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ORIGINAL RESEARCH

# Evaluating The Relationship Between Blood Transfusion Time Points and Mortality in Patients with Bladder Cancer Undergoing Radical Cystectomy

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**Abstract:** **Background:** Radical cystectomy as a crucial treatment approach for high-grade bladder cancer is often associated with substantial blood loss and a frequent necessity for blood transfusion. Investigating the correlation between perioperative blood transfusion and surgical outcomes is an area of contention. We aimed to examine the relationship between blood transfusion timing and mortality in patients undergoing radical cystectomy.
**Materials and methods** The clinical records of 274 patients who underwent radical cystectomy at Modarres Hospital in Tehran, Iran, during 2011-2021 were reviewed. Among them, 191 patients received perioperative blood transfusions. The 90-day mortality rate was compared between these groups, and the association between transfusion timing and mortality was assessed.
**Results:** The 90-day mortality rate was 14% in the blood recipient group and 11% in the non-transfusion group. However, no statistically significant relationship was observed between blood transfusion and 90-day mortality (P=0.4). The most prevalent timeframe for blood transfusion was before and during surgery. Mortality was highest in the group receiving blood before and during the operation, with a rate of 18%. Nevertheless, no statistically significant association was found between transfusion timing and mortality (P=0.346). When comparing the Charlson Comorbidity index (CCI) between the two groups, significantly higher CCI levels were observed in the blood recipient group (P=0.003).
**Conclusion:** In our retrospective review, no significant relationship was identified between blood transfusion, its timing, surgical outcomes, and 90-day mortality.

**Keywords:** Radical cystectomy, Blood transfusion, Mortality, Complication

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## 1. Introduction

Bladder cancer is the fourth most common cancer in men and the eighth most prevalent cancer in women. It accounts for approximately 4% of all malignancies and is 2.7 times more frequent in men than in women. Occupational exposure to carcinogens, smoking, chronic use of painkillers, and chronic inflammation of the bladder are among the known risk factors (1).

About 70-80% of bladder tumors do not invade the muscular wall of the bladder and can be effectively treated with transurethral resection of bladder tumor (TURBT) plus intravesical immunotherapy. However, in muscle invasive tumors, radical cystectomy is the standard treatment option (2).

Radical cystectomy (RC) is a high demanding surgery for both patients and surgeons with potential for multiple complications. Also, due to the rich vascular supply of pelvic organs, it has high propensity for blood loss and in need for multiple transfusions during and after surgery.

Additionally, since most of these patients have hematuria be-

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fore surgery or have undergone neoadjuvant chemotherapy, the hemoglobulin level is already plummeted, making them more susceptible to complications induced by blood loss (3,4). Although modifications in surgical procedures have been introduced over the years, RC is still among the most morbid urological procedures (5,6).

Blood transfusion alone has been mentioned in multiple studies as a risk factor for postoperative complications in multiple patients with urological cancer (7-11). Given the limited number of studies conducted on this subject in our country, we reviewed our database to explore the relationship between blood transfusion timing and mortality in patients with bladder cancer undergoing radical cystectomy.

## 2. Materials & Methods

A retrospective review of patients with bladder cancer who underwent radical cystectomy at Modarres Hospital in Tehran/ Iran, between 2011 and 2021 was conducted. Our Ethics Committee approved the protocol of the study (code: IR.SBMU.MSP.REC.1400.780). 276 records were included in the final analysis. The clinical and pathological variables including age, sex, body mass index, pre-surgical hemoglobin levels, presence of diabetes, smoking status, tumor stage and lymph node status of our study participants were recorded and analyzed.

Tumor grade and histological type were not individually reported or analyzed as most patients experiencing cystectomy present with high-grade urothelial carcinoma. Blood transfusion (BT) was defined as the administration of packed red blood cells (PC) during surgery (intraoperative BT) or during hospitalization after the surgery (postoperative BT). Patients who received neoadjuvant chemotherapy were excluded due to the potential confounding effect of chemotherapy-induced anemia.

### *2.1. Data Analysis*

Statistical analysis was performed using Chi-square test to evaluate the relationship between clinical and pathological variables with disease outcomes. A P<0.05 was considered statistically significant. SPSS software, version 22, was used for all analyses.

## 3. Results

We included 274 participants, consisting of 229 men with a mean age of 67 years and 45 women with a mean age of 72 years. Among the participants, 191 individuals had received packed red blood cells at various time points before, during, or after surgery, whilst 83 individuals did not. Among those who received blood, 157 (82%) were men and 34 (18%) were women. In the group without transfusion, there were 72 (87%) men and 11 (13%) women. No significant difference in sex distribution was observed between the two groups (P>0.05, Table 1).

