

Levels of quality of life in patients with muscle invasive bladder cancer after organ-preserving treatment

A.V. Sakalo ¹,
Z.V. Gatsereia ²,
V.S. Sakalo ¹

¹ SI “Institute of urology named after academic O.F. Voizianov” NAMS of Ukraine, Kyiv, Ukraine, e-mail: inurol@amnu.gov.ua

² KNP “Kyiv City Clinical Oncology Center”, Kyiv, Ukraine, e-mail: kmkoc.kiev@gmail.com

A.V. Sakalo

orcid: 0000-0001-5957-2562

Z.V. Gatsereia

orcid: 0000-0003-3705-7054

V.S. Sakalo

orcid: 0000-0002-8340-6895

For citation:

ДСТУ 8302 2015:

Сакало А. В., Гацереія З. В., Сакало В. С. Рівні якості життя пацієнтів із м'язово-інвазивним раком сечового міхура після органозберігаючого лікування. *Урологія*. 2023. Т. 27, № 1–2. С. 21–27.

DOI: <https://doi.org/10.26641/2307-5279.27.1-2.2023.291340>

APA:

Sakalo, A. V., Gatsereia, Z. V., & Sakalo, V. S. (2023). Levels of quality of life in patients with muscle invasive bladder cancer after organ-preserving treatment. *Urologiya*, 27(1–2), 21–27.

<https://doi.org/10.26641/2307-5279.27.1-2.2023.291340>

Надійшла: 10.11.2022

Акцептована: 01.03.2023

Keywords:

radical cystectomy, partial cystectomy, muscle-invasive bladder cancer, quality of life, chemoradiation therapy

Ключові слова:

радикальна цистектомія, часткова цистектомія, м'язово-інвазивний рак сечового міхура, якість життя, хіміопроменева терапія

SUMMARY

The aim of the study was to analyze the quality of life of MIBC patients' life after RC with orthotopic ileal neobladder, after partial cystectomy (PC) with adjuvant radiotherapy (RT) and after PC with adjuvant chemotherapy (CT). A retrospective analysis of 120 MIBC patients who were treated at the Kyiv city clinical oncological center which is the base of SI “Institute of urology named after academic O.F. Voizianov” NAMS of Ukraine during the period from 2008 to 2019 was performed. The patients were divided into 3 groups depending on the intervention extent. The 1st one included patients after RC (42), group 2 consisted the patients after PC and adjuvant RT, group 3 consisted the patients after PC and adjuvant CT. The patients' quality of life has been assessed by three questionnaires – EORTC QLQ-C30, EORTC SHQ-C22, ICIQ-UI. The results of the study confirm better quality of life after PC with adjuvant CT, especially with regard to physical condition, patients' adaptation in society (social scale), financial toxicity, gastrointestinal tract functioning (according to symptoms of vomiting, nausea and diarrhea). Our study has confirmed that PC can provide adequate control of MIBC in the individual cases and showed that it offers patients a good chance of long-term bladder preservation providing satisfactory overall postoperative health and quality of life. A critical approach should be taken into consideration when choosing the most appropriate regimen for treatment of MIBC and considering between radical cystectomy or partial cystectomy. However, it is important to inform patients that organ-preserving treatment allows them to achieve a better quality of life, the treatment process may be longer than that after radical cystectomy.

РЕФЕРАТ

Рівні якості життя пацієнтів із м'язово-інвазивним раком сечового міхура після органозберігаючого лікування. Сакало А. В., Гацереія З. В., Сакало В. С. Метою дослідження було проаналізувати якість життя пацієнтів із м'язово-інвазивним раком сечового міхура (МІРСМ) після РЦЕ з ортотопічним клубовим неосечовим міхуром, після

