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Research Article

Effects of neoadjuvant and adjuvant chemotherapy on survival in muscle-invasive bladder cancer: A multicenter study

Kas-İnvaziv mesane kanserinde neoadjuvan ve adjuvan kemoterapinin sağkalım üzerine etkinliği: Çok merkezli çalışma

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Abstract

Aim: Muscle-invasive bladder cancer requires systemic treatment due to its high risk of metastasis. However, studies comparing neoadjuvant and adjuvant therapy regimens are currently limited. Our goal in this study was to compare the treatment efficacy of patients receiving neoadjuvant or adjuvant treatment in locally advanced bladder cancer.

Material and Methods: We retrospectively included 107 bladder cancer patients from 6 centres who underwent radical cystectomy and received perioperative chemotherapy. Patients were divided into 2 categories: (i) neoadjuvant chemotherapy (n=54) and (ii) adjuvant chemotherapy (n=53).

Results: Median follow-up was 31.6 months (95%CI 21.8-41.4). 30-month disease-free survival (DFS) was 58.9% in the whole group, 56.3% in neoadjuvant and 61.5% in adjuvant. 30-month DFS after neoadjuvant treatment was 70.1% in <pT2N0 and 41.1% in ≥pT2, according to substaging. After neoadjuvant treatment, 30-month DFS was 85.7% and 45.9% in the pathologic complete response (CR) and non-CR group, respectively. 30-month overall survival (OS) was 69.8% in the whole group, 71.7% in neoadjuvant and 68.2% in adjuvant. This rate in patients with neoadjuvant downstaging was 81.4% and 62% in the <pT2N0 and ≥pT2 groups, respectively. At the same time, 30-month OS in the pathologic CR and non-CR group was 100% and 62.6%, respectively.

Conclusion: In patients with locally advanced bladder cancer who show a pathologically complete response to neoadjuvant chemotherapy, it is important to be evaluated in a multidisciplinary consultation in order to give cisplatin-based treatment before surgery since it has a significant contribution in terms of both DFS and OS.

Keywords: Bladder cancer, neoadjuvant chemotherapy, radical cystectomy, adjuvant chemotherapy, outcome analysis

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Öz

Amaç: Kasa invaze mesane kanserinin tedavisinde yüksek metastaz riski nedeniyle sistemik tedavi önerilmektedir. Neoadjuvan veya adjuvan tedaviyi karşılaştıran yeterli çalışma olmaması nedeniyle bu çalışmada amacımız lokal ileri evre mesane kanserinde neoadjuvan veya adjuvan tedavi alan hastaların tedavi etkinliğini karşılaştırmaktır.

Gereç ve Yöntemler: Radikal sistektomi yapılan ve perioperatif kemoterapi alan 6 merkezden 107 mesane kanseri hastası retrospektif olarak çalışmaya dahil edildi. Hastalar 2 kategoriye ayrıldı: (i) neoadjuvan kemoterapi (n=54) ve (ii) adjuvan kemoterapi (n=53). Ortanca takip süresi 31.6 aydı (%95CI 21.8-41.4). 30. ay hastalıksız sağkalım oranı (HSO) tüm grupta %58.9, neoadjuvanda %56.3 ve adjuvanda %61.5 idi. Neoadjuvan tedavi sonrası 30.ay HSS evrelemeye göre <pT2N0'da %70.1 ve ≥pT2'de %41.1 idi. Neoadjuvan tedavi sonrasında, 30.ay HSO patolojik tam yanıt (TY) ve TY olmayan grupta sırasıyla %85,7 ve %45,9 idi. 30.ay genel sağkalım oranı (GSO) tüm grupta %69,8, neoadjuvanda %71,7 ve adjuvanda %68,2 idi. Neoadjuvan tedavi ile evre gerilemesi olanlarda<pT2N0 ve ≥pT2 gruplarında 30.ay GSO sırasıyla %81.4 ve %62.0 idi. Aynı zamanda, patolojik TY ve TY olmayan grupta 30.ay GSO sırasıyla %100 ve %62.6 idi.