Fifty-seven patients had metastases (21%), with 44 cases in men and 13 cases in women. Among the group receiving PC, 38 cases (20%) had metastasis, while in the group without transfusion, 19 cases (23%) had metastasis. Although the numerical prevalence of metastasis was slightly higher in the group without transfusion, there was no statistically significant relationship between blood transfusion and the presence of metastasis (P=0.5).

In total, there were 36 mortalities within the first 90 days after surgery (13%). In the group receiving blood, there were 27 mortalities (14%), compared to 9 (11%) in the non-transfusion group. However, there was no statistically significant relationship between blood transfusion and the 90-day mortality rate (P=0.4).

Regarding tumor stage, T2 was the most common stage in both PC recipient (47%) and non-recipient group (37%). No statistically significant difference was found between the two groups in terms of mortality across different stages of the disease (P>0.05, Table 2).

Analyzing the timing of transfusion in the PC recipient group revealed that 15% of individuals received blood before surgery, 28% during surgery, 45% before and during surgery, and 12% after surgery. The most common timing for transfusion was before and during surgery. The group receiving blood before and during surgery had the highest mortality rate with 16 cases (18%), followed by the pre-operative group with 4 cases (14%), and the intra-operative group with 6 cases (11%). No significant relationship was observed between the timing of blood transfusion and the mortality rate in the transfusion group (P=0.3) (Table 3).

Regarding the correlation between mortality and the presence of metastasis, there were 13 mortality cases (23%) in the metastatic group and 23 mortality cases (11%) in the non-metastatic group. The presence of metastasis was associated with a significant increase in 90-day mortality in the overall population (P=0.015). Additionally, in the transfusion recipient group, the mortality rate was 26% in the metastatic cases and 11% in the non-metastatic group, indicating a significant relationship between metastasis and increased mortality (P=0.016).

In terms of the overall prevalence of postoperative complications, 94 complications (34%) were reported, with 70 (37%) in the blood recipient group and 24 (29%) in the non-transfusion group. There was no statistically significant difference between the two groups in terms of complications (P>0.05). The most common types of postoperative complications were ileus and intestinal obstruction (10%), followed by wound infection (8%), acute kidney injury (7%), urinary infection and deep vein thrombosis (6%). While the prevalence of wound infection, urinary infection, acute kid-

**Table 1:** General characteristics of the population based on blood transfusion

| | Group | Subgroup | Number (%) |
|---|---|---|---|
| Total | blood recipient | | 191 (69.7%) |
| | No transfusion | | 83 (30.3%) |
| Gender | Total | Male | 229 (83.6%) |
| | | Female | 45 (16.4%) |
| | blood recipient | Male | 157 (82.2%) |
| | | Female | 34 (17.8%) |
| | No transfusion | Male | 72 (86.7%) |
| | | Female | 11 (13.3%) |
| Metastasis | Total | | 57 (20.8%) |
| | | blood recipient | 38 (19.89%) |
| | | No transfusion | 19 (22.89%) |
| Death | Total | | 36 (13.13%) |
| | | blood recipient | 27 (14.13%) |
| | | No transfusion | 9 (10.84%) |

**Table 2:** Prevalence of tumor stages and mortality rates in each stage in relation to blood transfusion

| | Stage | Number (%) | Mortality (%) |
|---|---|---|---|
| Total | T1 | 55 (20.07%) | 2 (3.63%) |
| | T2 | 121 (44.16%) | 14 (11.57%) |
| | T3 | 73 (26.64%) | 16 (21.91%) |
| | T4 | 25 (9.12%) | 4 (16%) |
| Blood recipient | T1 | 33 (17.27%) | 1 (3.03%) |
| | T2 | 90 (47.12%) | 11 (12.22%) |
| | T3 | 52 (27.22%) | 11 (21.15%) |
| | T4 | 16 (8.37%) | 4 (25%) |
| No transfusion | T1 | 22 (26.5%) | 1 (4.54%) |
| | T2 | 31 (37.34%) | 3 (9.67%) |
| | T3 | 21 (25.3%) | 5 (23.8%) |
| | T4 | 9 (10.84%) | 0 |

**Table 3:** Frequency of blood transfusion in relation to timing and its association with mortality

| | Number (%) | Mortality (%) |
|---|---|---|
| Before the operation | 29 (15.2%) | 4 (13.79%) |
| During the operation | 53 (27.7%) | 6 (11.32%) |
| Before and during the operation | 87 (45.5%) | 16 (18.39%) |
| Post operation | 22 (11.5%) | 1 (4.54%) |

ney injury, and deep vein thrombosis was higher in the non-transfusion group, and the prevalence of ileus and intestinal obstruction was higher in the blood-recipient group, there was no significant difference between the two groups in any of those complications (P>0.05) (Table 4).