часткової цистектомії (ПЦ) з ад'ювантною променевою терапією (ПТ) та після РЦЕ з ад'ювантною хіміотерапією (ХТ). Проведено ретроспективний аналіз 120 хворих на МІРСМ, які перебували на лікуванні в Київському міському клінічному онкологічному центрі, який є базою ДУ «Інститут урології ім. академіка О.Ф. Возіанова» НАМН України в період з 2008 по 2019 рр. Пацієнти були розподілені на 3 групи залежно від обсягу втручання. До 1-ї належали хворі після РЦЕ (42), до 2-ї групи – пацієнти після ПК та ад'ювантної ПТ, до 3-ї – пацієнти після ПК та ад'ювантної ХТ. Якість життя пацієнтів оцінювали за трьома опитувальниками – EORTC QLQ-C30, EORTC SHQ-C22, ICIQ-UI. Результати дослідження підтверджують кращу якість життя після ПК з ад'ювантною ХТ, особливо щодо фізичного стану, адаптації пацієнтів у суспільстві (соціальний масштаб), фінансової токсичності, функціонування шлунково-кишкового тракту (за симптомами блювання, нудоти та діареї). Наше дослідження підтвердило, що ПК може забезпечити адекватний контроль МІРСМ в окремих випадках і показало, що він пропонує пацієнтам хороші шанси на тривале збереження сечового міхура, забезпечуючи задовільний загальний післяопераційний стан здоров'я та якість життя. При виборі найбільш підходящої схеми лікування МІРСМ і при виборі радикальної цистектомії або часткової цистектомії слід враховувати критичний підхід. Проте важливо інформувати пацієнтів, що органозберігаюче лікування дозволяє досягти кращої якості життя, процес лікування може бути довшим, ніж після радикальної цистектомії.

INTRODUCTION

The treatment choice (transurethral resection of the bladder, open resections or cystectomies) for muscle invasive bladder cancer (MIBC) is still controversial. According to the supporters of radical cystectomy (RC), the bladder removal in MIBC is a priority due to the high probability of recurrence (50-90%) after organ-preserving treatment of MIBC (Ebbing et al., 2018). At the same time, supporters of organ-preserving surgeries for MIBC point out the extremely low quality of life of patients after cystectomy, despite various types of urinary derivation (Halkin, 2007). Besides, the high injury rate and technical difficulties make RC unacceptable for some patients (Startsev, 2019). The advantage of organ-preserving complex MIBC treatment is the high quality of life figures, including social, physical, sexual, cognitive well-being as compared to patients who underwent RC.

The aim of the study was to analyze the quality of life of MIBC patients' life after radical cystectomy (RC), after partial cystectomy (PC) with adjuvant radiotherapy (RT) and after PC with adjuvant chemotherapy (CT).

MATERIALS AND METHODS

We observed 120 MIBC patients who were treated at the Kyiv city clinical oncological center which is the base of State Institution «Academician O.F. Vozianov Institute of Urology of the National Academy of Medical Sciences of Ukraine» during the period from 2008 to 2019. The patients were divided into 3 groups depending on the intervention extent. The 1st one included patients after RC with ICNP (42), group 2 consisted the patients after PC and adjuvant RT with a total dose to the bladder and pelvic lymph nodes 45 to 64 Gy and the single dose of 2 Gy for 6.5 weeks (using a linear accelerator (41)), group 3 consisted the patients after PC and adjuvant CT – 2-4 courses on the scheme of cisplatin

70 mg/m² on day 1 + gemcitabine 1000 mg/m² on days 1, 8, 15 (37). The mean age of the 1st patients' group was 62 years, in the 2nd group 63 years, in the 3rd group 58 years. According to the TNM classification, the distribution of patients was as follows: T2a-T2b – 72 (60%), T3a-T3b – 43 (35.8%), T4a-T4b – 5 (4.2%). Diagnosis was established in the all cases by US, CT or MRI data, transurethral biopsy (TUB) of bladder tumors in order to verify the diagnosis and determine the depth of neoplastic process invasion. Urothelial carcinoma of various tumor differentiation degrees was morphologically confirmed in all patients. According to the degree of tumor differentiation the patients were distributed as follows: high degree (G1) – 2 (1.6%), moderate degree (G2) – 46 (38.3%), low degree (G3) – 72 (60.1%). As for localization, in the 1st group 70% of tumors were located in the cervix, in the remaining 30% – on the lateral bladder walls. In 2nd and 3rd groups 80% of the tumors were located on the lateral walls, and 20% of them situated on the lateral walls with transition to the bladder neck. Cardiovascular diseases prevailed among comorbidities: in 1st group – 54%, in 2nd group – 56% and in 3rd group – 55%.

