

· 临床研究 ·

老年膀胱肿瘤手术前后生活质量比较及其影响因素分析

周萍*, 梁泽兰, 聂婷

(新疆维吾尔自治区人民医院泌尿中心, 乌鲁木齐 830001)

【摘要】目的 分析比较老年膀胱肿瘤手术前后生活质量, 并评估其生活质量不良的影响因素。**方法** 前瞻性对2021年6月至2023年9月新疆维吾尔自治区人民医院行经尿道膀胱肿瘤电切术(TURBT)治疗的158例老年非肌层浸润性膀胱癌(NMIBC)患者展开问卷调查, 分别在术前、术后1个月、术后3个月使用癌症患者生存质量核心量表-浅表性膀胱癌患者特异性量表(EORTC QLQ-BLS24)评估患者生活质量, 最终有147例患者完成3次问卷调查。147例老年NMIBC患者术后1个月EORTC QLQ-BLS24总分为(160.72±17.43)分, 根据术后1个月EORTC QLQ-BLS24总分将147例老年NMIBC患者分为生活质量良好组(QLQ-BLS24得分≤总分, 75例)与生活质量不良组(QLQ-BLS24得分>总分, 72例)。比较两组性别、年龄、术前老年营养风险指数(GNRI)等一般资料。采用SPSS 26.0软件进行数据分析。根据数据类型, 组间比较分别采用t检验、χ²检验及(或)Fisher精确概率法。采用logistic回归分析评估老年NMIBC患者TURBT术后1个月生活质量不良的影响因素。**结果** TURBT术后1个月, 老年NMIBC患者EORTC QLQ-BLS24尿路症状、治疗问题、肠道症状、性功能评分及总分均显著高于术前及术后3个月($P<0.05$), 担心将来评分低于术前($P<0.05$), 但高于术后3个月($P<0.05$)。生活质量不良组与生活质量良好组在术前GNRI、膀胱灌注方案、膀胱灌注不良反应及焦虑方面的比较, 差异均有统计学意义($P<0.05$)。logistic回归分析显示, 术前GNRI≤98($OR=3.397, 95\%CI 2.073\sim 5.567, P<0.05$)、膀胱灌注不良反应($OR=2.776, 95\%CI 1.517\sim 5.081, P<0.05$)及焦虑($OR=2.326, 95\%CI 1.186\sim 4.560, P<0.05$)均为TURBT术后1个月生活质量不良的危险因素, 膀胱灌注方案为吉西他滨为保护因素($OR=0.566, 95\%CI 0.013\sim 0.924, P<0.05$)。**结论** 老年NMIBC患者TURBT术后3个月内生活质量先降低后升高, 术前GNRI≤98及术后发生膀胱灌注不良反应、焦虑情绪是术后生活质量不良的高危因素, 吉西他滨膀胱灌注治疗可改善术后生活质量。

【关键词】 老年人; 非肌层浸润性膀胱癌; 经尿道膀胱肿瘤电切术; 生活质量; 影响因素; 老年营养风险指数

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Comparison of quality of life before and after surgery in elderly patients with bladder tumor and analysis of influencing factors

Zhou Ping*, Liang Zelan, Nie Ting

(Urinary Center, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi 830001, China)

【Abstract】 Objective To analyze and compare the quality of life (QoL) before and after surgery in elderly patients with bladder tumors and to evaluate the influencing factors of poor QoL. **Methods** A prospective questionnaire survey was conducted on 158 elderly patients with non-muscle invasive bladder cancer (NMIBC), who received transurethral resection of bladder tumor (TURBT) in People's Hospital of Xinjiang Uygur Autonomous Region from June 2021 to September 2023. European Organization for Research and Treatment of Cancer-Quality of Life in superficial bladder cancer patients (EORTC QLQ-BLS24) was used to evaluate the patients' QoL before surgery, and at 1 month and 3 months after surgery. Finally, 147 patients completed questionnaires three times. The total EORTC QLQ-BLS24 score in the 147 elderly NMIBC patients was (160.72±17.43) points at 1 month after surgery. According to this score, the patients were divided into a good QoL group (total QLQ-BLS24 score ≤ average, $n=75$) and a poor QoL group (total QLQ-BLS24 score > average, $n=72$). The two groups were compared in general data including gender, age, and preoperative geriatric nutritional risk index (GNRI). SPSS 26.0 was used for statistical analysis. Comparison between two groups was performed using t test, Chi-square test or Fisher's exact probability method depending on data type. Logistic regression analysis was used to evaluate the influencing factors of poor QoL in elderly NMIBC patients at 1 month after TURBT. **Results** At 1 month after TURBT, the scores of urinary tract symptom, treatment problems, intestinal symptom, sexual function, and total scores of EORTC QLQ-BLS24 in elderly NMIBC patients were significantly higher than those before surgery and at 3 months after surgery ($P<0.05$), and the score of worrying about the future was lower than that before

