Int J Physiol Pathophysiol Pharmacol 2021;13(5):132-139
www.ijppp.org /ISSN:1944-8171/IJPPP0137144

Original Article

Enhanced recovery open radical prostatectomy: costs and length of hospital stay

Thiago C Travassos, João Carlos N Pereira, Edison DS Monteiro, Bárbara Brunca, Carolina M Figueiredo, Giovanna SC Mouawad, Leonardo O Reis

Pontifical Catholic University of Campinas (PUC Campinas), Center for Life Sciences, Postgraduate Program in Health Sciences and UroScience, Campinas, SP, Brazil

Received July 7, 2021; Accepted October 11, 2021; Epub October 15, 2021; Published October 30, 2021

Abstract: Purpose: To evaluate factors related to the length of hospital stay and costs in patients undergoing local multimodal anesthetic solution compared to neuraxial block, both in association with general anesthesia. Methods: This is a retrospective cohort study of 77 consecutive patients submitted to open radical prostatectomies: 42 under general anesthesia plus neuraxial block, and 35 under enhanced recovery multimodal general anesthesia associated with preemptive target anesthetic solution (3 phases-P.T.A.S). Mann-Whitney, Chi-square, and Spearman correlation were applied with a 5% significance level. Results: There were no statistically significant differences between the two groups. The cost was positively and significantly related to the pathological report (PR), anesthetic time, use of crystalloid, and total drain volume. Length of hospital stay was positively and significantly related to the use of crystalloids and total drain volume, with a strong correlation with the latter. Conclusion: There was no statistically significant difference between the studied groups; however, there was a tendency to reduce the length of stay in the multimodal anesthetic solution group that may be better evidenced in studies with greater sampling power.

Keywords: Enhanced recovery after surgery, international preemptive Eurasian program, 3-phases PTAS, open radical prostatectomy

Introduction

More than just a subjective response learned through objective sensation, pain is part of a larger context that involves surgical procedures. It is a biopsychosocial phenomenon that is related to suffering and to mediators whose importance involves the entire process of medical care, from the communication of the diagnosis, to the post-operative (including pre and intra-operative) [1, 2].

There is a difficult balance between pain control and awakening in a way that allows early activity. In this regard, several studies have shown that the combination of general anesthesia and local anesthesia can improve postoperative results through synergistic effects on the pain path [3-10].

A recent meta-analysis including seven trials containing 784 prostate cancer patients showed that enhanced recovery after surgery (ERAS) can reduce length of hospital stay, time to flatus, time to defecate, time to ambulate, and time to remove drainage tube in prostate cancer patients who have undergone robotic assisted and laparoscopic radical prostatectomy compared with conventional care [11]. Also, the ERAS program was associated with a reduced hospitalization costs for patients undergoing minimally invasive radical prostatectomy [12], thought its impact on open radical prostatectomies is less clear.

This study innovates by comparing the data from patients who underwent open radical prostatectomies using enhanced recovery multimodal anesthetic solution (3 phases-PTAS) versus traditional neuraxial block, both in association with general anesthesia. We hypothesize that 3 phases-PTAS has potential to decrease costs and length of hospital stay and also evaluate to which clinical variables they might be correlated.

Methods

This is a retrospective study of consecutive patients operated for prostate cancer at a university hospital after local ethics committee approval (number 3.804.629).

Inclusion criteria: (a) histopathological diagnosis of prostate cancer; (b) open radical prostatectomy, with or without lymphadenectomy in the period from 06/01/2016 to 07/17/2018.

Exclusion criteria: (a) patients undergoing treatment modalities other than open surgery (e.g., laparoscopic); (b) metastatic prostate cancer; (c) insufficient and/or incomplete data in medical records.

Casuistic: Data from 117 patients undergoing radical prostatectomy for prostate cancer were selected, leaving 77 patients after applying the exclusion criteria. Of these, 42 underwent open radical prostatectomies from June 2016 to July 2017 using general anesthesia associated with a neuraxial block (NB) while 35 from August 2017 to July 2018 using general anesthesia associated with preemptive target anesthetic solution (3 phases-PTAS) in the context of E.R.A.S. protocol.

