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Original Article

Effect of multimodal analgesia on gynecological cancer patients after radical resection

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Abstract: Objective: This research was designed to probe into the effect of multimodal analgesia on gynecological cancer patients after radical resection. Methods: Ninety-eight cervical cancer patients undergoing laparoscopic radical resection in our hospital were included. Thereinto, 47 in the research group (RG) were given multimodal analgesia, and 51 in the control group (CG) were given conventional postoperative analgesia. The time of operation, anesthesia recovery room observation and extubation, postoperative NRS pain score, and the clinical manifestations of both groups were observed. The activity within three days after operation, the incidence of postoperative complications, hospitalization time and quality of life of both groups were compared. Results: The operation time of the RG was higher than that of the CG ($P < 0.05$), and the time of observation and extubation in the anesthesia room were lower than those in the CG ($P < 0.05$); the NRS pain score was lower than that of the CG ($P < 0.05$); the first time to get out of bed, and time of exhaust and diet were shorter than those of the CG ($P < 0.05$); the activity was better than that of the CG within three days after operation ($P < 0.05$); the incidence of complications was markedly lower than that in the CG ($P < 0.05$); the hospitalization time was shorter than that of the CG ($P < 0.05$); the postoperative quality of life was shorter than that in the CG ($P < 0.05$). Conclusion: Multimodal analgesia is safe and effective for patients after laparoscopic radical resection of gynecological malignancies, which can speed up the recovery of diseases and improve the quality of life. Thus, it is worthy of clinical application.

Keywords: Multimodal analgesia, laparoscopic radical hysterectomy for gynecological malignancies, analgesic effect, safety

Introduction

Cervical cancer (CC), endometrial cancer (EC), hysteromyoma and ovarian cancer (OC) are familiar gynecological tumors, which seriously threaten patients' lives and physical and mental health [1]. With the change of people's living habits, the morbidity has been on the rise [2], bringing a certain burden to the family and even the society. Surgery has always been the main treatment for gynecological tumors in early and middle stages [3]. However, the traditional open surgery produces great trauma, has long recovery time, and causes complications and poor postoperative prognosis [4]. The emergence of laparoscopic minimally invasive surgery will gradually replace it [5]. Compared with traditional surgery, laparoscopic surgery is popular, with less trauma, small incision, quick recovery, clear vision and less bleeding, which not only shows obvious advantages in treatment [6], but also greatly shortens the postoperative recovery time and speeds up the treatment progress [7]. Therefore, at the moment, most gynecological malignancies are completed under laparoscopy, which has been recognized by the majority of patients and medical workers [8]. Previous research data manifested that postoperative analgesia was a serious problem that was easily overlooked after gynecological laparoscopic surgery. Improper treatment of postoperative pain might delay patients' activities, prolong hospital stay and reduce their satisfaction [9]. It was reported that good analgesia could accelerate the recovery of diseases and avoid complications; otherwise, it

might affect the quality of life of patients for a long time [10]. Therefore, it is vital to pay attention to postoperative analgesia and choose appropriate analgesia methods for patients' recovery.

In recent decades, after various operations, continuous or bolus injection of different opioids has been widely used for patient-controlled analgesia; the side effects related to analgesia are also increasing, such as respiratory depression, itching, hallucination and postoperative nausea and vomiting [11]. The multimodal analgesia recommended by the concept of accelerated rehabilitation surgery has been well received in clinical practice [12]. It blocks different pain targets by different methods and drugs [13]. Huang et al. [14] proposed that multimodal analgesia has a positive effect on the rehabilitation of CC patients. In addition, Zhang [15] also pointed out that it could effectively reduce the pain degree of patients after gastric cancer surgery and speed up recovery. Based on the above analyses, we hypothesize that the application of multimodal analgesia in the recovery of patients with gynecological malignancies after radical resection may have unexpected effects. Thus, this research explores and analyzes the analgesic effect and safety of multimodal analgesia on patients with laparoscopic radical resection of gynecological malignancies, with the hope to provide practical guidance for future clinical practice.

Materials and methods

Data

From January 2016 to March 2019, 98 CC patients underwent laparoscopic radical resection in Tangshan People's Hospital were included. The experiment was approved by the ethics committee of our hospital. They were randomized into two groups. Research group (RG): 47 received multimodal analgesia; control group (CG): 51 received routine postoperative analgesia. All subjects signed informed consent, and the study was conducted in strict accordance with the Declaration of Helsinki.