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通信作者: 周萍, E-mail: zhoup96989@126.com

surgery ($P<0.05$) , but was higher than that at 3 months after surgery ($P<0.05$). There were statistically significant differences in preoperative GNRI, intravesical instillation regimen, adverse reactions to intravesical instillation, and anxiety between the poor QoL group and good QoL group ($P<0.05$). Logistic regression analysis showed that preoperative GNRI $\leqslant 98$ ($OR=3.397$, 95%CI 2.073–5.567; $P<0.05$), adverse reactions to intravesical instillation ($OR=2.776$, 95%CI 1.517–5.081; $P<0.05$) and anxiety ($OR=2.326$, 95%CI 1.186–4.560; $P<0.05$) were risk factors for poor QoL at 1 month after TURBT. Gemcitabine intravesical instillation was a protective factor ($OR=0.566$, 95%CI 0.013–0.924; $P<0.05$). **Conclusion** QoL in elderly NMIBC patients declines initially at 1 month after TURBT and improves by 3 months. Preoperative GNRI $\leqslant 98$, adverse reactions to intravesical instillation, and anxiety are risk factors for poor postoperative QoL. Gemcitabine intravesical instillation can improve postoperative QoL.

[Key words] aged; non-muscle invasive bladder cancer; transurethral resection of bladder tumor; quality of life; influencing factors; geriatric nutritional risk index

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Corresponding author: Zhou Ping, E-mail: zhoup96989@126.com

膀胱癌为泌尿外科常见恶性肿瘤,其中非肌层浸润性膀胱癌 (non-muscle invasive bladder cancer, NMIBC) 为主要类型,占比超过 70%,中老年为好发人群,随着全球老龄化现象加剧,老年 NMIBC 患病率显著升高^[1]。经尿道膀胱肿瘤电切术(transurethral resection of bladder tumor, TURBT) 可清除病灶,为 NMIBC 的主要治疗手段^[2]。但 NMIBC 复发率较高,临床常在 TURBT 术后联合膀胱灌注化疗,可有效延长患者生存期,近年对 NMIBC 患者 TURBT 围手术期的报道也集中于降低复发率的研究^[3]。然而,有研究指出,TURBT 术后未复发的 NMIBC 患者仍出现生活质量低下,影响患者预后^[4]。基于此,本研究对老年 NMIBC 患者 TURBT 手术前后生活质量变化展开分析,并评估其影响因素,为老年 NMIBC 患者 TURBT 术后的临床干预提供参考数据。

1 对象与方法

1.1 研究对象

前瞻性对 2021 年 6 月至 2023 年 9 月新疆维吾尔自治区人民医院行 TURBT 治疗的 158 例老年 NMIBC 患者手术前后展开问卷调查。本研究获得新疆维吾尔自治区人民医院医学伦理委员会审批(伦理号:WZ-20210359)。纳入标准:经手术病理学检查确诊为原发性 NMIBC, 肿瘤分期为 Ta~T1; 行择期 TURBT 治疗,且诊疗符合《中国非肌层浸润性膀胱癌治疗与监测循证临床实践指南(2018 简化版)》^[5]; 年龄 $\geqslant 60$ 岁; 意识清醒,沟通能力良好。排除标准:既往膀胱手术或介入治疗史;合并其他恶性肿瘤、凝血功能异常或肝肾功能异常等影响手术治疗的疾病;伴运动器官疾病、神经系统疾病等明显生理缺陷疾病;术前接受新辅助放化疗或膀胱灌注治疗;视听障碍。剔除标准:TURBT 中转开放手术;术后 3 个月内意识障碍或死亡。158 例老年 NMIBC 患者分别发放 3 次问卷,其中有 3 例患者术后离开

居住地,通过登记的联系方式无法取得联系,有 6 例患者术后未遵医嘱行膀胱灌注治疗,有 2 例患者所有问卷填写选项均为同一项判断为无效问卷,最终有 147 例患者完成 3 次问卷调查。