The 3 phases-PTAS consists of a multimodal solution of drugs, with synergistic action, for adequate pain control. The drugs used and their doses are: Ropivacaine 10 mg/ml (20 ml), Clonidine (1 ug/Kg), Chlorpromazine 25 mg, Sodium Bicarbonate 8.4%, 40 ml, Ketamine 10 mg, Hydrocortisone 500 mg, Dexamethasone 10 mg, 10% Magnesium Sulfate (1 ml); all diluted in 500 ml of 0.9% saline solution. 3-phases refers to the fact that the solution is infiltrated in all layers of the abdominal wall: skin, fascia, and muscles, to extend the sensory block to all planes of the surgical aggression site.

Data recovery: data were collected from the Patient Record Service and organized in tabular form for later statistical analysis. Data regarding age, weight, height, ASA, type of anesthesia, surgical time, and crystalloid infusion were obtained directly from the surgical form, present in each patient's medical record. Other data regarding the surgery and hospitalization, such as the number of days of hospitalization and drainage output volume, were obtained from the information recorded in the daily control forms and from those described in the patient's medical records.

We defined "open radical prostatectomy" in the context of this study as the surgical retro-pubic extirpation of the prostate gland due to a histopathological diagnosis of prostate cancer according to the Walsh technique.

All patients were admitted on the same day of the surgery, a few hours beforehand, thus "length of stay" was defined as the total hospitalization time for the surgical procedure and postoperative recovery, starting from the day of admission/surgical procedure until the day of drain removal and discharge.

Total cost was defined as the "total value" in Reais (R$), referring to the number of days, the procedure performed, medications, and materials dispensed for patient care, obtained from the hospital financial department.

Regarding other variables studied; "ISUP" refers to the International Society Of Urological Pathology (ISUP) consensus for prostate cancer grading, in which the traditional classification of prostate tumors based on Gleason criteria (<6, 3+4 = 7, 4+3 = 7, 8, and 9-10) is now classified into five groups by the ISUP consensus (e.g., ISUP 1, ISUP 2) to facilitate patient communication and understanding and better predict the outcome of interventions [13]. "PSA" (prostatic-specific antigen) refers to the blood marker, organ-specific, used in prostate cancer screening and follow-up.

To assess the severity of the disease and identify possible selection biases we subdivided the patients into PSA values <20 and greater than 20 because the last one is related to higher risk disease by D'Amico's classification system. The same rationale was used to classify the groups according to the clinical stage (using the TNM, Tumor, Node, Metastasis classification for malignant tumors of the UICC, The Union for International Cancer Control), with all patients with palpable nodules on digital prostate examination being ≥T2 [14-16].

"ASA" was defined as the physical status classification system adopted by the American Society of Anesthesiology. Crystalloid use was defined as the infusion of 0.9% saline solution

or ringer lactate; total drain, as the daily sum of drain volume, in milliliters (from the day of surgery to discharge) and lymphadenectomy as extirpation of pelvic lymph nodes in the surgical description.

Data analysis: Exploratory data analysis was performed using summary measures (mean, standard deviation, minimum, median, maximum, frequency, and percentage). To compare the two anesthesia groups the Mann-Whitney test (numerical variables) or the Chi-square test (categorical variables) were used.

Spearman's correlation coefficient was used to evaluate the correlation of cost and length of stay with clinical variables, rho coefficient (r^2) -1 to +1 classified as: "very weak": .00-.19; "weak": .20-.39; "moderate": .40-.59; "strong": .60-.79; and "very strong": .80-1.0 [17].

The level of significance adopted was 5%.

Results

Clinical features regarding patients and tumor characteristics are summarized and compared in **Table 1**. There were no statistical differences between the two groups for the analyzed characteristics; thereby it was not necessary to adjust the comparison between groups for cost and length of hospital stay for any of these variables.

The mean surgical and anesthesia time were 240.42 and 287.85 minutes in the 3PPTAS group and 232.87 and 293 minutes in the NB group, respectively. Pelvic lymphadenectomy occurred in 46% and 48% of 3PPTAS and NB, respectively. The intraoperative mean use of crystalloid solutions and mean drain volume during hospitalization were 2800.00 and 362.37 mL in the 3PPTAS and 3157.85 and 569.21 mL in the NB group, respectively.

The 3PPTAS group hospitalization time and costs were 2.77 days, and R$ 7255.93, while the NB group 3.19 days, and R$ 7307.40, respectively (**Figure 1**).

Table 2 presents the Spearman correlation coefficient between hospitalization time and costs and the quantitative variables (coefficients in bold are statistically different). Cost positively correlated with ISUP, anesthesia time, volume of crystalloids, and total drain volume. Length of hospital stay positively correlated with crystalloids and total drain, and the correlation with drain volume is strong.

