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ORIGINAL ARTICLE

Efficacy of on-pump coronary artery bypass grafting and stent implantation combined with surgery on lung cancer

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Summary

Purpose: *This study aimed to compare the application value of on-pump coronary artery bypass grafting (CABG) and stent implantation respectively combined with surgery for elderly patients with lung cancer and coronary heart disease (CHD).*

Methods: *69 elderly patients with lung cancer and CHD admitted to Liaoning Cancer Hospital and Institute from May 2010 to January 2014 were collected and analyzed retrospectively. Among them, 32 cases treated with on-pump CABG combined with lung cancer radical surgery served as group A, and the other 37 cases treated with coronary artery stent implantation combined with lung cancer radical surgery as group B. The total duration of operation, duration of lobectomy, intraoperative blood loss, thoracic drainage volume 24 h after surgery, hospital stay, postoperative complication rate, as well as pain scores before, 1 day after and 5 days after surgery in the two groups were compared.*

Results: *The duration of operation, duration of lobectomy, intraoperative blood loss, postoperative thoracic drainage volume and postoperative complications in group A were significantly higher than those in group B ($p<0.001$). The pain score in group B was significantly lower than that in group A at 1 day after surgery ($p<0.001$).*

Conclusion: *Stent implantation combined with surgery is safer than on-pump CABG combined with surgery in the treatment of elderly patients with lung cancer and CHD, but with a longer treatment duration. In clinical practice, careful consideration should be taken according to the actual situation of patients when selecting surgical treatment.*

Key words: *on-pump coronary artery bypass grafting, stent implantation, lung cancer and coronary heart disease, surgery, efficacy*

Introduction

Lung cancer is the most common primary malignant tumor of the lung, mostly beginning in the bronchial mucosal epithelium [1]. It is also one of the most common malignant tumors in the clinic at present with a high incidence rate [2]. The incidence is significantly higher in some regions with developed industries and large population base, such as China, than in other regions [3]. Furthermore, many research results at home and abroad [4,5] show that with the increase of motor vehicles and factories, the incidence of lung cancer is rising year by year, and the number of urban patients is significantly higher than that of rural ones. The pathogenesis is not yet clear, while its mortality

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rate ranks first among all malignant tumors [6]. Lung cancer is more common in the middle-aged and elderly people, but its incidence shows an increasing trend for the younger in recent years [7,8].

Coronary heart disease (CHD) is induced by myocardial ischemia, hypoxia or necrosis caused by stenosis or occlusion of vascular lumen due to coronary artery atherosclerosis, which is also one of the diseases with high incidence among the middle-aged and the elderly [9,10]. There are fewer cases of lung cancer complicated with CHD in clinical practice, but it is known to have a high death risk [11]. When dealing with such patients, it is not only necessary to complete the resection of tumor lesions, but also to deal with coronary artery lesions, which is extremely difficult to treat. At present, there are different clinical treatments for CHD, the most common of which are on-pump coronary artery bypass grafting (CABG) and stent implantation. On-pump CABG refers to the performance of distal vascular anastomosis with the aid of extracorporeal circulation machine under cardiac arrest, which makes the operation vision field clearer, the coronary artery better exposed, and the operation simpler [12]. However, in the stent implantation, the metal stent is permanently placed at the coronary artery lesion to support the vessel wall by balloon inflation or self-expansion in order to keep the coronary artery lumen open, thus preventing blockage due to local inflammatory reaction, thrombosis or intimal hyperplasia [13]. There is still no unified treatment plan for the choice of surgical methods and timing in clinic for patients with lung cancer and CHD due to lack of research worldwide. Therefore, this article aimed to provide effective and reliable references for future clinical treatment by analyzing the surgical effects of lung cancer and CHD patients admitted to Peking Union Medical College Hospital since 2010.

Methods

General data

Sixty-nine elderly patients with lung cancer and CHD admitted to Liaoning Cancer Hospital and Institute from May 2010 to January 2014 were collected and analyzed retrospectively, including 42 males and 27 females, aged 62±73 years and with an average age of 64.51±6.27 years. This study was approved by the Ethics Committee of Liaoning Cancer Hospital and Institute, and all the research subjects signed informed consent forms.