1.2 方法

1.2.1 治疗方法 老年 NMIBC 患者均使用离子双极内镜系统(英国 GYRUS 公司,国械注进 20153253043)行 TURBT 治疗,术者均为同一组医师,主刀医师均为副主任职称医师,TURBT 手术操作经历 $\geqslant 5$ 年;气管插管全身麻醉,膀胱截石位,电切功率为 140~160 W,电凝功率为 40~60 W。术后 24 h 行膀胱灌注治疗 1 次,随后每周膀胱灌注 1 次,连续治疗 8 周,改为膀胱灌注 1 次/月,连续灌注 10 个月。膀胱灌注方案包括 40 mg 注射用盐酸表柔比星(国药准字 H19990280, 规格: 10 mg, 瀚晖制药有限公司)、30 mg 注射用盐酸吡柔比星(国药准字 H20045983, 规格: 10 mg, 瀚晖制药有限公司)、1.0 g 注射用盐酸吉西他滨(国药准字 H20103523, 规格: 0.2 g, 北京协和药厂有限公司)。

1.2.2 资料收集方法 老年 NMIBC 患者实验室指标、手术病理资料等经查阅电子病历获得,所有患者在术前 1 d 常规采集清晨空腹外周肘静脉血,全自动生化分析仪(日本日立公司,型号:7600-220)检测血清白蛋白,计算老年营养风险指数(geriatric nutritional risk index, GNRI)^[6], $GNRI = 1.489 \times \text{血清白蛋白}(\text{g/L}) + 41.7 \times \text{实际体质量}(\text{kg}) / \text{理想体质量}(\text{kg})$, $GNRI > 98$ 为老年人营养状况良好。

1.2.3 问卷调查方法 在术前 1 d、术后 1 个月、术后 3 个月,于安静的病室(或随访门诊诊室)内行一对一问卷调查,问卷内容为癌症患者生存质量核心量表 - 浅表性膀胱癌患者特异性量表(European organization for research and treatment of cancer-quality of life in superficial bladder cancer patients, EORTC QLQ-BLS24)^[7], 包含 24 个项目, 3 个症状子量表

(尿路症状、治疗问题、肠道症状)及2个功能子量表(担心将来、性功能),项目以1(没有)~4分(非常多)计分,其中功能子量表反向计分,各子量表得分均经线性公式转换为0~100分的标准分,得分越低,生存质量越好。根据术后1个月EORTC QLQ-BLS24总分将147例老年NMIBC患者分为生活质量良好组(QLQ-BLS24总分≤平均分)与生活质量不良组(QLQ-BLS24总分>平均分)。术后1个月时对患者焦虑抑郁情况也进行问卷调查,使用焦虑自评量表(Zung self-rating anxiety scale, SAS)、抑郁自评量表(Zung self-rating depression scale, SDS)^[8],将初始得分转换为标准分,标准分=初始分×1.25,SAS标准分≥50分为可能存在焦虑状态,SDS标准分≥53分为可能存在抑郁状态。

1.3 统计学处理

采用SPSS 24.0统计软件进行数据分析。符合正态分布的计量资料用均数±标准差($\bar{x}\pm s$)表示,多时间点比较采用重复测量方差分析,两两比较使用LSD-t检验;计数资料用例数(百分率)表示,采用 χ^2 检验或Fisher精确概率法。采用多因素logistic回归分析老年NMIBC患者TURBT术后1个月生活质量不良的影响因素。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 老年NMIBC患者TURBT手术前后生活质量变化

术后3个月内,老年NMIBC患者均未出现复发病例。TURBT术后1个月时,老年NMIBC患者EORTC QLQ-BLS24尿路症状、治疗问题、肠道症状、性功能评分及总分平均分均显著高于术前及术后3个月($P<0.05$),担心将来评分低于术前($P<0.05$),但高于术后3个月($P<0.05$;表1)。

2.2 两组患者一般资料比较

147例老年NMIBC患者术后1个月EORTC

QLQ-BLS24总分为(160.72±17.43)分,根据术后1个月EORTC QLQ-BLS24总分将147例老年NMIBC患者分为生活质量良好组(QLQ-BLS24得分≤总分,75例)与生活质量不良组(QLQ-BLS24得分>总分,72例)。生活质量不良组与生活质量良好组患者在术前GNRI、膀胱灌注方案、膀胱灌注不良反应及焦虑方面比较,差异均有统计学意义($P<0.05$);其他指标比较,差异无统计学意义($P>0.05$;表2)。