In terms of the type of urinary diversion, uretero-cutaneous diversion was the most common type (61%), while orthotopic diversion was the least common (8%). There was no significant difference in the prevalence of diversion types between the blood recipient and non-recipient groups.

When comparing the Charlson Comorbidity Index (CCI) between the two groups, the CCI level was significantly higher in the blood recipient group (P=0.003). However, when comparing the average CCI in the blood recipient group, although patients who experienced mortality within 90 days after the operation had a higher CCI, this difference was not statistically significant (P=0.079). Among metastatic cases, metastasis to lymph nodes was the most prevalent (60%), followed by lung metastasis (30%). There was no significant difference in the prevalence of metastatic sites between the blood recipient and non-recipient groups.

## 4. Discussion

Radical cystectomy (RC) is recommended for NMIBC patients with high-risk features and for patients with muscle-invasive bladder cancer. Blood transfusion is often required during RC surgeries, and the relationship between preopera-

**Table 4:** Frequency of postoperative complications

| Type of complication | Group | Number |
|---|---|---|
| General complications | Overall frequency | 94 (34.3%) |
| | Blood recipient | 70 (36.64%) |
| | No transfusion | 24 (28.91%) |
| Wound infection | Overall frequency | 23 (8.39%) |
| | Blood recipient | 14 (7.32%) |
| | No transfusion | 9 (10.84%) |
| UTI | Overall frequency | 16 (5.83%) |
| | Blood recipient | 11 (5.75%) |
| | No transfusion | 5 (6.02%) |
| AKI and kidney | Overall frequency | 19 (6.93%) |
| | Blood recipient | 13 (6.8%) |
| | No transfusion | 6 (7.22%) |
| DVT | Overall frequency | 16 (5.83%) |
| | Blood recipient | 9 (4.71%) |
| | No transfusion | 7 (8.43%) |
| Intestinal obstruction and ileus | Overall frequency | 27 (9.85%) |
| | Blood recipient | 21 (10.99%) |
| | No transfusion | 6 (7.22%) |

tive blood transfusion (PBT) and outcomes has been studied in various surgeries, yielding conflicting results.

In our retrospective review of patients' records, we did not find any relationship between the timing of blood transfusion and the 90-day mortality rate. In the comparison of Charlson Comorbidity Index (CCI) between the two groups, the CCI level of the blood recipient group was significantly higher than the non-recipient group (P=0.003). This was no surprise since the more complicated the patient before surgery, there was greater chance of anemia and need for blood products.

Non-association of transfusion of blood products with survival and oncological outcomes has been shown in multiple studies. Diamantopoulos et al. (7) investigated the effect of postoperative allogeneic blood transfusion on oncological outcomes after radical cystectomy for bladder cancer. The study found no association between blood transfusion and recurrence-free survival, overall survival, or cancer-specific survival. Adjusting for baseline differences in patient characteristics did not show any adverse effect of blood transfusion on oncological outcomes. In another study by Lee et al. (8) the prognostic effect of postoperative blood transfusion on the survival of patients with urothelial carcinoma of the bladder treated with radical cystectomy was analyzed. Independent risk factors for overall mortality included female gender, lower hemoglobin level before surgery, blood loss estimate exceeding 800 ml, and the performance of neoadjuvant chemotherapy. Although univariate analysis showed an association between receiving preoperative blood transfusion and increased overall mortality, multivariate analysis did not confirm this relationship.

Conversely, some studies have reported a positive correlation between the timing of blood transfusion with bladder cancer mortality and recurrence (9,10). It is worth mentioning that in these studies, only pre- and intraoperative blood transfusion was associated with cancer recurrence and mortality while post-operative transfusion did not. Juan Gómez Rivas et al. (11) also reported that pre- and intra-operative transfusion is associated with increased infectious complications.