Table 3 presents the comparison of cost and hospitalization time between the categories of qualitative variables studied. Both cost (*P*-value = 0.003) and hospitalization time (*P*-value = 0.021) are higher in the lymphadenectomy group.

Considering the 5% significance level, the sample power to verify the difference between the two groups concerning cost was 3.6% and to verify the difference between the groups about length of hospital stay 46.9%. The minimum number of patients in each group, to verify the difference between the groups, about cost, would be 16,785, while concerning the length of stay this value would be lower, 84 patients.

Discussion

The groups were clinically homogeneous in terms of age, comorbidities, and ASA score. It was noted, however, that the average age of patients diagnosed and treated for prostate cancer was lower than those found in the literature, 62-63 years versus 65 years, respectively [18].

Regarding tumor characteristics and severity classification, there was also homogeneity between groups, with no statistically significant difference in PSA values >20 ng/mL (higher risk) and presence of palpable tumor at rectal examination (cT2) at the time of diagnosis. Confronting the internal data with the literature, 9% (NB group) to 20% (3PPTAS group) of patients had PSA >20 ng/mL, while the study by Erickson *et al*., showed a prevalence of this value of 12.3% [19]. Non-palpable tumors (T1) correspond to 60 to 75% of diagnosed cancers [20], while in the present study T1 stage tumors corresponded from 37% to 52%, in the 3PPTAS and NB groups, respectively, with the majority of tumors being palpable at the time of diagnosis.

It is worth mentioning that the physical examinations were performed by a series of different examiners with heterogeneous levels of training; however, both groups were subjected to

Table 1. Comparison between the two anesthesia groups (Mann-Whitney or Chi-square test)

Variable	3 phases-PTAS						*P*-value
	Total (N = 77)		No (N = 42)		Yes (N = 35)		
	Mean (SD)	Med [Min; Max]	Mean (SD)	Med [Min; Max]	Mean (SD)	Med [Min; Max]	
Age	63.3 (6.42)	64.0 [50.0; 75.0]	62.9 (6.57)	63.0 [50.0; 75.0]	63.9 (6.29)	65.0 [50.0; 75.0]	0.591
ISUP (Bx)	2.21 (1.06)	2.00 [1.00; 4.00]	2.26 (1.08)	2.00 [1.00; 4.00]	2.14 (1.03)	2.00 [1.00; 4.00]	0.650
ASA	2.00 (0.43)	2.00 [1.00; 3.00]	2.00 (0.38)	2.00 [1.00; 3.00]	2.00 (0.49)	2.00 [1.00; 3.00]	1.000
Anesthetic time	291 (58.6)	285 [180; 450]	293 (64.0)	285 [180; 450]	288 (52.4)	270 [210; 375]	0.894
Crystalloids	2995 (911)	3000 [1000; 5500]	3158 (909)	3000 [2000; 5500]	2800 (887)	2500 [1000; 5000]	0.086
Drain output	475 (934)	186 [20.0; 7166]	569 (1188)	192 [23.0; 7166]	362 (472)	185 [20.0; 2238]	0.751
Costs	7284 (2258)	6816 [3796; 14130]	7307 (2312)	6887 [4793; 14130]	7256 (2225)	6639 [3796; 12857]	0.894
Hospital stay	3.00 (1.25)	3.00 [1.00; 8.00]	3.19 (1.27)	3.00 [2.00; 8.00]	2.77 (1.19)	2.00 [1.00; 6.00]	0.062
PSA >20							0.285
No	66 (88.0%)		38 (92.7%)		28 (82.4%)		
Yes	9 (12.0%)		3 (7.32%)		6 (17.6%)		
Digital Rectal Examination ≥T2							0.188
No	35 (47.9%)		22 (56.4%)		13 (38.2%)		
Yes	38 (52.1%)		17 (43.6%)		21 (61.8%)		
Comorbidities							0.395
No	16 (24.2%)		7 (18.9%)		9 (31.0%)		
Yes	50 (75.8%)		30 (81.1%)		20 (69.0%)		
Lymphadenectomy							1.000
No	40 (52.6%)		22 (52.4%)		18 (52.9%)		
Yes	36 (47.4%)		20 (47.6%)		16 (47.1%)		

Numerical variables are summarized as mean (standard deviation) in the first column and median [Minimum; Maximum] in the second column. Qualitative variables are summarized in the form of frequency (percentage). ISUP: international Society of Uropathology. Bx: Prostate biopsy. ASA: American Society of Anesthesiology comorbidity index. PSA: Prostate Specific Antigen.