2.3 老年NMIBC患者TURBT术后1个月生活质量不良的影响因素分析

将上述有统计学意义的指标赋值带入logistic回归方程(术前GNRI:>98为0,≤98为1;膀胱灌注方案:吡柔比星为0,吉西他滨为0,表柔比星为1;膀胱灌注不良反应:无为0,有为1;焦虑:无为0,有为1),结果显示,术前GNRI≤98、膀胱灌注不良反应及焦虑均为TURBT术后1个月生活质量不良的危险因素($P<0.05$),膀胱灌注方案为吉西他滨为保护因素($P<0.05$;表3)。

3 讨论

TURBT+膀胱灌注化疗虽然能有效减少NMIBC复发风险,延长患者生存时间,但手术创伤难以避免,化疗对膀胱的刺激也会增加患者生理性疼痛,造成患者术后生活质量下降^[9]。本研究也发现,在术前,术后1、3个月的3个观察点中,老年NMIBC患者EORTC QLQ-BLS24尿路症状、治疗问题、肠道症状、性功能评分及总分在术后1个月时最高,提示老年NMIBC患者TURBT术后1个月不适症状较多,生活质量明显下降,与上述报道一致。值得注意的是,老年NMIBC患者术后EORTC QLQ-BLS24担心将来评分逐渐降低,提示患者的担心情绪随治疗的延长逐渐降低,可能与随着治疗的深入,患者对疾病及治疗的认知水平升高,治疗信心逐渐提升有关。

表1 老年NMIBC患者TURBT手术前后EORTC QLQ-BLS24评分比较

Table 1 Comparison of EORTC QLQ-BLS24 scores before and after TURBT in elderly patients with NMIBC

(n=147, points, $\bar{x}\pm s$)

Time point	Urinary tract symptom	Treatment problem	Intestinal symptom	Worrying about the future	Sexual function	Total score
Before surgery	17.26±2.56	125.12±4.79	112.29±2.13	127.66±5.04	115.49±3.11	197.82±12.35
1 month after surgery	21.22±3.88 [*]	26.65±5.02 [*]	57.24±9.44 [*]	26.25±4.93 [*]	29.36±4.84 [*]	160.72±17.43 [*]
3 months after surgery	12.36±2.34 ^{*#}	22.43±4.80 ^{*#}	32.06±7.13 ^{*#}	19.55±3.67 ^{*#}	16.34±3.21 ^{*#}	102.74±15.27 ^{*#}
F	320.730	28.281	1549.031	131.105	614.103	782.720
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

NMIBC: non-muscle invasive bladder cancer; TURBT: transurethral resection of bladder tumor; EORTC QLQ-BLS24: European organization for research and treatment of cancer-quality of life in superficial bladder cancer patients. Compared with before surgery, * $P<0.05$; compared with 1 month after surgery, # $P<0.05$.

表2 两组患者一般资料比较

Table 2 Comparison of general data between two groups

 $(\bar{x} \pm s)$

Item	Poor QoL group ($n=72$)	Good QoL group ($n=75$)	χ^2/t	P value
Male/female (n)	59/13	58/17	0.481	0.488
Age [$n(\%)$] 60~70 years	24 (33.33)	36 (48.00)	3.271	0.071
>70 years	48 (67.67)	39 (52.00)		
Body mass index (kg/m^2 , $\bar{x} \pm s$)	21.12 ± 1.98	21.65 ± 2.04	1.597	0.112
Educational level [$n(\%)$] Junior high school and below	35 (48.61)	29 (38.67)		
Technical secondary school or senior high school	25 (34.72)	31 (41.33)		
Junior college or above	12 (16.67)	15 (20.00)		
Marital status [$n(\%)$] Married	51 (70.83)	61 (81.33)	2.233	0.135
Unmarried/divorced/widowed	21 (29.17)	14 (18.67)		
Smoking history [$n(\%)$]	39 (54.17)	37 (49.33)	0.344	0.558
Tumor staging [$n(\%)$] Ta	32 (44.44)	38 (50.67)		
T1	40 (55.56)	37 (49.33)		
Tumor diameter (cm, $\bar{x} \pm s$)	1.56 ± 0.29	1.48 ± 0.27	1.732	0.085
Preoperative GNRI [$n(\%)$] ≤98	35 (48.61)	21 (28.00)		
>98	37 (51.39)	54 (72.00)		
Postoperative complications [$n(\%)$]	8 (11.11)	4 (5.33)	1.636	0.201
Urinary tract infection [$n(\%)$]	5 (6.94)	3 (4.00)	0.179	0.431 *
Bladder urinary fistula [$n(\%)$]	3 (4.17)	1 (1.33)	0.301	0.583 *
Bladder perfusion regimen [$n(\%)$] Epirubicin	37 (51.39)	19 (25.33)	10.802	0.005
Pirarubicin	13 (18.06)	18 (24.00)	10.575	0.001
Gemcitabine	22 (30.56)	38 (50.67)	0.780	0.377
Adverse reactions of bladder perfusion [$n(\%)$] Bladder irritation symptom [$n(\%)$]	26 (36.11)	13 (17.33)	6.151	0.013
Hematuria [$n(\%)$]	18 (25.00)	10 (13.33)	6.645	0.010
Fever [$n(\%)$]	5 (6.94)	2 (2.67)	3.243	0.072
Anxiety [$n(\%)$]	3 (4.17)	1 (1.33)	0.689	0.406 *
Depression [$n(\%)$] QoL: quality of life; GNRI: geriatric nutritional risk index. * Continuous corrected Chi-square test.	36 (50.00)	23 (30.67)	0.301	0.583 *
	32 (44.44)	22 (29.33)	5.715	0.017
			3.609	0.057