Inclusion and exclusion criteria

Inclusion criteria: conforming to clinical manifestations of lung cancer [14]; conforming to clinical manifestations of CHD [15]; diagnosed with lung cancer by biopsy in the pathology department of the hospital; diagnosed with CHD in the imaging department of the hospital; normal coagulation function; operated in our hospital after diagnosis; complete case data; cooperating with the arrangement of medical staff in our hospital; aged 60-70 years. *Exclusion criteria:* complicated with multiple tumors; tumor metastasis; complicated with other cardio-cerebrovascular diseases; important organs failure; hepatic and renal insufficiency; contraindications to surgery; mental illness; physical disability; not able to take care of themselves; transferred halfway.

Methods

Sixty-nine patients were operated by senior chief surgeons in Peking Union Medical College Hospital. Among them, 32 cases undergoing on-pump CABG combined with lung cancer radical surgery were regarded as group A. Surgery procedures: Routine general anesthesia was performed before surgery. Afterwards double lumen tube was used for intubation, and a median sternal incision was made, then on-pump CABG was conducted assisted by a cardiac stabilizer. Doppler blood flow probe was used to detect graft blood flow in real time during the operation. At the same time of transplantation, lung cancer radical surgery was carried out with an axillary incision. Pulmonary vein and pulmonary artery were separated, ligated and cut off, and the leaf fissure was also separated. Bronchus was closed with a bronchial occluder after its dissociation, and the lobectomy then a systemic lymph dissection were carried out. Pericardial, mediastinal and thoracic drainage were performed after the surgery. Aspirin (Bayer Health Care Co., Ltd., SFDA Approval No. J20171021) was taken for anti-platelet therapy after 6 h of weaning from ventilator. The other 37 cases treated with coronary artery stent implantation combined with lung cancer radical surgery were regarded as group B.

Surgery procedures for group B: Aspirin and clopidogrel bisulfate (Hangzhou Sanofi Pharmaceutical Co., Ltd., SFDA Approval No. J20130083) were taken before surgery. Local anesthesia was administered, and coronary angiography was performed. The coronary stent was placed according to the arterial lesion condition, and heparin (100 U/kg) was given according to the patient's body mass during placement. Aspirin and clopidogrel bisulfate were taken daily for anti-platelet therapy after surgery. Lung cancer radical surgery was performed 3 weeks after stent placement. General anesthesia was performed before surgery, then double lumen tube was used for intubation. Radical resection of lung cancer, hilar and mediastinal lymph node dissection were performed with one-lung ventilation at the healthy side. Anti-platelet therapy was performed according to the above scheme after surgery.

Outcome measures

Surgical indicators: total surgical duration of patients in the two groups (total time of CHD surgery and lung cancer surgery); duration of lobectomy; intraoperative blood loss; thoracic drainage volume 24 h after surgery and hospital stay. Postoperative indicators: post-

operative complications in the two groups were recorded and the incidence rate was calculated. Incidence rate of complications = number of complications/total number ×100%. Pain scoring: visual analogue scale (VAS) [16] was used to evaluate the pain of patients in the two groups before, 1 day after and 5 days after surgery. The higher the score, the more severe the pain. Prognosis: All patients were followed up for 5 years with letters, phone calls, home visits and hospital reexamination. Deadline and cutoff events were December 30, 2018 and death of patients respectively. The 5-year survival rate of patients was calculated.

Statistics

SPSS24.0 statistical software (Beijing Strong-Vinda Information Technology Co., Ltd.) was used to calculate all experimental results. Graphpad8 (Shenzhen Soft Head Software Technology Co., Ltd.) was used to draw all figures and to double check the results. Counting data were expressed as rate, and chi-square test was used for comparison between groups. All measurement data were expressed as mean±standard deviation, repeated measurement analysis of variance (ANOVA) was used for the comparison among multiple time points in the group, and *t*-test was used for comparison

