C., RADULESCU, A., POPESCU, R., MARCU, D., MISCHIANU, D., ARMEAN, P. Romanian Journal of Military Medicine, **119**, no. 2, 2016, p. 12-16. 7.BRATU, O., SPINU, D., OPREA, I., POPESCU, R., MARCU, D., FARCAS, C., DINU, M., MISCHIANU, D. Romanian Journal of Military Medicine, **118**, no. 3, 2015, p. 23-25.

8.SPINU, D., BRATU, O., MARCU, D., MISCHIANU, D., HUICA, R., SURCEL, M., MUNTEANU, A., SOCEA, B., BODEAN, O., URSACIUC, C., Rev Chim (Bucharest), **69**, no. 3, 2018, p. 645-649.

9.BRATU, O., MISCHIANU, D., CONSTANTINOIU, S., Chirurgia (Bucur), **108**, no. 2, 2013, p.250-255.

10.SCARNECIU, I., ANDREI, C., SCARNECIU, C., LUPU, A.M., BRATU, O.G., LUPU, S., Urology Journal, **15**, no. 5, 2018, p. 297-299.

11.PANDI, E., MAXIM, L.S., CRISTIAN, A., HOGEA, M.D., DOCHIT, C.M., SCARNECIU, C.C., SCARNECIU, I., MIRONESCU, A., Urol J, **13**, no. 4, 2016, p. 2797-9.

12.MARCU, R.D., SPINU, A.D., MISCHIANU, D., OPREA, I.S., DIACONU, C., SOCEA, B., BRATU, O.G., Farmacia, **67**, no. 1, 2019, p. 50-55.

13. TATARU, A.L., FURAU, G., AFILON, J., IONESCU, C., DIMITRIU, M., BRATU, O.G., TIT, D.M., BUNGAU, S., FURAU, C., *J. Clin. Med.*, *8*, *no.* 1, 2019, E96; https://doi.org/10.3390/jcm8010096.

14.SINESCU, R.D., NICULĂE, A., PERIDE, I., VASILESCU, F., BRATU, O.G., MISCHIANU, D.L., JINGA, M., CHECHERITA, I.A., Rom J Morphol Embryol., **56**, no. 2, 2015, p. 601-605.

15.SAARNI, S.I., HARKANEN, T., SUVISAARI, J., KOSKINEN, S., AROMAA, A., LONNQVIST, J., Qual Life Res, **15**, no. 8, 2006, p. 1403-14.

16.SUBAK, L.L., BRUBAKER, L., CHAI, T.C., CREASMAN, J.M., DIOKNO, A.C., GOODE, P.S., KRAUS, S.R., KUSEK, J.W., LENG, W.W., LUKACZ, E.S., NORTON, P., TENNSTEDT, S., Obstet Gynecol, **111**, no. 4, 2008, p. 899-907.

17.GANZ, M.L., SMALARZ, A.M., KRUPSKI, T.L., ANGER, J.T., HU, J.C., WITTRUP-JENSEN, K.U., PASHOS, C.L., Urology, **75**, no. 3, 2010, p. 526-32.

18.IRWIN, D.E., MUNGAPEN, L., MILSOM, I., KOPP, Z., REEVES, P., KELLEHER, C., BJU Int., **103**, no. 2, 2009, p. 202-9.

19.PRICOP, C., DRAGOMIR, S., MARDARI, B., BARDAN, R., SCARNECIU, I., ORSOLYA, M., Biol Sci, **66**, no. 4, 2014, p. 1581-1584.

20.RADULESCU, A., MADAN, V., AUNGURENCI, A., BRATU, O., FARCAS, C., DINU, M., MISCHIANU, D., Romanian Journal of Military Medicine, **118**, no. 3, 2015, p. 20-22.

21.SPINU, D., BRATU, O., POPESCU, R., MARCU, D., RADULESCU, A., MISCHIANU, D., Romanian Journal of Military Medicine, **118**, no. 3, 2015, p. 12-15.

22.BUMBU, A., NACER, K., BRATU, O., BERECHET, M., BUMBU, G., BUMBU, B., Proceedings: 14th National Congress of Urogynecology and The National Conference of the Romanian Association for the Study of Pain, Eforie, Romania, 2017, p. 82.