Sonuç: Neoadjuvan ve adjuvan kemoterapi, kas-invaziv mesane kanseri tedavisinde sağkalımı önemli ölçüde etkileyen yaklaşımlardır. Patolojik tam yanıt ve sisplatin bazlı rejimler, daha iyi sağkalım sonuçları ile ilişkilidir. Bu bulgular, tedavi planlamasında patolojik tam yanıtın ve rejim seçiminin önemini vurgulamaktadır ve tedavi kararı multidispliner olarak verilmelidir.

Anahtar Kelimeler: mesane kanseri, neoadjuvan kemoterapi, radikal sistektomi, adjuvan kemoterapi, sağkalım sonuçları

Introduction

Bladder cancer (BC) is the fourth most prevalent cancer among all new cases of cancer in men, with a prevalence three times higher than in women, according to recent statistics (1). The histopathological diagnosis of the patients is urothelial carcinoma with a rate of 90% (2). When the tumour invades the detrusor muscle, it is called muscle-invasive bladder cancer. The primary method of treatment is surgery, which includes pelvic lymph node dissection and radical cystectomy (RC). However, it's important to recall that 50% of patients have micro-metastases, which increase the risk of metastasis to distant organs and intra-abdominal lymph nodes. As a result, current guidelines suggest that systemic treatment should be considered in addition to local treatment at this stage (clinically T2) (3).

Systemic therapies can be administered as neoadjuvant (NAC) or adjuvant (AC) treatment from T2 clinically in non-metastatic bladder cancer. According to current treatment guidelines, adjuvant treatment should consist of platinum plus gemcitabine therapy and immunotherapy in selected patients. While studies have shown that AC contributes to DFS, no significant contribution to OS has been observed (4). However, it is important to note that serious complications after RC can delay AC for an average of 3 months in 30% of patients. Moreover, it has been observed that the risk of distant metastasis increases when AC is administered after 8 weeks (5). Therefore, it is recommended that NAC be administered whenever possible. While several studies have demonstrated that adjuvant platinum-based chemotherapies can enhance DFS, no improvement in OS has been observed (6).

The benefits of neoadjuvant treatment are to provide systemic control of the disease, to reduce the clinical and radiological stage, and to observe in-vivo treatment efficacy. Neoadjuvant treatment is also known to contribute to survival in bladder cancer (7). In the trial comparing the neoadjuvat regimen of vinblastine, doxorubicin, cisplatin, and methotrexate (MVAC) with surgery alone, the median overall survival in the NAC arm was 77 months, representing a two-fold increase compared to surgery alone. In addition, the pathological complete response (CR) rate is 38% (8). However, MVAC treatment is not a regimen that we actively use because of its haematological and gastrointestinal side effects. Phase 3 data for this regimen is not available and is mostly used based on metastatic disease data. In 40-67% of cases who underwent surgery alone without neoadjuvant treatment, pT3-T4a or lymph node positivity is observed, and 5th year survival is 25-30% (7). There is not a significant difference in the pathological CR rate between the cisplatin and gemcitabine with MVAC regimen compared to other studies that used NAC choosing. However, pathological complete response rate and survival results are more negative with gemcitabine and carboplatin (9).

In light of this information, our aim in this study was to compare the clinical efficacy of neoadjuvant and adjuvant

treatments in bladder cancer and to evaluate the parameters affecting survival.

Material and Methods

Patient characteristics

In our study, we included 107 patients with locally advanced bladder cancer, aged over 18 years, from six centers, who were followed between 2008 and 2023 at medical oncology clinics.

Patients with non-muscle-invasive bladder cancer who did not receive systemic chemotherapy (neoadjuvant or adjuvant) were excluded from the study. All patients received cisplatin-based treatment as neoadjuvant therapy. However, carboplatin was given to patients for whom cisplatin was ineligible (ECOG performance stats of > 1; creatine clearance less than 30 ml/min; grade 2 or greater peripheral neuropathy etc.) for adjuvant treatment.

Data on age at bladder cancer diagnosis, histological features of the tumor, ECOG-PS status, demographic, clinical and pathological characteristics (including gender, lymphovascular invasion, and surgical margin), treatments, and treatment response were recorded.