Table 1. Comparison of clinical data

	Group A (n=32)	*Group B (n=37)*	t/χ^2	*p*
Age (years), mean±SD	65.11±5.21	64.82±5.06	0.234	0.816
BMI (kg/m^2), mean±SD	22.62±5.24	23.15±5.91	0.391	0.697
Course of disease (days)*, mean±SD	14.82±6.21	15.20±5.94	0.260	0.796
Plateles (×10^9/L), mean±SD	316.22±56.92	320.41±58.14	0.301	0.764
Red blood cells (×10^{12}/L), mean±SD	5.21±1.15	5.09±1.22	0.418	0.677
White blood cells (×10^9/L), mean±SD	7.16±1.84	7.35±1.92	0.418	0.677
Gender, n (%)			0.067	0.796
Male	22 (68.75)	22 (59.46)		
Female	10 (31.25)	15 (40.54)		
Smoking, n (%)			2.309	0.129
Yes	26 (81.25)	24 (64.86)		
No	6 (18.75)	13 (35.14)		
Educational background, n (%)			0.166	0.684
<high school	18 (56.25)	19 (51.35)		
≥ high school	14 (43.75)	18 (48.65)		
Residence, n (%)			0.089	0.765
Urban	21 (65.63)	23 (62.16)		
Rural	11 (34.38)	14 (37.84)		
Nationality, n (%)			0.993	0.319
Han	30 (93.75)	32 (86.49)		
Minority	2 (6.25)	5 (13.51)		
CHD manifestation, n (%)			0.198	0.657
Unstable angina	19 (59.38)	20 (54.05)		
Acute myocardial infarction	13 (40.63)	17 (45.95)		
Diseased vessels, n (%)			0.336	0.845
Single vessel	16 (50.00)	17 (45.95)		
Double vessels	10 (31.25)	14 (37.84)		
Triple vessels	6 (18.75)	6 (16.22)		
Tumor staging, n (%)			0.166	0.684
I-II	14 (43.75)	18 (48.65)		
III-IV	18 (56.25)	19 (51.35)		
Tumor distribution, n (%)			0.442	0.979
Left upper lobe	3 (9.38)	4 (10.81)		
Left lower lobe	6 (18.75)	8 (21.62)		
Right upper lobe	12 (37.50)	13 (35.14)		
Right middle lobe	1 (3.13)	2 (5.41)		
Right lower lobe	10 (31.25)	10 (27.03)		

* represents the time from onset of clinical symptoms to hospital visits

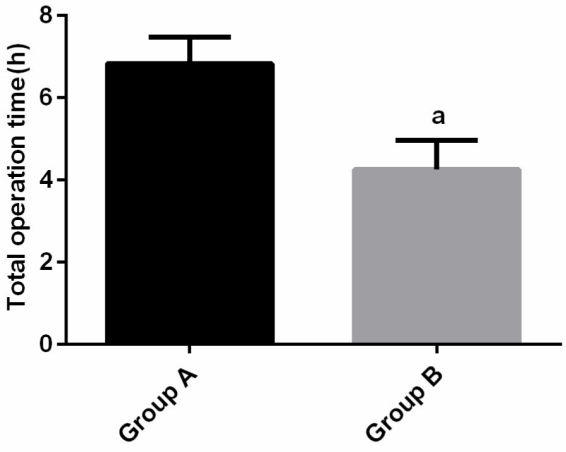

Figure 1. Comparison of the total surgical duration. The total surgical duration in group B was significantly shorter than that in group A; a indicates that compared with the total surgical duration in the group A, p<0.001.

among the groups. The survival rate was calculated by Kaplan-Meier method, and the comparison of survival rate with Log-rank test. P<0.05 indicated statistical significance.

Results

Comparison of clinical data

There was no significant difference in age, body mass index (BMI), course of disease, platelet (PLT), red blood cell (RBC) and white blood cell (WBC) counts, gender, smoking, educational background, residence, nationality, CHD manifestations, diseased vessels, tumor staging and distribution between the two groups (p>0.05), proving a good comparability between the two groups (Table 1).

