Am J Clin Exp Urol 2023;11(2):177-184
www.ajceu.us /ISSN:2330-1910/AJCEU0146701

Original Article

Evaluation of postoperative bleeding control employing Surgicel: a clinical trial

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Received September 26, 2022; Accepted April 12, 2023; Epub April 15, 2023; Published April 30, 2023

Abstract: Introduction: Various techniques have been developed for the rapid control of bleeding as a potential surgical complication. Research shows that the Surgicel has a significant effect on reducing bleeding in most surgeries; however, in our experimental observations on patients undergoing open prostatectomy, not only no significant reduction was seen in the amount of bleeding, but in some cases, Surgicel led to infection. Therefore, in this study, the effect of the Surgicel on infection and bleeding in open prostatectomy was investigated. Materials and methods: Thirty patients undergoing open prostatectomy were randomly divided into two groups. To control bleeding after suturing the bladder neck, the Surgicel was installed in the first group, while it was not in the second group. Hemoglobin, hematocrit, PT, PTT, INR, bleeding rate, and postoperative complications were evaluated in all patients. Results: In the studied groups, hemoglobin level and hematocrit percentage before surgery and on the first and second days after surgery, along with coagulation status, were compared in terms of PT, PTT, and INR. There were no significant differences between the studied variables and baseline variables. Conclusion: The present study revealed that the Surgicel in open prostatectomy was ineffective in controlling bleeding and can lead to infection.

Keywords: Prostatectomy, the Surgicel, post-operative bleeding, post-operative infection

Introduction

Bleeding is a potential Surgical complication and a significant challenge for surgeons and anesthesiologists. While inadequate local homeostasis can cause severe bleeding, taking care of bleeding during and after surgery is one of the most critical points to consider in treating patients. Besides, the hemodynamic instability in patients and the need for blood transfusion prolong the hospital stay [1], so in one study, the rate of bleeding in 13% of the patients undergoing prostatectomy was reported to be more than one liter, causing hemodynamic disorders [2]. Therefore, the first important step in patient management is early detection and control of bleeding since the mortality rate increases from 1% to 20% in severe bleeding. Although hidden bleeding does not affect hemodynamic instability, such complications can cause infection, inflammation, and adhesions [3]. To control and reduce bleeding, drugs such as anti-fibrinolytic and intravenous injections of coagulation agents such as fibrinogen are typically used, which can have many side effects. Therefore, hemostatic agents are used topically for better results and reduction of the drug's side effects [4-6]. Topical hemostatic agents are used based on their ability to activate the coagulation cascade locally to control bleeding before surgery at the surgery site, stimulating and facilitating the formation of blood clots at the site of bleeding. These local factors rely on a healthy coagulation mechanism; their use is limited in patients with coagulation disorders. Several hemostatic methods, such as mechanical devices, thermal devices, and local hemostatic agents, prevent postoperative bleeding. Each of these techniques has advantages and disadvantages, considered by surgeons to use selectively depending on the field of surgery. One of these factors is mechanical homeostasis. The most common method used in surgery is direct pressure which is not stable in controlling bleeding. Another method of controlling bleeding in hemostatic agents is the chemical method, causing vasoconstriction by administering epinephrine. Heat

hemostasis (electrocautery) is another hemostatic agent that can pursue large areas of tissue by creating short-term hemostasis by denaturing proteins. Although this method can save time and shorten homeostasis, its use can be restricted by the complication of tissue rupture, burns, and electric shock [7]. Cellulose-based products (Surgicel) are utilized only for the local control of light bleeding, and local hemostatic consisting of oxidized cellulose in the absence of plasma compounds, especially factors VIII and XII, is not able to induce platelet activity and control bleeding [8]. The main ingredient of the Surgicel is a resorbable oxidized cellulose material in a sterile fabric meshwork [8]. In treating benign prostatic hyperplasia (BPH), the most common cause of urinary obstruction is often seen in men over the age of 50. If it does not respond to drug therapy as the first line of treatment, various Surgical methods are employed. Prostate hysterectomy (TURP), a common surgical treatment, has risky complications such as bleeding during and after surgery [9-11]. The extreme enlargement of prostate hypertrophy and the past medical of hypertension and diabetes in patients may contribute to bleeding exceeding 1000 ml in patients undergoing prostatectomy [11]. In experimental observations of prostatectomy patients in Imam Reza Hospital in Tabriz, no difference was observed in the amount of bleeding (drainage, hemoglobin loss) in patients for whom the Surgicel was implanted compared to the group without the Surgicel, where in some cases, it led to infection at the operation site. Therefore, in the present study, prostatectomy patients were evaluated for bleeding and infection in prostatectomy patients with or without the Surgicel.