Follow-up time, DFS, OS data were also calculated.

The primary endpoint of DFS was defined as the time from the date of diagnosis to first progression, death, or last disease-free visit. OS was defined as the time from the date of diagnosis to death or last visit.

Every piece of data was analyzed using SPSS 23.0 software. Both univariate and multivariate analyses were conducted. In the study, results with $p<0.1$ in univariate analysis were included in multivariate analysis results. The standard deviation was represented by the symbol (±). To compare parametric variables between groups, the independent variable t test was employed. The nonparametric variables were assessed using the chi-square test. Cox Regression was used for multivariate analysis. The Kaplan-Meier test was used to analyze survival. A 95% confidence interval was assigned. A significant p-value was defined as <0.05.

This study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was granted by Marmara University School of Medicine Ethics Committee dated 05.05.2023 and numbered 05.05.2023.627

Results

In this retrospective and multi-center study, 107 patients were investigated (Table 1). NAC was administered to 54 (50.4%) and AC to 53 (49.6%) patients. The median age of the patients was 63 years (IQR:39-86). In 93% of the patients, urothelial histopathology was normal. All patients underwent radical cystectomy. Table 1 also compares the demographic characteristics and treatment response of patients receiving neoadjuvant and adjuvant treatment. Perineural invasion, lymphovascular invasion and surgical margin positivity were less in the NAC group, which were statistically significant (p=0.004 vs p=0.005; p=0.02, respectively). All patients received cisplatin plus gemcitabine as NAC. Adjuvantly, 64% received cisplatin plus gemcitabine and 36% received carboplatin plus gemcitabine. The groups differed significantly in terms of the pathological T and N stages. The rate of pT0-1 was 58% in the NAC group and 6% in the AC group, and N0 was 96% vs 40%, respectively (p=0.001). In the NAC group, CR rate was 28% and pathological down-staging was 57%.

The median follow-up period of all patients was 31.6 months (95% CI 21.8-41.4). 30-month DFS was 58.9% in the whole group, 56.3% in those who received neoadjuvant treatment and 61.5% in those who received adjuvant treatment. 30-month DFS was according to down staging after neoadjuvant, <pT2N0 70.1% and 41.1% in the group with ≥ pT2. After neoadjuvant treatment, 30-month DFS was 85.7% vs 45.9% in pathological CR vs non-CR group, respectively. 30-month OS was 69.8% in the whole group, 71.7% in those receiving neoadjuvant treatment and 68.2% in those receiving adjuvant treatment. This rate in patients with neoadjuvant downstaging was 81.4% and 62% in the <pT2N0 and ≥pT2 groups, respectively. Meanwhile, 30-month OS in the pathological CR vs non-CR group was 100% vs 62.6%, respectively.

30-month OS and DFS rates are summarized in Table 2. 30-month OS was 69.8% in the whole group, 100% in the group with pathological CR and 62.6% in the non-CR group. This rate was 81.4% in the down staging (<pT2N0) group and 62% in the ≥ pT2 group. Cisplatin treatment was superior to carboplatin in both 30-month DFS and 30-month OS groups.

30-month DFS was 58.9% in the whole group, 85.7% in the group with pathological CR and 45.9% in the non-CR group. 30-month DFS was 70.1% in the down staging (<pT2N0) group and 41.1% in the ≥ pT2 group. Median DFS was 44.5 months (95% CI 23.4-65.6) in all patients. The median DFS was 25.4 months ((95% CI 5.6-45.1) in the non-CR group (p=0.02), while the median DFS was not reached in the CR group (Figure 1).

The group that achieved CR after neoadjuvant treatment had longer overall survival times than the group that received both non-CR and adjuvant treatment (Figure 2).