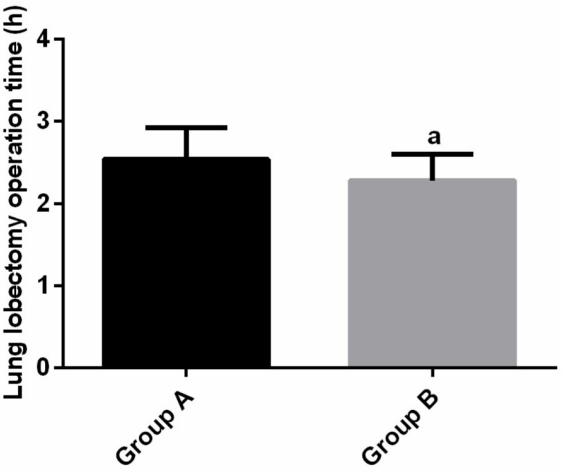

Figure 2. Comparison of the duration of lobectomy. The duration of lobectomy in group B was significantly shorter than that in group A; a indicates that compared with the duration of lobectomy in group A, p<0.001.

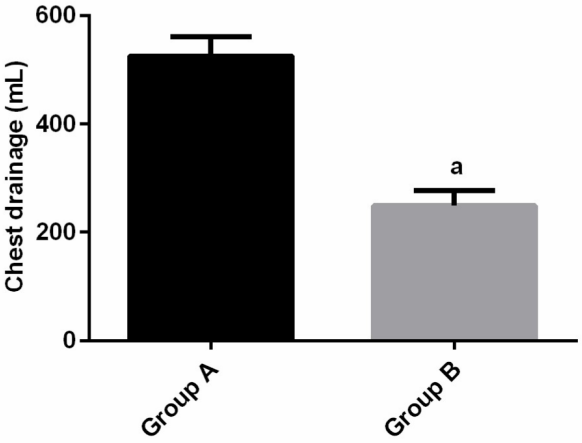

Figure 4. Comparison of the thoracic drainage volume 24 h after surgery. The thoracic drainage volume 24 h after surgery in group B was significantly lower than that in group A; a indicates that compared with the thoracic drainage volume 24 h after surgery in the group A, p<0.001.

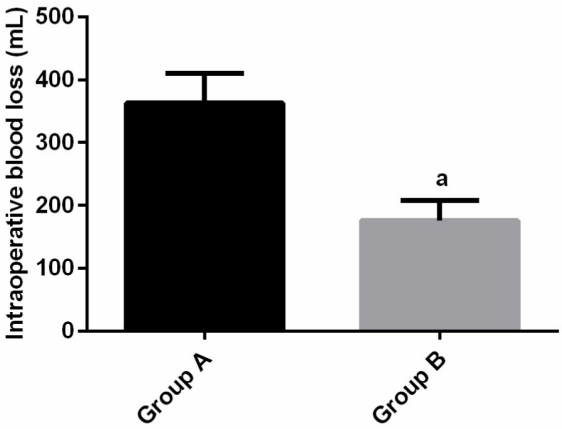

Figure 3. Comparison of the intraoperative blood loss. The intraoperative blood loss in group B was significantly less than that in group A; a indicates that compared with the intraoperative blood loss in the group A, p<0.001.

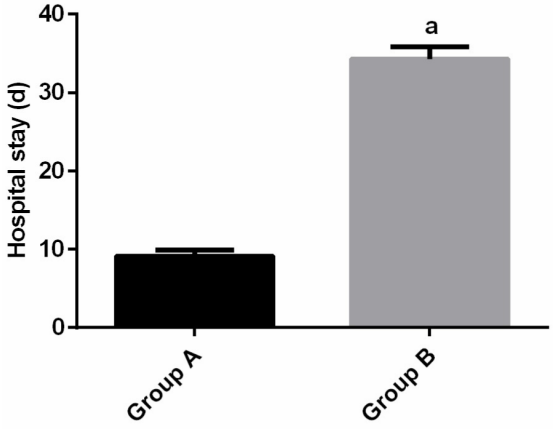

Figure 5. Comparison of the hospital stay. The hospital stay in group B was significantly longer than that in group A; a indicates that compared with the hospital stay in group A, p<0.001.

Comparison of surgical indicators

The total surgical duration in group A (6.82±0.65 h) was significantly longer than that in group B (4.25±0.71 h; p<0.001). The duration of lobectomy in group A (2.54±0.38 h) was significantly longer than that in group B (2.28±0.32 h; p< 0.001). The intraoperative blood loss in group A (362.61±48.16 mL) was significantly more than that in group B (175.62±31.52 mL; p<0.001). The thoracic drainage volume 24 h after surgery in group A (525.16±36.11 mL) was significantly higher than that in group B (248.62±28.21 mL; p<0.001). The hospital stay in group A (9.14±0.74 d) was significantly shorter than that in group B (34.25±1.57 d; p<0.001) (Figures 1, 2, 3, 4 and 5).