23.EBBESEN, M., HUNSKAAR, S., RORTVEIT, G., HANNESTAD, Y., BMC Urology, **13**, 2013, p. 27.

24.SPINU, A.D., MARCU, R.D., SOCEA, B., DIACONU, C.C., SCARNECIU, I., SCARNECIU, C., BODEAN, O.M., DRAGOMIRESCU, R.I.F., STANESCU, A.M.A., MISCHIANU, D.L.D., BRATU, O.G., Rev Chim (Bucharest), **69**, no. 8, 2018, p. 2061-2063.

25.SCARNECIU, I., BRATU, O.G., COBELSCHI, C.P., NECULOIU, C.D., SCARNECIU, C.C., LUPU, S., BRINZA, A., MARCU, D., SOCEA, B., MAXIM, L., Rev Chim (Bucharest), **69**, no. 12, 2018, p. 3406-3409.

26.RADULESCU, D., BALCANGIU STROESCU, A., PRICOP, C., GEAVLETE, B., NEGREI, C., BRATU, O., GINGHINA, O., VACAROIU, I., Rev Chim (Bucharest), **68**, no. 1, 2017, p. 52-54.

27.BUMBU, G.A., BERECHET, M.C., KARIM, N., BUMBU, G., MAGHIAR, O.A., BRATU, O.G., VICAS, R.M., TICA, O., BUMBU, B.A., Romanian Journal of Morphology and Embriology, **59**, no. 4, 2018, p. 1173–1177. 28.THOM, D., J Am Geriatr Soc, **46**, no. 4, 1998, p. 473-80.

29.HUANG, A.J., JAMA Intern Med, **173**, no. 15, 2013, p. 1463-4.

30.ABDEL-DAIM, M.M., ABO-EL-SOOUD, K., ALEYA, L., BUNGAU, S.G., NAJDA, A., SALUJA, R., Oxid. Med. Cell. Longev., 2018, ID 6276438, 2018 https://doi.org/10.1155/2018/6276438.

31.DIACONU, C.C., DEDIU, G.N., IANCU, M.A. Acta Cardiologica, **73**, no. 6, 2018, p. 511-517.

32.DIACONU CC, ARSENE D, BALACEANU A, BARTOS D. Romanian Journal of Morphology and Embryology, **55**, no. 3, 2014, p. 973-976. 33.RICHTER, H.E., BURGIO, K.L., BRUBAKER, L., NYGAARD, I.E., YE, W., WEIDNER, A., BRADLEY, C.S., HANDA, V.L., BORELLO-FRANCE, D., GOODE, P.S., ZYCZYNSKI, H., LUKACZ, E.S., SCHAFFER, J., BARBER, M., MEIKLE, S., SPINO, C., Obstet Gynecol, **115**, no. 3, 2010, p. 609-17.

34. WEBER, M.A., KLEIJN, M.H., LANGENDAM, M., LIMPENS, J., HEINEMAN, M.J., ROOVERS, J.P., PLOS ONE, **10**, no. 9, 2015, p. e0136265. 35.NOVARA, G., GALFANO, A., SECCO, S., D'ELIA, C., CAVALLERI, S., FICARRA, V., ARTIBANI, W., Eur. Urol., **54**, no. 4, 2008, p. 740-63.

36.MANEA, M., MARCU, D., PANTEA STOIAN, A., GAMAN, M.A., GAMAN, A.M., SOCEA, B., NEAGU, T.P., STANESCU, A.M.A., BRATU, O.G., DIACONU, C.C. Rev Chim (Bucharest), **69**, no. 11, 2018, p. 4180-4184. 37.JOST, W., MARSALEK, P., Clin. Auton. Res., **14**, no. 4, 2004, p. 220-7.

38.ABDEL-DAIM, M.M., ZAKHARY, N.I., ALEYA, L., BUNGAU, S.G., BOHARA, R.A., SIDDIQI, N.J., Oxid. Med. Cell. Longev., 2018, ID 2098123, 2018 https://doi.org/10.1155/2018/2098123.

39.ABDEL-DAIM, M.M., AHMED, A., IJAZ, J., ABUSHOUK, A.I., AHMED, H., NEGIDA, A., et al., Environ. Sci. Pollut. Res., **26**, no. 8, 2019, p. 8080.