Materials and methods

Sample selection

This study was conducted as a double-blind and prospective randomized clinical trial at Imam Reza Educational and Medical Center of Tabriz from September 2019 to December 2021. The results of the previous studies were used to determine the sample size [12]. The study protocol was approved by the ethical committee of Tabriz of Medical sciences (IR.TBZMED.REC.1398.1215). Also, the current study was registered in the Iranian Registry of Clinical Trials (IRCT20200219046557N1, https://www.irct.ir/trial/46049). All patients signed written consent for participation in the study. Inclusion criteria comprised having the classic indications for prostate surgery, age 60 years and older, and completing the informed consent form by the patient. Exclusion criteria included patients with coagulation disorders, patients taking anticoagulants, patients with a history of deep vein thrombosis and embolism, and ischemic heart disease and arrhythmia. The sample included 30 adult patients with class II-I ASA with a mean age of 71.6 years who were candidates for prostatectomy based on the treating physician's diagnosis. Consecutive sampling was performed based on the order of patients' referrals to the operating room.

Procedures

The titles of the treatments were placed in sealed envelopes, and each patient candidate for proctectomy was asked to choose one of the envelopes by lot, and the main researcher prescribed the selected treatment for the patient. Thus, patients were randomly (using random allocation software) divided into two treatment groups. For the first group, the surgeon implanted the Surgicel to control bleeding. For the second group, patients were not implanted with the Surgicel, and only a bladder neck suture was performed. All patients were evaluated for demographic information such as weight, height BMI and age, cardiopulmonary evaluation, pulmonary complications, heart rate, blood pressure, arterial oxygen saturation, ECG, and daily fluid balance of each patient during hospitalization before spinal anesthesia. In addition, all patients were blood variable tested for hemoglobin, hematocrit, PT, PTT, and INR before surgery.

Evaluations

A few hours after surgery, the Surgicel and drainage, hemoglobin and hematocrit levels, and coagulation tests such as PT, PTT and INR were carried out again on the first and second days after surgery. Furthermore, the amount of bleeding during the operation was estimated and recorded using the blood volume in the suction, blood-stained gases, and blood spilled from the operation site.

Statistical analysis

The sample size was calculated using the following formula: $N = (Z1\text{-}\alpha/2 + Z1\text{-}\beta/2)^2 (S12 + S22)/(\mu1 - \mu2)^2$ (formulation 1).