Inclusion and exclusion criteria

Inclusion criteria were as follows: All patients were diagnosed as CC for the first time in our hospital and received follow-up treatment; the diseases were in early and intermediate stages; they were treated with laparoscopic radical resection; all patients and their families agreed to take part in the experiment and signed an informed consent form.

Exclusion criteria were as follows: those with drug allergy, other malignant diseases, impaired physical function, communication disorder and low cooperation.

Methods

All the patients were treated by the same surgeon, and the same drugs and doses were used for preoperative anesthesia.

CG: the operating room was prepared, the vital signs were monitored routinely, and patients were induced by general anesthesia; they took no pain prevention drugs before the operation, and controlled intravenous analgesia was provided after the operation. Fentanyl 0.8 mg+100 mL normal saline was dripped into the peripheral vein every hour, 2 mL per hour, and the dosage of single intravenous self-control was 1 mL, lasting for 48 h.

RG: the operating room was prepared, the vital signs were monitored routinely, and patients were induced by general anesthesia; flurbiprofen axetil 50 mg was injected intravenously before operation for preventive analgesia, 0.5% ropivacaine was given for local incision infiltration, and controlled intravenous analgesia was provided after operation; flurbiprofen axetil 100 mg, sufentanil 100 μg and morphine 2 mg were added into 100 mL normal saline twice a day, and the dosage of single intravenous self-control was 1 mL, lasting for 48 h.

Outcome measures

The time of operation, anesthesia recovery observation and extubation of patients in both groups were observed, and the NRS pain scores [16] on the first, the second and the third days after operation were assessed. The time of getting out of bed, air-out and eating were compared, and the activities of patients within three days after operation were evaluated via functional activity score method (FAS) [17]. The incidences of complications after surgery were

Table 1. General data table [n (%)]

	Research group (n=47)	Control group (n=51)	t or χ^2	P
Age (years)	49.8±5.6	49.2±5.9	0.608	0.515
BMI (KG/cm^2)	25.52±3.05	26.46±4.72	1.160	0.249
Living environment			0.059	0.808
Towns	34 (72.34)	38 (74.51)		
Countryside	13 (27.66)	13 (25.49)		
History of smoking			0.029	0.865
Yes	14 (29.79)	16 (31.37)		
No	33 (70.21)	35 (68.63)		
History of drinking			0.133	0.715
Yes	25 (53.19)	29 (56.86)		
No	22 (46.81)	22 (43.14)		
Nationality			0.170	0.680
Han	41 (87.23)	43 (84.31)		
Ethnic minorities	6 (12.77)	8 (15.69)		
Have children or not			0.088	0.767
Yes	38 (80.85)	40 (78.43)		
No	9 (19.15)	11 (21.57)		
ASA grading			0.003	0.954
Grade I	27 (57.45)	29 (56.86)		
Grade II	20 (42.55)	22 (43.14)		
TNM staging			0.145	0.704
Stage I	24 (51.06)	28 (54.90)		
Stage II	23 (48.94)	23 (45.10)		
Hypertension			0.097	0.756
Yes	17 (36.17)	20 (39.22)		
No	30 (63.83)	31 (60.78)		

analyzed, and the hospitalization time and quality of life of patients were compared by the FACT-Cx score of CC quality of life scale [18].

Statistical methods

The experimental results were statistically analyzed using SPSS24.0 (Shanghai Yuchuang Network Technology Co., Ltd.), and all the graphical results were drawn via Graphpad8 (Shenzhen Qiruitian Software Technology Co., Ltd.). The counting data were expressed in (%), and inter-group comparison was assessed by Chi-square test. The measurement data were represented as mean ± standard deviation, and the inter-group comparison was made by t test. The comparison among multiple groups was analyzed by one-way analysis of variance (ANOVA) and LSD post hoc testing, and that among multiple time points was evaluated by repeated measures ANOVA and Bonferroni post hoc testing. $P < 0.05$ revealed that the difference was statistically significant.