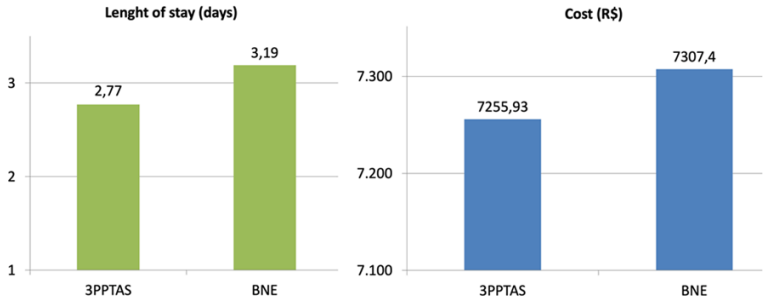

Figure 1. Average length of stay and cost of hospitalization. 3PPTAS (3 phases-PTAS); NB (neuraxial block).

the same variation, reducing the importance of this fact as a selection bias.

From the surgical point of view, there were no significant differences between the groups regarding anesthetic time, use of crystalloids, or even the total value of postoperative secretion drainage; however, these three factors showed a positive correlation with the total cost involved. This relationship between anesthetic time and the cost was also observed by Hu & He in 2015 when comparing the use of varying doses of propofol for performing radical gastrectomy and also Macario *et al.*, who estimated that 3% of the total costs of a patient undergoing a surgical procedure are in the hands of the anesthesiologists [21, 22].

It can be inferred, in a more objective way, that longer anesthetic time will demand greater use of intraoperative medications that may be related to increased costs. However, considering the rationale involved in optimized postoperative recovery protocols, it must be noted that longer anesthetic time is also related to longer exposure to low operating room temperatures, greater infusion of crystalloids and drugs to prolong anesthesia. All these factors delay recovery in the immediate postoperative period, retarding ambulation and diet and influencing to increase the final hospitalization time and costs involved. On the other hand, longer anesthetic time can also be related to more complicated and difficult surgeries that can influence recovery time, hospitalization, and consequently costs.

In addition to its relationship with costs, the use of crystalloids has also shown a direct relationship with the length of stay. Doherty and Buggy demonstrated that the decision of the fluid infusion therapy (restricted versus liberal) can influence postoperative results. The liberal option involved the use of volumes ranging from 2700 to 5400 mL while in the restricted model volumes ranged from 998 to 2740 mL, similar to the values obtained in the present study [23].

One of the steps within the E.R.A.S. model is precisely the rational use of crystalloids to maintain the normovolemia of patients, reducing interstitial edema. As well as the possible relationship already described, as a consequence of longer anesthetic time, the excessive use of crystalloids can increase the extravasation of liquids into the third space, leading, for example, to intestinal and pulmonary interstitial edema. The first, by being directly related to peristalsis, influences in a way to reduce gastrointestinal transit and bowel movements, causing discomfort to the patient, reducing mobility and increasing hospitalization time and consequently costs. The pulmonary interstitial edema can be related to the decrease of expansibility and atelectasis, factors related to the postoperative outcome of patients [24].

For the drain volume, the relationship between the total volume during hospitalization and the length of hospital stay in days was somewhat expected. The drain is one of the major limiting factors for the discharge of patients submitted to radical prostatectomies and, although some institutions nowadays adopt hospital discharge with drain, it is still an important limiting factor for discharge. The point is that, probably, the drain volume is related more to the operative technique than to the protocol used. It can be observed that in the group of patients undergoing lymphadenectomy, in which drainage is expected in larger quantities, there was an increase in length of stay and costs. Lymphadenectomy, drain volume, length of stay, and costs are related and probably independent of the type of anesthetic protocol used.

Despite a tendency of correlation within the study for the length of stay and the multimodal solution, there was no statistically significant

Table 2. Spearman's correlation coefficient of the outcome variables with the other numerical variables (marked coefficients are statistically significant)

	Age	ISUP (Bx)	ASA	Anesthesia Time	Crystalloids	Drain output
Costs	0.16	0.35*	0.14	0.39*	0.34*	0.43*
Hospital Stay	0.03	0.19	0.01	0.25	0.34*	0.70*

ISUP: international Society of Uropathology. Bx: Prostate biopsy. ASA: American Society of Anesthesiology comorbidity index. *Statistically significant.