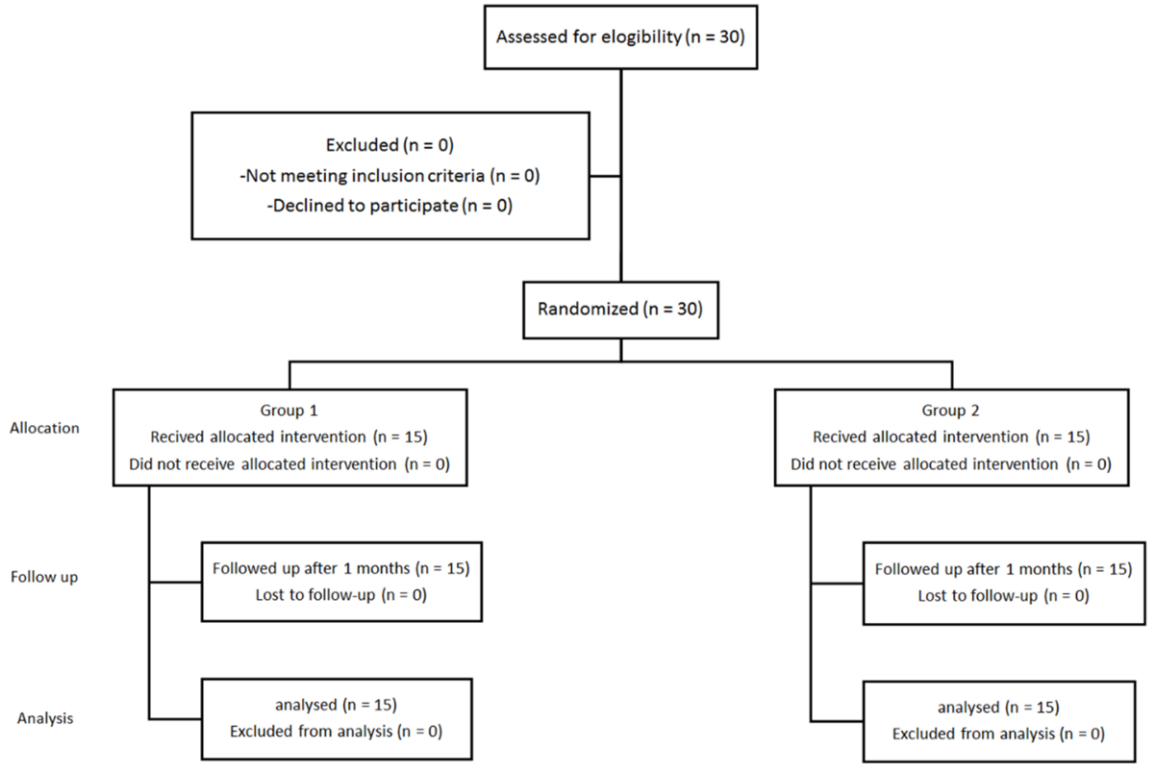

Figure 1. CONSORT flow chart.

Where N is a sample size and Z is a constant (set by convention according to accepted α error) [23].

The data obtained in the present study were analyzed by descriptive statistical methods (mean ± standard deviation). The quantitative variables were shown as mean and the qualitative variables were shown as frequency (percentage). To compare the means of weight, height, BMI, age, blood variables such as PT, PTT, INR, hemoglobin, hematocrit, and amount of blood in the drain of the two groups, the independent t-test was used. For qualitative variables, the chi-square test was utilized. The Independent t-test was carried out to compare age and BMI. Data were analyzed using SPSS 25 statistical software. In this study, a *P*-value less than 0.05 was considered statistically significant.

Result

Preintervention data

In this study, 30 patients who were candidates for electro prostatectomy were divided into two groups of 15 and then examined. After the random assignment of the patients to the relevant groups, they were present until the end of the intervention; In other words, the sample loss rate in this study was zero (**Figure 1**). A Surgicel (a topical hemostatic cellulose material) was implanted with chromic thread after suturing the bladder neck to control bleeding in the first group. And in the second group, for the same purpose, only bladder neck suture was performed without using a Surgicel. The mean age, weight, and height of participants in the first group were 73.6 ± 3.3, 3.4, and 173.8 ± 4.1, and in the second group, were 71.6 ± 6.7, 81.2, and 174.7 ± 4.1, respectively. There was no significant difference in mean age, weight, height, and body mass (**Table 1**).

Analysis of blood characteristics

Before the intervention, blood samples were taken to measure the hemoglobin, hematocrit, PT, PTT, and INR levels from all patients in two groups. The mean deviations of hemoglobin hematocrit, PT, PTT, and INR in the first group were 14.3, 38.2, 12.5, 28.8, and 90, while in the second group, they were 14.8, 38.3, 13.1,

Table 1. Mean ± standard deviation of height, weight, BMI and age

Variable	Group	Mean	*P*-value*
Height	Intervented without Surgicel (n = 15)	174.7 ± 4.1	0.570
	Intervented with Surgicel (n = 15)	173.8 ± 4.1	
Weight	Intervented without Surgicel (n = 15)	81.2 ± 5.82	0.255
	Intervented with Surgicel (n = 15)	83.4 ± 4.80	
BMI	Intervented without Surgicel (n = 15)	27.0 ± 2.05	0.458
	Intervented with Surgicel (n = 15)	27.6 ± 1.92	
Age	Intervented without Surgicel (n = 15)	71.6 ± 6.73	0.267
	Intervented with Surgicel (n = 15)	73.6 ± 3.39	

*independent T test.