The patients' quality of life has been assessed by three questionnaires. The first one is a modern version of the EORTC quality of life questionnaire (EORTC QLQ-C30) officially approved by the EORTC Quality of Life Study Group and approved for use in scientific studies (Aaronson, 1993). The second questionnaire is the Sexual Health Questionnaire (EORTC SHQ-C22) which was recently developed by the European Organization for Research and Treatment of Cancer to assess the sexual health of cancer patients (European Organisation for Research and Treatment of Cancer, 2014). A third tool, the International Consultation on Incontinence Questionnaire–Urinary Incontinence (ICIQ-UI) is a questionnaire to assess the frequency, severity and

impact on quality of life (QoL) of urinary incontinence in men and women in research and clinical practice worldwide (International consultation on incontinence questionnaire-urinary incontinence short form, 2019).

All 120 patients participating in the study answered three questionnaires. The hypothesis of the difference between the groups was verified using the nonparametric Kruskal-Wallis H-test.

Descriptive statistics were performed (table on pages Stat QLQ-30 and Stat ICIQ), including average value, median, minimal value, maximal value, upper and lower quantile (25 and 75%), standard deviation and standard error of the mean.

A comparison was made between the three groups based on the EORTC QLQ-30 and ICIQ scales (stat file page QLQ-30 and Stat ICIQ). Processing and analysis of the obtained results were carried out using the method of statistical analysis by the "STATISTICA for Windows v12.0" software. In order to compare the quality of life, the Mann-Whitney U-test was applied – a non-parametric statistical test used to assess the differences between two independent samples according to the level of the characteristic. p is the level of statistical significance, which is present in the calculation of all statistical criteria, and highlights the accuracy degree of the conclusion regarding the presence of differences. $p \leq 0.01$ – indicates the presence of differences, the probability of error is 1% means that there are no differences; $p \leq 0.05$ – shows the probability of error comprises 5%.

RESULTS AND DISCUSSION

In a retrospective study of 120 cases of patients with MIBC after RC, PC with pelvic lymphadenectomy, and adjuvant RT or CT, a 5-year overall survival (OS) rate was achieved in 50%; 53%; 68% of patients, respectively. Cancer-specific survival were 56%; 54%; 66%, respectively. Recurrence-free survival (RFS) was 60%; 36%; 38% of patients, respectively.

EORTC QLQ-30 questionnaire

The results of the study confirm better quality of life after PC with adjuvant CT, especially with regard to physical condition, patients' adaptation in society (social scale), financial toxicity, gastrointestinal tract functioning (according to symptoms of vomiting, nausea and diarrhea).

Quality of life figures were lower after RC as compared to those after PC. The only scale for which the scores in group 1 were better than in groups 2 and 3 was the Fatigue scale which may be associated with a longer follow-up period, presence of repeated

surgeries for MIBC relapses among group 2 and 3 patients that had the influence on the patients prolonged stay in the hospital (Table 1).

a) High median on the other scales means the higher intensity of dysfunction.

b) High median on the Quality of Life scale means a high living standard.

When assessing the overall scale Quality of Life, the median scores were equal in all groups. However this scale is not the integral one, so when interpreting the data one should take into account the values obtained in all scales of the questionnaire. When analyzing the graph, the maximum deviation towards the 25th percentile (towards the worst indicators) was found in group 1, and the maximum deviation towards the 75th percentile (towards the best indicators) in groups 2 and 3 (Table 1). *It was found for patients after open resection of the bladder to be higher quality of life* (Sveklina and Krupin, 2012). When comparing the average indices according to the role scale, the indices in the 2nd group were worse than those in the 3rd group, but during detailed analysis the maximum deviations towards the worse indices were revealed in the 1st group. According to the emotional scale the medians of groups 2 and 3 are equal; however a detailed evaluation of all deviations revealed that group 2 has patients with less pronounced emotional deviations, and group 1 has a higher level of psycho-emotional disorders. The median scores on the Pain symptom scale were equal in groups 2 and 3, but scores deviation towards worse side was greater among group 1 patients, indicating a greater pain severity in patients in this group. No statistically significant differences were found among patients in all groups on the cognitive scale (whose questions concerned interest in books and TV watching).

According to the EORTC QLQ-30 questionnaire, a higher level of quality of life was found among group 3 patients. Low level of quality of life was confirmed in patients after RC (group 1). At the same time, intermediate results were obtained in group 2 after RC with LT. These results were associated with a smaller extent of surgery than that in group 1, bladder preservation, the long follow-up period, and an older age composition of patients as compared to group 3 (Table 1).

As shown in Table 2, the group of patients with PC and CT, PC and RT had better sexual health indices according to the EORTC SHQ-C22 questionnaire, as compared to the group of patients after RC. These findings are further evidence of the better quality of life in patients after partial cystectomy with CT and RT.