Results

General data of patients

There was no difference in age, BMI, living environment, history of smoking and drinking, nationality, childbirth, ASA grade, TNM stage and hypertension of patients between the two groups ($P > 0.05$) (**Table 1**).

Comparison of time of operation, anesthesia recovery observation and extubation of patients between the two groups

Comparing the perioperative conditions between the two groups, we found that the operation time of the RG was longer than that of the CG ($P < 0.05$), while the time of observation and extubation of the anesthesia room of the CG were higher than those of the RG ($P < 0.05$) (**Figure 1**).

NRS pain scores on the first, the second and the third days after operation in the two groups

The pain of both groups on the first, the second and the third days after operation were evaluated via the NRS pain scores. The results manifested that the pain scores decreased with the increase of time, and the scores of the RG were lower than those of the CG on the first, the second and the third days after operation ($P < 0.05$) (**Figure 2**).

Comparison of first time of getting out of bed, exhausting and eating time between the two groups after operation

Comparing the first time of getting out of bed, exhausting and eating time between the two groups, we found that the times in the RG were shorter than those in the CG ($P < 0.05$) (**Figure 3**).

Comparison of activities of patients between the two groups within three days after operation

Comparing the activities of patients in the two groups within three days after operation, we

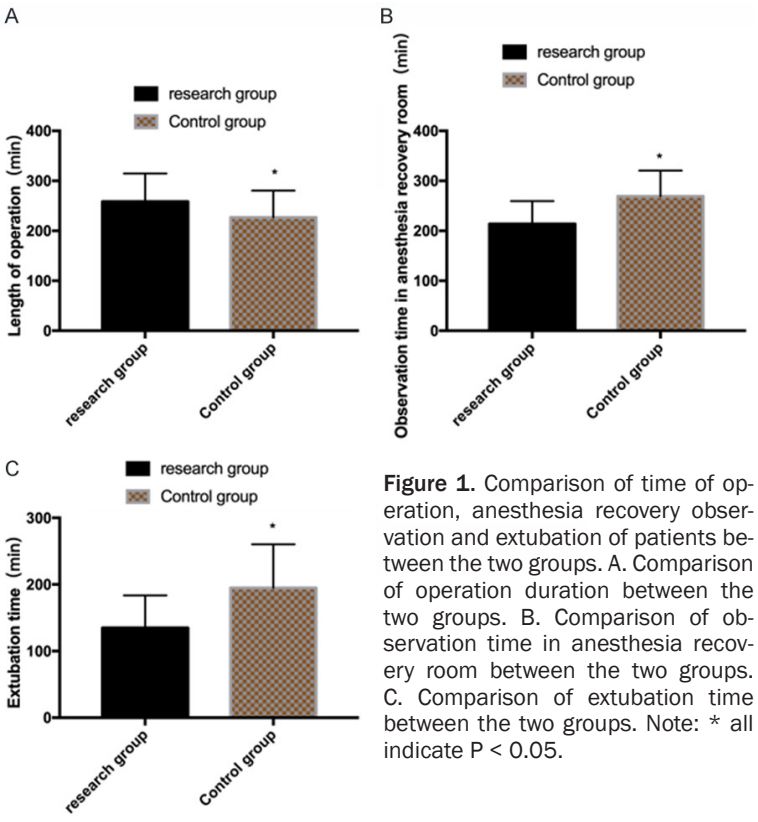

Figure 1. Comparison of time of operation, anesthesia recovery observation and extubation of patients between the two groups. A. Comparison of operation duration between the two groups. B. Comparison of observation time in anesthesia recovery room between the two groups. C. Comparison of extubation time between the two groups. Note: * all indicate P < 0.05.

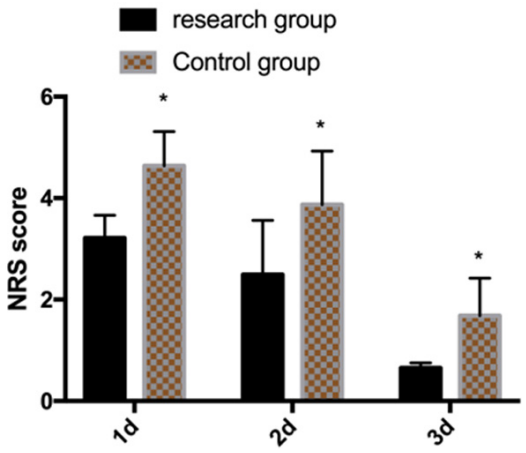

Figure 2. NRS pain scores on the first, the second and the third days of patients after operation in both groups. Note: * all indicate P < 0.05.

discovered that the total activity time, frequency and distance in the RG were higher than those in the CG (P < 0.05) (**Figure 4**).