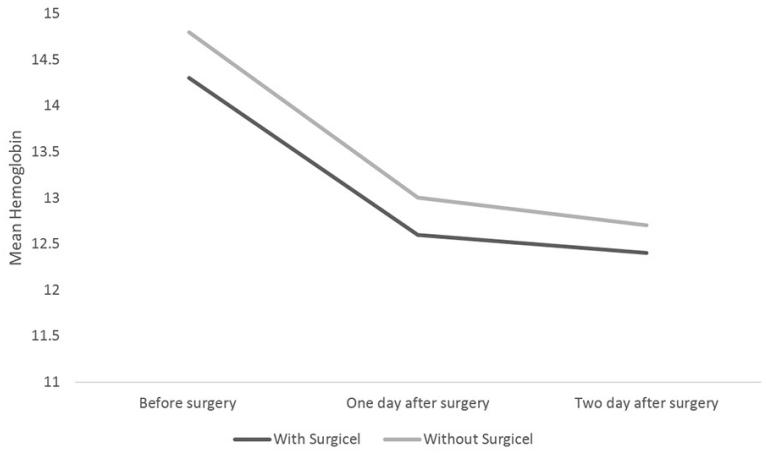

Figure 2. Mean hemoglobin.

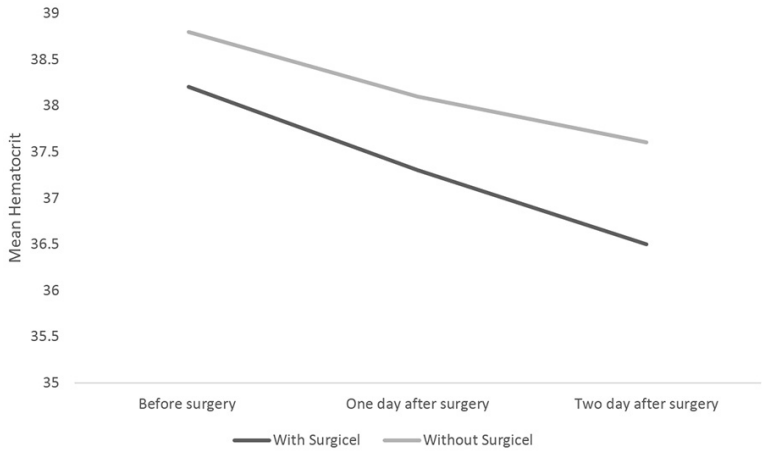

Figure 3. Mean hematocrit.

30 and 91, respectively. These parameters were measured one and two days after the operation. The mean deviations of hemoglobin hematocrit, PT, PTT, and INR after one day in the first group were 12.6, 37.3, 12.3, 28.4, and 94, while in the second group, they were 13, 38.1, 12.9, 30.7 and 97, respectively; while these blood parameters after two days in the first group were 12.4, 30.5, 12.9, 27.9 and 90 and in the second group 12.7, 37.6, 13, 29.7 and 91, respectively (**Figures 2**, **3**). There was no significant difference between the two groups in terms of decreased hemoglobin (*P*-value = 0.599) in post-operative compared to pre-operative hematocrit (*P*-value = 0.503) in the first and second days after surgery (**Figure 5**). PT (*P*-value = 0.132), PTT (*P*-value = 0.065), and INR (*P*-value = 0.53) in participants in this study did not show a significant decrease between the two groups (**Figure 5**).

Analysis of blood in the drain

The blood in the drain was determined one and two days after the intervention. The mean amounts of blood in the drain after a day in the Surgicel and non-Surgicel groups were 84.3 and 86, respectively. This parameter on the day after the first day was 14.0 and 14.6, respectively. This result demonstrated that the amount of blood in the drain declined, but there was no significant difference between the two groups in terms of decreased blood in the drain (*P*-value = 0.80) in the first and second days after surgery (**Figure 4**).

Analysis of bleeding during surgery

The mean bleeding during surgery in the first and second groups was 216 and 196.33, respectively. Reduced bleeding during surgery did not show a significant difference when the Surgicel was employed (**Figures 5**, **6**).