Tablo 1. Characteristics of patients by the treatment types				
	All (107)	NAC (54)	AC (53)	P
Age, year (median IQR)	63 (39-86)	62 (42-79)	63 (39-86)	0.350
Gender, n (%)				0.960
Female	18 (16.8)	9 (16.6)	9 (16.9)	
Male	89 (83.2)	45 (83.4)	44 (83.0)	
ECOG-PS, n (%)				0.780
0	72 (67.3)	37 (68.5)	35 (66.1)	
≥1	35 (32.7)	17 (31.5)	18 (33.9)	
Clinical T stage, n (%)				0.690
cT2	64 (59.8)	32 (59.3)	32 (60.4)	
cT3	28 (26.2)	13 (24.1)	15 (28.3)	
cT4	15 (14.0)	9 (16.6)	6 (11.3)	
Clinical N stage, n (%)				0.090
cN0	62 (57.9)	27 (50.0)	35 (66.1)	
cN+	45 (42.1)	27 (50.0)	18 (33.9)	
Clinical stage, n (%)				0.002
2	41 (38.3)	13 (24.1)	28 (52.8)	
3	66 (61.7)	41 (75.9)	25 (47.2)	
Lymphovascular invasion, n (%)				0.004
Absent	44 (41.1)	29 (53.7)	15 (28.3)	
Present	52 (48.5)	19 (35.1)	33 (62.2)	
Perineural invasion, n (%)				0.005
Absent	47 (43.9)	30 (55.5)	15 (28.3)	
Present	44 (41.1)	15 (27.7)	29 (I54.7)	
Surgical Margin, n (%)				0.020
Absent	82 (76.6)	44 (81.4)	38 (71.6)	
Present	14 (13.1)	3 (5.5)	11 (20.7)	
Treatment, n (%)				0.001
Cisplatin+gemcitabine	89 (83.1)	54 (100)	34 (64.1)	
Carboplatin+gemcitabine	20 (16.9)	0	19 (35.9)	
Pathological T stage, n (%)				0.001
pT0	14 (13.1)	14 (25.9)	0	
pT1	20 (18.7)	17 (31.4)	3 (5.7)	
pT2	22 (20.6)	11 (20.3)	11 (20.8)	
pT3	33 (30.8)	6 (11.1)	27 (50.9)	
pT4	18 (16.8)	6 (11.1)	12 (22.6)	
Pathological N stage, n (%)				0.001
pN0	73 (68.2)	52 (96.2)	21 (39.6)	
pN+	34 (31.8)	2 (3.7)	32 (60.3)	
Pathological stage, n (%)				0.001
0	15 (14.0)	15 (27.7)	0	
1	16 (15.0)	16 (29.6)	0	
2	18 (16.8)	10 (18.6)	8 (15.1)	
3	58 (54.2)	13 (24.1)	45 (84.9)	
Pathological down staging, n (%) *				
Yes	31 (57.4)	31 (57.4)		
No	23 (42.6)	23 (42.6)		

AC: Adjuvant chemotherapy; ECOG-PS: Eastern Cooperative Oncology Group-Performance score; NAC: Neoadjuvant chemotherapy; N: Node; p: Pathological; T: Tumor; * Pathological down staging are only given for patients who received neoadjuvant chemotherapy

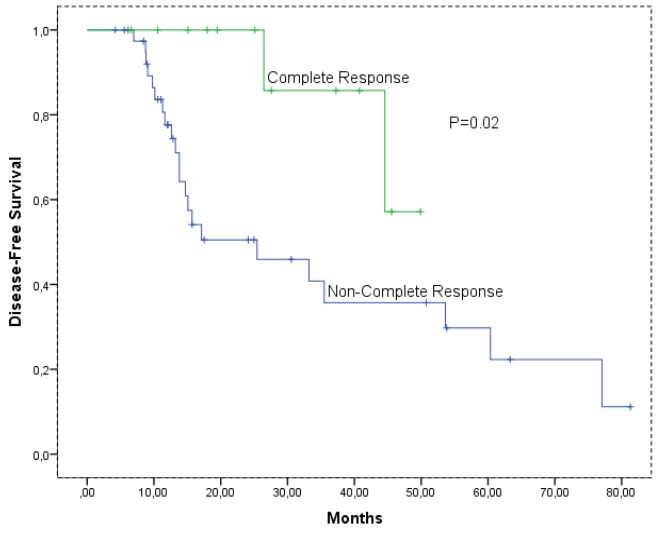

Figure 1. Comparison of Disease-Free Survival Between Complete Response and Non-Complete Response Groups