Comparison of postoperative complications between the two groups

Comparing the incidence of postoperative complications between the two groups, we discovered that the number of vomiting, fever and chills in the CG was markedly higher than that in the RG; the total incidence of complications in the CG was 37.25%, while that in the RG was 17.02%, which was dramatically lower than that in the CG (P=0.025) (**Table 2**).

Hospitalization time and quality of life scores of patients in the two groups

The hospitalization time and quality of life of both groups were recorded and compared. And the results showed that the hospitalization time of the RG was shorter than that of the CG (P < 0.05), and the postoperative quality of life scores of the RG were higher than those of the CG (P < 0.05) (**Figure 5**).

Discussion

CC is the most familiar and prone malignancy in gynecological tumors, which has become a burden for women all over the world [19]. It is reported that the annual morbidity and mortality are higher [20]. Lack of awareness, ineffective screening procedures, and lack of attention to women's health are important factors leading to the rising incidence of gynecological tumors such as CC [21]. The biggest obstacle to effective treatment of gynecological tumors is still the delay of diagnosis and treatment [22]. Open total resection is one of the most commonly used methods for treating gynecological tumors such as early CC, but the complications caused by surgery have always plagued the quality of life of patients [23]. With the advancement of medicine, minimally invasive surgery is becoming more and more popular. It has been proved that the recovery of patients after radical laparoscopic surgery is obviously better than that of those undergoing open surgery [24]. However, with the continuous improvement of the efficacy, many scholars have found that the pain of patients after radical laparoscopic surgery is easy to be ignored, which is easy to cause dissatisfaction with the treatment effect and reduce the efficacy [25]. Multimodal analgesia has been mentioned in

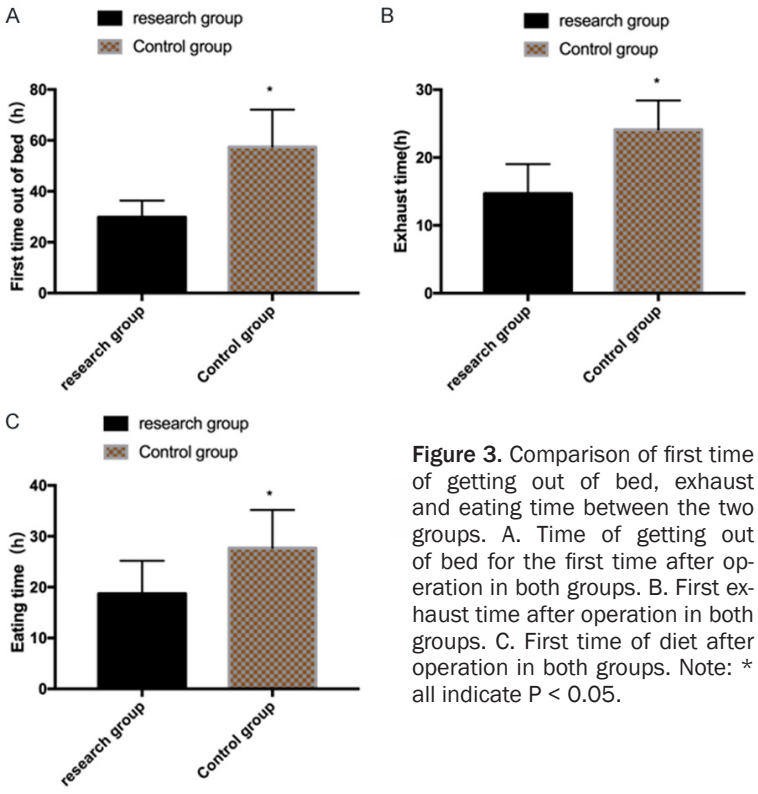

Figure 3. Comparison of first time of getting out of bed, exhaust and eating time between the two groups. A. Time of getting out of bed for the first time after operation in both groups. B. First exhaust time after operation in both groups. C. First time of diet after operation in both groups. Note: * all indicate $P < 0.05$.