TABLE 1. Assessment of patients' quality of life according to the EORTC QLQ-30 questionnaire

Scale of the questionnaire	Radical cystectomy with orthotopic ileal neobladder	Partial cystectomy with adjuvant radiation therapy M±SE	Partial cystectomy with adjuvant chemotherapy
	1	2	3
General scale of life quality	63.88±1.90 p1-2=0.000	81.04±1.84 p2-3=0.560	80.64±1.74 p1-3=0.000
Functional scale			
Physical scale	77.76±1.92 p1-2=0.409	79.00±1.73 p2-3=0.087	76.36±1.49 p1-3=0.969
Role scale	72.44±2.38 p1-2=0.193	68.40±1.80 p2-3=0.001	60.36±1.31 p1-3=0.000
Emotional scale	79.20±1.40 p1-2=0.000	60.80±2.07 p2-3=0.478	62.16±2.14 p1-3=0.000
Cognitive scale	88.72±2.09 p1-2=0.915	89.32±1.95 p2-3=0.001	81.56±2.12 p1-3=0.010
Social scale	85.48±2.31 p1-2=0.001	76.44±2.12 p2-3=0.534	78.4±2.04 p1-3=0.005
Symptomatic scale			
Tiredness	27.92±2.85 p1-2=0.554	29.60±2.34 p2-3=0.003	44.56±3.44 p1-3=0.002
Nausea/vomiting	63.08±2.64 p1-2=0.000	22.96±1.10 p2-3=0.000	31.76±1.08 p1-3=0.000
Pain	38.36±2.34 p1-2=0.000	23.08±1.35 p2-3=0.502	21.48±1.23 p1-3=0.000
Dyspnea	0.00±0.00 p1-2=0.000	2.60±0.44 p2-3=0.017	4.52±0.70 p1-3=0.000
Loss of appetite	7.40±0.86 p1-2=0.003	4.24±0.46 p2-3=0.814	4.32±0.63 p1-3=0.007
Sleep disturbance	23.64±1.45 p1-2=0.000	15.52±1.16 p2-3=0.004	10.68±0.97 p1-3=0.000
Constipation	10.36±0.57 p1-2=0.000	4.36±0.80 p2-3=0.976	3.84±0.43 p1-3=0.000
Diarrhea	4.00±0.41 p1-2=0.000	10.64±0.79 p2-3=0.000	5.56±0.42 p1-3=0.011

TABLE 2. Estimates of the sexual health of cancer patients

Sex		Radical cystectomy	Partial cystectomy + chemotherapy	Partial cystectomy + radiation therapy
Men	Erection	25.2	12.1	14.1
	Hardness	3.1	1.2	2.5
	Desire	5.1	2.7	3.2
	Ejaculation	13.3	3.4	5.3
Women	Lubrication / Dryness	10.1	4.2	3.2
	Desire	11.6	3.4	4.2
	Orgasm	13.7	2.8	4.5
	Dyspareunia	11.4	3.3	3.1

Note. A higher indicator means a higher severity of dysfunction.

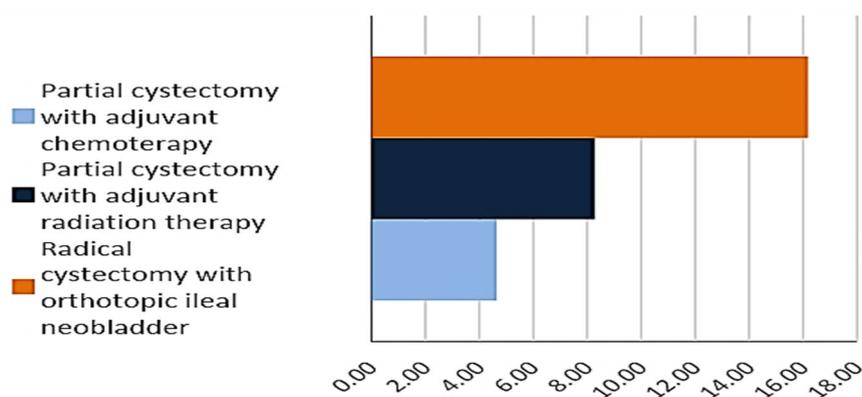
ICIQ-UI SF questionnaire

The ICIQ-UI is used to assess the incidence, severity and impact on quality of life (QoL) associated with urinary incontinence in men and women in research and clinical practice worldwide.