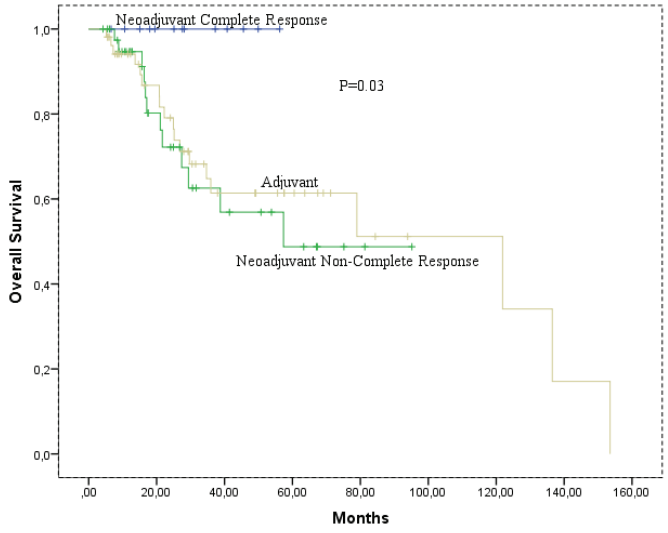

Figure 2. Comparison of Overall Survival Between Groups

Table 3 shows the univariate and multivariate analysis of potential prognostic factors for disease-free survival. Complete response (CR vs non-CR) was significant in both univariate and multivariate analyses. In multivariate analysis, there were HR=0.23 (0.10-0.49) P=0.01 patients with complete response.

In terms of OS, being treated with a cisplatin regimen longer overall survival times in both univariate and multivariate analyses. In multivariate analysis, there were HR=0.39 (0.17-0.86) P=0.01. In addition, patients older than 65 years had shorter overall survival times (HR=1.39 (1.27-3.86) P=0.03) (Table 4).

Table 2. 30-month DFS and OS in bladder cancer patients

	30-month DFS (%)	30-month OS (%)
General (n=107)	58.9	69.8
Age		
≤ 65	65.3	78.2
> 65	45.1	52.9
Gender		
Male	58.6	72.1
Female	59.6	62.3
Treatment		
Neoadjuvant	56.3	71.7
Adjuvant	61.5	68.2
Clinical stage		
2	62.7	75.2
3	57.3	70.5
Down staging		
<pT2N0	70.1	81.4
≥ pT2	41.1	62.0
Neoadjuvant treatment, platin		
1-3 cycles	63.5	76.2
4 cycles	55.4	68.8
Adjuvant treatment		
Cisplatin	75.1	81.0
Carboplatin	35.9	44.4
Pathological response		
Complete response (CR)	85.7	100
Presence of residue (non-CR)	45.9	62.6

DFS: disease free survival; OS: Overall survival

Discussion

The study findings suggest that patients who responded to neoadjuvant treatment for locally advanced bladder cancer (complete response or down staging) had a better prognosis than those who did not respond to adjuvant and neoadjuvant treatment. Additionally, the study identified advanced age as a factor that impacted overall survival.

According to current guidelines, cisplatin-based neoadjuvant treatment is recommended for bladder cancer starting from clinically staged T2. However, despite being the standard treatment for muscle-invaded bladder cancer, only 15% of patients receive it (7). This data emphasizes the importance of multidisciplinary evaluation. While neoadjuvant cisplatin-based combined chemotherapy regimens have demonstrated an overall survival advantage, it is important to acknowledge that 50% of these patients still have residual tumors at postoperative T2 and above (7). In our study, 54% of the patients received neoadjuvant treatment and all of them received cisplatin plus gemcitabine. In comparison with the literature, the CR rate after neoadjuvant treatment was 28% and pathologic down-staging was 57%. Therefore, it is important to explore alternative treatment strategies that may improve response rates and survival outcomes.