The results of these studies have provided conflicting results mostly due to the heterogenous patient population and retrospective design of the studies. Despite our previous notion that patients with the need for blood products are defacto poor-risk patients, our results did not provide the expected results. Possibly our lack of association is partly due to the preponderance of the uretero-cutaneous type of diversion since most of the complications of RC patients originate from intestinal origin.

We did evaluate the mortality rates in different stages of the disease and the highest mortality in the overall population was observed in T3 stage (22%), followed by T2 (12%). In the blood transfusion and non-transfusion group the highest mortality rate was again observed in T3 patients (21% for the former and 24 % for the latter). However, no statistically significant difference was found in terms of mortality among disease stages between the blood recipient and non-recipient groups (P>0.05).

The drawback of our study is its retrospective design with limitations inherent to it. The preponderance of T2 stage and uretero-cutaneous diversion in our group of patients could create bias in study results.

## 5. Conclusion

Timing of blood transfusion in RC patients did not show any correlation with 90-day mortality and post-operative complications. This could imply that other factors inherent to the nature of the bladder cancer and surgical details during cystectomy and diversion have defining role in patients' mortality and complication rate.

## 6. Appendix

### 6.1. Acknowledgment

None.

### 6.2. Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

### 6.3. Funding and support

None.

### 6.4. Author's contributions

Study design: N.Masoumi; Data gathering and analysis: H. Chaabi, A. Jouzi; Original draft preparation: H. Chaabi, M. Darzi; Final edit and submission: N.Masoumi.

## References

1- Masui K, Gini B, Wykosky J, Zanca C, Mischel PS, Furnari FB, et al. A tale of two approaches: complementary mechanisms of cytotoxic and targeted therapy resistance may inform next-generation cancer treatments. Carcinogenesis. 2013;34(4):725-38.

2- Lorusso D, Bria E, Costantini A, Di Maio M, Rosti G, Mancuso A. Patients' perception of chemotherapy side effects: Expectations, doctor–patient communication and impact on quality of life–An Italian survey. European journal of cancer care. 2017;26(2):e12618.

3- Yun SJ, Kim S-K, Kim W-J. How do we manage high-grade T1 bladder cancer? Conservative or aggressive therapy? Investigative and clinical urology. 2016;57(Suppl 1):S44-S51.

4- Martini A, Sfakianos JP, Renstrom-Koskela L, Mortezavi A, Falagario UG, Egevad L, et al. The natural history of untreated muscle-invasive bladder cancer. BJU international. 2019.

5- Soleimani M, Moradkhani E, Masoumi N, Gholivandan J. Extra-Peritoneal versus Trans-Peritoneal Open Radical Cystectomy - Comparison of Two Techniques in Early Post-Operative Complications. Urol J. 2021 Nov 7;18(5):519-524. doi: 10.22037/uj.v16i7.6147. PMID: 32827149.

6- Hosseini A, Adding C, Nilsson A, Jonsson MN, Wiklund NP. Robotic cystectomy: surgical technique. BJU Int. 2011 Sep;108(6 Pt 2):962-8. doi: 10.1111/j.1464-410X.2011.10566.x. PMID: 21917098.

7- Diamantopoulos LN, Sekar RR, Holt SK, Khaki AR, Miller NJ, Gadzinski A, et al., editors. Patterns and timing of perioperative blood transfusion and association with outcomes after radical cystectomy. Urologic Oncology: Seminars and Original Investigations; 2021: Elsevier.

8- Lee JS, Kim HS, Jeong CW, Kwak C, Kim HH, Ku JH. The prognostic impact of perioperative blood transfusion on survival in patients with bladder urothelial carcinoma treated with radical cystectomy. Korean journal of urology. 2015;56(4):295-304.

9- Abel EJ, Linder BJ, Bauman TM, Bauer RM, Thompson RH, Thapa P, et al. Perioperative blood transfusion and radical cystectomy: does timing of transfusion affect bladder cancer mortality? European urology. 2014;66(6):1139-47.

10- Moschini M, Dell'Oglio P, Capogrosso P, Cucchiara V, Luzzago S, Gandaglia G, et al. Effect of allogeneic intraoperative blood transfusion on survival in patients treated with radical cystectomy for nonmetastatic bladder cancer: results from a single high-volume institution. Clinical genitourinary cancer. 2015;13(6):562-7.

11- Rivas JG, y Gregorio SA, Ledo JC, Gómez ÁT, Sebastián JD, de la Peña Barthel J. The role of perioperative blood transfusion on postoperative outcomes and overall survival in patients after laparoscopic radical cystectomy. Journal of cancer research and therapeutics. 2016;12(1):146.