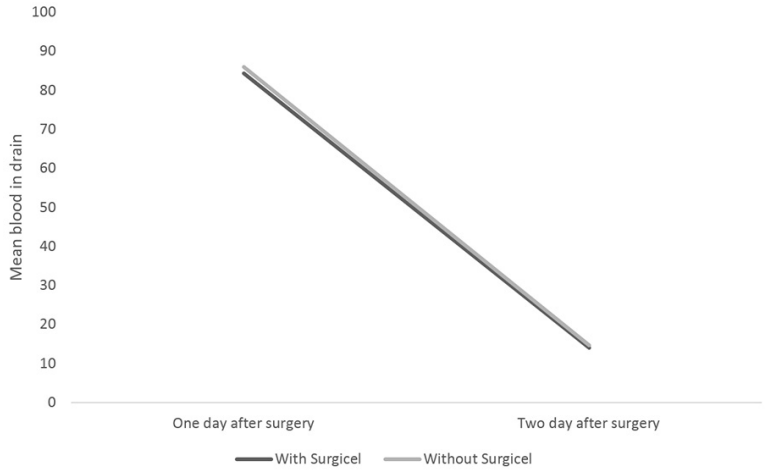

Figure 4. Mean blood in drain.

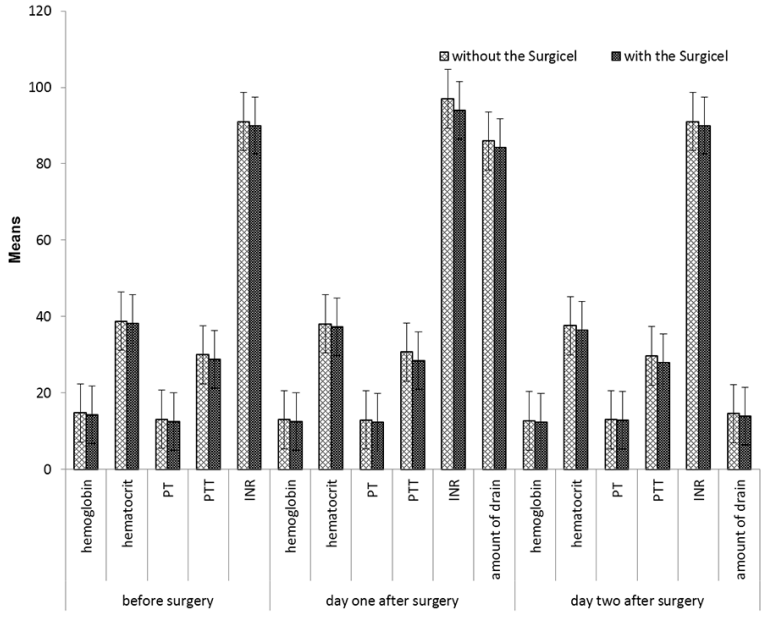

Figure 5. Mean hemoglobin, hematocrit, PT, PTT, INR, and blood in the drain before surgery, first and second days after prostatectomy. Independent T test (*P*-value ≤ 0.05), non-significant.

Analysis of the infection complication

Post-operative infection in patients with the Surgicel increased from 6.6% to 33.3% compared to those without the Surgicel; however, this was not statistically significant (**Figure 6**).

Discussion

Surgicel is a strategy to reduce the incidence rate of bleeding and infection after any surgical procedure and can benefit patients. In experimental observations of prostatectomy patients in the amount of bleeding in patients for whom the Surgicel was implanted, compared to the group without the Surgicel, no difference was observed, where in some cases, it led to infection at the operation site. In the study of Myung et al., they reported that in the duration of hospital stay, fever and bleeding significantly decreased in patients with implanted Surgicel [22]. However, Surgicel brought some disadvantages. Some studies have shown that localized Surgicel has side effects such as cysts, local swelling, and infection, probably due to an increase in the pH of the surrounding environment [13]. In our study, controlling bleeding in the Surgicel group did not have enough positive results compared with the other group, failing to prove its efficiency to be generally used in any surgery. Contrary to the results of our study, Waleed et al. [19], Pringle et al. [20], and Corbridge et al. [21] reported that the success rate of implantation of Surgicel were 96%, 91.5%, and 92.6% in patients with epitaxies treatment with Surgicel.