Table 3. Univariate and multivariate analysis of potential prognostic factors for disease-free survival

Parametres	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	p
Age, >65 years vs <65 years	1.65 (0.89-3.04)	0.10	0.55 (0.40-1.70)	0.27
Gender, Male vs Female	0.72 (0.35-1.46)	0.36		-
Histopathology, Urotelyal vs Other	0.88 (0.27-2.86)	0.84		-
Smoking, Yes vs No	0.66 (0.33-1.31)	0.24		-
Alcohol, Yes vs No	0.77 (0.32-1.89)	0.57		-
BMI>25 vs <25	0.83 (0.45-1.52)	0.55		-
Stage, 3 vs 1-2	1.28 (0.66-2.46)	0.45		-
Treatment, Neoadjuvant vs Adjuvant	1.40 (0.77-2.56)	0.26		-
Cisplatin, Yes vs No	0.58 (0.29-1.15)	0.12		-
Complete Response, Yes vs No	0.21 (0.05-0.92)	0.03	0.23 (0.10-0.49)	0.01
Neoadjuvant treatment, 4 cycles vs 1-3 cycles	0.69 (0.32-1.48)	0.35		-
Down staging,<pT2N0 vs >pT2	0.55 (0.23-1.29)	0.17		-

CI: Confidence interval; HR: Hazard ratio

Table 4. Univariate and multivariate analysis of potential prognostic factors for overall survival

Parametres	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	p
Age, >65 vs <65 years	2.58 (1.20-3.54)	0.01	1.39 (1.27-3.86)	0.03
Gender, Male vs Female	0.60 (0.26-1.38)	0.23		-
Histopathology, Urotelyal vs Other	0.52 (0.15-1.73)	0.28		-
Smoking, Yes vs No	0.46 (0.20-1.06)	0.15		-
Alcohol, Yes vs No	0.31 (0.07-1.39)	0.12		-
BMI>25 vs <25	0.65 (0.30-1.40)	0.27		-
Stage, 3 vs 1-2	0.95 (0.44-2.07)	0.91		-
Treatment, Neoadjuvant vs Adjuvant	0.86 (0.40-1.84)	0.71		-
Cisplatin, Yes vs No	0.49 (0.21-1.13)	0.09	0.39 (0.17-0.86)	0.05
Complete Response, Yes vs No	0.03 (NR-7.79)	0.21		-
Neoadjuvant treatment, 4 cycles vs 1-3 cycles	0.54 (0.20-1.46)	0.22		-
Down staging,<pT2N0 vs >pT2	0.60 (0.19-1.93)	0.40		-

CI: Confidence interval; HR: Hazard ratio; NR: Not reached

Tablo 5. Clincal trials outcomes

Pathologic Stage	MSK (n = 154)	Dash et al (n = 42)	Yeshchina et al (n = 37)	Majidova et al (n = 54)
Regimen	GC	GC	GC	GC
pT0N0, %	20	26	25	27
< pT2N0, %	44	36	50	55
≥ pT2, %	56	64	50	45

GC: gemcitabine plus cisplatin

Moreover, it is important to note that a significant proportion of patients who undergo radical cystectomy are unable to receive adjuvant treatment due to prolonged complications and comorbidities. Therefore, it is imperative to carefully assess eligible patients for neoadjuvant treatment.

As it is widely acknowledged, neoadjuvant chemotherapies have been shown to yield complete response rates of 30-40%. Unfortunately, even with these treatments, 50% of patients still have >pT2 residual tissue after radical cystectomy. In order to improve these response rates, it may be worth considering combinations of chemotherapy and immunotherapy, as has been seen in studies on lung cancer treatment (10). However, it is important to note that phase 2 studies did not show a significant increase in pathological response rates. It is possible that the results of phase 3 studies will lead to changes in clinical practice (11). As seen in Figure 2, it is a well-established fact that neoadjuvant treatment leads to longer survival times and is particularly beneficial for patients who achieve a complete response. The findings were consistent with the literature. While the 30-month OS rate was 71.7% in those who

received neoadjuvant treatment, this rate was 68.2% in those who received adjuvant treatment. As previous studies have shown, neoadjuvant treatment provides a survival advantage for patients who achieve a complete pathological response with NAC (12). Platinum-based NAC can increase the 5-year survival rate by 5-10% in the relevant population. Patients who respond to NAC have a 5-year survival rate of 80-90%, whereas non-responders have a rate of 30-40% (13).