Functional outcome – urinary incontinence after RC is one of the main problems affecting the long-term quality of life (Yang, 2016). Published continence figures in large series range from 90 to 92% for daytime continence, and 80% for nocturnal continence. The high incidence rate of urinary incontinence after cystectomy was associated with the

technical aspects of surgery, in particular the necessity to remove the prostate and neurovascular complex to provide better oncological outcomes. The worst indicators of urinary incontinence in the group of radiation therapy were due to radiation cystitis and formation of microcysts.

According to Figure, the best outcomes with a lower incontinence rate were in patients after PC, and the worst ones after RC. These data serve as further evidence of the benefits of PC with adjuvant chemoradiation therapy.



Note. A higher index means a higher severity of dysfunction

Assessment of patients' quality of life according to the ICIQ-UI questionnaire

Unsatisfactory oncological results after cystectomy may be due to surgical intervention resulting in erectile dysfunction and urinary incontinence. However, PC has been considered as the least traumatic and oncologically effective treatment (Hamad et al., 2020; Knoedler and Frank, 2015; Knoedler et al., 2012; Holzbeierlein et al., 2004; Kassouf et al., 2006; Capitanio et al., 2009). Our data based on the questionnaire usage suggesting that organ-preserving complex MIBC treatment is an alternative to radical cystectomy for the selected patients. Over the last decade the efficiency of organ-preserving complex MIBC treatment was confirmed in literature, this approach not only allows to achieve similar oncological results as in case of RC, but also gives an opportunity to improve patients' long-term quality of life (Knoedler and Frank, 2015).

Sexual dysfunction is characterized by impaired libido and psychophysiological changes related to the sexual response cycle in men and women, or pain during sexual intercourse (Sveklina and Krupin, 2012). The World Health Organization (WHO) defines sexual health as a state of physical, emotional, mental and social well-being related to sexuality, and it is not simply the absence of disease, dysfunction or impairment (Bessa et al., 2020). So, sexual health must be assessed holistically through the complex interplay between biological, psychological, interpersonal, and social/cultural factors since all of these factors can affect sexual function

and well-being. Although the European Association of Urology (EAU 2019) and National Comprehensive Cancer Network (NCCN guidelines, 2020) recommend that the standard treatment for MIBC is RC with pelvic lymph node dissection, our retrospective analysis shows a quality-of-life advantage of organ-preserving comprehensive treatment for MIBC (Table 2).

Our study is limited by its retrospective nature and small sample size. However, we confirmed that PC can provide adequate control of MIBC in the individual cases and showed that it offers patients a good chance of long-term bladder preservation providing satisfactory overall postoperative health and quality of life. It is our belief that the patient's age, psycho-emotional status, and the spread of the tumor process are important factors contributing to the achievement of better quality of life especially in terms of erectile function and urination quality.

CONCLUSION

A critical approach should be taken into consideration when choosing the most appropriate regimen for treatment of MIBC and considering between radical cystectomy or partial cystectomy. However, it is important to inform patients that organ-preserving treatment allows them to achieve a better quality of life, the treatment process may be longer than that after radical cystectomy.

REFERENCES

- Ebbing, J., Heckmann, R. C., Collins, J. W., Miller, K., Erber, B., Friedersdorff, F., Fuller, T. F., Busch, J., Seifert, H. H., Ardelt, P., Wetterauer, C., Hossaini, A., Jentzmik, F., & Kempkensteffen, C. (2018). Oncological outcomes, quality of life outcomes and complications of partial cystectomy for selected cases of muscle-invasive bladder cancer. *Scientific Reports*, 8, Article number: 8360. <https://doi.org/10.1038/s41598-018-26089-x>
- Halkin, N. H. (2007). Kachestvo zhizni posle tsistektomii s razlichnymi sposobami otvedeniya mochi [Quality of life after cystectomy with various methods of urinary diversion]. *Meditinskii nauki. Klinicheskaia meditsina*, 4, 77-84.
- Startsev, V. Yu., Dylenok, I. N., & Dzhemilev, T. R. (2019). Sovremennyye vozmozhnosti organosokhraniayushchego lecheniya bolnykh myshechno-invazivnym rakom mochevogo puzyrja [Modern possibilities of organ-preserving treatment of patients with muscle-invasive bladder cancer]. *Urolohicheskie vedomosti*, 1. <https://doi.org/10.17816/uroved9129-38>
- Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N.J., Filiberti, A., Flechtner, H., Fleishman, S. B., de Haes, J. C. J. M., Kaasa, S., Klee, M., Osoba, D., Razavi, D., Rofe, P. B., Schraub, S., Sneeuw, K., Sullivan, M., & Takeda, F. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J. Natl. Cancer Inst.* 85, 365-376. <https://doi.org/10.1093/jnci/85.5.365>
- European Organisation for Research and Treatment of Cancer. (2014) *Sexual Health Questionnaire (EORTC SHQ-C22)*.
- International consultation on incontinence questionnaire-urinary incontinence short form. (2019).
- Bessa, A., Martin, R., Häggström, C., Enting, D., Amery, S., Khan, M. S., Cahill, F., Wylie, H., Broadhead, S., Chatterton, K., Malde, S., Nair, R.,