QoL: quality of life; GNRI: geriatric nutritional risk index. * Continuous corrected Chi-square test.

表3 TURBT术后1个月生活质量不良的logistic回归分析

Table 3 Logistic regression analysis of poor quality of life at 1 month after TURBT

Factor	β	SE	Wald χ^2	P value	OR	95%CI
Preoperative GNRI ≤ 98	1.223	0.324	14.248	<0.001	3.397	2.073~5.567
Bladder perfusion regimen of gemcitabine	-0.569	0.180	9.993	0.002	0.566	0.013~0.924
Adverse reactions of bladder perfusion	1.021	0.316	10.439	0.001	2.776	1.517~5.081
Anxiety	0.844	0.282	8.957	0.003	2.326	1.186~4.560

TURBT: transurethral resection of bladder tumor; GNRI: geriatric nutritional risk index.

吡柔比星、表柔比星及吉西他滨均为TURBT术后膀胱灌注的常用化疗药物,其中吡柔比星、表柔比星为蒽环类抗肿瘤药物,可通过阻断肿瘤细胞脱氧核糖核酸合成,将细胞增殖周期终止于G2期,达到抗肿瘤的作用^[10]。吉西他滨为脱氧胞苷类似物,可阻止肿瘤细胞G1期向S期进展,也能影响肿瘤细胞核糖核酸分子合成,对恶性肿瘤细胞特异

性高^[11]。本研究也发现,膀胱灌注不良反应为TURBT术后1个月生活质量不良的危险因素,而膀胱灌注方案为吉西他滨为保护因素,提示吉西他滨膀胱灌注不良反应较少,患者耐受性良好,对生活质量的不良影响较小。究其原因可能为吉西他滨脂溶性良好,且分子量大,膀胱局部给药时不易被黏膜吸收,而对膀胱刺激性小^[12]。

老年恶性肿瘤患者身体素质差,营养状态被认为是影响其预后的重要因素,GNRI是评估老年人营养不良的重要工具,近年被发现与老年肺癌、头颈癌等恶性肿瘤的预后死亡风险有关^[13]。本研究结果显示,术前GNRI≤98为TURBT术后1个月生活质量不良的危险因素,提示术前营养不良可能对老年NMIBC患者TURBT术后生活质量产生不良影响。究其原因可能为营养状态较差者维持生理稳态能力低下,对手术及膀胱灌注化疗的耐受性差,更易发生膀胱刺激症状等不良反应,而生活质量下降^[14]。因此,对于术前存在营养状态不良的老年患者可尽早予以营养干预,以提升术后生活质量。另据文献报道,负性情绪是影响生活质量的重要因素,长期焦虑情绪还可诱导膀胱黏膜血管舒缩功能紊乱,促进膀胱刺激症状的发生^[15]。本研究发现,焦虑也是TURBT术后1个月生活质量不良的危险因素,提示焦虑情绪可能增加患者不适症状,对身心健康均产生不利影响,导致生活质量下降,与上述报道相似。故心理干预也是TURBT围手术期的重要临床工作,缓解老年患者焦虑情绪可能对提升术后生活质量有利。然而,本研究仅通过logistic回归分析评估生活质量不良的危险因素,针对危险因素予以相应的预防措施是否能有效提升患者术后生活质量,还需后续前瞻性大样本量研究的验证。

综上,老年NMIBC患者TURBT术后1个月生活质量显著下降,术前营养状态较差及术后发生膀胱灌注不良反应、焦虑均为TURBT术后1个月生活质量不良的危险因素,行吉西他滨膀胱灌注治疗者生活质量较好。

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