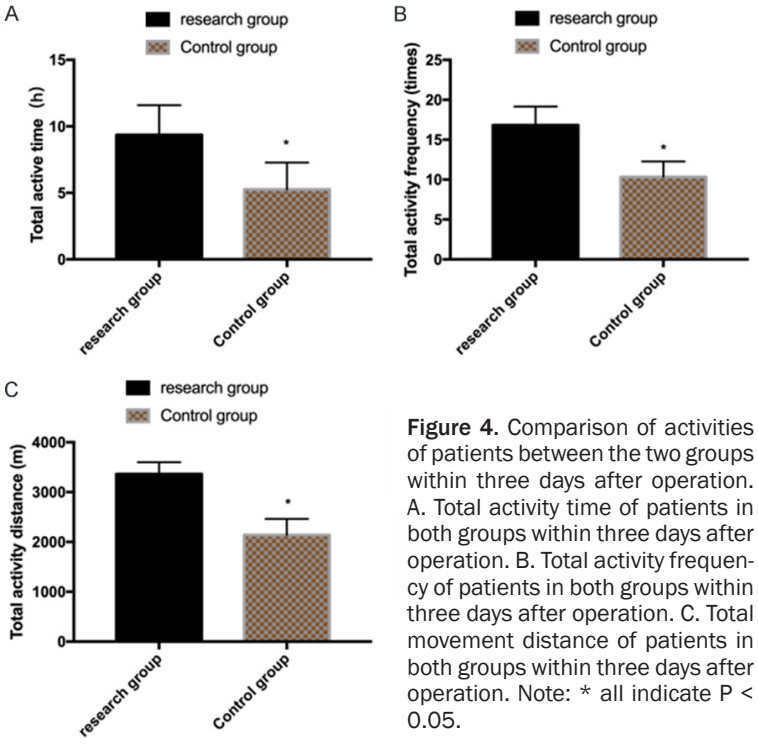

Figure 4. Comparison of activities of patients between the two groups within three days after operation. A. Total activity time of patients in both groups within three days after operation. B. Total activity frequency of patients in both groups within three days after operation. C. Total movement distance of patients in both groups within three days after operation. Note: * all indicate $P < 0.05$.

many references to have good analgesic effect. Hence, this paper explored the influence of multimodal analgesia after laparoscopic radical surgery on gynecological tumors.

First of all, we compared the general data such as age, BMI, living environment, history of smoking and drinking, nationality, childbirth, ASA grade, TNM stage, hypertension, etc., and found that there was no difference between the two groups; it suggested that we could conduct follow-up experiments. We first compared the perioperative conditions, and found that the operation time of the RG was longer than that of the CG, while the times of observation and extubation of the CG were higher than those of the RG. It suggested that patients with multiple analgesia modes could recover quickly after operation. Multimodal analgesia is an active, objective, regular assessment of patients' pain and timely and effective analgesia for patients based on their own conditions; it reduces the additional side effects brought by more drug intake. Memtsoudis et al. [26] confirmed that multiple analgesia model could effectively improve the perioperative outcomes. It could support our experimental results. Then, the pain of both groups on the first, the second and the third days after operation was evaluated by the NRS pain scores. The results showed that the pain scores decreased with the increase of time, and the scores of the RG were lower than those of the CG on the first, the second and the third days after operation, suggesting that multiple analgesia model could effectively relieve the pain of patients and promote recovery. The main idea of multimodal analgesia is to prevent different pain conditions

Table 2. Incidence of postoperative complications in both groups

	Research group (n=47)	Control group (n=51)	X^2	P
Vomiting	3 (6.38)	8 (15.69)		
Fever	2 (4.26)	5 (9.80)		
Urinary retention	1 (2.13)	1 (1.96)		
Intestinal obstruction	1 (2.13)	1 (1.96)		
Chill	0 (0.00)	3 (5.88)		
Pulmonary infection	1 (2.13)	1 (1.96)		
Total	8 (17.02)	19 (37.25)	5.017	0.025