Evaluation of hemoglobin, hematocrit, blood in the drain in the first and second days after surgery, and PT, PTT, and INR in patients

In the present study, a relative decrease in post-operative hemoglobin and hematocrit was observed in the group using the Surgicel compared to the pre-operative period; however, this decrease was not statistically significant (**Figures 2**, **3**). This indicates that the Surgicel did not have a significant effect on controlling bleeding during prostatectomy. In the present study, the coagulation-determined factors such as PT, PTT, and INR before and after surgery were not significantly different in both groups (**Figure 5**). Pani et al. obtained the same results

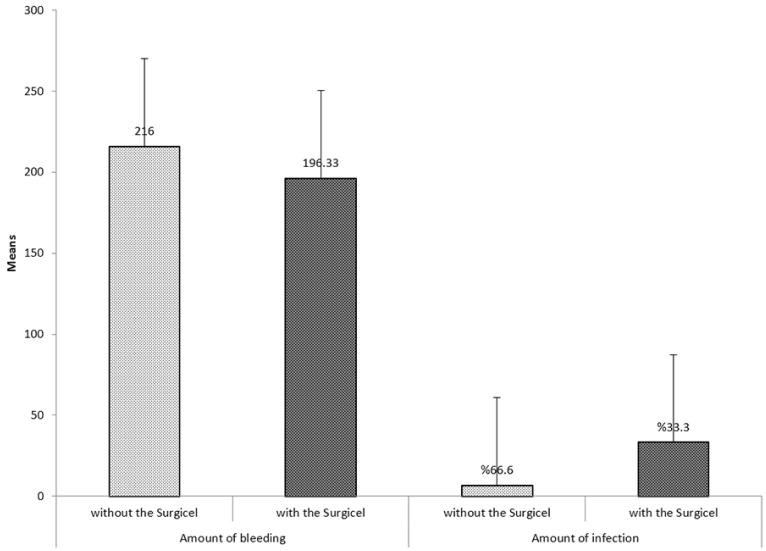

Figure 6. Mean bleeding and percentage of infection with the Surgicel and without the Surgicel after prostatectomy. Independent T test (*P*-value ≤ 0.05), non-significant.

using topical fibrinogen in high-risk patients. They reported that coagulation parameters did not change significantly, and plasma fibrinogen concentrations did not differ significantly before and after surgery [18]. Francisco et al., in a study on patients undergoing percutaneous nephrolithotomy (PCNL) surgery, did not observe a significant difference in the benefit of the Surgicel implantation between the Surgicel implanted and non-implanted surgeries in terms of hemoglobin and urinary leakage [16], whose results matched with ours.

Evaluation of reduction of bleeding during surgery in patients

In our study, the reduction of bleeding during surgery did not show a significant difference when the Surgicel was employed. It indicated that the amount of bleeding during surgery was not significantly different between the two groups. In the study of Wang et al., blood leakage in the joint and tissues and bleeding due to hemolysis after tuberculosis surgery at the end of hip arthroplasty led to the accumulation of intra-articular blood, resulting in failed surgery [14]. Wolfe et al. assessed the effect of the Surgicel during corporotomy closure after penile prosthesis surgery on reducing bleeding that potentially reduced the complications of scrotal hematoma [17], the results of which were inconsistent with those of our study.

Evaluation of infections complication

In the present study, the incidence rate of postoperative infection in the patients with implanted Surgicel was more than that in the group without implanted Surgicel (**Figure 5**). Theoretically, it can cause infection and increase the risk of delayed recovery as a foreign substance. Surgicel may act as a foreign body and increase inflammation, causing a delay in the repair of the prostate and increasing the possibility of infection. Wang et al. showed that Surgicel caused postoperative intra-articular infection [14]. Kim et al. reported that the Surgicel did homeostatic action through blood uptake, surface interaction with platelets and proteins, and activation of the coagulation cascade, while it was resistant to bacterial infection and prevented it [15]; however, these results are not in line with those of our study. Myung et al. showed that the Surgicel caused a significantly lower rate of infection incidence, signs, and infection parameters, such as fever, leukocytosis, and C reactive protein in the use of Surgicel in colorectal endoscopic submucosal dissection (ESD) in treatment of large colorectal tumors [22].

Conclusion

Our study suggests no significant difference between the groups' blood volume lost during surgery. The Surgicel used in prostatectomy may not be an effective agent in controlling bleeding and, in some cases, may cause infection; however, further studies are needed to determine the clinical usage of the Surgicel to prevent postoperation bleeding and infection.

Limitation

The empirical results reported herein should be considered in light of some limitations. The small sample size and the use of a single center are the limitations of this study, which may change the accuracy of the results of the pres-

ent study. It would be better to repeat the survey for medical centers to have more sample size to increase the precision of results.

Acknowledgements

The research team would like to thank the individuals who participated in this study. This study was financially supported by funds from the Department of urology, Tabriz University of Medical Sciences.

Disclosure of conflict of interest

None.

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