When we look at other studies with neoadjuvant chemotherapy selection, there is no significant difference in terms of pathological complete response rate in the comparison of cisplatin plus gemcitabine and MVAC regimen. However, pathological complete response rate and survival results are more favorable with MVAC regimen. In the study comparing donse dens MVAC with gemcitabine cisplatin, although the pathological complete response rate (42% vs 35%) was not statistically significant, it was slightly superior in the dd-MVAC arm (p=0.2). However, pathological down-staging rates were better in the dd-MVAC arm (p=0.007). 3-year PFS with dd-MVAC was 64% and statistically significant (p=0.02) (9). Carboplatin is not recommended as a substitute for cisplatin, as the complete response rate with carboplatin is below 10% in patients for whom cisplatin is not suitable (14). The results of immunotherapy studies for these patient groups are encouraging (15, 16).

Apart from immunotherapies, pathological complete response rate is 35% when antibody drug conjugate (ADC) anti-Nectin-4 enfortumab and cisplatin are given neoadjuvantly in unsuitable patients. In terms of squamous histology, the efficacy of chemotherapy has not been clearly demonstrated and surgery may be a priority (17). In our study, 8 patients had squamous cell carcinoma. Seven patients received adjuvant treatment after direct surgery, 1 patient was operated only after neoadjuvant treatment and no pathological complete response was achieved. In our study, all patients received cisplatin plus gemcitabine as neoadjuvant treatment and our results are compared with other studies in Table 5, and our results are similar to other studies.

The role of postoperative adjuvant chemotherapy in BC remains unclear. So far, prospective randomised trials have demonstrated a contribution to progression-free survival in patients receiving cisplatin-based adjuvant chemotherapy, but this has not been reflected in overall survival (18). In the adjuvant immunotherapy group (nivolumab), 40% of patients underwent surgery after cisplatin-based chemotherapy and had residual tumors staged >T2, while the remaining patients were directly operated on because they were not suitable for cisplatin. This approach provided a two-fold advantage in disease-survival, which was the primary outcome. In conclusion, platinum base adjuvant therapy or nivolumab is recommended for patients with >T3 and node positivity after radical cystectomy without neoadjuvant treatment due to its contribution to DFS. In addition, adjuvant nivolumab may be considered for patients with residual disease after cisplatin-based postoperative treatment (19). In our study, adjuvant treatment was given to patients with residual disease who had not received neoadjuvant treatment before. While 60% of the patients received cisplatin combination therapy, 40% were treated with carboplatin-based therapy. We were unable to administer adjuvant immunotherapy to any of our patients due to the lack of reimbursement coverage in our country. However, 30-month OS was two times higher with cisplatin compared to carboplatin (81% vs 44%, respectively). If the patient has not received neoadjuvant treatment, cisplatin should be strongly considered for adjuvant therapy.

Limitations

The major limitation of our study is that data may be lost due to its retrospective nature and confounding factors may not be controlled. Although the number of patients was small and none received neoadjuvant dose-dense MVAC or immunotherapy as adjuvant treatment, the most important conclusion of this study is that neoadjuvant treatment and the response that it generates play a crucial role in determining patient prognosis.

Conclusion

In conclusion, neoadjuvant cisplatin-based chemotherapies significantly improved both pathologic response and survival in muscle- invasive bladder cancer. Age and chemotherapy intensity were found to be important prognostic factors, with younger patients and more cisplatin-based treatments achieving better outcomes. Surgery, radiotherapy and systemic treatment options in muscle invasive bladder cancer can be evaluated in multidisciplinary tumor consultations. Patients who can respond to neoadjuvant therapy should receive neoadjuvant therapy, but if neoadjuvant therapy is not feasible, adjuvant therapy can be considered. The lack of significant difference between the two treatment strategies emphasizes the importance of adjuvant therapy for patients who cannot undergo neoadjuvant treatment. Further prospective studies are needed to explore optimized chemotherapy regimens that may improve survival while minimizing toxicity, especially in elderly or high-risk patients.

Conflicts of interest

Authors declare no conflicts of interest.

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