Table 3. Comparison of cost and length of stay among the categories of qualitative variables (Mann-Whitney test)

PSA >20		
No (N = 66)	Yes (N = 9)	*P*-value
6782 [3796; 13146]	6987 [4805; 14130]	0.536
3.00 [1.00; 8.00]	3.00 [2.00; 7.00]	0.918
Digital Rectal Examination ≥T2		
No (N = 35)	Yes (N = 38)	*P*-value
6414 [3796; 11884]	6928 [4805; 13146]	0.164
3.00 [1.00; 5.00]	3.00 [2.00; 8.00]	0.519
Comorbidities		
No (N = 16)	Yes (N = 50)	*P*-value
5914 [3796; 12857]	7030 [4805; 14130]	0.088
3.00 [1.00; 6.00]	3.00 [2.00; 8.00]	0.679
Lymphadenectomy		
No (N = 40)	Yes (N = 36)	*P*-value
6017 [3796; 11884]	7161 [4805; 14130]	0.003
2.50 [1.00; 5.00]	3.00 [1.00; 8.00]	0.021

Median [Minimum; Maximum]. PSA: Prostate Specific Antigen.

difference between groups regarding the total time of hospitalization and costs, the main motivators of this work. Especially for costs, even adjusting the results to the sample power it seems to be no direct difference at all.

It should be considered that while perhaps reflecting-in larger sample studies-a decrease in length of stay, the consequent reduction in cost, in the enhanced recovery 3PPTAS group, may be outweighed by the variety of drugs used in the solution composition. This analysis, although, seems too simplistic and studies with greater statistical power and causal correlation need to be conducted.

An important flaw to be considered in the present work was the lack of a more detailed analysis of the pain in patients submitted or not to the enhanced recovery solution. However, as usual, in many retrospective studies, there was not enough reliable and objective data for this evaluation. In the vast majority of cases, pain assessment was described using subjective and non-comparable criteria (e.g., mild pain, moderate pain) and not evaluated using standardized pain scales (e.g., analog and visual pain scale).

It is already clear that patients undergoing E.R.A.S. protocols have faster recovery, with less postoperative morbidity and more quality recovery; with impact also on patient satisfaction with the services that provide them care and with the professionals involved. The main question to be answered in future studies is how these protocols can be used and adapted to the reality of urologic surgeries.

Limitations of current study are related to the retrospective design, relatively small number of patients and single center experience. It is also important to emphasize that "the solution is not the solution". It is part of a process that begins in the preoperative period, through the better insertion of the individual in his or her treatment process; and postoperative care that enables early mobilization and patient autonomy. The solution is, therefore, a bridge to movement, and movement is anti-nausea, anti-constipation, anti-atelectasis, anti-thrombosis; factors related to a decrease in hospitalization time.

Conclusion

There was no statistically significant difference between the groups studied and it is not possible to affirm that the use of the enhanced recovery 3 phases-PTAS solution effectively reduces the length of hospital stay or costs. However, a tendency towards a reduction in hospital stay was observed in the multimodal anesthetic solution that may be better evidenced in studies with larger sample size.

Acknowledgements

To the involved institution(s), the patients, and those that provided and cared for study patients. CNPq Research Productivity, Brazil - grant: 304747/2018-1 (Reis LO).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Leonardo O Reis, UroScience, University of Campinas and Pontifical Catholic University of Campinas, Av. John Boyd Dunlop, Jardim Ipaussurama, Campinas 13034-685, SP, Brazil. Tel: +19-3343-8600; E-mail: reisleo.l@gmail.com

References

[1] Melnyk M, Casey RG, Black P and Koupparis AJ. Enhanced recovery after surgery (eras) protocols: time to change practice? Can Urol Assoc J 2011; 5: 342-8.

[2] Moseley GL and Butler DS. Fifteen years of explaining pain: the past, present, and future. J Pain 2015; 16: 807-13.

[3] Kaufman E, Epstein JB, Gorsky M, Jackson DL and Kadari A. Preemptive analgesia and local anesthesia as a supplement to general anesthesia: a review. Anesth Prog 2005; 52: 29-38.

[4] Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ and Wu CL. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of anesthesiologists committee on regional anesthesia, executive committee, and administrative council. J Pain 2016; 17: 131-57.

[5] Chakravarthy M. Regional analgesia in cardiothoracic surgery: a changing paradigm toward opioid-free anesthesia? Ann Card Anaesth 2018; 21: 225-227.

[6] Renghi A, Gramaglia L, Casella F, Moniaci D, Gaboli K and Brustia P. Local versus epidural anesthesia in fast-track abdominal aortic surgery. J Cardiothorac Vasc Anesth 2013; 27: 451-8.