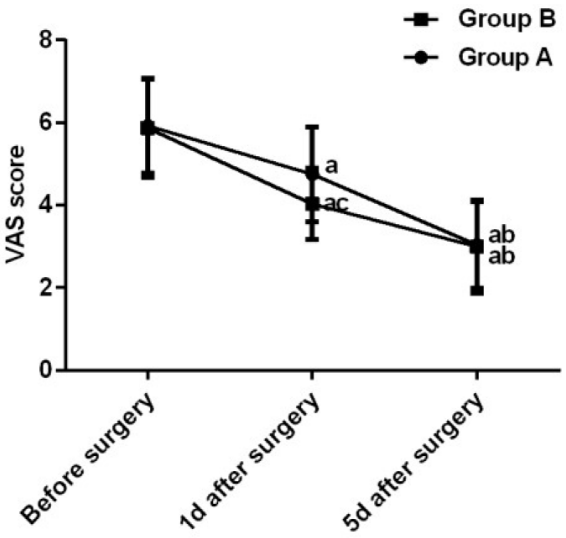

Figure 6. Comparison of VAS pain score. The VAS pain scores in group A were significantly higher than those in group B at 1 day after surgery. The scores in both groups were significantly lower than those in the same group at 1 day after surgery, and the scores at 5 days after surgery were significantly lower than those at 1 day after surgery. a indicates that compared with the VAS pain score in the same group before treatment, p<0.001; b indicates that compared with the VAS pain score in the same group at 1 day after surgery, p<0.001; c indicates that compared with the VAS pain score in group A at 1 day after surgery, p<0.001.

Comparison of postoperative conditions

Both groups of patients were successfully operated with no perioperative death. In group A, postoperative pulmonary infection occurred in 6.25% (2 cases), atelectasis occurred in 3.13% (1 case), arrhythmia 6.25% (2 cases), lung leakage for more than 7 days 6.25% (2 cases), and with an incidence of complications of 21.88%. In group B, chylothorax occurred in 2.70% (1 case) and arrhythmia occurred in 2.70% (1 case), with an incidence of complications of 5.41%. The incidence in group A was significantly higher than that in group B (p=0.043). There was no significant difference in VAS scores between the two groups before and 5 days after surgery (p>0.050), while the scores in group A were significantly higher than those in group B at 1 day after surgery (p<0.001). The postoperative VAS scores in both groups were significantly lower than those before surgery (p<0.001) and reached the lowest at 5 days after surgery (p<0.001) (Table 2 and Figure 6).

Comparison of prognosis

Five-year follow-up was performed in 69 patients, and 68 (98.55%) of them were followed-up successfully. Among them, there were 32 cases in

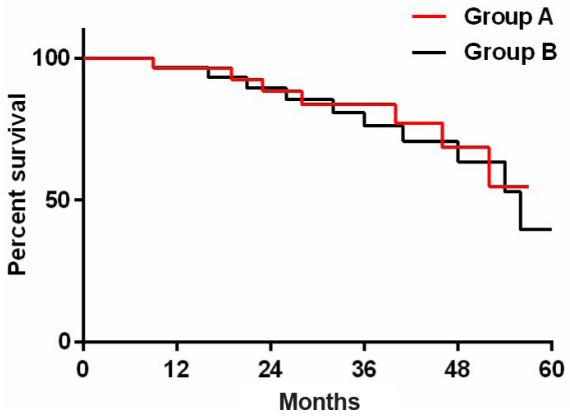

Figure 7. Kaplan-Meier 5-year overall survival. There was no significant difference in the 5-year survival rate between the two groups (p>0.05).