- Thurairaja, R., Kumar, P., Haire, A., Green, S., Northover, M., Briggs, K., & Van Hemelrijck, M. (2020). Unmet needs in sexual health in bladder cancer patients: a systematic review of the evidence. *BMC Urology*, 20, Article number: 64. <https://doi.org/10.1186/s12894-020-00634-1>
- Yang, L. S., Shan, B. L., Shan, L. L., Chin, P., Murray, S., Ahmadi, N., & Saxena, A. (2016). A systematic review and meta-analysis of quality of life outcomes after radical cystectomy for bladder cancer. *Surg. Oncol.* 25, 281-297. <https://doi.org/10.1016/j.suronc.2016.05.027>
- Hamad, J., McCloskey, H., Milowsky, M. Royce, T., & Smith, A. (2020). Bladder preservation in muscle-invasive bladder cancer: a comprehensive review. *Int Braz J Urol.*, 46(2), 169-184. <https://doi.org/10.1590/s1677-5538.ibju.2020.99.01>
- Knoedler, J., & Frank, I. (2015). Organ-sparing surgery in urology: partial cystectomy. *Curr. Opin. Urol.* 25, 111-115. <https://doi.org/10.1097/MOU.0000000000000145>
- Knoedler, J., Boorjian, S. A., Kim, S. P., Weight, C. J., Thapa, P., Tarrell, R. F., Cheville, J. C., & Frank, I. (2012). Does partial cystectomy compromise oncologic outcomes for patients with bladder cancer compared to radical cystectomy? A matched case-control analysis. *J Urol. Oct.*, 188(4), 1115-9. <https://doi.org/10.1016/j.juro.2012.06.029>
- Holzbeitrlein, J. M., Lopez-Corona, E., Bochner, B. H., Herr, H. W., Donat, S. M., Russo, P., Dalbag-
ni, G., & Sogani, P. C. (2004). Partial cystectomy: a contemporary review of the Memorial Sloan-Kettering Cancer Center experience and recommendations for patient selection. *J. Urol.*, 172, 878-881. <https://doi.org/10.1097/01.ju.0000135530.59860.7d>
- Kassouf, W., Swanson, D., Kamat, A., Leibovici, D., Siefker-Radtke, A., Munsell, M. F., Grossman, H. B., & Dinney, C. P. N. (2006). Partial cystectomy for muscle invasive urothelial carcinoma of the bladder: a contemporary review of the M. D. Anderson Cancer Center experience. *J. Urol.* 175, 2058-2062. [https://doi.org/10.1016/S0022-5347\(06\)00322-3](https://doi.org/10.1016/S0022-5347(06)00322-3)
- Capitiano, U., Isbarn, H., Shariat, S., Jeldres, C., Zini, L., Saad, F., Graefen, M., Montorsi, F., Perrotte, P., & Karakiewicz, P. I. (2009). Partial cystectomy does not undermine cancer control in appropriately selected patients with urothelial carcinoma of the bladder: a population-based matched analysis. *Urology*, 74, 858-864. <https://doi.org/10.1016/j.urology.2009.03.052>
- Knoedler, J., & Frank, I. (2015). Organ-sparing surgery in urology: partial cystectomy. *Curr. Opin. Urol.* 25, 111-115. <https://doi.org/10.1097/MOU.0000000000000145>
- Sveklina, T. A., & Krupin, V. N. (2012). Quality of life in patients with muscle-invasive bladder cancer stages T2B AND T3A after surgical treatment. *Cancer Urology*, 8(3). 55-59.