[7] Soffin EM, Wetmore DS, Beckman JD, Sheha ED, Vaishnav AS, Albert TJ, Gang CH and Qureshi SA. Opioid-free anesthesia within an enhanced recovery after surgery pathway for minimally invasive lumbar spine surgery: a retrospective matched cohort study. Neurosurg Focus 2019; 46: E8.

[8] Li C, Qu J, Pan S and Qu Y. Local infiltration anesthesia versus epidural analgesia for postoperative pain control in total knee arthroplasty: a systematic review and meta-analysis. J Orthop Surg Res 2018; 13: 112.

[9] Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalez M, Ljungqvist O, Petersen RH, Popescu WM, Slinger PD and Naidu B. Guidelines for enhanced recovery after lung surgery: recommendations of the enhanced recovery after surgery (ERAS®) society and the European society of thoracic surgeons (ESTS). Eur J Cardiothorac Surg 2019; 55: 91-115.

[10] Williams JB, McConnell G, Allender JE, Woltz P, Kane K, Smith PK, Engelman DT and Bradford WT. One-year results from the first US-based enhanced recovery after cardiac surgery (ERAS cardiac) program. J Thorac Cardiovasc Surg 2019; 157: 1881-1888.

[11] Zhao Y, Zhang S, Liu B, Li J and Hong H. Clinical efficacy of enhanced recovery after surgery (ERAS) program in patients undergoing radical prostatectomy: a systematic review and meta-analysis. World J Surg Oncol 2020; 18: 131.

[12] Ye Z, Chen J, Shen T, Yang H, Qin J, Zheng F and Rao Y. Enhanced recovery after surgery (ERAS) might be a standard care in radical prostatectomy: a systematic review and meta-analysis. Ann Palliat Med 2020; 9: 746-758.

[13] Egevad L, Delahunt B, Srigley JR and Samaratunga H. International society of urological pathology (ISUP) grading of prostate cancer-an ISUP consensus on contemporary grading. APMIS 2016; 124: 433-5.

[14] Ross AE and Rodriguez R. Development, molecular biology, and physiology of the prostate. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, editors. Campbell-Walsh urology. 11th ed. Philadelphia; 2016. pp. 2393-424.

[15] Reis LO, Travassos T da C, Andrade DL and Gon LM. Biomarcadores no Câncer de Próstata. In: Carvalhal GF, Nogueira L, editors. PROUROLOGIA-Sociedade Brasileira de Urologia. Ciclo 2. Porto Alegre: Artmed Panamericana; 2020. pp. 71-95.

[16] Reis LO, Simão AF, Baracat J, Denardi F and Gugliotta A. Digital rectal examination standardization for inexperienced hands: teaching medical students. Adv Urol 2013; 2013: 797096.

[17] Laranja WW, Pereira TA, Guimarães PVB, Tobias-Machado M, Leandro-Merhi VA, de Aquino JLB and Reis LO. Do rapid emotional thermometers correlate with multidimensional validated structured questionnaires in low-risk pros-

tate cancer? Int Urol Nephrol 2020; 52: 1073-1078.
[18] Rawla P. Epidemiology of prostate cancer. World J Oncol 2019; 10: 63-89.
[19] Erickson A, Sandeman K, Lahdensuo K, Nordling S, Kallajoki M, Seikkula H, Bützow A, Vasarainen H, Boström PJ, Taimen P, Rannikko A and Mirtti T. New prostate cancer grade grouping system predicts survival after radical prostatectomy. Hum Pathol 2018; 75: 159-166.
[20] Stephenson AJ and Klein EA. Epidemiology, etiology, and prevention of prostate cancer. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, editors. Campbell-Walsh urology. 11th ed. Philadelphia: Elsevier; 2016. pp. 2542-64.
[21] Hu J and He Z. Cost of general anesthesia during radical gastrectomy using different specifications of propofol: cost-minimization analyses. Int J Clin Exp Med 2015; 8: 21266-78.
[22] Macario A, Vitez TS, Dunn B and McDonald T. Where are the costs in perioperative care? Analysis of hospital costs and charges for inpatient surgical care. Anesthesiology 1995; 83: 1138-44.
[23] Doherty M and Buggy DJ. Intraoperative fluids: how much is too much? Br J Anaesth 2012; 109: 69-79.
[24] Brandstrup B. Fluid therapy for the surgical patient. Best Pract Res Clin Anaesthesiol 2006; 20: 265-83.