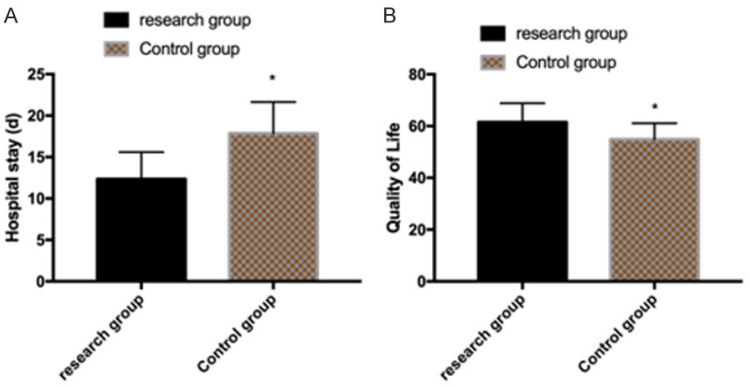

Figure 5. Hospital stay and quality of life scores of patients in both groups. A. Hospital stay of patients in both groups. B. Quality of life scores of patients in both groups. Note: * all indicate $P < 0.05$.

through different methods and drugs. Previous studies have shown that postoperative pain, especially after tumor surgery, cannot be alleviated; it will not only prolong the recovery time of patients, but also aggravate their anxiety, tension, anxiety, fear of uneasiness and other bad emotions, thus worsening their illness [27]. In this experiment, the pain scores of patients with multimodal analgesia were obviously superior to those with routine analgesia. Chang et al. [28] proved that multimodal analgesia could effectively reduce patients' sensitivity to pain, and it was more helpful to improve their compliance with later treatment, which supported this experiment. Then, we compared the first time of getting out of bed, exhaust and eating time of patients between the two groups. The results revealed that the times of patients in the RG were shorter than those in the CG, which further showed that multimodal analgesia could obviously promote the recovery of patients. Laparoscopic radical surgery is minimally invasive, but it is still invasive, which will inevitably cause some damage to patients, but most of them can be adjusted to return to normal. Multimodal analgesia, on the other hand, can directly relieve pain by taking targeted analgesia measures according to patients' pain conditions, to speed up the recovery of various physical functions after operation and then promote the recovery of diseases. We think that the value of multimodal analgesia may be that it will not only use opioids for pain relief, but will target inhibition based on self-conduction pain, thus reducing the use of opioids and the side effects caused by drugs. Comparing the activities of patients in the two groups within three days after operation, we found that the total activity time, frequency and distance of patients in the RG were higher than those in the CG, which further confirmed our above experimental results and reflected the value of multimodal analgesia. Next, we analyzed the incidence of postoperative complications in both groups. The results showed that the number of patients with vomiting, fever and chills in the CG was markedly higher than that in the RG; the total incidence of complications in the CG was 37.25%, while that in the RG was 17.02%, suggesting that multimodal analgesia was safe and more helpful for patients to recover. Cozowicz et al. [29] demonstrated that multimodal analgesia could effectively reduce postoperative complications and save resources, similar to our research results. Finally, the hospital stay and quality of life of both groups were recorded and compared. The results manifested that the hospital stay of the RG was shorter than that of the CG, and the postoperative quality of life score was higher than that of the CG. It further confirms our above conjecture and reflects its utility value. In addition, we also found that multimodal analgesia had high application value in spinal surgery and craniotomy [30, 31]. This further demonstrates the great potential of multimodal analgesia in future clinical application. Although there are few studies on the application of multimodal analgesia in radical gynecological surgery, Shen et al. [32] have pointed

out that multimodal analgesia has an excellent effect on abdominal and pelvic surgery, which also lays a good foundation for CC and OC among gynecologic tumors.

Conclusion

Multimodal analgesia is safe and effective for patients with gynecological malignancies after laparoscopic radical resection. It can speed up the recovery of disease and improve the quality of life, which is worthy of clinical application. However, there are still some shortcomings, such as short experimental time, failure of long-term follow-up investigation, and a small number of experiments. The experiment only focuses on CC, which has the highest incidence of gynecological tumors, and does not rule out differences when compared with other diseases. The above limitations will also be the focus of our future research. We will conduct a more comprehensive and effective experimental analysis on the application of multimodal analgesia in gynecological tumors as soon as possible, and provide more accurate guidance for clinical practice.

Disclosure of conflict of interest

None.

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