Table 2. Comparison of postoperative complications

	Group A (n=32) *n (%)*	*Group B (n=37)* *n (%)*	x^2	*p*
Pulmonary infection	2 (6.25)	0 (0.00)		
Atelectasis	1 (3.13)	0 (0.00)		
Chylothorax	0 (0.00)	1 (2.70)		
Arrhythmia	2 (6.25)	1 (2.70)		
Lung leakage >7 d	2 (6.25)	0 (0.00)		
Incidence of complications (%)	21.88	5.41	4.104	0.043

group A and 36 cases in group B. The 5-year overall survival rate in group A was 78.13%, while that in group B it was 75.00%, showing no significant difference between the two groups (p>0.050) (Figure 7).

Discussion

Lung cancer is one of the most common malignant tumors in clinic with a top mortality rate [17]. The unclear manifestations of early lung cancer cause most patients to be not diagnosed and treated in time. As a result, most lung cancer patients have reached the middle and late stages once diagnosed, missing the golden time for effective treatment [18]. Therefore, "early detection and early treatment" has always been advocated in the clinical treatment of lung cancer. The treatment difficulty is greatly increased in the elderly patients due to their decline of body functions and immune functions. Moreover, they usually suffer from complications [19], so the surgical process not only needs to complete the treatment of tumors, but also to effectively remove the threat of complications. At present, there is still controversy regarding clinical treatment options for patients with lung cancer and CHD. The stent implantation increases the possibility of bleeding during and after lung cancer surgery, and the hypercoagulable state caused by tumor may affect the patency rate of the implanted stent [20]. While on-pump CABG can effectively cure CHD, renal perfusion damage is likely to occur under the condition of revascularization of lateral and posterior cardiac walls [21]. Through advanced statistical software, precise inclusion and exclusion criteria and strict adherence to scientific research spirit, this paper investigated the therapeutic effects of two surgical treatment methods on lung cancer patients with CHD.

The results of this study showed that the surgical duration, duration of lobectomy, intraoperative blood loss, postoperative thoracic drainage volume, postoperative complications and pain scores in group A using on-pump CABG and surgery were significantly higher than those in group B using coronary stent implantation and surgery, suggesting that the stent implantation and surgery are safer for lung cancer patients with CHD. However, the total hospital stay in group A was significantly shorter than in group B, indicating that the treatment cycle of lung cancer complicated with CHD by on-pump CABG and surgery is shorter. There was no significant difference in 5-year survival between the two groups, suggesting that the two surgical treatment methods have little difference in the prognosis of patients, but not excluded whether it is a statistical calculation problem caused by too few research samples. It is speculated that the differences between the two groups are mainly systemic inflammatory reaction, pulmonary edema, and lung function damage caused by on-pump CABG. Besides, the heparinization of the body during cardiopulmonary bypass increases the probability of hemorrhage during tumor surgery [22]. However, coronary stent implantation can avoid the disadvantages of cardiopulmonary bypass, reduce the damage to lung function and lay a foundation for lymph node dissection. Since tumor surgery can only be performed about 3 weeks after stent implantation, the overall rehabilitation period of the patient will be greatly prolonged, but with smaller surgical trauma, lower surgical risk, and milder postoperative pain. Moreover, coronary stent is very beneficial for patients to excrete sputum during the perioperative period [23], which is also one of the reasons why the postoperative complications in group B were significantly lower than those in group A.

This study compared the application value of on-pump CABG and coronary artery stent implantation respectively combined with surgery for lung cancer patients with CHD. Nevertheless, there are still deficiencies due to insufficient experimental conditions. Firstly, lung cancer patients with CHD are not common in clinical practice, so the number of cases collected in Peking Union Medical College Hospital was small, leading to the absence of statistical analysis of big data. We will conduct joint experiments with several hospitals to further explore the best choice for surgical treatment of lung cancer complicated with CHD. Secondly, the race in this study was single and the age span was relatively small, so it cannot be excluded that the experimental results may differ among different races and different ages. Thirdly, the surgical treatment of lung cancer and CHD is not limited to the two methods studied in this paper. Therefore, we will incorporate more treatment schemes and conduct more detailed comparison in order to obtain the best experimental results.

In conclusion, stent implantation combined with surgery is safer than on-pump CABG combined with surgery in the treatment of elderly patients with lung cancer and CHD, but with a longer treatment duration. In clinical practice, careful consideration should be taken according to the actual situation of patients when selecting a surgical treatment scheme.

Conflict of interests

The authors declare no conflict of interests.

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