40.YEUNG, A.W.K., TZVETKOV, N., EL-TAWIL, O.S., BUNGAU, S.G., ABDEL-DAIM, M.M., ATANASOV, A.G., Oxid. Med. Cell. Longev., 2019, ID 8278454, 2019. https://doi.org/10.1155/2019/8278454.

41.SOCEA, L.I., VISAN, D.C., BARBUCEANU, S.F., APOSTOL, T.V., BRATU, O.G., SOCEA, B., Rev Chim (Bucharest), **69**, no. 4, 2018, p. 795-797.

42.DUMITRU, N., COCOLOS, A., CARAGHEORGHEOPOL, A., DUMITRACHE, C., BRATU, O.G., NEAGU, T.P., DIACONU, C.C., GHEMIGIAN, A., Rev Chim (Bucharest), **69**, no. 7, 2018, p. 1706-1709. 43.TIGLIS, M., NEAGU, T.P., ELFARA, M., DIACONU, C.C., BRATU, O.G., VACAROIU, I.A., GRINTESCU, I.M., Rev Chim (Bucharest), **69**, no. 10, 2018, p. 2877-2880.

44.MOGA, M.A., BANCIU, S., DIMIENESCU, O., BIGIU, N.F., SCARNECIU, I., J Pak Med Assoc, **65**, no. 1, 2015, p. 76-80.

45.FORD, A.A., ROGERSON, L., CODY, J.D., OGAH, J., Cochrane Database Syst Rev, 7, 2015, p. CD006375.

46.SCARNECIU, I., LUPU, S., SCARNECIU, C., COCUZ, M.E., SCARNECIU, V., Metalurgia International, **16**, no. 9, 2011, p. 43-45.

47.LATTHE, P.M., SINGH, P., FOON, R., TOOZS-HOBSON, P., BJU Int., **106**, no. 1, 2010, p. 68-76.

48.BRATU, O., MARCU, D., SPINU, D., RADULESCU, A., OPREA, I., MISCHIANU, D., Romanian Journal of Military Medicine, **118**, no. 3, 2015, p. 40-44.

49.DELORME, E., DROUPY, S., DE TAYRAC, R., DELMAS, V., Prog. Urol., **13**, no. 4, 2003, p. 656-9.

50.BODEAN, O., BRATU, O., BOHILTEA, R., MUNTEANU, O., MARCU, D., SPINU, D.A., VACAROIU, I.A., SOCEA, B., DIACONU, C.C., FOMETESCU GRADINARU, D., CIRSTOIU, M., Rev Chim (Bucharest), **69**, no. 6, 2018, p. 1411-1415.

51.MEHEDINTU, C., ANTONOVICI, M., BRINDUSE, L., BRATILA, E., STANCULESCU, R., BERCEANU, C., BRATU, O., PITURU, S., ONOFRIESCU, M., MATASARIU, D.R., Rev Chim (Bucharest), **69**, no. 3, 2018, p. 581-584.

52.STANIMIR, M., CHIUTU, L.C., WESE, S., MIULESCU, A., NEMES, R.N., BRATU, O., Rom J Morphol Embryol, **57**, no. 2 Suppl, 2016, p. 849-852.

53.SERATI, M., BAUER, R., CORNU, J.N., CATTONI, E., BRAGA, A., SIESTO, G., LIZÉE, D., HAAB, F., TORELLA, M., SALVATORE, S., Eur. Urol., **63**, no. 5, 2013, p. 872-8.

54.SERATI, M., BRAGA, A., ATHANASIOU, S., TOMMASELLI, G.A., CACCIA, G., TORELLA, M., GHEZZI, F., SALVATORE, S., Eur. Urol., **71**, no. 4, 2017, p. 674-679.

55.CHAE, J., YOO, E.H., JEONG, Y., PYEON, S., KIM, D., Obstet Gynecol Sci., **61**, no. 3, 2018, p. 404-412.

56.SCARNECIU, I., LUPU, S., SCARNECIU, C.C. Procedia – Social and Behavioral Sciences, **127**, 2014, p. 442-447.

57.DIACONU, C.C., MANEA, M., MARCU, D.R., SOCEA, B., SPINU, A.D., BRATU, O.G. Acta Cardiologica 2019. DOI 10.1080/ 00015385.2019.1590498

Manuscript received:22.11.2018